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Anthrax: Management of Pediatric Cases After Exposure

Şarbon: Temas Sonrası Çocuk Olguların Yönetimi

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Abstract

Objective: Anthrax is a zoonotic disease caused by *Bacillus anthracis* that can be transmitted to humans from herbivorous animals such as sheep, goats and beef cattle, with infection passing through direct contact with the skin of infected animals, meat and wool, the ingestion of infected meat or the inhalation of spores. Depending on the point of entry of the bacteria, the disease can take three clinical forms, namely skin, respiratory and gastrointestinal system anthrax. Although there is a suggested prophylaxis following the inhalation of *B. anthracis* spores as a biological weapon, there is a lack of data on treatment after direct contact with infected animals or the ingestion of infected meat. This study proposes a post-contact management method for children who come into contact with an anthrax-infected animal.

Material and Methods: The history of a 36-year-old female living in the Trabzon province who died from *B. anthracis* sepsis indicated that she had helped in the butchering of a cow with anthrax and in the distribution of the meat. All of the children living in the area that came into contact with the meat were evaluated in pediatric emergency and pediatric infectious disease polyclinics.

Results: A total of 48 children applied to the outpatient clinics in the province after coming into contact with the anthrax-infected meat, of which 33 (68.8%) had ingested the meat, 11 (22.9%) had had direct contact with the sick cow and four (8.3%) lived in the same house as the cutaneous anthrax case. The 33 children who had ingested the infected meat, received a prophylaxis of oral ciprofloxacin for 10 days, and five children are admitted to the pediatric infectious disease service. No intestinal or cutaneous anthrax was detected in any patient.

Özet

Giriş: Şarbon, *Bacillus anthracis*'in etken olduğu; koyun, keçi, sığır gibi otçul hayvanlardan insanlara bulaşan zoonotik bir enfeksiyondur. İnsanlara enfekte hayvanların derisi, eti ve yünüyle doğrudan temas ile, enfekte etlerin yenmesi veya sporların inhale edilmesi ile bulaşır. Bakterinin vücuda giriş yerine göre deri, solunum ve gastrointestinal sistem şarbonu olmak üzere üç klinik form görülmektedir. Biyolojik silah olarak *B. anthracis* sporlarının inhalasyonu sonrası profilaksi ile ilgili bilgiler olmakla birlikte, enfekte hayvanla doğrudan temas veya enfekte etlerin yenmesi sonrası profilaksi ile ilgili yeterli veri bulunmamaktadır. Bu yazının amacı şarbonlu hayvan ile teması olan çocuk olguların temas sonrası yönetiminin paylaşılmasıdır.

Gereç ve Yöntemler: Trabzon'da yaşayan 36 yaşındaki kadın hasta *B. anthracis* sepsisinden kaybedildi. Hastanın şarbonlu ineğin kesimine ve dağıtılmasına yardım ettiği öğrenildi. O bölgede yaşayan tüm temaslı çocuklar çocuk acil ve çocuk enfeksiyon polikliniklerinde değerlendirildi.

Bulgular: Kırk sekiz çocuk şarbonlu hayvan ile temas etmesi nedeniyle polikliniğimize başvurdu. Otuz üç (%68.8) çocuğun hasta hayvan etinden yediği, 11 (%22.9) çocuğun hayvan ile doğrudan temas ettiği, 4 (%8.3) çocuğun cilt şarbonu olan kişi ile aynı evde yaşadığı tespit edildi. Hasta hayvan etinden yiyen 33 çocuğa oral siprofloksasin ile 10 gün profilaksi verildi. Beş çocuk çocuk enfeksiyon servisine yatırıldı. Hiçbir olguda intestinal veya cilt şarbonu tespit edilmedi.

Sonuç: Sıklığı giderek azalsa da şarbon, ülkemiz için önemli bir halk sağlığı problemi olmaya devam etmektedir. Şarbonlu hayvan ile temas

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Conclusion: Anthrax continues to be a major public health problem in our country, although the number of cases is in a gradual decline. After coming into contact with anthrax, patients should be followed up closely and an appropriate prophylaxis should be initiated when necessary.

Keywords: Anthrax, contact, prophylaxis

sonrası olguların yakın takip edilmesi ve gerekli durumlarda profilaksi başlanması gerekmektedir.

Anahtar Kelimeler: Şarbon, temas, profilaksi

Introduction

Anthrax is a zoonotic infection caused by *Bacillus anthracis* that can be transmitted to humans by herbivorous animals such as sheep, goat and cattle. *B. anthracis* is a gram-positive, aerobic or facultative anaerobic, endospore-forming rod, and is transmitted to humans through direct contact with the skin, meat or wool of an infected animals, through the ingestion of infected meat or via the inhalation of spores. The disease can manifest in three clinical forms, being cutaneous, inhalation and gastrointestinal anthrax, depending on the point of entry into the body, although skin anthrax accounts for the majority of cases (95 percent) (1). The bacteria can spread via lymphatic and hematogenous routes and may cause meningitis and sepsis, leading potentially to mortality (2).

It is estimated that 2.000 to 20.000 human cases of anthrax occur in the world every year (2), and while it continues to be an endemic disease, its occurrence in Turkey has decreased gradually over the years. Infections can occur at any age and in any gender, and of the 32 reported cases in 2016, one patient died of anthrax. The morbidity and mortality rates of anthrax cases between 2006 and 2016 are presented in Table 1 (3). Anthrax is considered to be a bioterrorism threat in most industrialized countries, and has been responsible for the death of livestock and a limited number of human cases (4). Although there is a suggested prophylaxis following the inhalation of *B. anthracis* spores as a biological weapon, there is a lack of data on treatment after direct contact with infected animals or the ingestion of infected meat. The present study shares our experience of the post-exposure management of pediatric cases after contact with an infected animal.

Materials and Methods

A 36-year-old female patient living in the Ağaçlı district of the Akçaabat county in Trabzon died of *B. anthracis* sepsis in the intensive care unit of Karadeniz Technical University (KTU) Faculty of Medicine. Her medical history revealed that she had assisted her neighbor in slaughtering a diseased cow and distributing its meat to the villagers 10 days previously, and had developed a skin wound developed on her hand. The patient consulted a doctor and was prescribed antibiotics, and three days later was brought to the emergency room of the KTU Faculty of Medicine due to fever and syncope. A physical examination upon admission revealed a body temperature of

Table 1. Number of anthrax cases and morbidity rates, Turkey, 2006-2016

Years	Population	Number of cases	Anthrax morbidity rate (100.000)	Number of deaths	Anthrax mortality rate (1.000.000)
2006	72.974.000	272	0.37	1	0.01
2007	70.586.256	262	0.37	0	0.00
2008	71.517.100	235	0.33	1	0.01
2009	72.561.312	149	0.21	1	0.01
2010	73.722.988	94	0.13	0	0.00
2011	74.724.269	165	0.22	2	0.03
2012	75.627.384	135	0.18	0	0.00
2013	76.667.864	197	0.26	2	0.03
2014	77.695.904	150	0.19	1	0.01
2015	78.741.053	139	0.18	0	0.00
2016	79.814.871	32	0.04	1	0.01

38.8°C and blood pressure of 60/40 mmHg. After three loading doses of a serum physiologic solution, the patient still had hypotension, and so a dopamine, dobutamine, adrenalin and noradrenalin infusion was initiated. The patient was intubated in the anesthesiology intensive care unit and went into cardiac arrest two days after admission, and cardiopulmonary resuscitation was performed. Despite all interventions, the patient died of *B. anthracis* sepsis that developed after cutaneous anthrax. It was reported that the owner of the cow had also contracted cutaneous anthrax and was undergoing therapy. The Provincial Directorate of Agriculture identified the presence of anthrax in the slaughtered animal. All children living in the vicinity with a contact history were called to the pediatric emergency and pediatric infectious diseases outpatient clinics, and their age, gender, contact history, complaints, institution of prophylactic measures, drugs used for prophylaxis and duration, test results, hospitalization requirement, laboratory results of the hospitalized patients, length of hospital stay and therapies administered were recorded. The blood samples collected from the hospitalized patients were sent to the National High-Risk Pathogens Reference Laboratory of the Turkish Public Health Agency for the detection of *B. anthracis*.

The statistical analyses were performed using the SPSS program (15.0. version, Chicago, SPSS Inc.). Quantitative data was presented as mean ± standard deviation, and categorical data was presented as frequency (n) and percentage (%). The quantitative data was analyzed with a Student's t-test if normally distributed, and with a Mann-Whitney U-test when abnormally distributed. Categorical data was analyzed with a Chi-Square test. P values lower than 0.05 were considered statistically significant.

Results

Of the 48 children admitted to the pediatric emergency and pediatric infectious diseases outpatient clinics due to a history of contact with infected animals, 21 (43.8 percent) were female and 27 (56.3 percent) were male. The median age of the female patients was 9 (minimum: 1, maximum: 17), and the median age of the male patients was 11 (minimum: 1, maximum: 16). Of the total, 33 (68.8 percent) of the patients had eaten infected meat, 11 (22.9 percent) patients had direct contact with the animal and four (8.3 percent) lived in the same house as the index patient with cutaneous anthrax. As no antibiotic susceptibility testing was performed for *B. anthracis* isolated from the blood culture of the deceased patient, the 33 children that consumed the meat of the sick animal were initiated with a 10-day prophylaxis of ciprofloxacin. One four-year-old boy continued prophylaxis with high dose amoxicillin due to a lack of tolerance for ciprofloxacin. The children who did not consume the meat of the infected animal but had a history of direct contact with the animal and those who lived in the same house with the index case received no prophylaxis, but were monitored at the pediatric infectious diseases outpatient clinics for two weeks.

All of the children who consumed the meat of the infected animal underwent abdominal ultrasound examinations at 3 and 7 days. Of the total, five cases were found to have mesenteric reactive lymphadenopathy on an abdominal USG; and the content of the bowel loops in the upper quadrant had a hyperechogenic appearance in three cases, indicating an intestinal hemorrhage; and one case had an incidentally detected hepatic hemangioma and calcification. The abdominal USG showed normal findings in 23 cases, and three cases with a suspected intestinal hemorrhage, while two other children had nausea, vomiting and abdominal pain on admission and were hospitalized in the pediatric infectious diseases ward. Of the hospitalized cases, one was female and four were male, with a median age of 8 (minimum: 4, maximum: 13). Oral intake was stopped after admission to the ward, and intravenous (IV) fluid infusions adjusted for age were initiated. The laboratory results of the cases are shown in Table 2. Therapy of intravenous ciprofloxacin and clindamycin was initiated, and blood samples were sent to the National High-Risk Pathogens Reference Laboratory of the Turkish Public Health Agency for the PCR detection of *B. anthracis* in the blood and *B. anthracis* culture. No growth of *B. anthracis* was noted in the blood cultures, and the PCR results were negative for *B. anthracis* in all cases. The median length of hospital stay until the results were available was five days (minimum: 2, maximum 5 days), and the prophylaxis and therapy was completed at 10 days. All cases were invited to attend control visit one month later, although none of the cases were identified with intestinal or cutaneous anthrax in follow-up visit.

Discussion

Anthrax is a zoonotic infection transmitted to humans through contact with infected animals and contaminated animal products. Although the incidence of anthrax in Turkey has declined in recent years, it continues to be an endemic disease, and still results in the death of animals and people, although in limited numbers. Close cooperation and the sharing of knowledge between institutions, taking precautions and applying regulations are required in order to avoid human cases of anthrax and to control the disease in animals. In order to protect against anthrax, animal breeding must be monitored, uncontrolled animal slaughter must be prevented, animals must be vaccinated against anthrax, particularly in endemic regions, animals in places where the disease occurs must be kept in quarantine, and animal carcasses with anthrax should be buried deep. Furthermore, efforts need to be made to raise public

Table 2. Laboratory results of the hospitalized anthrax cases

	n	Median	(Minimum-Maximum)
Hemoglobin (g/dL)	5	13.4	(10.4-15)
Platelets (/mm^3)	5	31.6000	(248.000-418.000)
White blood cell (/mm^3)	5	7000	(5200-9800)
AST (U/L)	5	26	(19-42)
ALT (U/L)	5	9	(4-17)
LDH (U/L)	3	262	(195-283)
GGT (U/L)	3	12.5	(12-13)
Total bilirubin (mg/dL)	5	0.58	(0.17-1.54)
Direct bilirubin (mg/dL)	5	0.11	(0.04-0.27)
BUN (mg/dL)	5	11	(8-19)
Creatinine (mg/dL)	5	0.46	(0.31-0.54)
Uric acid (mg/dL)	4	3.3	(2.7-3.7)
Erythrocyte sedimentation rate	5	7	(5-9)
CRP (mg/dL)	5	0.05	(0.02-1.07)

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: lactate dehydrogenase, GGT: Gamma glutamyl transferase, BUN: Blood urea nitrogen, CRP: C-reactive protein.

awareness on the danger of the uncontrolled slaughter and skinning of infected or dead animals without the control of a veterinary physician, avoiding contact with animal carcasses with bare hands, and reporting suspicious animal deaths to the authorities should be among the primary precautions. (5,6). It was found that the deceased patient became sick after unknowingly aiding in the slaughter of the infected animal and in the distribution of its meat.

The disease occurs in humans as a result of the transmission of *B. anthracis* spores through inhalation, ingestion or skin contact (7). The spores are resistant to dryness, heat, ultraviolet light, gamma irradiation and various disinfectants. *B. anthracis* spores used as a biological weapon in aerosol form can lead to mass disease and mortality, and anthrax is regarded as a bioterrorism threat in the majority of industrialized countries (8). Gastrointestinal system (GIS) anthrax occurs in Turkey as a result of consuming the meat of an infected animal, while cutaneous anthrax develops as a result of direct contact with the infected animal (4). Post-exposure prophylaxis for inhalation anthrax should be initiated as soon as possible and continued for 60 days, as the incubation period is long, and any delay in initiating therapy will decrease its efficacy (7,9). Although the transmission of anthrax from animals through inhalation is theoretically possible, it is considerably rare when compared to transmission through industrial activities and bioterrorism attack. Long-term prophylaxis with antibiotics is recommended only in cases of exposure to abundant aerosolized spores resulting from biological weapons or industrial sources. Aside from these, no prophylaxis for inhalation anthrax is recommended (9). The 11 children with a history of direct contact with the infected animal received no prophylaxis, but made control visits to pediatric infectious diseases outpatient clinics. As no prophylaxis is required for cutaneous anthrax, the four children who lived in the same house as the patient with cutaneous anthrax received no prophylaxis. A 10-day antibiotic prophylaxis is recommended if undercooked meat contaminated with anthrax spores has been consumed. In the present study, the 33 children who had consumed infected meat were admitted to the pediatric emergency and pediatric infectious diseases outpatient clinics, and were placed on a 10-day course of prophylaxis. In post-exposure prophylaxis, the first choice of drug is ciprofloxacin or doxycycline until the susceptibility profile of the agent becomes known. If both drugs are contraindicated or cannot be tolerated, high-dose penicillin (i.e. amoxicillin or penicillin V) is another option (9). A four-year-old boy who was on follow-up who was found to be intolerant of oral ciprofloxacin and the prophylactic antibiotic course was completed with amoxicillin, while the other

cases completed the prophylaxis with ciprofloxacin without any problems.

Gastrointestinal anthrax is common in herbivorous animals that serve as the usual host for anthrax, while it is quite rare in humans, accounting for only 1 percent of all anthrax cases in developing countries, and particularly in rural areas. It results from the consumption of undercooked or raw dried meat contaminated with anthrax spores, and epidemics may occur in communities in which the meat of the infected animal is shared (10,11). The incubation period for gastrointestinal anthrax is 3-7 days, and anthrax lesions can occur in any part of the gastrointestinal tract. Single or multiple ulcers, diffuse mucosal edema, intestinal hemorrhage, mesenteric lymphadenopathy and ascites develop, and patients may experience nausea, vomiting, loss of appetite, malaise, abdominal pain, hematemesis and bloody diarrhea. Abdominal pain may become severe and may mimic the findings of surgical acute abdominal conditions, and bacteremia, meningitis and sepsis can develop secondary to gastrointestinal anthrax. If left untreated, it has a lethal course in 40 percent of cases. The cases in the present study were evaluated twice during the outpatient control visit throughout the entire course of the incubation period, and complaints were inquired during examinations. Although there have been no previous studies in literature suggesting a recommended follow-up of patients after the consumption of contaminated meat, all cases underwent an abdominal USG examination of the gastrointestinal system. Subsequently, four cases were identified with an intestinal hemorrhage and started on intravenous therapy with a combination of ciprofloxacin and clindamycin after admission to the hospital. As no human-to-human transmission of anthrax has been demonstrated, aside from standard isolation, no other precautions are required for the hospitalized patients other than air-filtering masks or devices to detect particles in the air (12,13). Standard isolation measures were applied for the hospitalized patients, and the patients had no complaints during the follow-up period. A control USG examination revealed normal findings, and no growth of *B. anthracis* was identified in the culture of the blood samples referred to the National High-Risk Pathogens Reference Laboratory of the Turkish Public Health Agency. Furthermore, a PCR analysis showed negative results for *B. anthracis*, and so treatment was completed after a total of 10 days.

Although its spread from person to person is rare, the disease can be transmitted through direct or indirect contact with the infected wound or discharge. All of the cases had cutaneous anthrax, and so no additional measures, such as vaccination or antibiotic prophylaxis, was needed for people who came into contact with the patient (family members, friends, colleagues) (13). Among the children with a contact history that were followed-up, those who were living in the same house as the patient with cutaneous anthrax received no prophylaxis, and no cutaneous anthrax was observed in these children during follow-up at the pediatric infectious diseases outpatient clinic. In conclusion, anthrax continues to be an important health problem in Turkey, although its incidence has decreased. The vaccination of animals for anthrax in endemic areas is the most important step in controlling the disease, as this will reduce the number of human cases. Avoiding the consumption of meat from animals that have died of anthrax should be ensured, and in cases where the meat has been consumed, a prophylaxis with ciprofloxacin or high-dose penicillin is recommended.

Ethics Committe Approval: Ethics committee approval was not received due to the retrospective nature of this study.

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