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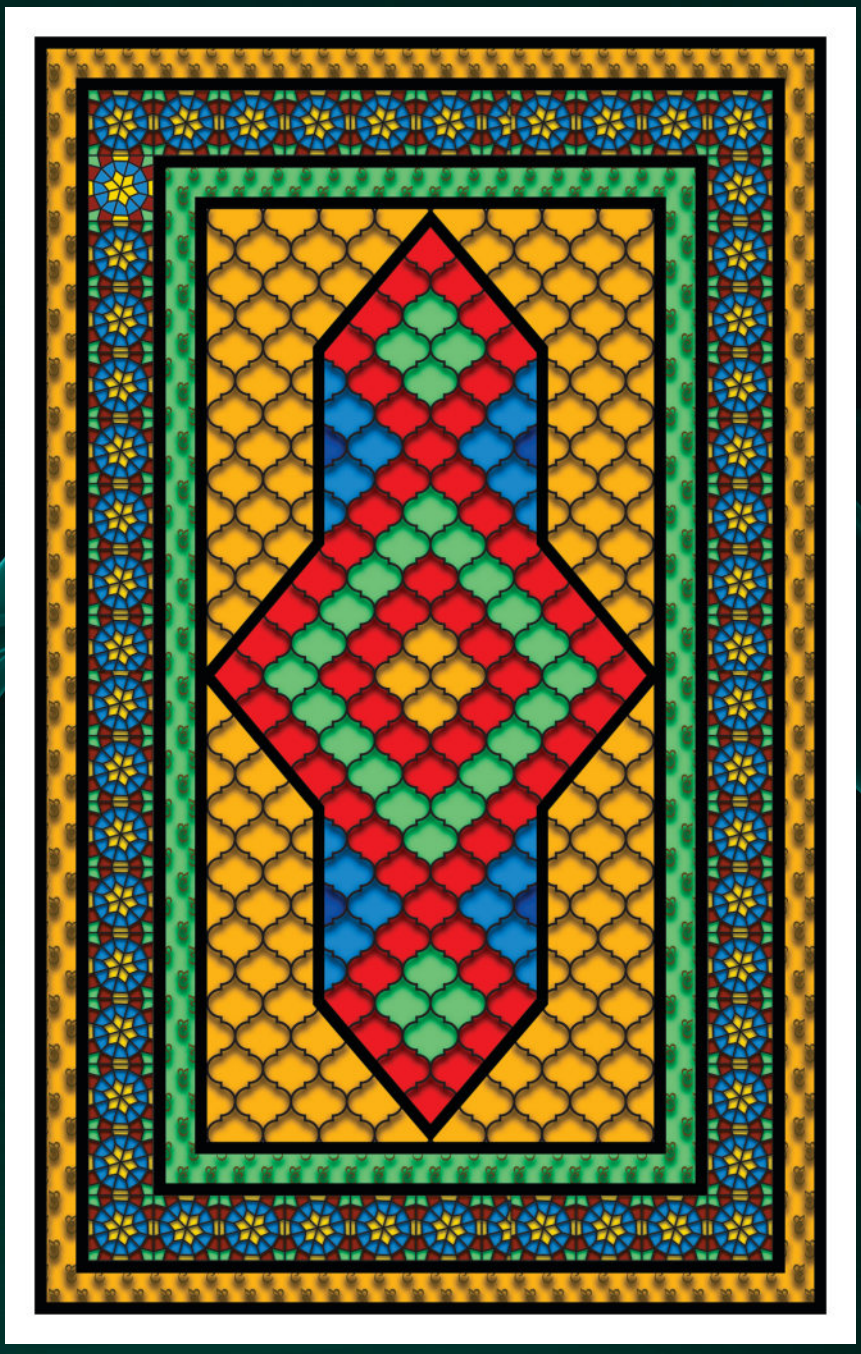

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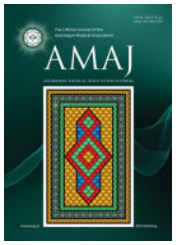

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Case Report
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Multicystic Perivascular Spaces Mimicking Cystic Neoplasm of Brain

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Background: Virchow-Robin (VR) spaces are the fluid-filled perivascular spaces adjacent the brain vessels. The signal intensities of the VR spaces are very similar to those of cerebrospinal fluid (CSF). VR spaces should be distinguished various pathologic conditions, including lacunar infarctions, cystic periventricular leukomalacia, cryptococcosis, cystic neoplasms and neuroepithelial cysts.

Case presentation: 32-year-old female with 6 month history of worsening severe headaches. The clinical examination and laboratory findings were congruent with hypothyroidism. MR imaging revealed multiloculated, thin-walled, "soap bubble" like lesions cystic lesions involving anterior part of left cingulated gyrus. Cystic lesions showed the same signal intensity characterstics with CSF. There was no any mass effect, enhancement, peripheral edema and no restriction in diffusion-weighted images. After 10 month follow-up there was no any change in size or in MRI features.

Conclusion: Knowledge of the signal intensity characteristics, locations of VR spaces and absence of any change in follow up prevents unnecessary biopsy.

Keywords: Virchow-Robin spaces, perivascular spaces, cingulate gyrus, cystic lesion of brain, neuroepithelial cyst

Introduction

Virchow-Robin (VR) spaces are perivascular spaces surrounding the brain vessels. Although, the signal intensities of the VR spaces are identical to those of CSF, they do not communicate directly subarachnoid space or ventricles. One of the most basic roles of the VR spaces is the regulation of CNS fluid movement and drainage [1].

VR spaces can be distinguished by it's signal characterictics and location from various pathologic conditions, including lacunar infarctions, cystic periventricular leukomalacia, cryptococcosis, cystic neoplasms and neuroepithelial cysts.

Case Report

A 32-year-old female, presented with 6 month history of severe headache. The clinical examination and was laboratory findings were congruent with hypothyroidism (fT3=2.16 Pg/ml; fT4=0.33 ng/ml; TSH=76.45 µIU/ml;). MR imaging examination was performed and revealed multiloculated, clusters of variable-sized, thin-walled, "soap bubble" like lesions cystic lesions involving anterior part of left cingulated gyrus (figure 1). Cystic lesions showed the same signal intensity characterstics with CSF. There was no any mass effect, enhancement and peripheral edema, calcification or haemorrhagia. Diffusion-weighted images showed no restricted diffusion. The patient has a history of traumatic brain injury 20 years before. We decided to follow-up and after 10 month there was no any change in size or in MR imaging features (figure 2).

Discussion

Virchow-Robin spaces surround the walls of vessels as they course from the subarachnoid space through the brain parenchyma. Dilated VR spaces typically occur in three characteristic locations: Type I VR spaces found along the lenticulostriate arteries entering the basal ganglia; Type II VR

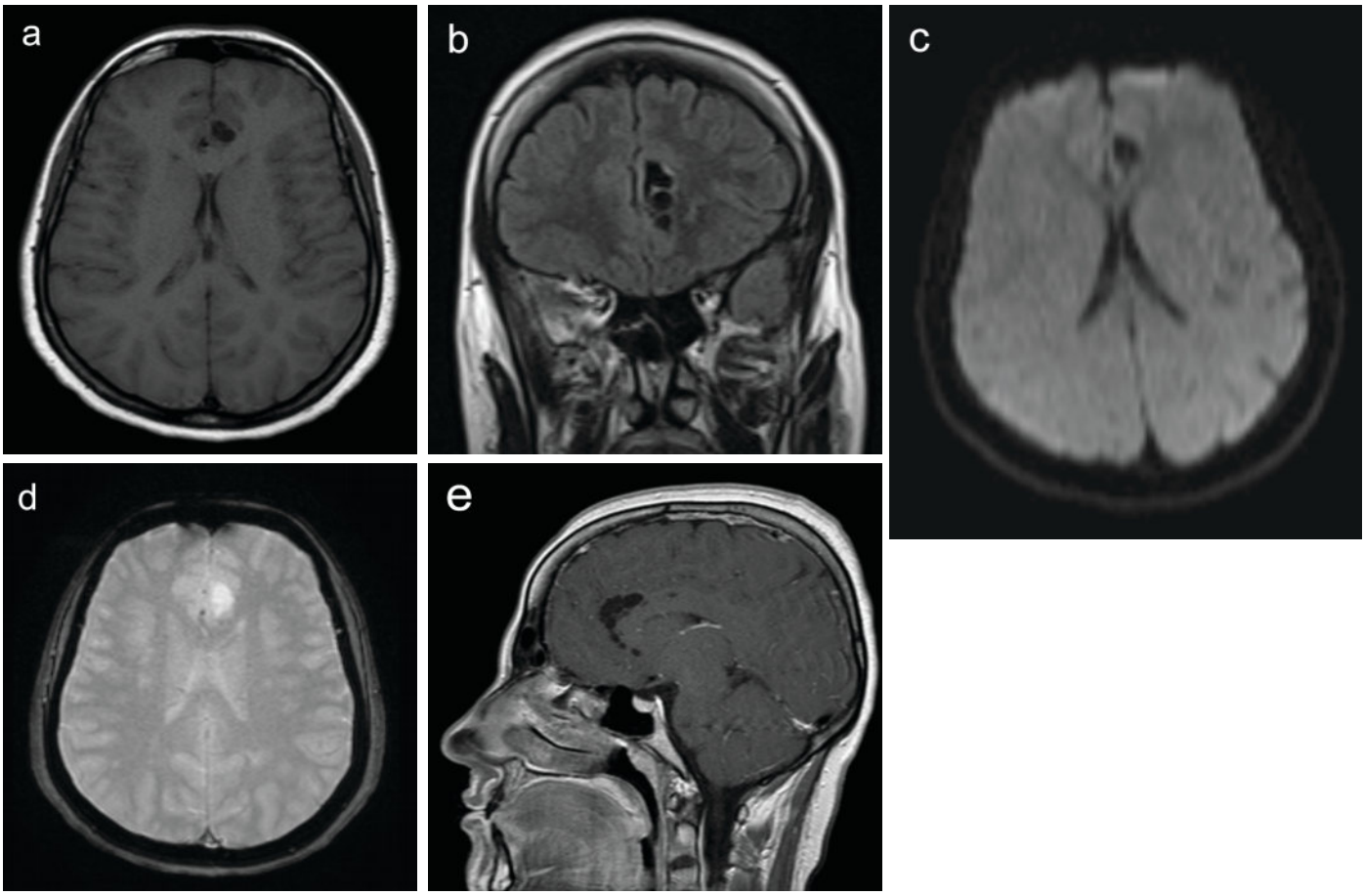

Figure 1. Axial T1-weighted (repetition time - TR:550ms, echo time - TE:10ms, averages:4, flip angle:90°) images **(a)** shows parasagittal hypointense multicystic lesions in cingulate gyrus that completely suppressed in FLAIR (TR:8000ms, TE:118ms, averages:1, flip angle:150°) images **(b)**. There is no restriction diffusion-weighted (b-value:1000) images **(c)** and no calcification or haemorrhage in T2W-Fast Field Echo (TR:757ms, TE:23ms, averages:2, flip angle:18°) sequence **(d)**. No contrast enhancement in T1-sequence was detected **(e)**.

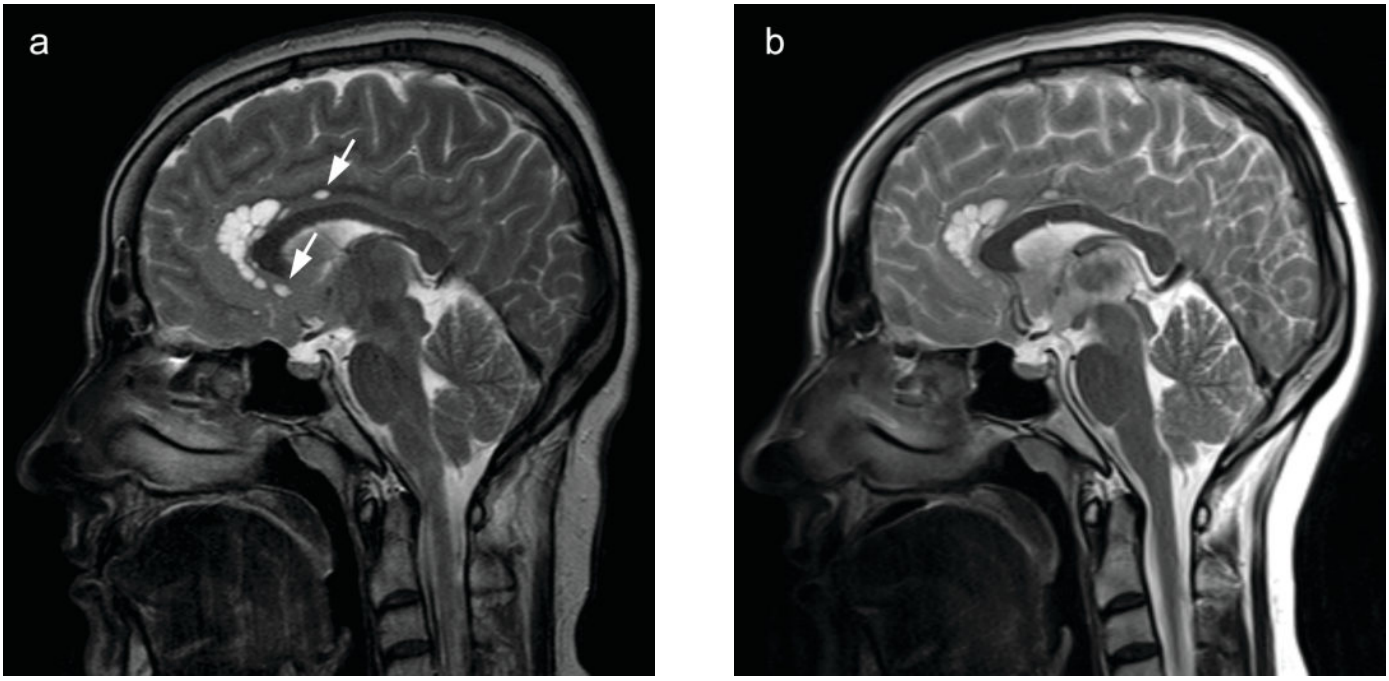

Figure 2. a. Sagittal T2-weighted image shows hyperintense multicystic "soap-bubble"like Virchow-Robins spaces with some small cysts (arrows) that isolated from grouped ones and lined along the cingulate gyrus. **b.** Nearly the same section T2-weighted image shows no change after 10 months follow-up.

spaces found along the paths of perforating medullary arteries as they enter the cortical gray matter over the high convexities; and Type III VR spaces in the midbrain [1]. Occasionally, VR spaces appear markedly enlarged, cause mass effect, and assume weird cystic formations.

Awareness of the signal intensity characteristics and locations of VR spaces helps differentiate them from various pathologic conditions, including cystic tumors, parasitic cysts, cystic infarctions, non-neoplastic neuroepithelial cysts, cystic periventricular leukomalacia, multiple sclerosis, mucopolysaccharidoses, and arachnoid cysts [1]. Rarely, as seen in the present patient, they can also occur at an atypical location causing diagnostic confusion. There is no adjacent T2W or FLAIR hyperintensity, that excludes multiple sclerosis, cystic infarctions and cystic periventricular leukomalacia. No contrast enhancement excludes cystic neoplasms. No restriction in diffusion-weighted images excludes cryptococcosis.

The imaging features of neuroepithelial cysts are very identical to those of VR spaces. Both suppresses in FLAIR, there is no contrast enhancement, no restriction in diffusion-weighted images. Certain differentiation can be made only by pathologic study. The best radiological clue to exclude neuroepithelial cysts is being its single, unilocular cystic nature and greater in size [2]. Besides, in our case, some small cysts that isolated from grouped ones are lined along the cingulate gyrus (figure 2). Whereas, neuroepithelial cysts are tending to group concentrically.

The causes of enlarged VRS are still remain unclear. Commonly, size and frequency of VR spaces increase with advancing age. An association shown with neuropsychiatric disorders, recent-onset multiple sclerosis and diseases associated with microvascular abnormalities [1]. Inglese M. et al found a correlation between dilated VR spaces and mild traumatic brain injury [3]. In our case, the past traumatic brain injury may support this hypothesis. However, it is hard to prove injury, that been 20 years ago.

Conclusion

Virchow-Robin spaces are benign lesions with unknown ethiology. Awareness of the signal intensity characteristics and locations of VR spaces helps differentiate them from various pathologic conditions and avoids unnecessary biopsies.

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Case Report
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Reconstruction of Pharyngeal Defect with Prelaminated Pectoralis Major Pedicled Flap

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Pharyngeal reconstruction remains a considerable challenge in head and neck surgery. Defects of pharynx combined with anterior neck soft tissues deficiency require both external skin and lining for their reconstruction. Flap prelamination is a powerful method, which can provide two epithelial surfaces simultaneously.

Here we describe pharyngeal reconstruction by prelaminated pectoralis major flap. Two clinical cases are presented.

We performed a two-stage reconstruction, which included implantation of skin graft under pectoralis major muscle and subsequent transfer of a myocutaneous flap onto the neck, where the grafted surface was used for pharyngeal lining. A functionally consistent pharyngeal tube and satisfactory anterior neck coverage have been achieved.

Although more clinical experience is needed, the prelamination of pectoralis major myocutaneous flap can be an alternative for reconstructions of complex pharyngeal defects, as shown in our cases.

Keywords: pharyngeal, defect, reconstruction, prelaminated, pectoralis, major, flap, anterior, neck

Introduction

Pharyngeal reconstruction presents clinical challenge because of the complexity of the region, poor health state of the patients and relatively high percentage of complications, including flap failure, fistula formation, stenosis, etc. [1, 2].

The most common cause of pharyngeal wall defects is a surgical resection of the larynx alone or in combination with the pharynx for cancerous affections.

Nowadays many methods of pharyngeal reconstructions have been proposed. These can be classified into reconstruction with local fasciocutaneous and muscle flaps (platysma, sternocleidomastoideus and infrahyoid), regional flaps (trapezius, pectoralis major) and free flaps (jejunum, radial forearm). Nevertheless, defects of pharynx combined with soft tissue deficiency of the neck require substantial efforts for successful reconstruction [1, 6]. The classic option is a muscle flap together with skin graft for anterior neck resurfation. However, graft coverage is known to be prone to unstable scar formation, color and texture mismatch and lack of sufficient bulkiness to provide normal neck contour [2]. Although additional flap can be used to provide skin cover for neck, this definitely adds donor site morbidity and prolongs time of operation. Insufficiency in insurance cover and all consequences that follows should also been taken in consideration. As a result, even though we perform all kinds of microsurgical procedures in our clinic, we decided to use a non microsurgical technique on our patients, because they and their family members insisted on the use of a procedure with no risk of total flap failure.

Here we present post pharyngectomy patients with deficient anterior neck soft tissue who were successfully treated by prelaminated pectoralis major pedicled flap technique.

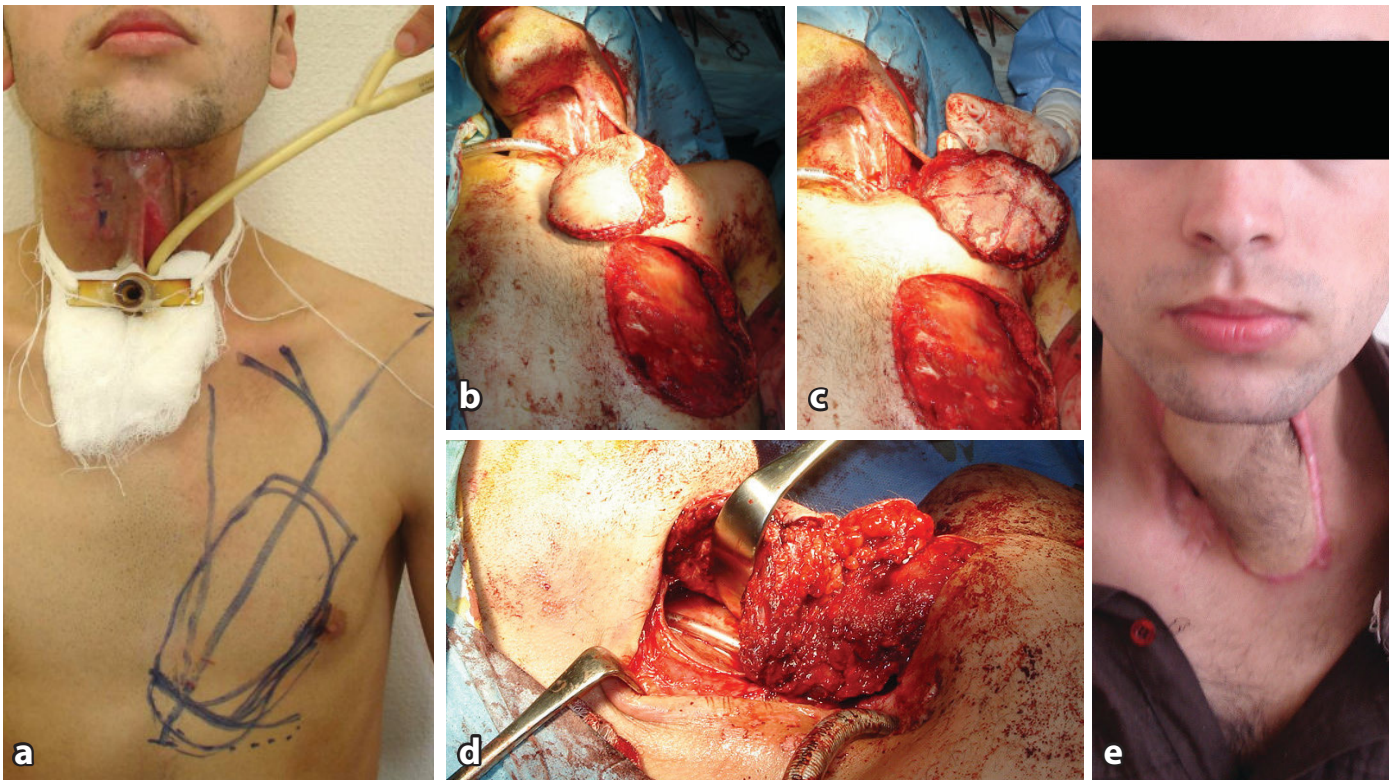

Figure 1. a - Pre-op neck contour; **b -** Pectoral flap, skin surface ; **c -** Prelaminated lining (skin graft) on undersurface of the pectoralis flap; **d -** Suturing of the lining to remnant of posterior pharyngeal mucosa; **e -** Final neck contour.

Case 1

A 26-year-old male was referred to our clinic for the treatment of a neck disfigurement. He underwent total laryngectomy and subtotal pharyngectomy with subsequent course of chemo and radiotherapy in another clinic, for low grade pharyngeal carcinoma (T3N0M0). According to an oncologist's report, the patient had been free of disease for two years at the time of admission (13.02.2012).

Physical examination showed a soft tissue defect on anterior neck surface with narrow strip of pharyngeal mucosal remnant in its depth. (Fig. 1 a).

We planned the operation in two stages. The first stage included skin grafting on the undersurface of the left pectoralis major muscle (i.e. prelamination). Three strips of split thickness skin graft obtained from the left thigh were fixed by absorbable sutures to the dermis of the skin island and through the substance of the pectoralis muscle The second stage was performed 3 weeks later and consisted of the transfer of prelaminated myocutaneous pectoralis major flap onto the neck (Fig. 1 b, c and d).

A mucocutaneous junction between the posterior pharyngeal remnant and neck skin was released and circumferential suturing of the skin graft to the edges of the mucosal remnant was performed. We used Donatti sutures piercing through both epithelial and muscle layers. After the completion of mucosal suturing, the muscle portion of the flap was anchored to the muscles of the neck.

The postoperative course was even. After the second operation the patient was placed on nasogastric feeding for a 4 weeks. A small fistula on the right superior edge of the flap closed spontaneously.

Finally, partial debulking of the muscle and division of the flap pedicle were performed. Hypertrophied scars of donor area were injected by steroid solution at the same time.

As of the last control, the patient had normal oral feeding and satisfactory anterior neck contour (Fig 1 e). In addition, he had esophageal speech. His psychological condition had become better as apparent from his own statements and reports of family members.

Endoscopic examination by means of flexible endoscope reveals moistened and white-coated surface of the skin graft and normal act of swallowing (Video 1).

Some asymmetry in the nipple position and hypertrophic scarring has occurred on the donor area, which is currently treated by additional procedures.

Case 2

A 63 years old male patient referred to us with neck infection. He previously was diagnosed larynx carcinoma, stage T4N1Mx and underwent total laryngectomy. Reconstruction was done by right-sided pectoralis major flap. Clinical examination showed dehiscence of sutured hemi- Apron incision on the right side of the neck together with offensive discharge from the wound (Fig. 2 a) General state of patient was severe; with great fatigue, malaise, malnourishment, elevated WBC count and anemia. First of all, we performed debridment of all necrotic tissues and opened pharyngostoma. Then, taking in account fragile general state of the patient, we planned two stage reconstruction and got

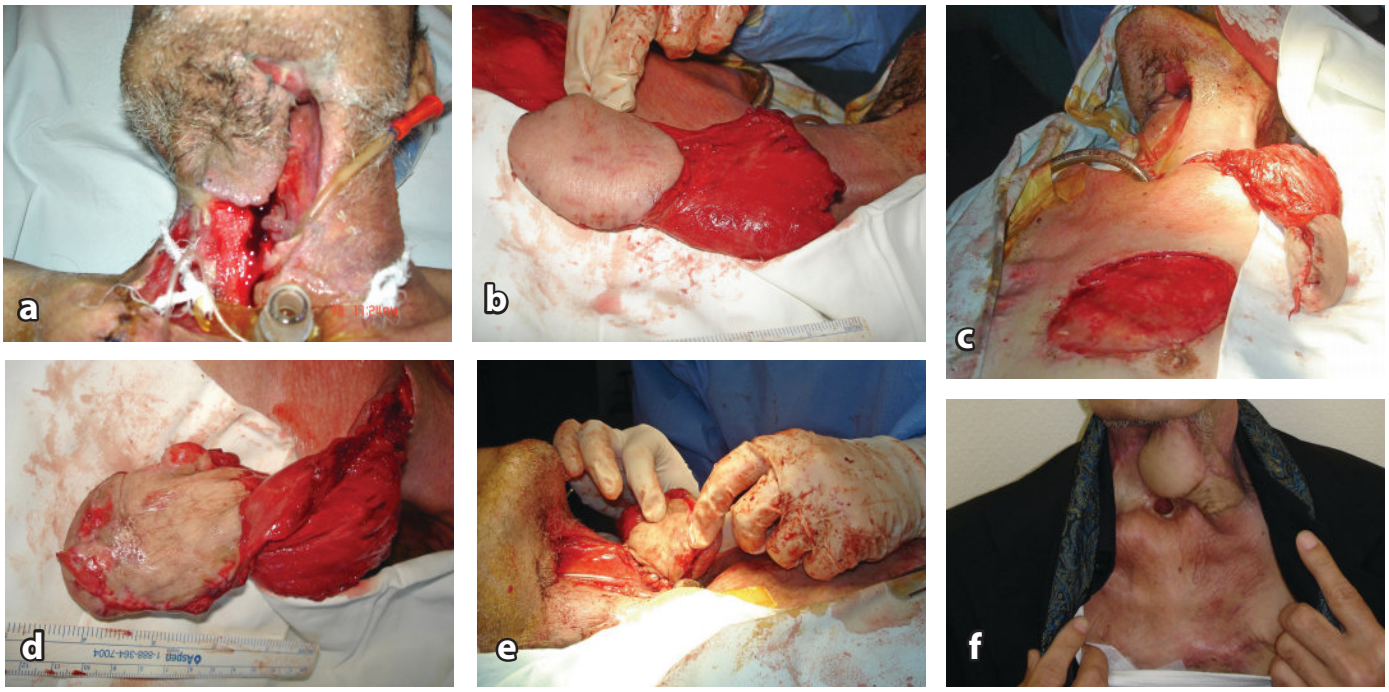

Figure 2. a - Pre-op neck contour; **b -** Pectoral flap, skin surface; **c -** Pectoral flap elevated with both side (i.e. skin and grafted-surface) visible; **d -** Prelaminated lining (skin graft) on undersurface of the pectoralis flap; **e -** Suturing of the lining to remnant of posterior pharyngeal mucosa; **f -** Final neck contour.

informed consent from the patient and his relatives.

First, the left pectoralis major musle was grafted by full thickness skin graft (obtained from left groin) on its undersurface.

After 3 weeks the musculocutaneous flap was transferred to the neck so that the grafted surface was used for reconstruction of the wall of pharynx and the native skin of the flap was used fot coverage of the neck (Fig. 2 b, c, d, e)

The postoperative course was even. A small fistula on the superior edge of the flap closed spontaneously in 1 week period. Oral feeding began at 5th week and flap pedicle was divided 2 months later. As of the last control, the patient had normal oral feeding and satisfactory anterior neck contour (Fig 2 f). He also has developed esophageal speech. Endoscopic examination by means of flexible endoscope reveals moistened and white-coated surface of the skin graft and normal act of swallowing (Video 2).

Discussion

Pharyngeal wall defects constitute a clinical challenge. The main goals of pharyngeal reconstruction include restoration of the continuity of digestive tract and maintenance of speech production [1, 2, and 6]. Pharyngeal defects generally occur after oncological resections in the form of partial pharyngectomies, total laryngectomy with subtotal pharyngectomy and total laryngopharyngectomy.

Today the use of free microvascular flaps and pedicled pectoralis major flap are considered among the most reliable options for the reconstruction of subtotal and total pharyngeal defects [2].

The pectoralis major flap, despite of wide use of microsurgical techniques, is still considered a work-horse in the head and neck reconstruction. It can be used for closing partial pharyngeal defects as well as in total pharyngoplasties. Because of a relatively high rate of complications, the use of a tubed flap has been replaced by use of a U-flap [1, 4]. Also local cutaneous flaps, platysma, infrahyoid and sternocleidomastoid muscle flaps can be used for small to medium pharyngeal defects [5, 6]. However, there is no standard treatment in cases where a pharyngeal defect is combined with a defect in the soft tissues of the neck. The use of skin grafting for anterior neck can be an option; however it leaves the skin poorly matched and lacking sufficient bulk. Anterior neck can also be reconstructed by additional flaps: supraclavicular, local cervicoplatysmal or even free ones [2, 6]. Nevertheless, this adds technical challenges, prolongs the operational time and creates additional donor site morbidity.

Flap prelamination is defined as a two-stage procedure, which allows the addition of different tissue layers into the axial vascular territory. After maturation of the added tissues, the composite structure is transposed on the original pedicle to cover the defect (3). Prelamination allows the added layers to heal properly with less chance of breaking down, which is particularly useful in the formation of functional units like neo-urethra or neo-esophagus. In the case of a free flap reconstruction of the esophagus, prelamination was reported as tubing of radial foramen and TFL flap “in situ” with subsequent transfer after formation of the tubular structure [3, 6].

We used prelaminated myocutaneous pectoralis major flap for reconstruction of the nearly total pharyngeal defect combined with soft tissue deficiency of the anterior neck. Our patients had major disfigurement of the neck, inability to sustain normal oral feeding and constant discharge challenging daily life. Thus, there was need in both functional and aesthetic restoration. After the discussion of the available options we chose the usage of the prelaminated flap. As a result, we achieved wa-

ter-tight pharyngeal wall closure together with anterior neck restoration.

Our method provides simultaneous reconstruction of a pharyngeal defect and cervical skin insufficiency. The prelaminated "sandwich"-like structure of the flap allows the use of both of its sides and eliminates the need in a second flap for neck skin. We believe that our method, being both simple and effective, can be included in the armamentarium of surgeons engaged in pharyngeal reconstruction.

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Review Article
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Technical Review On Phrenic Nerve Stimulation During Biventricular Pacing – How To Avoid And How To Treat?

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Phrenic nerve stimulation (PNS) is one of the undesired complications associated with left ventricular stimulation. Absence of PNS during implantation procedure does not guarantee its absence in the future. It is may be managed with reprogramming but sometime it may necessitate repositioning of lead either with percutaneous or open surgical approach. The aim of this review article is to discuss peri and postprocedural management of patients with PNS. Here we also present data on frequency and management of PNS at our Institution.

Keywords: biventricular pacing, phrenic nerve stimulation

Introduction

Biventricular stimulation is one of the essential tools in the management of sympthomatic heart failure. Phrenic nerve stimulation with subsequent diaphragmatic contraction is one of the frequent complication associated with left ventricular stimulation via branches of coronary sinus and may be observed with it's frequency varying between 3 and 20 % of patients [1]. Some of patients with PNS can be managed by reprogramming of stimulation parameters, however some of them must undergo lead repositioning procedure. In this review article we aimed to present our own data and also to discuss methods that may help to avoid PNS and management of this complication. This will be discussed, in four different sections such as 1) peri-procedural considerations 2) postprocedural reprogramming for management of PNS, 3) selection of percutaneous or surgical approach for repositioning of left ventricular lead and 4) our own data and observations.

Peri-procedural Considerations

One of the important first steps during the procedure is to obtain coronary sinus venograms in all available views (AP, RAO 30, LAO 30) and to keep this data. In case of need for repositioning in the future, operator will be able to decide whether to proceed with percutaneous or surgical approach.

Any muscle relaxants and curarizing agents should be avoided in patients, who require periprocedural general anesthesia.

Implantation procedure is always performed in supine position and this ameliorates PNS and makes patient to sense it much more weaker that he or she will sense it in the upright position. For this reason, after implantation of left ventricular lead pacing at high output should be performed to evaluate presence of PNS, and in case of it lead should be repositioned if possible. In case of absence of alternative side branch lead should be withdrawn to more basal part of left ventricle, because more apical locations are more frequently associated with PNS. Operator should look for a small side branch within the target vein, where it could be possible to stabilize led. If it is also impossible and stable position could not be achieved, active fixation lead (Attain Starfix®4195, Medtronic, MN, USA) should be preferred. However at sometimes, and it is not so infrequent, proximal portion of target vessel tends to be widened and this precludes implantation of even this above mentioned active fixation lead. This is more

frequently observed in inferolateral vein, when compared to lateral and anterolateral side branches. In this situation, operator should look for another target site, or use newly introduced lead (Attain Ability®4196 Medtronic MN, USA), which has two electrodes, with interlectrode distance of 21 mm. It allows separate pacing from each of these two electrodes. So when pacing from distal electrode results in PNS, then device can be reprogrammed to pace from proximal electrode.

Previous studies performed with passive configuration LV leads showed no difference in frequency of PNS between various manufacturers and models [2, 3]. However it can be speculated that newer designs may result in decreased frequency of PNS.

Post-procedural Reprograming For Management Of PNS

The easiest way of management of PNS is decreasing pacing output. However this may also result in failure of LV capture, or PNS may continue despite absence of LV capture. This is frequently observed in patients with high ventricular pacing thresholds. For this reason, if PNS when pacing at high output is an unavoidable during implantation procedure, sites with lowest pacing threshold should be preferred.

New CRT systems have capability of programming of multiple LV pacing configuration. One recent study compared frequency and management strategy in patients with new and older models of CRT devices [3]. PNS was observed in 12 % of study group(new generation device) and 24 % of control group (old generation device). They observed that PNS was easily managed by reprogramming of new generation devices, however all patients with old generation devices had to undergo repositioning procedure.

Reprogramming includes several approaches, and all of these approaches should be tried before attempting re-operation. This include:

1. Decreasing of pacing output
2. In patients with true bipolar left ventricular leads one may try to use the tip or the ring/coil of the lead as either cathode or anode. Mechanism by which, configuration of left ventricular pacing results in decreased pacing threshold is not clearly understood, but it is suggested that this phenomenon occurs as a result of change in magnitude of current flowing through an excitable myocardial mass between electrodes (current density theory) [4]. Another important underlying mechanism is change in myocardial fiber orientation in relation to the electrical pacing vector. This theory is supported by observation, that stimulation threshold is lowest, when the stimulating electrical field is parallel to fiber orientation [5].
3. It was suggested that increasing of pulse duration during left ventricular stimulation could help to overcome PNS. This was related to different excitability properties of left ventricle (LV) and phrenic nerve (PN). One study investigated this relationship, and compared excitability properties (rheobase and chronaxie) of LV and PN in 44 patients with biventricular devices (Roka A, Szilagyi S, Geller L, Merkely B, Zima E. Prevention of diaphragm stimulation during biventricular pacing with long left ventricular pulse. Abstract of this study was presented at World Congress on Heart Disease which was held on July 26-29 2008 in Toronto, Canada). And they found that LV chronaxie was longer and its rheobase was lower, when compared to PN. With prolonging of LV pulse duration with setting of pacing output at twice of the threshold value, they achieved elimination of PNS in 5 of 6 patients. This approach seems logical and should be tried in every patient presenting with PNS.
4. Changing LV-RV pacing sequence (V-V delay) may also be of value in selected group of patients. We for the first time observed and report here beneficial effect of this approach in one of our patients with PNS. However, it should be noted that this may result in inappropriate hemodynamic response, and echocardiographic evaluation should be performed in these cases to avoid decline in cardiac output and subsequent deterioration of heart failure symptoms. Mechanism underlying this observation is not clear.

Selection of Surgical Or Percutaneous Approach For Repositioning of LV Lead

When all attempts of reprogramming failed, repositioning or reimplantation of lead should be performed. As we mentioned before, images of coronary sinus venogram with inflated balloon catheter should be obtained in all cases during initial implantation procedure. Pacing values and information about presence of PNS in any of side branches where measurements were made should be also noted on a separate procedural sheet. Based on these findings, one may decide whether to proceed with surgical implantation or percutaneous repositioning. In patients with leads positioned in the basal part of LV wall and no alternative side branches it seems better to proceed with surgical implantation.

When patient has an alternative side branch it is reasonable to try the second procedure of implantation using the same technique used during initial procedure.

When pacing lead moved distally in to the vessel or when it is somewhere in the middle wall good results can be achieved by slight withdrawal of lead in more basal position. But one must be careful when withdrawing active fixation lead, because it may cause dissection and perforation of coronary sinus.

Another technique that may be used in patients with the only one enlarged vein and apical displacement of LV lead, is stenting of coronary side branch when lead placed in a desired position [6, 7]. This will result in stable position of the lead. This procedure may be performed either by subclavian approach or recently introduced femoral approach [8]. During femoral vein approach, ablation catheter and Amplatz 2 left type guiding catheter must be introduced to the right atrium. This is followed by cannulation of coronary sinus with Amplatz catheter, and advancement of guide wire and stent to desired vein. Stent size should be selected according to reference vein diameter. Because of the presence of enlarged vein, stents suitable for coronary intervention may not suffice and larger diameters stents, ahich are used in peripheral arterial intervention should be available. Then ablation catheter must be looped around the LV lead in right atrium, and slightly withdrawn until lead positioned in

desired position. Stent should be inflated only when all the measurements confirm desired location. These technique was successfully performed all nine patients included to this study. The advantage of this technique is obviating need for reoperation of generator pocket, which may increase risk of pocket infection, and other related complications. Another advantages is less invasive nature and shorter duration of hospitalization. It may be used more successfully if the LV lead is displaced in a distal position, but one must be careful to avoid displacement of right ventricular an/or atrial lead during the procedure. However it should be noted, that stabilization of coronary sinus lead with stenting, makes it impossible to extract this lead in the future, and patients should undergo surgery. This is the most important disadvantage of this procedure. Implantation of active fixation screw-in leads was suggested as alternative for stenting within coronary veins, however safety concerns of this technique are still exist [9].

When all percutaneous approaches fail, patient must be referred for surgical placement of left ventricular lead. Surgical techniques are out of the scope of this review, but we think that it is important to mention here that favorable hemodynamic results can be achieved with posterolateral approach, rather that standart lateral thoracotomy, and special attention should be given here to appropriately localize phrenic nerve, and this is especially important in patients with PNS.

Conclusion

PNS is one of the frequent complications associated with biventricular stimulation. It has negative psychological effects, and may result in failure of biventricular pacing. Its management includes both, simple reprogramming and complex interventional or surgical procedures. In this review article we presented currently available scientific data on prevention and management of this clinical entity and presented our own point of view, experience and observations.

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Case report
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Acute Renal Insufficiency Caused by Total Uterine Prolapse: A Case Report and Review of the Literature

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We aimed to report a case with acute renal insufficiency and hydronephrosis treated by surgical repair of the total uterine prolapse. A 61-year-old woman presented to our clinic with a general weakness, lower abdominal pain, decreased urination and dysuria. Her pelvic examination revealed the fourth-degree uterine prolapse and blood tests demonstrated failure of renal function tests. Abdominal computed tomography showed bilateral hydroureteronephrosis and the prolapsed uterus and the bladder through the pelvis. After acute vital intervention surgical repair of the pelvic floor with vaginal hysterectomy was performed. There were no complications associated with the surgery. The patient's renal function tests returned to normal and urine extraction increased. We suggest renal evaluation should be considered for cases with severe prolapse of the uterus and if hydroureteronephrosis exists, surgical treatment should be performed as soon as possible to prevent irreversible consequences.

Keywords: hydronephrosis, renal function, renal insufficiency, uterine prolapse, vaginal hysterectomy.

Introduction

Pelvic organ prolapse (POP) is the downward displacement of structures that are normally located at the level of or adjacent to the vaginal vault. Due to this anatomical displacement, hydronephrosis is one of the various complications which was first reported in 1923 by Brettauer and Rubin [1]. This easily overlooked complication can cause irreversible results if not treated properly. We report a case of postrenal acute renal failure caused by total uterine prolapse.

Case report

61-year-old woman was admitted with a three day history of general weakness, vomiting and lower abdominal pain. She also described decreased urination and dysuria. She had one term pregnancy terminated by vaginal delivery. She had hypertension for several years which was kept under control with medical treatment. Her family history was not significant.

On physical examination, her temperature was 36°C, blood pressure was 70/40 mmHg, pulse rate was 105 beats/min and her respiratory rate was 22 breaths/min. Both lungs were clear on auscultation, her abdomen was not distended and no abdominal bruit was heard. She had no pretibial pitting edema. On admission, her serum blood urea nitrogen was 229 mg/dL and creatinine was 20.26 mg/dL. Other laboratory findings included Hb of 7.2 g/dL, sodium of 138 mmol/L, potassium of 8 mmol/L, chloride of 114 mmol/L. Arterial blood gas analysis showed pH: 7.268, pCO_2 17.2 mmHg and HCO_3^- 7.9 mmol/L. The urinalysis showed pH 6.5, specific gravity 1005, protein (2+) and blood (2+).

The pelvic examination revealed fourth-degree uterine prolapse according to the Baden-Walker Halfway system and vaginal eversion with ulcerated mucosa (Fig. 1). Transabdominal ultrasonography showed bilateral severe hydroureteronephrosis but no additional remarkable finding. Abdom-

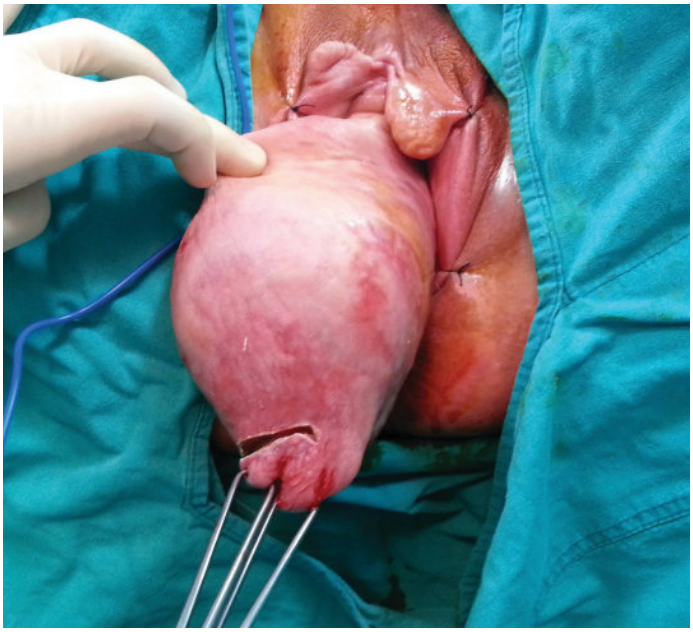

Figure 1 - Fourth-degree uterine prolapse (vaginal eversion) and marked vesico-cervical border.

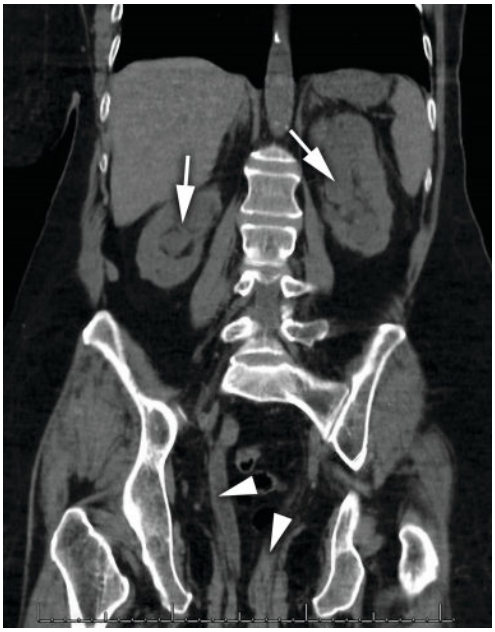

Figure 2. Abdominal computed tomography: coronal view of bilateral hydronephrosis (arrows) and hydroureter (arrowheads); pelvic cavity with nonvisible uterus and bladder.

inal computed tomography presented that the uterus and the bladder were prolapsed through the pelvis, bilateral hydroureteronephrosis with renal cortical thinning (Fig. 2). Catheterisation of the bladder revealed anuria. Due to these findings, she was diagnosed with postrenal acute renal failure. She was resuscitated with intravenous fluids and placed on hemodialysis. After acute vital intervention, bilateral nephrostomy catheterisation was performed.

After stabilization of the renal function tests and the patient's physical condition, a POP surgery was planned. The cervical cytologic examination showed chronic inflammation. The endometrial biopsy was reported as "squamous metaplastic changes of the epithelial fragments, surface epithelial changes and atrophy of the glandular tissues". Vaginal hysterectomy with anterior and posterior colporraphy and right sacrospinous fixation procedures were performed. There were no complications associated with the surgery. The patient's follow-up renal functional tests were normal and urination volume increased up to 6L/day.

A postoperative transabdominal ultrasonography showed a receding pattern of hydroureteronephrosis. The nephrostomy catheters were removed 2 days after the surgery. The patient was discharged on the seventh postoperative day. Despite the normal preoperative endometrial sampling, the specimen's pathological examination revealed endometrioid adenocarcinoma (Grade 1) with absence of myometrial and lymphovascular space invasion.

Discussion

The 37% prevalence of POP in the general population increases to 64.8% in older women [2]. The studies of large patient cohorts list prevalence of 25/323 (7.7%) and 31/189 (17.4%) [3, 4]. In a recent publication, Constantini et al. reported that the 5% overall prevalence of hydronephrosis in the 257 patients who underwent surgery for POP decreased to 3.5% when POP-related hydronephrosis was assessed [5]. Hence, as these studies included symptomatic preoperative patients, the prevalence of hydronephrosis associated with POP might be higher if undiagnosed or overlooked asymptomatic patients were included.

Several theories have been suggested to explain the mechanism of developing hydroureteronephrosis secondary to POP. In 1980, Hader and Meiraz proposed that the ureters become entrapped by the genital hiatus against the fundus of the uterus [6]. Although widely approved, this hypothesis fails to explain hydroureteronephrosis in patients who have undergone hysterectomy previously and the unilateral cases. Alternatively, Lieberthal and Frankenthal described a mechanism for hydroureteronephrosis with uterine prolapse that might be considered as a plausible mechanism with vaginal vault prolapse cases [7]. They theorized that cardinal ligaments form a sling over the ureters at the uterocervical junctional level and pull them downward when the uterus descends, which causes kinking of the ureters.

In the literature, there are several reported cases such as incidental diagnosis of hydroureteronephrosis due to uterine prolapse, bilateral hydronephrosis caused by vaginal vault prolapse or end-stage renal failure at neglected prolapse cases [8, 9]. To the best of our knowledge, our report is the second acute renal failure case caused by uterine prolapse in the literature [10]. We suggest renal evaluation should be considered for severe POP cases and if hydroureteronephrosis exists, surgical treatment should be performed as soon as possible to prevent irreversible consequences.

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Case report
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Fibrous Dysplasia of the Temporal Bone Presenting with Vertigo

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Fibrous dysplasia (FD) is a slowly progressive, benign, chronic fibro-osseous tissue disease, which is characterized by abnormal proliferation of fibrous tissue interspersed with normal or immature bone.

In this report we describe a patient with monostotic fibrous dysplasia that involved temporal bone presenting with vertigo, and discuss diagnostic work-up, histopathology, and treatment options of the disease, reviewing the literature.

Keywords: fibrous dysplasia, vertigo,

Introduction

Fibrous dysplasia (FD) is a slowly progressive, benign, chronic fibro-osseous tissue disease, which is characterized by abnormal proliferation of fibrous tissue interspersed with normal or immature bone.

Von Recklinghausen first described the term fibrous dysplasia, although Lichtenstein first suggested the terms fibrous dysplasia and polyostotic fibrous dysplasia in 1938. Ten to 25% of the monostotic form of FD involves craniofacial region [1]. Anatomically, the most commonly involved area in the skull is the ethmoid bone (71%) [1]. The next most common site of skull involvement is the sphenoid bone (43%), followed by the frontal bone (33%) and maxilla (29%) [1]. 24% of the disease involves temporal bone [2]. In this report we describe a patient with monostotic fibrous dysplasia that involved temporal bone presenting with vertigo, and discuss diagnostic work-up, histopathology, and treatment options of the disease, reviewing the literature.

Case Report

A 35-year-old woman attended the outpatient clinic of Azerbaijan Medical University, Otorhinolaryngology Department with the complaints of a vertigo, headache, and dizziness for 6 months. Previously she had applied to a public hospital with the same complaints and medical treatment was administered with the diagnosis of vestibular neuritis but as the complaints did not regress, she was referred to our clinic. The previous medical and family history was nonspecific. In her physical examination, the external auditory canal and tympanic membrane were normal. Nasal, nasopharyngeal, oral and oropharyngeal, hypopharyngeal examinations with rigid and fiberoptic endoscopy were otherwise normal. Audiologic tests, including pure-tone and impedance audiometry, were normal and other laboratory investigations were all in normal limits. Neurological and cranial nerve exams were within normal range except for vestibuler nerve dysfunction demonstrated by caloric testing and electronystagmography that showed reduced vestibuler function on the left side. Temporal bone computed tomography (CT) demonstrated bone growth with temporal bone sclerosis and narrowing of internal auditory canal on the left, compatible with picture of temporal bone fibrous dysplasia on the left and normal right temporal bone. As the other system and neurological examinations were normal the

vestibular symptoms were related to temporal bone fibrous dysplasia due to irritation or compression of vestibular nerve. High dose corticosteroids were administered (1mg/kg metilprednisolon) and the symptoms regressed one week after the treatment.

Discussion

Fibrous dysplasia (FD) is a slowly progressive, benign, chronic fibro-osseous tissue disease, which is characterized by abnormal proliferation of fibrous tissue interspersed with normal or immature bone. The precise etiology of fibrous dysplasia is currently unknown. The disease tends to develop in the pre-adolescence years, and is predominant in male patients (2:1).

Fibrous dysplasia can be classified as unifocal (the monostotic form of the disease, MFD involving only one bone) 70%, multifocal (the polyostotic form of the disease, PFD involving multiple bones) 30% or part of McCune Albright Syndrome (bone involvement associated with skin lesions and endocrinopathies) 3%. Unifocal type typically involves the ribs and femur. The lesions grow slowly and growth usually stops after puberty. Because many patients are asymptomatic and are often diagnosed incidentally, the incidence of the monostotic form is considered to be highest. 10 to 25% of the monostotic form of the disease involves craniofacial region. Ethmoid bone is the most commonly involved region in the skull followed by sphenoid and frontal bone. Involvement of temporal bone is seen %24 of the cases. Determining the true incidence of fibrous dysplasia, particularly for the more prevalent monostotic form, is difficult because many patients are asymptomatic and are often diagnosed incidentally after radiographic evaluation for other reasons [4].

Temporal bone involvement usually presents with clinical symptoms because narrowing of external auditory canal leads to progressive conductive hearing loss [3]. Other symptoms include retroauricular bulging, otalgia tinnitus and otorrhea. When the ear capsule is involved then sensorineural hearing loss may occur. In about 40% of the cases cholesteatoma may develop, and it is the most frequent complication of the disease [5]. Also the involvement of the facial nerve is seen in 10% of the patients. In our case, the fibrous lesions of the temporal bone led to narrowing of the left internal auditory canal causing vestibular nerve dysfunction. The reduced activity of the vestibular nerve on the left side was was demonstrated by caloric ENG and balance tests. We believe that the reduced diameter of the internal auditory canal compressed the vestibular nerve causing irritation and dysfunction of the nerve.

The differential diagnoses of temporal bone fibrous dysplasia include Paget's disease, hyperparathyroidism, local reaction to meningioma, osteoma, eosinophilic granuloma, osteochondroma, and sarcomatous neoplasm [6].

It is not always possible presently, to control fibrous dysplasia since there is no conservative treatment. The simple presence of the lesion does not justify surgical intervention. The bone invasion of external auditory canal (enough to produce conductive hearing loss), recurrent infections and secondary cholesteatoma in the external auditory canal are the indications for surgery of temporal bone fibrous dysplasia. The secondary complications of fibrous dysplasia may be secondary external cholesteatoma behind the canal stenosis or obliteration (16-40 %), erosion of the middle ear ossicles inner ear capsule and fallopian canal leading to a labyrinthitis and facial palsy. Involvement of the middle and posterior cranial fossa dura, lateral sinus, jugular bulb and carotid artery may also be seen. If the hearing is affected or recurrent infection or secondary canal cholesteatoma is detected, surgical intervention must be performed. The surgeon must be aware that surgery of the dysplastic temporal bone can be hazardous because landmarks are often obliterated and intra-operative bleeding can be vigorous [7].

As hearing of our patient was within normal limits and the only symptom was vertigo we started medical treatment with steroids and the symptoms regressed.

In cocnclusion, we report a rare lesion effecting internal audiotry canal and interestingly affecting only vestibular nerve in same side. the symptom regressed via steroid. Otherwise we need operated and enlareged the canal.

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Case report
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First Living Donor Liver Transplantation For Congenital Hepatic Fibrosis In Azerbaijan.

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Congenital hepatic fibrosis (CHF) is a rare autosomal recessive disease. Cases have been reported from all over the world but the exact incidence of the disease is not known. The diagnosis sometimes is difficult to establish and one of the main diagnostic method is histological evaluation. The management and prognosis of CHF is dependent on alimentary bleeding secondary to portal hypertension. In late childhood abdominal pain, cholangitis and features of hypersplenism complicate the problem. Herein we present the case report of patient with CHF. Our choice of treatment was living donor liver transplantation. This procedure is a very difficult but only life – saving chance for patients with CHF.

Keywords: liver fibrosis, living donor liver transplantation, congenital hepatic fibrosis, chronic liver failure

Introduction

Congenital hepatic fibrosis (CHF) is an unusual condition in which portal hypertension (PH) occurs without significant hepatic or renal functional impairment and characterized histologically by defective remodeling of the ductal plate. CHF is a subtype of group of congenital disorders described as fibropolycystic disease with a wide clinical spectrum depending upon the time of presentation and degree of hepatic involvement. Herein we report a case of living donor liver transplantation for patient with CHF.

Case Report

An 21-year-old man was admitted with slowly progressive distension of abdomen and fullness in upper abdomen of 7 months duration, and history of 3 time hematemesis during last 7 months and 3 times of EVL. There was no history of pain abdomen, jaundice, or any skin bleeds or hyperpigmentation. On tracing the pedigree no other family member was known to be affected. The man weighed 62.7kg, with a height of 167 cm. Body mass index was 22.5. General examination revealed pallor and conjunctival xerosis without any signs of liver cell failure or icterus. Temperature, pulse and BP were normal. On abdominal examination spleen measured 9 cm below costal margin with tip below umbilicus without signs of hypersplenism, liver span was 6 cm with no evidence of free fluid in the abdomen. Kidneys were not palpable and other systemic examination was normal. On investigations, hemoglobin was 10.5 g/dl, total leukocyte count was 3060/mm3, platelet count was 106000/mm3, and peripheral blood smear revealed thrombocytopenia, leukopenia, normal erythrocytes and no malarial parasite (MP). Liver function tests revealed total bilirubin of 1.1 mg/dl and serum aspartate transaminase was 9.6 IU/ L, serum alanine transaminase was 10.5 IU/L and alkaline phosphatase was 75 IU/L.

Bone marrow aspiration showed erythroid hyperplasia with normoblastic reaction and no abnormal cells, LD bodies or MP. HBsAg, anti HCV, ANCA, ASMA and serol-

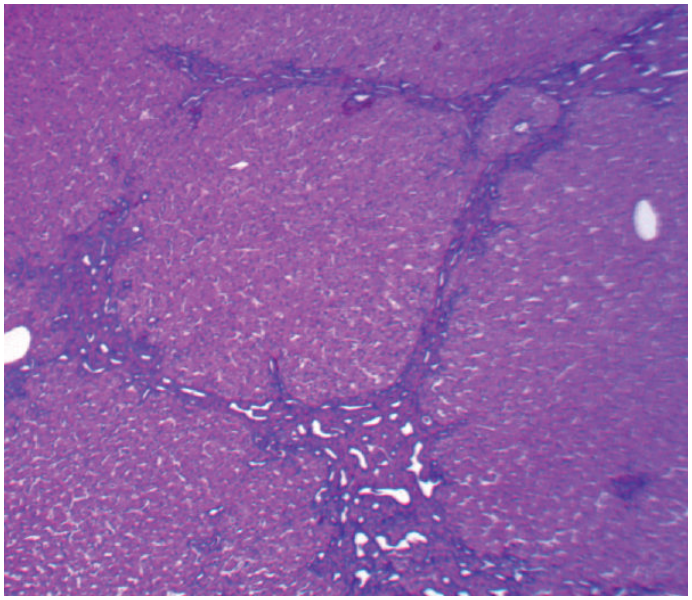

Figure 1. Histological examination. Liver tissue with distorted architecture composed of nodules of different sizes surrounded by fibrous septa.

ogy malaria were negative. Alpha 1 antitrypsin was 2.01 gr/L. Ultrasound of abdomen showed normal liver, kidneys and normal caliber of portal vein with no evidence of ascites. Upper GI endoscopy revealed grade III esophageal varices. Slit lamp examination of eyes was normal. Prothrombin time and INR were also within normal limits. Abdominal contrast CT shows the signs of chronic liver decease without any mass and splenomegaly, the dilated intrahepatic bile ducts particularly in right lobe and many portocaval shunts especially around spleen.

Liver biopsy showed liver tissue with distorted architecture composed of nodules of different sizes surrounded by fibrous septa. On fibrous septa dilated bile ducts and marked cholangiolar proliferation was seen. Inflammatory infiltration is minimally on fibrous septa. There was focal mild dilatation of interlobular ducts. These histological features confirmed the diagnosis of CHF and possibility of inactive cirrhosis. During the hospital stay, the patient remained asymptomatic and had no evidence of active bleeds.

This patient was treated by living donor liver transplantation. Procedure was performed without any deviations from standard technique.

Discussion

Congenital hepatic fibrosis is a rare autosomal recessive disease named by Kerr in 1961. Clinically reserved for a condition in which PH occurs without significant impairment of liver or kidney function [1]. Cases have been reported from all over the world [2-7] but the exact incidence of the disease is not known. CHF has usually autosomal recessive inheritance and initial presentation may be at around 3-6 months. The presentation ranges between 1.8-14 years [8], PH is a usual accompaniment and renal involvement is seen with < 10% tubules being affected. Classically affected patients are asymptomatic until the age of 5 or 7 years when manifestations of PH or cholangitis lead to the diagnosis. Several clinical forms are described which depend on the variable predominance of PH and cholangitis. Cholangitis form of CHF is more severe and usually occurs in late childhood and adult life [9]. Blyth and Ockenden(10) have divided their patients into 4 groups called perinatal, neonatal, infantile and juvenile in accordance with the age at clinical presentation. Renal involvement is maximal in perinatal group and minimal in juvenile group. Our patient had presented with PH, with no clinical or histological evidence of cholangitis and renal abnormalities.

The usual presentation of CHF is with abdominal distension(4), hematemesis or melena, failure to thrive, jaundice, anemia, hepatomegaly and splenomegaly [1,8]. The other features of CHF are abdominal pain (splenic infarction), fever (cholangitis in dilated ductules), ascites, etc. [2-5]. CHF is particularly associated with infantile polycystic kidney disease or intrahepatic bile duct dilatation (Caroli's disease) [1]. The diagnosis is based on liver functions which are well preserved, features of hypersplenism, elevation in levels of alkaline phosphatase and gamma glutamyl transferase [1, 5]. Other associated disorders with CHF are medullary sponge kidney, Ivemark's Familial Dysplasia, Meckels syndrome, vaginal atresia and rarely adult type polycystic kidney disease or nephronopthises, Jenunne's syndrome, tuberous sclerosis, etc. These conditions were ruled out in our case by absence of other clinical features/malformations associated with these conditions and relevant investigations. Biliary hamartomas (von Meyenberg complexes) are frequently associated with CHF and are detected on histology and by imaging. Hallmark of diagnosis is liver biopsy which shows bands of fibrous tissues often containing linear or circular spaces lined by cuboidal epithelium. There is diffuse portal and perilobular fibrosis varying in thickness but it does not distort lobular structures. The limiting plate is intact and parenchyma is separated by islands of fibrosis. There are no inflammatory changes and regenerative nodules are absent or few [8]. The cholangitis form of CHF is difficult to differentiate from Caroli's disease characterized by nonobstructive dilatation of intrahepatic bile ducts occurring as an isolated abnormality without portal fibrosis. This suggests a spectrum of congenital biliary tree disease with portal fibrosis and normal caliber ducts at one end and multiple intrahepatic, even extrahepatic, dilatations without fibrosis at the other end. Overlapping of CHF and Caroli's disease has been confirmed by histological studies [9].

The management and prognosis of CHF is dependent on alimentary bleeding secondary to PH. In late childhood abdominal pain, cholangitis and features of hypersplenism complicate the problem. However, prognosis may be greatly improved by shunt surgery but survival in some patients may be limited by degree of renal failure (I). In our case choice of treatment was living donor liver transplantation.

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Case report
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Risperidone-Induced Hiccups in an Adolescent

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Hiccups are involuntary spasmodic contractions of the diaphragm and inspiratory intercostal muscles followed by sudden closure of glottis which leads to halting the start of an inspiration. There are many factors which may cause hiccups. Although the exact pathophysiological processes involved have not yet been established, the neurotransmitters dopamine, serotonin and gamma amino butyric acid (GABA) have been documented to play a significant role in the generation of hiccups. Here, we present a case of risperidone-induced hiccups in a 14-year old adolescent to discuss the probable causes, the etiology and the clinical outcomes of this side effect.

Keywords: Adolescent, Hiccups, Risperidone

Introduction

Hiccups are involuntary spasmodic contractions of the diaphragm and inspiratory intercostal muscles followed by sudden closure of glottis which leads to halting the start of an inspiration [1]. The neurobiologic reflex system of hiccup includes the vagus and phrenic nerves, and the sympathetic chain from thoracic segments T6–T12 in the afferent limb; and the brain stem, hypothalamus, the respiratory center, medullary reticular formation, phrenic nerve nuclei in the efferent limb. The C3–C5 segments and the brain stem form the main link between the efferent and the afferent limbs [2].

It is called intractable persistent hiccup when the duration of hiccup exceeds 48 h [3]. There are many factors which may cause hiccups. Vagus and phrenic nerve irritation (resulting from e.g., tumors, goiters, cysts, gastroesophageal reflux disease, hiatal hernia), central nervous system disorders (e.g., trauma, infection, structural, or vascular lesions) , toxic metabolic disorders (e.g., medications, general anesthesia, alcohol abuse, diabetes, gout, electrolyte deficiencies), psychogenic factors (e.g., anxiety, stress, excitement) are main categories of possible mechanisms that lead to persistent hiccups [1]. Although the exact underlying mechanisms have not been established, gamma amino butyric aid (GABA), serotonin, and dopamine have been shown to have a role as an etiological factors for hiccups [2, 4].

Hiccups caused by dopaminergic agents and treatment with antidopaminergics have been reported [1, 5, 6]. The serotonin`s role for producing hiccups is thought because of reported treatment of hiccups by olanzapine and sertraline. Also there is a report for clozapine that causes hiccups [3, 7, 8].

Risperidone is an atypical antipsychotic, used for psychotic disorders, behavioral problems and tic disorders in childhood. It has the strongest affinity for D2 dopamine and 5-HT2 receptors; strongest affinity for α1 adrenergic, M muscarinic and H1 histamine receptors. The main mechanism of action of risperidone is known to be the blockage of serotonin and dopamine systems through actions especially at the D2 and 5-HT2 receptors [10, 11]. Risperidone has a adverse effect profile as extrapyramidal symptoms, increased weight, and metabolic problems.

We are going to present a risperidone-induced hiccups case to discuss the probable etiological mechanisms, the causes, and the clinical outcomes of this side-effect.

Case Report

A 14-year-old girl who had been referred to psychiatry outpatient clinic from pediatric nephrology department with complaints of irritable mood, diminished interest in daily activities, fatigue and feeling of worthlessness for about a month. At last days, she complained about hearing voices, which had been calling her name. She suffered from chronic renal failure diagnosed nearly 2 years ago. Recently, she was given hemodialysis. Her blood and urine analysis had been shown no recent pathological sign, including electrolyte imbalance. The psychiatric examination revealed depressed affection, psychomotor retardation and auditory halucinations. We put the diagnosis of major depressive episode with psychotic features according to *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition criteria [12]. She was started on risperidone 0.5 mg/day. Within 2-3 h after taking risperidone, the patient started to have hiccups. The hiccup didn`t disappear on that day. We evaluated all other possible organic causes, including neurologic examination for acute neurologic problems, physical, blood and urine examinations for acute infections and sudden medical causes. We also asked to her and her parents about history of drinking carbonated beverages, alcohol, eating too much in last two days. We couldn`t find any cause explaining the hiccups. We discontinued risperidone after 60 hours and the hiccups ended a day later. There were no hiccups following 3 days.

Because of this, further analysis were not done and we decided to restart a risperidone. After restart of risperidone, the hiccups begin again within a few hours. Risperidone was ordered to stop, immediately. And again, after 12-14 hours the hiccups disappeared. There were no hiccups following two weeks.

Discussion

Our case describes the possible role of risperidone for inducing hiccups. It is one of the rare reports in the literature [13] documenting this fact. Previously, hiccups resulting after aripiprazol and clozapine treatment were reported [2, 3]. As we mentioned earlier, risperidone has the strongest affinity for D2 dopamine and 5-HT2 receptors; strongest affinity for α1 adrenergic, M muscarinic and H1 histamine receptors. The main mechanism of action of risperidone is known as the blockage of serotonin and dopamine systems at the D2, 5-HT2 receptors [11]. Risperidone also has adverse effects as extrapyramidal symptoms, increased weight, and metabolic problems.

In contrast to the previous reports of hiccups caused by antipsychotics, electrolyte disturbances (e.g. hyponatremia) seem to be an unlikely etiology in our patient [14]. Although our patient had a kidney problem, the electrolyte and biochemical analysis were normal during the presence of hiccups. According to these, we offer the modulation of neurotransmitters as a possible mechanism for the hiccups after risperidone in our patient. And also the beginning time, lasting time, and relationship between drug discontinuation and hiccups are compatible with literature [2, 13].

As both hypo- and hyperdopaminergic states have been associated with the development of hiccups, the antagonism of dopamine by risperidone may be the cause. But, the obvious neuronal mechanism through which dopamine effects the hiccup reflex circle remains unknown.

The other possible mechanism is through serotonin which has a role in the underlying process of hiccups. Risperidone has an action on 5HT2 receptor, but the consequence of hiccups through this action also remains unclear.

Conclusion

The duration and relationship of hiccups with risperidone and the absence of any neurologic and physical signs and symptoms seem to ignore the systemic cause for the hiccups. Although hiccup is a benign side effect, it can be very stressful and may cause disruption of treatment. More studies are needed to understand mechanism of neurotransmitters involved in the hiccup reflex system and the pathways for the different medications effects.

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Original article
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Our Initial Results of Off-pump Coronary Artery Bypass Grafting

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Background. On-pump coronary artery bypass grafting (CABG) remains a procedure of choice in patients with ischemic heart disease despite nearly two decades of utilization of off-pump techniques. Nearly all aspects of off-pump CABG operations are still debatable, including indications and contraindications to this procedure. We report here our initial experience with routine application of off-pump CABG in patients with ischemic heart disease.

Methods. Results of 96 off-pump CABG procedures performed from May 2015 to date are analyzed. Preoperative demographic and clinical data, intraoperative data and results of postoperative course are analyzed. Our results are compared with the results of other authors and mortality rates are compared to predicted by risk-stratification system "EuroScore" values.

Results. The mean number of distal anastomoses was 3.01 +/- 0.07 per patient. In 75 (78.1%) patients we constructed 3 or more grafts, in 22 cases (23%) - we used complex types of surgical technique (sequential, "Y-graft" or "T-graft"). 28 (29.2%) patients required inotropic support in ICU for initial recovery with an average duration of 3.14 +/- 0.74 hours. In 3 (3.1%) patients in the postoperative period were episodes of sustained atrial fibrillation. In 1 (1.04%) patient course of OPCABG procedure was complicated with emergent conversion to on-pump CABG. Mortality was 1.04% (1 patient).

Conclusions. A modern OPCABG approach offers low mortality, excellent clinical outcomes, and does not come at the price of less complete revascularization.

Keywords: coronary artery disease, myocardial revascularization, off-pump coronary artery bypass grafting

Introduction

The first coronary artery bypass grafting (CABG) procedures performed in the 60s - 70s of the past century were the operations on the beating heart without using cardiopulmonary bypass (CPB) and cardioplegia (CP) [1, 2]. However, the universal spread and popularity acquired performing CABG using CPB-machine – so-called on-pump CABG, popularized by Favaloro and colleagues [3]. Very soon this technique became very popular and demonstrated the possibility of performing these operations on the motionless and bloodless operative field, as well as the ways of its standardization, widespread dissemination and training. Several decades of performing CABG operations on-pump revealed a number of complications associated directly with cardiopulmonary bypass itself and cardioplegia, as well as with connecting the patient to the heart-lung machine (cannulation of the great vessels) and clamping of the aorta. Consequently, many eyes were again turned to the possibility of performing coronary bypass surgery on the beating heart without CPB and cardioplegia (off-pump CABG or OPCABG), which also falls into the category of minimally invasive cardiac surgery [4].

However, despite of the nearly two decades of utilization and numerous reports, this method remains not standardized, its use is not reflected in the leading American and European guidelines, indications and contraindications for these operations are not specified. Most of the issues related to the OPCABG procedure remains debated [4]. In this regard, we would like to present our initial experience with using OPCABG in the newly created surgical department.

Material and Methods

Since the beginning of our activity in May 2015 we have operated on 110 patients with coronary artery disease who underwent 110 isolated OPCABG procedures (Table 1). In 5 cases (4.5%) operations were performed with CPB and cardioplegia (conventional on-pump CABG). In 9 cases (8.2%) operations were performed with CPB on a beating heart ("on-pump beating heart"). In 96 patients (87.3%) procedures were performed without CPB – off-pump CABG or OPCABG.

The average age of patients was 59.14 +/- 0.4 years (range from 33 to 77 years). 45 patients (46.9%) were older than 60 years. Most of our patients were male (79 patients, representing 82.3% of all population). The vast majority of patients - 81 (92%) - were in the III-IV NYHA functional class. Factors such as obesity, diabetes and chronic obstructive pulmonary disease (COPD) occurred in 39 (40.6%), 28 (29.2%) and 26 (27.1%) of the operated patients respectively. Also, in 28 cases (29.2%) there were carotid artery lesions of varying degree. In 4 (4.2%) patients there was renal failure not requiring hemodialysis.

It should be noted that 63 patients (65.6%) had a history of myocardial infarction. Most of the patients who have suffered myocardial infarction had 1 MI in anamnesis - 47 (74.6% of patients with previous MI). Another 12 patients (19%) had a history of 2 MI and 3 patients (4.8%) had 3 MI. 11 patients (11.5%) had a history of previous PCI with stenting of coronary arteries. It should be noted that t46 patients (47.9%) were with acute coronary syndrome, including 13 (13.5%) with acute phase of myocardial infarction. Angiographic picture in the vast majority of patients was characterized by high complexity of coronary lesions. So, 76 patients (79.2%) had three-vessel coronary disease, and 17 (17.7%) – two-vessel disease. Left mainstem disease (or its equivalent) was noted in 43 (44.8%) patients. Although the incidence of stenotic lesions was similar in all three regions, distribution of occlusive vascular lesions was uneven. So, most frequently were observed occlusions of the left anterior descending artery (LAD) and right coronary artery (RCA) distributions – they were registered in 45.7% and 42.9% respectively, while the occlusive lesions in the circumflex artery (Cx) artery area were met less frequently - in 21.7% of cases.

According to preoperative echocardiography, signs of left ventricular dilatation were observed in 26% of patients – LVEDD of more than 60mm was in 23 (23.9%) patients, and the LVEDD>70 mm – was in 2 patients (2.1%). 33.3% of patients had a decrease in LVEF. For instance, LVEF<50% was in 27 (28.1%) patients, and less than 40% was observed in 5 (5.2%).

Table 1. Preoperative demographics and clinical data

Variable	n (96)	%
Age (mean), years	59,14 +/- 0,4 (33-77)	
Older than 60 years	45	46,9%
Male	79	82.3%
Female	17	17.7%
FC III NYHA	78	88.6%
FC IY NYHA	3	3.4%
Obesity	39	40,6%
COPD	26	27,1%
Diabetes	28	29,2%
Renal failure	4	4,2%
History of MI	63	65,6%
1 MI	47	74,6%
2 MI	12	19%
3 MI	3	4,9%
PCI, stenting in anamnesis	11	11,5%
Acute coronary syndrome	46	47,9%
Acute MI	13	13,5%
3-vessel disease	76	79,2%
2-vessel disease	17	17,7%
Left mainstem disease (or its equivalent)	43	44,8%
Echo LVEDD>60 mm	23	23,9%
EchoLVEDD>70 mm	2	2,1%
LVEF <50%	27	28,1%
LVEF <40	5	5,2%
Urgent procedure	15	15,6%
EuroScore mean (logistic)	3,69 +/- 0,27	
EuroScore mean (percent)	3,85 +/- 0,43%	

20% of patients had I-II degree of mitral insufficiency.

In 15 patients (15.6%) operation had urgent status.

The risk of surgical intervention predicted by risk-stratification system "EuroScore" averaged 3.69 +/- 0.27 (logistic) or 3.85 +/- 0.43% (by percentage).

Surgical Technique

All operations were carried out through median sternotomy. We also routinely used high thoracic epidural anesthesia with bupivacaine in combination with a conventional general anesthesia. Standard monitoring technique was used in all cases.

Internal thoracic artery (ITA) was harvested whether skeletonized without opening of the left pleural cavity or pedicled the opening of the left pleural cavity, depending on the preferences

Table 2. Intraoperative data

Variable	n (96)	%
Operation times, min	263,8 +/- 5,4	
(160-460)		
Blood loss, ml	597 +/- 24,49	
Usage of internal thoracic artery	95	98,9%
Mean number of distal anastomoses per patient	3,01 +/- 0,07	
3 grafts	75	78,1%
4 grafts	20	20,8%
Sequential technique	11	11,5%
Complex conduits (Y-graft, T-graft)	11	11,5%
"Internal thoracic artery-LAD first" technique	72	75,8%
"Other vessel first" technique	24	24,2%
Conversion to CPB	1	1,04%

Table 3. Postoperative data

Variable	n (96)	%
Conversion to CPB	1	1,04%
Need for inotropic support	28	29,2%
Inotropic support time, hours	3,14 +/- 0,74	
Ventilation time, hours	5,78 +/- 0,37	
Prolonged ventilation (>24 hours)	1	1,04%
Atrial fibrillation	3	3,1%
RBC transfusikon, ml	358,43 +/- 19,7	
FFP transfusion, ml	410,71 +/- 16,63	
Length of stay in ICU, hours	47,8 +/- 1,8	
Length of stay in hospital after surgery, days	6,83 +/- 0,3	
Chest re-open for hemostasis	2	2,08%
Superficial wound infection	1	1,04%
Mortality	1	1,04%

of the operating surgeon. Heparin was administered at the dose of 1.5 mg/kg of patient weight. Opening the pericardium was performed in a standard inverted "T" fashion. For the positioning of the heart, we used a deep pericardial stitch (Lima-stitch), by manipulation of which we had access to different surfaces of the heart. Also, sometimes for better visualization of the arteries of the Cx artery area we put additional deep pericardial sutures on the left edge of the pericardium near left pulmonary veins. Also we actively changed operating table positions to assist in heart positioning (Trendelenburg position with turns to the left and to the right to visualize different areas of the heart). To stabilize the myocardium, we used the commercially available tissue stabilizers (Octopus 4 Tissue Stabilizer; Medtronic, Minneapolis, MN). Additionally, a mister-blower (Guidant, Indianapolis, IN) was used. For temporary occlysion of revascularized vessel we used silicone vessel loops. Coronary arteriotomy was performed with a beaver blade, and shunt insertion (ClearView Intracoronary Shunt; Medtronic) was used whenever possible.

Myocardial revascularization we always started with occluded and collaterilized artery (in half of the cases it was the LAD, in other half - RCA). If it was LAD – we constructed anastomosis with internal thoracic artery. Then, the operation proceeded in a standard fashion. If the occluded artery was RCA - then first we anastomosed safenous vein to the RCA or PDA, then constructed the proximal anastomosis of that vein to the ascending aorta (as well as other proximals if other arteries were planned to be grafted). Then we continued with ITA-LAD distal anastomosis and other distals with other arteries (DV, OM etc.). If there was no occluded arteries, myocardial revascularization was always started with anastomosis of the ITA with LAD. Prior to arteriotomy we always performed a short period (30 seconds) of ischemic preconditioning using silicone vessel loop. Anastomoses of the ITA and sequential anastomoses were constructed using polypropylene 8/0 suture, the remaining distal anastomoses - polypropylene 7/0 sutures. For the construction of proximal anastomoses we used polypropylene 6/0 suture. Upon completion of the revascularization, if there were no excess bleeding, we neutralized only half the dose of heparin.

Results

In 95 patients the ITA was used (98.9%).The mean number of distal anastomoses was 3.01 +/- 0.07 per patient (range 1 to 5 grafts). In 75 (78.1%) patients we constructed 3 or more grafts (Table 2): in 55 (57.3%) were grafted 3 vessels, and in 20 (20.8%) patients - 4 vessels. In 22 cases (23%) - we used complex types of surgical technique: in half of the cases (11 patients) we used sequential technique, when with one conduit two or more vessels were revascularized, and in the remaining 11 (11.5%) patients were constructed complex conduits - in the form of a "Y-graft" or "T-graft".

In 72 (75.8%) patients initially ITA-LAD anastomosis was constructed first followed by other coronary areas. In the remaining 24.2% of cases other regions were revasculaized first followed by ITA-LAD anastomosis.

Mean operative time was 263.8 +/- 5.4 minutes (160-460 minutes). Blood loss on the average was 597.06 +/- 24.49 mL (300-1500 mL).

28 (29.2%) patients required inotropic support in ICU for initial recovery with an average duration of 3.14 +/- 0.74 hours (Table 3). Duration of ventilation support (respiratory support) after surgery was 5.78 +/- 0.37 hours. Prolonged ventilation (more than 24 hours) was needed in 1 (1.04%) patient.

In 3 (3.1%) patients in the postoperative period were episodes of sustained atrial fibrillation (AF), which were treated

(managed) pharmacologically. Red blood cell (RBC) transfusions averaged 358.43 +/- 19,7ml/patient during surgery and in surgical intensive care unit (ICU), and fresh frozen plasma (FFP) transfusuions reached on average - 410.71 +/- 16.63 ml/patient.

Mediastinitis and other wound infection problems after surgery were not registered. In 1 (1.04%) patient there was superficial wound infection without any serious consequences. In 2 (2.08%) patients due to bleeding chest reopening for hemostasis was performed.

In 1 (1.04%) patient course of OPCABG procedure was complicated with emergent conversion to on-pump CABG due to uncontrollable outbreak of arrhythmias. In this case operation was continued on-pump beating heart with good postoperative results.

One patient (1.04%) died due to malignant cardiac arrhythmias on the third postoperative day.

Discussion

We present our consecutive series of patients operated by our group and reflecting our daily practice. The complexity of our population is demonstrated by the large number of patients with comorbidities and other risk factors as obesity, COPD and diabetes, as well as the presence of other important factors, as a left mainstem (LM) lesions, combined lesions of the carotid vessels, the high proportion of multivessel coronary disease etc. Also an important factor was the fact that about half of our patients preoperatively were clinically unstable (acute coronary syndrome, acute phase of myocardial infarction). But in contrast to other author's data, we did not have patients with redo heart surgery or with preoperatively inserted intra-aortic balloon counterpulsator [5,6].

The proportion of patients with LM disease (or its equivalent) was 44,8%. W.Turner et al [5] in their first series of 100 patients report about 3% of patients with LM-disease, though at the same period proportion of such patients in STS registry was about 15%. According to M.Y. Emmert [7], of the 983 patients 343 were with LM lesions, which accounted for 34.9% of the operated. Close to our data, the proportion of patients with left main stem lesion reported by Ki-Bong Kim et al (8) - of 1345 operated in 9 years 42.2% had LM disease or three-vessel coronary lesions. Very low rate of such patients in our opinion could talk about patient selection (or selection bias).

The main argument, which opponents of OPCABG put – is performing off-pump CABG procedures at the expense of completeness of revascularization. Thus, a low number of distal anastomoses per patient can talk about patient selection (selection bias), or actual incomplete myocardial revascularization. For example, in our series of operated patients, the mean number of distal anastomoses was 3.01 +/- 0.07 per patient. Given the presence of patients with two- and three-vessel disease, this figure seems to us high enough to demonstrate the adequacy and completeness of revascularization. As another example, in W.Turner [5] series of 100 OPCABG mean number of distal anastomoses per patient was 1.9, in E.Buffalo [6] series - 1.9 and M.Y.Emmert et al [7] report - 3.62 anastomoses/patient.

Another indicator of the success of implementation of CABG operations on the beating heart is the rate of conversion to CPB. Thus, according to the different authors [9-11], it ranges from 1% to 15%, with an average of 3-4%. In our series of patients conversion rate was 1.04% (1 patient converted to on-pump beating heart CABG due to arrhythmic complications). It is believed that the most common cause of complications, causing the emergent intraoperative conversion is local ischemia, thus, global ischemial accompanying cardioplegic cardiac arrest in such patients may lead to catastrophic heart failure [4, 6, 11]. In this connection, the authors recommend at conversions on CPB, to continue the operation on-pump beating heart in order not to aggravate ischemic state of the myocardium [4].

In general, among our initial series of 110 patients with isolated ischemic heart disease, 87.3% of CABG surgeries were performed off-pump. Thus, by different authors reports, this parameter ranges from 49% to 99% [4-6, 10, 11], and exploring various approaches of different groups can also shed light on additional anesthetic, surgical and technical aspects of the problem.

One of the most common complications that occur after conventional CABG is an episode of atrial fibrillation, which complicates the postoperative period in approximately 30-45% of patients. In our series of operations we registered three patients (3.1%)with this complication, which is quite a low figure, demonstrating the effectiveness of OPCABG surgery. According to the RA Archbold et al [12] paroxysms of atrial fibrillation observed in 4% -26% of all operated off-pump CABG patients. As you can see, our findings fit into the overall picture of the post-operative course after OPCABG surgery.

And finally, the mortality rate we observed was 1.04% (1 patient) – in contrast to the expected by the EuroScore risk-stratification system which was 3,85 +/- 0,43% [13]. According to Ki-Bong Kim et al [8] in the 1345 operated patients mortality rate was 1,6%, to W.Turner et al [5] - 3% of 100 operated patients, E.Buffalo [6] – reported about 1.9 % mortality on 3866 patients operated and M Y.Emmert [7] observed 2.2% mortlity. One can see that our mortality rate was close to the range of other group reports.

Study limitations

Of course, this is a retrospective and observational study and all associated disadvantages apply. An ideal approach would be a trial of prospective and randomized nature. Next, our results lack the force of numbers, and certainly a higher level of signi - cance may have been obtained had we analyzed a larger cohort of patients. However, we present a homogenous population with a 100% standardized and modern approach to OPCABG. This approach is supported by at least 90% of CABG cases being done in off-pump fashion currently, which is far above the international standard, and also by our excellent overall outcome as well as our overall low conversion rate to CPB.

Conclusion

The isolated off-pump CABG surgery is a safe alternative that provides low rates of complications and mortality, rapid clinical recovery and rehabilitation of patients without compromising the adequacy of myocardial revascularization.

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Case Report
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Splenic Artery Pseudoaneurysm – Unusual Pediatric Case

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Splenic artery is the third most frequently place of aneurysm in abdominal vessel taking place after abdominal aorta and iliac arteries. Pseudoaneurysm although differs from true one by histological point of view generally has same symptoms, complication. But aneurysms and pseudoaneurysms of the splenic artery require different management strategies. This entity can encounter in adult population not so rare but it is very unusual to see it in children. In our case we show complicated splenic artery pseudoaneurysm, it background and endovascular treatment.

Keywords: splenic artery, pseudoaneurysm, pediatric, endovascular treatment

Introduction

Complicated with the hemorrhage splenic artery pseudoaneurys could be life-treating condition, which required prompt intervention, ranging from embolization to radical surgery. Splenic artery pseudoaneurysm generally symptomatic and the most common presentation is abdominal pain upper or lower GI bleed, hemorrhage into pancreatic duct and hematemesis. Only small percentage of patient is asymptomatic [1]. In children population, unlike in adult where pancreatitis plays an important role most common cause of splenic artery pseudoaneurysm is blunt abdominal trauma. Although non-invasive methods like multidetector computed tomography (MDCT) angiography and magnetic resonance (MR) angiography become more popular in diagnosis of splenic aneurysm conventional digitally subtracted angiography is gold standard modality. Not only for diagnosis but endovascular treatment of aneurysms could be also possible in a same procedure [2]. Splenic artery aneurysms and pseudoaneurysms require different management strategies. Management of true aneurysm depends on size of aneurysm, patient status, pregnancy and of course symptoms. Follow up generally advised asymptomatic small size aneurysm except pregnancy. Because of high rite of hemorrhagic complication, which could be, life-threatening prompt intervention is advised in pseudo aneurysm cases [3].

Case Report

Eight years old female patient was admitted to our hospital with symptoms of epigastric pain lasting 14 days. Ultrasound reviled cystic lesion around duodenum in size of 3 x 4 cm. Upper abdominal magnetic resonance imaging (MRI) was performed with contrast administration. On MRI there was cystic lesion in oval shape located para-duodenal space without evidence of hemorrhage. Another cystic lesion was found in pancreatic glands caudate segment in size of 2 x 3 cm. Patient denied any trauma or symptoms of pancreatitis. Acute phase reactants were not elevated. Because of epigastric pain the patient was undergone to surgery. During operation there was found cystic lesion located para-duodenal `qspace, no evidence of clot but fluid content of the cyst was hemorrhagic. Cyst was removed totally. Pancreatic cyst was not touched because of absence of symptoms. The patient releases from hospi-

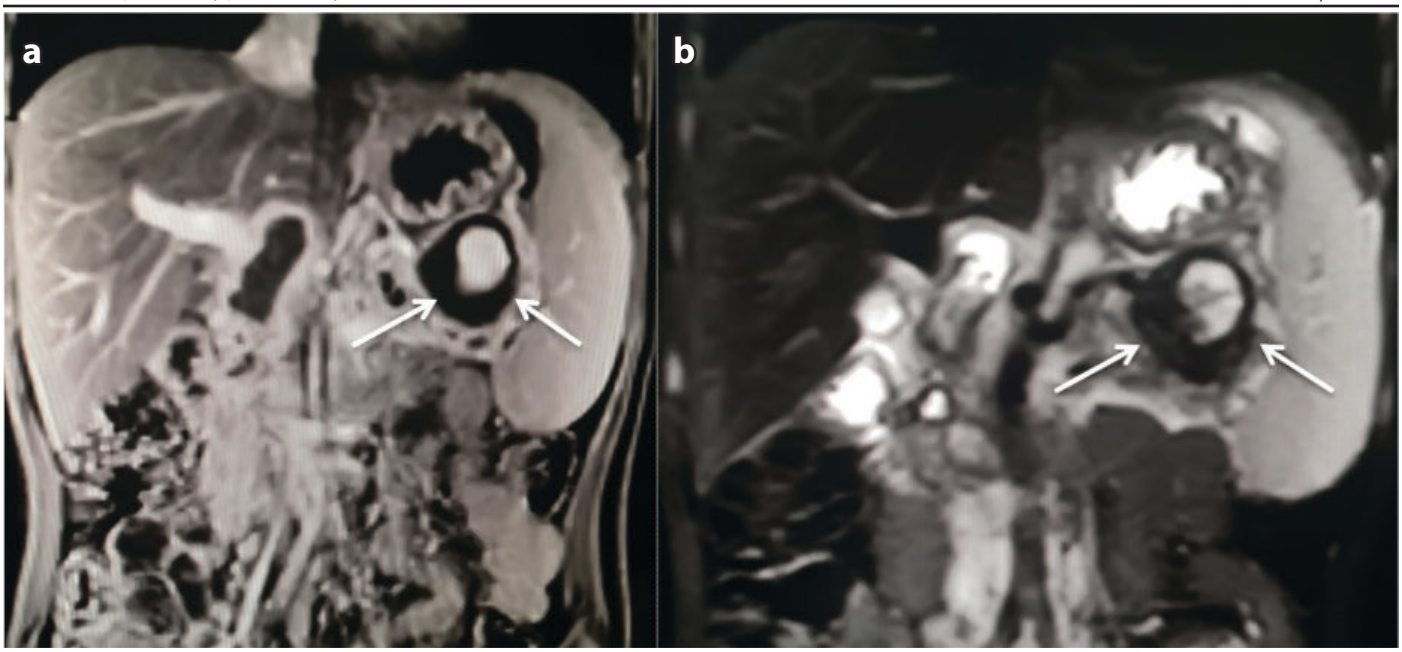

Figure 1. Coronal T*2 weighted **(a)** and contrast enhanced MRI **(b)** shows pseudoaneurysm arising from the distal segment of splenic artery (white arrows).

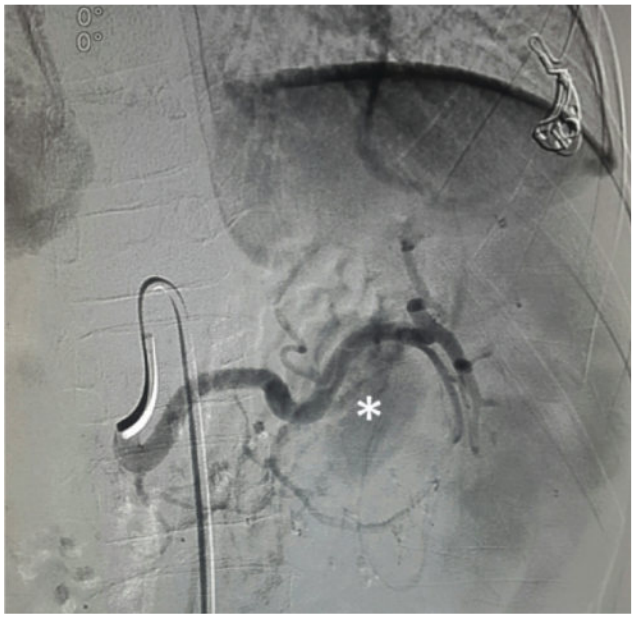

Figure 2. Digital subtracted angiography demonstrated contrast filling into the aneurysmal sac (asterisk).

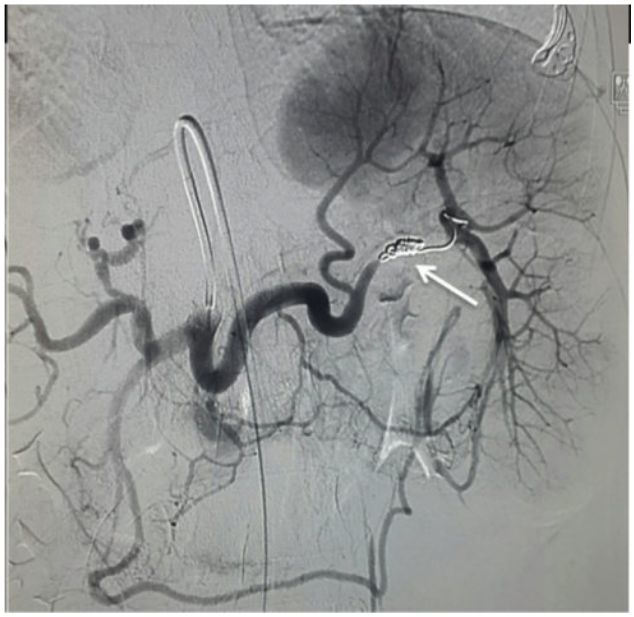

Figure 3. Digital subtracted angiography - post embolization image. There is no flow with in the sac (arrow).

tal after 7 days. 2 years later she admitted to our hospital again with episodes of epigastric pain, hematemesis and bloody dearie lasting 6 days. On examination there was severe pallor. Hb was 4.0 gm/dL, Attempt for blood transfusion caused three more episodes of vomiting which was red in color and melena. Gastroscopy was performed and blood coming out from pancreatic duct was found. Contrast administrated upper abdominal MRI revealed splenic artery pseudo-aneurysm formation with in the pancreatic cyst, which was diagnosed previously. Conventional angiography was performed and splenic artery aneurysm was confirmed. Coil embolisation of splenic arteries (damaged part, where pseudoaneurysm was located) was performed, so pseudo aneurysm was thrombosed consequently. The patient releases from hospital after 2 days with symptom free.

Discussion

Etiology of the splenic artery pseudoaneurysm differs from case to case but most leading cause of this entity is pancreatitis. Second and third causes are abdominal trauma and postoperative complication. In our case there was not history of pancreatitis and trauma but we thought it was due to incomplete history gathering because of urban circumstances where she lives.

Splenic artery pseudoaneurysm generally symptomatic and the most common presentation is abdominal pain. Upper or lower GI bleed, hemorrhage into pancreatic duct and hematemesis are also common symptoms. Around 2.5% of cases present incidentally [1]. In children population, unlike in adult most common cause of splenic artery pseudoaneurysm is blunt abdominal trauma. The most common symptom is abdominal pain. Conventional angiography is steel remain gold standard for diagnosis of splenic artery pseudoaneurysm and true aneurysm. It provides more detailed information about blood inflow and out flow of aneurismal sac, presents of extravasations and leakage, collateral blood supply of spleen and small vessel architecture. But because of invasive procedure there are still angiography related complication like puncture site complication, vessel dissection or rupture during catheterization, inflectional complication and contrast nephropathy. Gray-scale and Doppler ultrasonography is used as an initial modality and could play some role for the diagnosis of splenic artery aneurysm in curtain patients. But there are some limitations like it is operator-dependent and may be limited due to obesity, shadowing from bowel gas, and arteriosclerosis aneurysms [2].

With current MDCT and MRI technology, patient scan be imaged quickly during the arterial phase, which is essential for detecting these lesions. There are some relative contraindications for non invasive angiography so especially MR angiography being used widely. Current generation scanners are capable of high spatial resolution and short breath-hold times. The high temporal resolution facilitates acquisition of data during a purely arterial phase and results in decreased motion artifact [3].

Due to high risk of rupture and high mortality rate if splenic artery pseudoaneurysm ruptures, various interventions have been used for both ruptured and intact pseudoaneurysms. Aneurysms and pseudoaneurysms of the splenic artery require different management strategies. Recent data suggest that symptomatic and high risk splenic artery aneurysms should be promptly treated. However, no consensus has been reached regarding intervention in asymptomatic patients with splenic artery aneurysm. The appropriate treatment for splenic artery aneurysms depends on the location of the lesion (proximal, middle or distal part of artery), the age of the patient, operative risks like comorbidities, size of the aneurysm, and clinical status of the patient. There are several surgical and endovascular methods for treatment of the aneurysm. Surgery is still remain radical solution bur has high mortality and morbidity rates. Selected patient may be undergone for huge surgery like splenectomy and distal pancreatectomy whereas small size aneurysm in distal segment of splenic artery could be simply dissected [4].

Approach for pseudoaneurysm is different. As this pseudoaneurysm is more prone to rupture and carries high mortality rate, the earliest possible intervention is warranted. Same as in true splenic arteries aneurysm in this entity there several way to go. Endovascular embolization is safe and mini invasive method, which has been gaining favor. Although success rates of approximately 85% are lower than those of direct surgical intervention, associated operative morbidity and mortality rates are significantly reduced. A major dilemma is whether transarterial catheter angioembolization should be the definitive approach or if it should always be followed by surgical intervention [5].

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Original Research
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Fatal Mushroom Poisoning in Syrian Refugees

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Objective: The aim of this study was to evaluate the deaths of Syrian refugees caused by mushroom poisoning in the light of patient data, living conditions and autopsy findings.

Methods: An evaluation was made of 6 Syrian refugees who died at Malatya Turgut Ozal Medical Centre as a result of mushroom poisoning in 2014. Diagnosis of mushroom poisoning was made from the anamnesis, laboratory test results and clinical evaluation of the patients. The autopsy procedures for all the cases were performed at the Malatya Local Authority Forensic Medicine Institution. All the cases were evaluated in respect of age, gender, height, weight, symptoms of poisoning, duration of hospitalization, month of poisoning, laboratory parameters, autopsy findings and histopathological findings.

Results: The 6 cases included in the study comprised 4 males and 2 females with a mean age of 27±18.7 years. Some of the cases were related. It was determined that all the cases were poisoned after eating wild mushrooms that they had collected. In all the cases, the liver function tests were impaired, with values determined of mean ALT 5456.83±2556.47 U/L, AST 2517.66±2351.56 U/L, INR 5.04±2.04 and ammoniac 904.16±308.6 µg/dl. In the autopsy, widespread foci of bleeding were determined in the internal organs, a jaundiced appearance and fluid accumulation in the body cavities (pleural effusion and acid). Thrombosis in the vena porta hepatica was determined in 1 case. In the histopathological examination, massive liver necrosis was seen in all the cases.

Conclusion: Mushroom poisoning as a definitive cause of death must be determined with a detailed history, autopsy findings and histopathology together. Furthermore, refugees should be warned that there could be similar species of mushrooms growing in different natural environments and that they could be poisonous.

Keywords: mushroom poisoning, organ transplant, death, autopsy

Introduction

Although there are approximately 140,000 species of mushrooms worldwide, 2000 of these are accepted as safe for human consumption and approximately 700 of these have been reported to have therapeutic properties [1]. Approximately 100 mushroom species lead to toxicity in humans [2]. The gathering of mushrooms as food from woods and fields is a widespread tradition among communities of a low socio-economic level [4]. In studies related to mushrooms, they have been reported to have a significant place in the human diet due to high protein content, health benefits and the taste [3]. With the trend in recent years for a return to organic foodstuffs, there has been an increase in the consumption of natural mushrooms by city-dwellers. Mushroom poisoning has been reported to almost always occur from the consumption of mushrooms gathered for food from wild areas [5].

As mushrooms are generally eaten cooked, poisoning is seen from only a few species with heat-resistant toxins. Amanita phalloides, which is a heat-resistant toxin, is responsible for the majority of deaths occurring from these toxic species [6]. The consumption of toxic mushrooms may lead to reactions such as gastroenteritis, psychological problems and acute liver failure [5]. The most important factors affecting the prognosis are the degree of liver damage and complications developing after the poisoning [7].

As a consequence of the civil war in Syria, more than 7 million refugees have had to leave their homes for safer countries, primarily Turkey. According to United Nations data in December 2015, there were 2,287,360 Syrian refugees in Turkey [8]. As the socioeconomic level of the refugees is low, mushrooms are often gathered and eaten, especially in the summer and autumn months and thus mushroom poisoning is often seen [9].

The aim of this study was to evaluate the deaths of Syrian refugees caused by mushroom poisoning in the light of patient data, living conditions and autopsy findings.

Material and Methods

The study included cases of death as a result of mushroom poisoning at Malatya Turgut Ozal Medical Centre in 2014. All the cases were Syrian refugees. As Malatya Turgut Ozal Medical Centre was the first transplantation hospital in the world which specialised in the field of liver transplantation, the cases were transferred here when a table of liver failure developed during clinical follow-up. All the cases died in the intensive care unit while waiting for a liver organ transplant.

Diagnosis of mushroom poisoning was made from the anamnesis, laboratory test results and clinical evaluation of the patients.

The anamnesis was taken from relatives of the patients. The autopsy procedures, and toxicology and histopathology examinations for all the cases were performed at the Malatya Local Authority Forensic Medicine Institution.

All the cases were evaluated in respect of age, gender, height, weight, symptoms of poisoning, duration of hospitalization, month of poisoning, laboratory parameters, autopsy findings and histopathological findings. The data obtained were transferred to a form prepared for this study.

Analysis of the data obtained was made using SPSS 17.0 (Statistical Package for Social Science) software. The defined mean values were stated as arithmetic mean±standard deviation.

Results

The 6 cases comprised 4 males and 2 females with a mean age of 27±18.7 years (range, 9-50 years). The mean duration of hospitalisation was 7.5±5.46 days (Table 1).

Of the total 6 cases, 2 were mother and son, who presented at hospital with complaints of nausea after eating mushrooms that they had gathered in a rural area of Ankara in October. Another 3 cases were all members of the same family who had presented at a hospital in Syria with complaints of vomiting and diarrheoea after eating mushrooms that they had gathered in a rural area in Syria in the month of November. Two family members had died in Syria of Amanita poisoning. The other case in this study presented at hospital with complaints of abdominal pain after eating mushrooms in December in Hatay.

In all the cases, an increase was seen in the liver enzymes, ammoniac and International Normalised Ratio (INR) values. The laboratory test results were determined as mean ALT 5456.83±2556.47 U/L, AST 2517.66±2351.56 U/L, INR 5.04±2.04 and ammoniac 904.16±308.6 µg/dl. The laboratory parameters of the cases are shown in Table 2.

In the evaluation of the autopsy findings, fluid accumulation in the body cavities (pleural effusion and acid) occurred in all the cases. There were widespread foci of bleeding in the internal organs, and a jaundiced appearance (Figure 1). The macroscopic and histopathological findings of the cases are given in detail in Table 3. In Case no.2, thrombus was observed in the vena hepatica porta (Figure 2).

In the histopathological examination, there was congestion in the internal organs and findings of varying degrees of necrosis were determined particularly in the liver and kidneys (Table 3).

Discussion

Poisoning is a significant public health problem throughout the world. According to World Health Organisation data, 41,000 deaths were the result of unintentional poisoning in the USA in 2008, of which a significant number were cases of mushroom poisoning [11]. Studies in Turkey have reported mushroom poisoning within all poisoning cases at rates of 2.8% in chil-

Table 1. Details of the cases

Case No	Sex	Age (year)	Height (cm)	Weight (kg)	Sign of posoning	Duration of hospitalization	Month of poisoning
1	F	50	165	78	Nausea	2 days	October
2	M	25	168	70	Nausea	5 days	October
3	M	9	130	30	Vomiting	6 days	November
4	M	18	171	71	Vomiting	7 days	November
5	F	10	137	34	Vomiting	18 days	November
6	M	50	182	92	Abdominal pain	7 days	December

Table 2. Laboratory parameters of cases

Parameter	Case						Unit	Normal values
	1	2	3	4	5	6		
WBC	13,4	34,8	3,4	5,9	25,6	8,3	10^3/ML	4,3-10,3
Hgb	7,6	7,0	8,7	8,9	9,3	9,4	g/dL	13,6-17,2
Plt	79	59	82	33	12	88	10^3/ML	156-373
Na	135	119	152	144	152	129	mmol/L	136-145
K	4,4	6,1	3,6	4,5	4,16	5,2	mmol/L	3,5-5,1
Cl	92	95	105	107	117	98	mmol/L	98-107
Glucose	52	182	73	25	202	134	mg/dl	70-105
BUN	26	28	20	9	96	11	mg/dl	8,9-20,6
Creatinine	3,96	3,07	2,22	1,27	1,03	6,09	mg/dl	0,72-1,25
AST	3278	6622	2723	1865	285	333	U/L	5-34
ALT	2443	6873	4914	5062	307	1142	U/L	0-55
GGT	36	45	70	47	35	53	U/L	12-64
INR	4,4	7,3	4,6	7,5	2,1	4,4		0,8-1,2
T.Bilirubin	3,98	10,12	5,9	13,8	5,2	9,86	g/dl	0,2-1,2
Ammoniac	1306	1240	779	818	499	783	µg/dl	31-123
Albumin	2,5	3,5	2,8	2,7	5,4	3,1	g/dl	3,5-5
Lactate	>120	56,4	62,3	45,4	34	51	mg/dl	4,5-19,8

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BUN: Blood Urea Nitrogen, GGT: Gamma-glutamyl transferase, INR: International Normalized Ratio, WBC: White Blood Cell, Hgb: Hemoglobin, Plt: Platelet

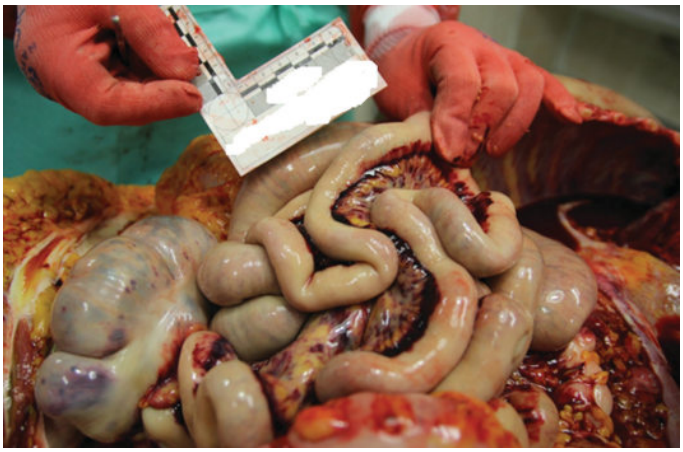

Figure 1. Haemorrhagic foci in bowels mesentery

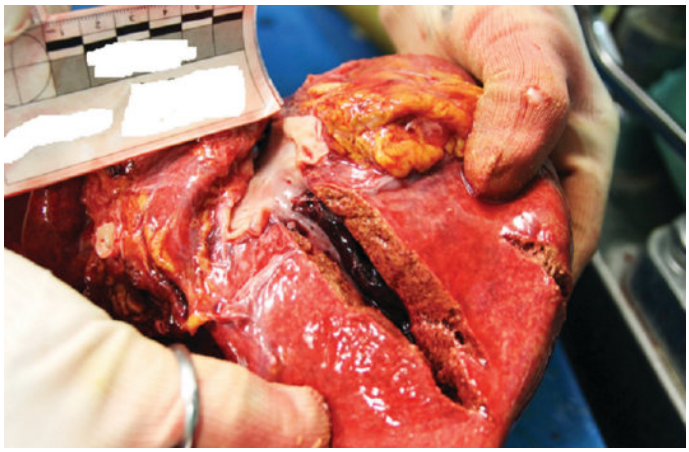

Figure 2. Thrombosis in Vena Porta Hepatica

dren and 2.5% in adults [12]. Mushroom poisoning has been reported to constitute approximately 50% of deaths caused by plant-related poisoning [13].

Mushrooms are a part of the human diet worldwide because of the taste, nutritional value and medical properties [10]. There has been a global increase in reports of poisoning cases related to the consumption of wild mushrooms [14]. There has also been a significant increase in recent years in the tendency for consumption of organic foods grown in a natural environment [15]. However, the current cases were all Syrian refugees with a low socio-economic level and who in these conditions of hunger were gathering mushrooms to meet the basic need for food.

When the characteristics of the cases in the current study are examined, 3 cases were Syrians who had come to Turkey as refugees and had been poisoned from mushrooms they had collected. The reason for this was thought to be that they could not differentiate the mushroom species growing in a different place than their own natural environment. Another 3 cases were poisoned by mushrooms they had eaten in Syria. This was thought to be due to a lack of food because of the civil war in Syria and that they had not been able to differentiate mushroom species growing all together in the same natural environment.

Mushrooms grow in any place that has sufficient organic matter, rain and a damp environment. Therefore, although the

Table 3. Findings of autopsy and histopathology

Case	Autopsy Findings	Histopathological Findings
1	Petechial haemorrhage on surface of heart and lungs, Pleural effusion (1300 cc), liver 1653 gram, haemorrhagic and icteric liver, haemorrhagic and icteric kidneys ve icteric, haemorrhage in the bowels mesentery, ascites (1000 cc)	Congestion in brain, kidneys, heart and pancreas, diffuse alveolar damage in lungs (ARDS), karaciğerde diffuse massive necrosis, macro and vesicular steatosis and congestion in liver, perimuscular and subserosal fresh haemorrhage in gall bladder
2	Petechial haemorrhage on surface of heart and lungs, Pleural effusion (1100 cc), liver 2234 gram, haemorrhagic and icteric liver, thrombosis in vena porta hepatica and vena hepatica sinistra, paleness in kidneys, haemorrhage in the bowels mesentery and omentum, ascites (1200 cc)	Congestion in brain, kidneys, heart and pancreas, bronchopneumonia in lungs, massive diffuse necrosis in the liver
3	Paleness and haemorrhage on heart surface, patchy haemorrhagic areas in the lungs, Pleural effusion (60 cc), haemorrhage in gastric mucosa, liver 662 gram, icteric appearance and millimetric nodules in liver, icteric and haemorrhagic bowels, ascites (300 cc)	Congestion in brain and heart, intraalveolar fresh haemorrhage and emphysematous changes in lungs, vacuolization in the renal tubular epithelium and eosinophilic proteinaceous material in the lumen
4	(compatible with toxic substances), focal fresh haemorrhage in peripancreatic fatty tissue, massive necrosis in zone 2 and 3, macro and micro vesicles in hepatocytes zone 1, steatosis in the liver	Fresh subarachnoid haemorrhage in the brain and cerebellum, Congestion in heart, intraalveolar fresh haemorrhage (due to resuscitation) in lungs, vacuolization in the renal tubular epithelium and eosinophilic proteinaceous material in the lumen (compatible with toxic substances), focal fresh haemorrhage in peripancreatic fatty tissue, massive necrosis in zone 2 and 3, macro and micro vesicles in hepatocytes zone 1 in the liver
5	Paleness and haemorrhage on heart surface, patchy haemorrhagic areas in the lungs, Pleural effusion (650 cc), liver 943 gram, icteric appearance and millimetric nodules in liver, icteric and haemorrhagic bowels, ascites (400 cc)	Fresh subarachnoid haemorrhage in the brain and cerebellum, Congestion in heart, intraalveolar fresh haemorrhage (due to resuscitation) in lungs, vacuolization in the renal tubular epithelium and eosinophilic proteinaceous material in the lumen
6	Subepicardial haemorrhage , subpleural haemorrhage in right lung and bullous structures in both lungs, Pleural effusion (150 cc), liver 1163 gram and icteric, haemorrhagic areas in bowels and omentum majus, ascites (400cc),	Congestion in brain and heart, bronchopneumonia and intraalveolar fresh haemorrhage (due to resuscitation) in lungs, previous chronic phyelonephritis in kidneys, massive diffuse necrosis in liver

growing periods show changes according to seasonal climate conditions, it is generally in early summer and autumn when there is greater rainfall. Previous studies have reported that the majority of mushroom poisoning cases occur in the autumn (5, 17, 18). The cases in the current study were consistent with the data in literature as 5 cases occurred in October and November and 1 in December (Table 1). These months are generally the periods of the heaviest rainfall in this region.

The cases in the current study presented at hospital with gastrointestinal complaints such as vomiting and abdominal pain. Previous studies have reported the most frequent complaints to be nausea and vomiting [20]. Early presentation at hospital is of great importance to be able to reduce mortality from mushroom poisoning [15]. In poisoning by mushroom species containing Amatoxin, there may be asymptomatic latent periods which can last up to 8-14 hours [5]. Therefore, it is thought that the current cases presented late at a healthcare centre as they either waited throughout the asymptomatic period or because they were in Turkey as refugees from the war in Syria.

Depending on the mushroom species, mushroom poisoning may show a wide clinical table ranging from mild gastrointestinal complaints to liver failure resulting in death [15]. Amatoxin is responsible for 90% of deaths related to mushroom poisoning and the most important effects are seen on the liver [3, 16]. All of the current cases were diagnosed with Amanita species mushroom poisoning and all died in the intensive care unit due to liver failure. All of these cases had been transferred to our university Liver Transplantation Unit as they were selected as severe cases. However, liver transplantation could not be performed due to the shortage of organ donors.

As the clinical table deteriorates in mushroom poisoning there is a progressive loss of liver and kidney functions [22]. A significant relationship has been shown between mortality and liver enzyme levels (AST, ALT) and prothrombin time and in

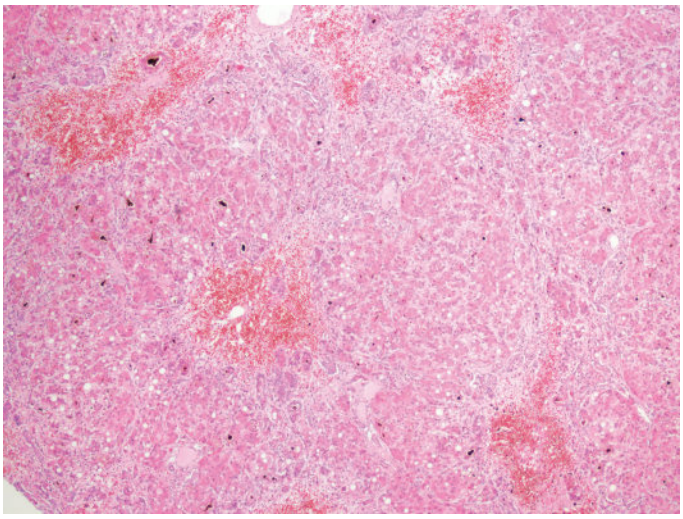

Figure 3. Pericentral (zone 3) haemorrhagic necrosis. (H&E×40)

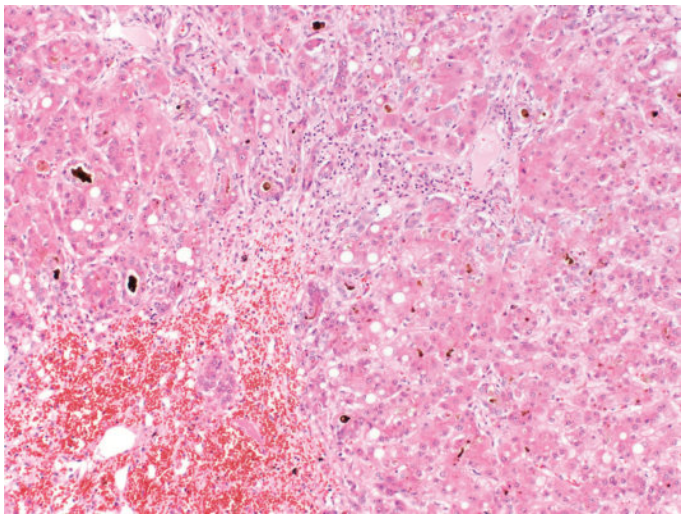

Figure 4. Focal macrovesicular steatosis and canalicular cholestasis. (H&E×100)

deaths because of hepatic coma, values have been reported of AST: 2075-3464 U/L and ALT: 2345-4048 U/L (15-19). These elevated enzyme levels have been reported to be a good indicator of mushroom poisoning and a need for liver transplantation [19]. In the current study, the mean values of the cases were determined as ALT 5456.83±2556.47 U/L, AST 2517.66±2351.56 U/L, creatinine 2.94±1.89 mg/dl and INR 5.04±2.04. The reason for the enzyme values to be this high in the current cases is that they were at an advanced clinical stage and as seen in the liver histopathology (Table 3), severe liver damage had developed.

In the autopsies of mushroom poisoning cases, there are no specific findings. However, bleeding in the internal organs associated with liver failure, areas of bleeding in the intestinal tract with the direct effect of Amatoxin and congestion may be encountered [21]. In addition there may be widespread clotting within the blood vessels associated with reduced production of clotting inhibitors in the liver [23]. In case no 2, thrombus was observed in the hepatic portal vein (Figure 2). In cases of mushroom poisoning, widespread haemorrhagic foci and necrosis may be seen in both the liver and kidneys [24]. In histopathologic evaluation pericentral (zone 3) haemorrhagic necrosis, focal macrovesicular steatosis and canalicular cholestasis has been observed in cases (Figure 3 and 4).

Conclusion

Mushroom poisoning as a definitive cause of death must be determined with a detailed history, autopsy findings and histopathology together. There must be better organisation to meet the nutritional and healthcare needs of refugees with poor living conditions because of the civil war in Syria. Furthermore, refugees should be warned that there could be similar species of mushrooms growing in different natural environments and that they could be poisonous.

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WMA International Code of Medical Ethics

Adopted by the 3rd General Assembly of the World Medical Association, London, England, October 1949 and amended by the 22nd World Medical Assembly, Sydney, Australia, August 1968 and the 35th World Medical Assembly, Venice, Italy, October 1983 and the 57th WMA General Assembly, Pilanesberg, South Africa, October 2006.

DUTIES OF PHYSICIANS IN GENERAL

A PHYSICIAN SHALL always exercise his/her independent professional judgment and maintain the highest standards of professional conduct.

A PHYSICIAN SHALL respect a competent patient's right to accept or refuse treatment.

A PHYSICIAN SHALL not allow his/her judgment to be influenced by personal profit or unfair discrimination.

A PHYSICIAN SHALL be dedicated to providing competent medical service in full professional and moral independence, with compassion and respect for human dignity.

A PHYSICIAN SHALL deal honestly with patients and colleagues, and report to the appropriate authorities those physicians who practice unethically or incompetently or who engage in fraud or deception.

A PHYSICIAN SHALL not receive any financial benefits or other incentives solely for referring patients or prescribing specific products.

A PHYSICIAN SHALL respect the rights and preferences of patients, colleagues, and other health professionals.

A PHYSICIAN SHALL recognize his/her important role in educating the public but should use due caution in divulging discoveries or new techniques or treatment through non-professional channels.

A PHYSICIAN SHALL certify only that which he/she has personally verified.

A PHYSICIAN SHALL strive to use health care resources in the best way to benefit patients and their community.

A PHYSICIAN SHALL seek appropriate care and attention if he/she suffers from mental or physical illness.

A PHYSICIAN SHALL respect the local and national codes of ethics.

DUTIES OF PHYSICIANS TO PATIENTS

A PHYSICIAN SHALL always bear in mind the obligation to respect human life.

A PHYSICIAN SHALL act in the patient's best interest when providing medical care.

A PHYSICIAN SHALL owe his/her patients complete loyalty and all the scientific resources available to him/her. Whenever an examination or treatment is beyond the physician's capacity, he/she should consult with or refer to another physician who has the necessary ability.

A PHYSICIAN SHALL respect a patient's right to confidentiality. It is ethical to disclose confidential information when the patient consents to it or when there is a real and imminent threat of harm to the patient or to others and this threat can be only removed by a breach of confidentiality.

A PHYSICIAN SHALL give emergency care as a humanitarian duty unless he/she is assured that others are willing and able to give such care.

A PHYSICIAN SHALL in situations when he/she is acting for a third party, ensure that the patient has full knowledge of that situation.

A PHYSICIAN SHALL not enter into a sexual relationship with his/her current patient or into any other abusive or exploitative relationship.

DUTIES OF PHYSICIANS TO COLLEAGUES

A PHYSICIAN SHALL behave towards colleagues as he/she would have them behave towards him/her.

A PHYSICIAN SHALL NOT undermine the patient-physician relationship of colleagues in order to attract patients.

A PHYSICIAN SHALL when medically necessary, communicate with colleagues who are involved in the care of the same patient. This communication should respect patient confidentiality and be confined to necessary information.

Azerbaijan Medical Association

ABOUT

The Azerbaijan Medical Association (AzMA) is the country's leading voluntary, independent, non-governmental, professional membership medical organization for physicians, residents and medical students who represent all medical specialties in Azerbaijan.

Founded in 1999 by Dr. Nariman Safarli and his colleagues and at the founding meeting physicians adopted the Statutes and Code of Ethics of the AzMA. The association was officially registered by Ministry of Justice of Azerbaijan Republic in December 22, 1999.

Since its inception, the AzMA continues serving for a singular purpose: to advance healthcare in Azerbaijan.

- Founded in 1999, the Azerbaijan Medical Association provides a way for members of the medical profession to unite and act on matters affecting public health and the practice of medicine.
- We are the voice of physicians who support the need for organized medicine and want to be active within their profession.
- We are the representative for Azerbaijan doctors on the world–wide level and the voice of Azeri physicians throughout the world.

MISSION

The mission of the Azerbaijan Medical Association -is to unite all members of the medical profession, to serve as the premier advocate for its members and their patients, to promote the science of medicine and to advance healthcare in Azerbaijan.

GOALS

- Protect the integrity, independence, professional interests and rights of the members;
- Promote high standards in medical education and ethics;
- Promote laws and regulation that protect and enhance the physician-patient relationship;
- Improve access and delivery of quality medical care;
- Promote and advance ethical behavior by the medical profession;
- Support members in their scientific and public activities;
- Promote and coordinate the activity of member-specialty societies and sections;
- Represent members' professional interests at national and international level;
- Create relationship with other international medical associations.
- Increase health awareness of the population

The association's vision for the future, and all its goals and objectives are intended to support the principles and ideals of the AzMA's mission.

INTERNATIONAL RELATIONSHIPS

Since its establishment AzMA built close relationships with many international medical organizations and national medical associations of more than 80 countries. The following are the AzMA's international affiliations:

- Full membership in the World Medical Associations (WMA) (since 2002)
- Full membership in the European Forum of Medical Associations (EFMA) (since 2000)
- Full membership in the Federation of Islamic Medical Associations (FIMA) (since 2002)
- Associate membership in the European Union of Medical Specialists (UEMS) (since 2002)

Especially the year 2002 remained with memorable and historical events for AzMA such as membership to the World Medical Association (WMA). Today we are extremely pleased to represent our Association and to be a part of the WMA family.

MEMBERSHIP

A person with medical background, who accepts and follows the AzMA Statutes and AzMA Code of Ethics, may become a member of the Association. The Code of Ethics of the Association shall be the members' guide to professional conduct.

Membership in the AzMA is open to:

- Physicians residing and practicing in Azerbaijan and in abroad.
- Medical students enrolled at medical universities or schools
- Retired physicians

Members can access a special members only area of the AzMA website designed to provide the most up-to-date, and timely information about organized medicine in our country.

To the non-member, we hope you'll discover, through our web site how valuable Azerbaijan Medical Association (AzMA) is to medicine in Azerbaijan and will join us.

MEDICINE'S VOICE IN AZERBAIJAN

As the largest physician membership organization in Azerbaijan the AzMA devotes itself to representing the interests of physicians, protecting the quality of patient care and as an indispensable association of busy professionals, speaks out with a clear and unified voice to inform the general public and be heard in the highest councils of government.

The AzMA strives to serve as the Medicine's Voice in Azerbaijan.

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Azerbaijan Medical Association

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