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

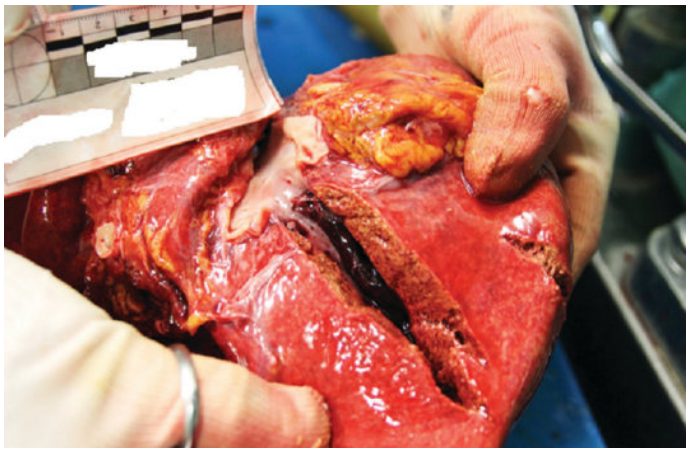

Figure 2. Thrombosis in Vena Porta Hepatica

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

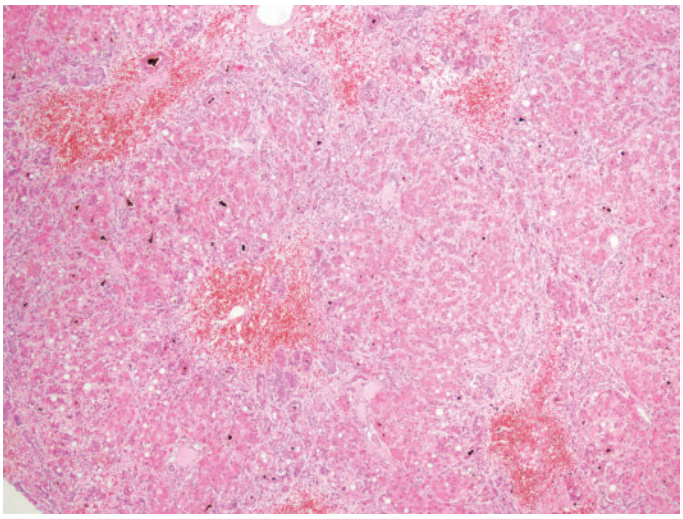

Figure 3. Pericentral (zone 3) haemorrhagic necrosis. (H&E×40)

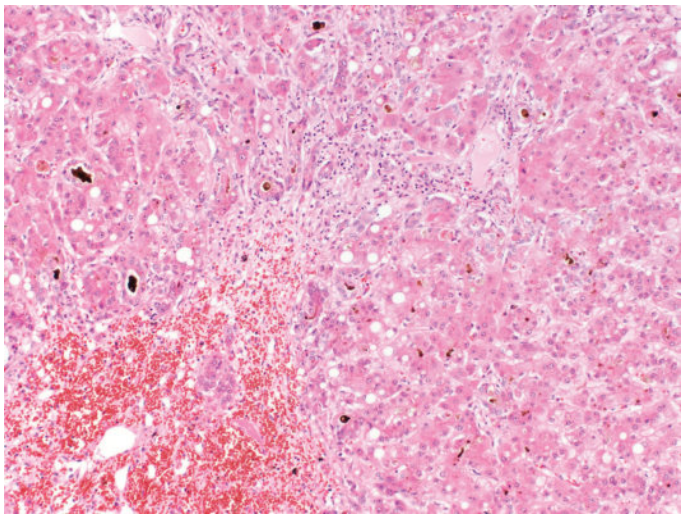

Figure 4. Focal macrovesicular steatosis and canalicular cholestasis. (H&E×100)

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.

References:

1. Lima ADL, Fortes RC, Garbi Novaes MRC, Percario S. Poisonous mushrooms; a review of the most common intoxications. Nutr Hosp. 2012;27:402-408.
2. Erguven M, Yilmaz O, Deveci M, Aksu N, Dursun F, Pelit M, et al. Mushroom poisoning. Indian J Pediatr 2007;74:847-852.
3. Garcia J, Costa MR, Carvalho A, Baptista P, Pinho PG, Bostos ML, Carvalho F. Amanita phalloides poisoning: mechanism of toxicity and tratment. Food and Chemical Toxicology 2015; 86:41-55.
4. Köksal T, Demirçeken FG, Köksal AO, Araslan z. Çocuklarda mantar zehirlenmesi: 26 olgunun değerlendirilmesi. Yeni Tıp Dergisi 2012; (29)3:155-58.
5. Yardan T, Baydin A, Eden AO, Akdemir HU, Aygün D, Acar E, Arslan B. Wild mushroom poisonings in the Middle Black Sea region in Turkey: Analyses of 6 years. Human and Experimental Toxicology 2010;29(9):767-771.
6. Güler K, Güven Ö, Bozfakıoğlu S. 22 mantar intoksikasyon vakasının klinik, laboratuar özellikleri ve tedaviye cevapları: Tedaviye erken başlamanın prognostik önemi. T Klin Gastrohepatoloji 1991; 2(2):122-25.
7. Zarafyants GN. Forensic medical diagnostics of intoxication with certain poisonous mushrooms in the case of the lethal outcome in a hospital. Sud Med Ekspert 2016;59(1):22-28.
8. UNHCR Turkey External Updates. (2015, December 7). Retrieved from http://www.unhcr.org/turkey/uploads/root/november_-_external_update_2015.pdf (Access date: 22.04.2016)
9. Ergüven M, Çakı S, Deveci M. Mantar zehirlenmesi: 28 vakanın değerlendirilmesi. Çocuk Sağlığı ve Hastalıkları Dergisi 2004;47:249-53.
10. Jo WS, Hossain MA, Park SC. Toxicological profiles of poisonous, edible, and medicinal mushrooms. Mycobiology 2014; 42(3):215-20.
11. Warner M, Chen LH, Makuc DM, Anderson RN, Miniño AM. Drug poisoning deaths in the United States, 1980-

2008 Atlanta: Centers for Disease Control and Prevention, 2011. Retrieved from http://www.cdc.gov/nchs/data/databriefs/db81.htm (Access date: 23.04.2016)
12. Akköse AŞ, Köksal Ö, Fedakar R, Emircan Ş, Durmuş O. 1996-2004 yılları arasındaki erişkin zehirlenme olguları. Uludağ Üniversitesi Tıp Fakültesi Dergisi 2006; 32(1): 25-27.
13. Eren ŞH, Oğuztürk H, Korkmaz İ, Varol O. 2004 Yılı İçerisinde Cumhuriyet Üniversitesi Tıp Fakültesi Acil Tıp Anabilim Dalı'na Başvuran Mantar Zehirlenmesi Vakalarının Değerlendirilmesi. C. Ü. Tıp Fakültesi Dergisi 2005; 27 (1): 15-18.
14. Diaz JH. Evolving global epidemiology, syndromic classification, general management, and prevention of unknown mushroom poisonings. Crit Care Med 2005; 33: 419-426.
15. Eren SH, Demirel Y, Ugurlu S, Korkmaz İ, Aktaş C, Güven FMK. Mushroom poisoning: retrospective analysis of 294 cases. Clinics 2010;65(5):491-96.
16. Barbato MP. Poisoning from accidental ingestion of mushrooms. Med J 1993;158:842-47.
17. Ishihara Y, Yamaura Y. Descriptive epidemiology of mushroom poisoning in Japan. Nippon Eiseigaku Zasshi. 1992;46:1071-8.
18. Deniz T, Saygun M. Investigation of 62 mushroom poisoning cases applied to the emergency service during one month period. Akademik Acil Tip Dergisi. 2008;7:2 9-32.
19. Pajoumand A, Shadnia S, Efricheh H, Mandegary A, HassanianMoghadam H, Abdollahi M. A retrospective study of mushroom poisoning in Iran. Hum Exp Toxicol. 2005;24:609-13.
20. Durukan P, Yildiz M, Cevik Y, Ikizceli I, Kavalci C, Celebi S. Poisoning from wild mushrooms in Eastern Anatolia region: analyses of 5 years. Hum Exp Toxicol 2007;26:579-582.
21. Amini M, Ahmadabadi A, Kazemifar A.M, Solhi YJ. Amanita phalloides intoxication misdiagnosed as acute appendicitis: a case report. Iran. J. Toxicol 2011;5:527-530.
22. Becker CE, Tong TG, Boerner U, Roe RL, Sco TA, Macquarrie MB, Bartter F. Diagnosis and treatment of Amanita phalloides-type mushroom poisoning: use of thioctic acid West J. Med 1976;125:100-109.
23. Soysal D, Çevik C, Saklamaz A, Yetimalar Y, Unsal B. Coagulation disorders secondary to acute liver failure in Amanita phalloides poisoning: a case report. Turk J. Gastroenterol. 2006;17:198-202.
24. Fineschi V, Di Paolo M, Centini F. Histological criteria for diagnosis of amanita phalloides poisoning J. Forensic Sci 1996; 41:429-432.