

EVALUATION OF OCULOCUTANEOUS ANTHRAX. A SERIES OF 20 CASES

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ABSTRACT

Introduction: Cutaneous anthrax is the most common clinical presentation of human anthrax. This study presents an evaluation of cases of ocular lesions from cutaneous anthrax.

Methods: A total of 20 patients who attended the emergency department of Yuzuncu Yil University, School of Medicine between 2007 and 2013 were enrolled in the study.

Results: 65% of the cases were female and 35% were male. The mean age was 29.16 ± 14.80 . In 60% there were periorbital lesions in the right eye. 90% of the patients had a history of contact with animals or had eaten animal meat. The mean starting time of lesion was 3.2 ± 1.2 days before admittance. In 75% of the cases the diagnosis was based on the characteristic appearance of the lesion and the patient's history. All the patients spent 9.9 ± 4.3 days in hospital. Upper eyelid scar tissue and ectropion were found respectively in 20 % and 10 % of the cases.

Conclusions: Early diagnosis and appropriate antibiotic treatment can facilitate recovery and prevent the development of eyelid complications.

Key words: anthrax, oculocutaneous, emergency department.

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Introduction

Anthrax is one of the oldest infectious diseases known that is caused by *Bacillus anthracis*. It is mainly an animal disease rarely affecting human beings under normal conditions^(1,2). It consists most frequently as an epizootic or enzootic disease of herbivores (e.g., cattle, goats, or sheep) that acquire spores from direct contact with contaminated soil⁽³⁾. Anthrax is also a significant problem in Central America, Romania, Greece and Turkey^(4,5), representing in this last country an endemic disease, although its incidence is decreasing⁽⁶⁾. Also, cases of anthrax associated with intentional exposure in the United States are occurred for public health threat⁽³⁾.

There are three clinical types of anthrax: cutaneous, gastrointestinal (GI) and inhalational. Cutaneous anthrax (CA) is the most common form and accounts for 95% of all cases and is contracted when spores enter the body through a cut or erosion in the skin⁽⁷⁾. Inhalational anthrax (IA) is rare but it is usually fatal⁽⁸⁾. It reported that IA, resulting from inhalation of anthrax spores. Clinical features of IA comprise haemorrhagic thoracic lymphadenitis, pulmonary oedema, pleural effusions, leptomeningeal involvement, septic shock and respiratory distress, with death often following within 24 h⁽⁹⁾.

GI anthrax is characterized by rapid onset, fever, and septicemia and originates after eating contaminated meat. Most of previous cases of sep-

ticemic anthrax were related to injection drug users⁽¹⁰⁾. Human-to-human transmission has not been reported⁽³⁾. Clinicians and clinical laboratorians should be alert to the presence of *Bacillus anthracis* when *B. anthracis* is suspected. Because, notification of anthrax disease is mandatory⁽³⁾. CA lesions are usually seen on exposed parts of the body, generally on the face, neck, hands and arms⁽⁷⁾. In the face, the eyelid is the most common area of infection⁽¹¹⁾. Oculocutaneous anthrax (OA) should be suspected in the differential diagnosis of ulcerative preseptal cellulitis in subjects belonging to risk group such as exposure to contaminated animal products^(8,11).

The diagnosis of CA can be very difficult. CA is characterized by a skin lesion evolving from a papule, through a vesicular stage, to a depressed black eschar; edema, erythema, or necrosis without ulceration may be present⁽³⁾. In the majority of cases it must base on clinical grounds and confirmed by the isolation of bacteria from an infected ulcer or a blood sample⁽¹²⁾. Early and accurate diagnosis positively affects the prognosis of the (OA) however, if early diagnosis and treatment are not achieved, serious ophthalmic complications may develop⁽¹³⁾.

In this study, we present demographic features, clinical presentation, diagnosis and treatment of 20 OA cases. To the best of our knowledge, our series is one of the largest of adult OA in the literature.

Material and Methods

In this retrospective study, 22 patients with OA who attended the emergency department (ED) of Yuzuncu Yil University from 01.01.2007 to 31.10.2013 were enrolled. Two patients were excluded due to failure of records. The study protocol was conducted in accordance with the Helsinki Declaration as revised in 2000 and was approved by the local ethics committee.

The cases were evaluated from the hospital records in terms of age, gender, month of admission, occupation, duration of lesion, transmission mode, laboratory parameters, treatment administered in the emergency department, place of hospitalization and outcomes.

The definite diagnosis of anthrax confirm as 1) a clinically compatible case of cutaneous, inhalational, or gastrointestinal illness* that is laboratory confirmed by isolation of *B. anthracis* from an the

affected tissue and next to or 2) other laboratory evidence of *B. anthracis* infection based on at least two supportive laboratory tests such as polymerase chain reaction, immunohistochemical staining, serology⁽³⁾. A suspected case was defined as 1) a clinically compatible case of illness without isolation of *B. anthracis* and none alternative diagnosis, but with laboratory evidence of *B. anthracis* by one supportive laboratory test or 2) a clinically compatible case of anthrax epidemiologically linked to a confirmed environmental exposure, but without corroborative laboratory evidence of *B. anthracis* infection⁽³⁾.

The diagnosis of OA for suspected case was based on dermatological findings in a patient who have an appropriate history. This dermatologic lesion onset was characterized by appearance a of pruritic papule and followed by a painless ulcer with a characteristic necrotic eschar in the center. In the some cases, diagnosis was confirmed by the isolation of bacteria from the infected ulcer or from a blood sample. In all cases the bacteria were not isolated because of local technical limitations. The peripheral blood leukocyte, lymphocyte, neutrophil and monocyte counts, erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) levels were measured.

Exclusion criteria included that patients had other dermatological diseases and anthrax diagnosis could not be completely defined.

Statistical analysis

Data obtained from the hospital records. This data was expressed with mean +/-, standard deviation, median and as a percentage using analytical procedures as named PROC MEANS and PROC frequency in SAS.

Results

In this study, a total 20 patients with ocular anthrax were evaluated. Females were 13 (65%) and 7 (35%) were male. The female/male proportion was 1.85. The mean age was 30.45 ± 14.29 (range 16-63 years). Eighteen patients (90%) had a history of contact with animals or had eaten meat. All the patients were characterized by the appearance of an ocular lesion. The demographic and laboratory features of the cases are shown in table 1. The blood leukocyte counts, lymphocyte and neutrophil counts were higher than normal in the patients with OA.

The mean starting time of lesion was 3.2 ± 1.2 (1-6 days) before admittance. Of the 20 patients, 6

(30%) had received antibiotherapy before admission to our emergency department. The most common symptoms on admission were swelling and redness on the skin (Figure 1). There were periorbital lesions in the right eye in 12 (60%) cases and in the left eye in the remaining 8 (40%). The definite diagnosis of OA was based on the isolation of bacteria from the infected ulcer in 5 (25%) cases and fifteen (75%) cases were suspected by the characteristic appearance of the lesion and the patient's history. The diagnoses of suspected cases were supported by according to their response to treatment and appearance of lesion.

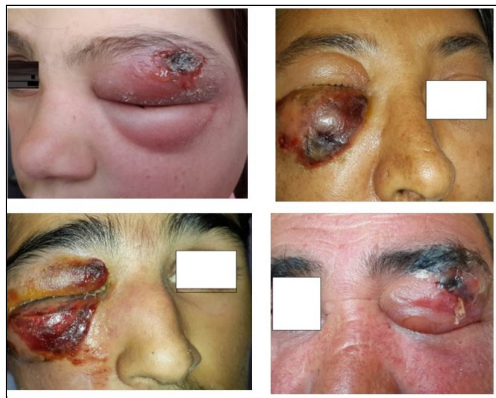


Figure 1: Swelling and redness on the periorbital area.



Figure 2: A case with orotracheal intubation.

Laryngeal edema developed in three (15%) cases and in two patients orotracheal intubation was administered (Figure 2). Massive face and neck edema evolved in three (15%) of the cases. Penicillin treatment was administered to all the 20 patients. Two patient with laryngeal edema and three patients with massive face and neck edema were treated as symptomatic with drugs including steroids and antihistamines. There was upper eyelid scar tissue due to necrosis in the 20% (n=4) and ectropion was seen in 10% (n=2) of cases.

Mortality were not reported in this study. Mean hospitalization length of stay was 9.9 ± 4.3 (5-22 days).

Discussion

Anthrax is a common disease in parts of Africa, Latin America, Asia and Eastern Europe however, the bacillus anthracis infection is rare in developed countries⁽¹¹⁾. Anthrax is an endemic zoonosis in Turkey and it is a serious threat to health in eastern Turkey⁽¹²⁾.

CA is the most common form of the disease⁽⁸⁾. Bacillus anthracis spores enter the body through a cut or abrasion in the skin⁽¹¹⁾. Lesions spread by inoculation of contaminated material transported from the hands and fingers into eyes, face or neck⁽⁶⁾. On the face, the eyelid is the most common site of infection⁽¹¹⁾. In literature, there are few case reports of anthrax affecting the eyes and the area around the eyes^(11,14-16). However, Yorston and Foster presented eleven cases with anthrax of the eyelids developing sequelae⁽¹⁷⁾. Tekin et al.,⁽¹³⁾ reported that CA generates 95% of anthrax in humans but palpebral involvement is rare. They presented series of twenty-one cases with palpebral anthrax over a 12 years period. In our study, we report on a series of twenty cases with OA over a six-year period.

In our study, OA was more frequently according to literature.

Yorston and Foster⁽¹⁷⁾ presented that the age ranges at the infection onset from 4 months to 45 years. Tekin et al.,⁽¹³⁾ reported series of twenty-one cases with palpebral anthrax in which the mean age was 31 ± 21.2 and eight patients were male (38.1%) and 13 patients were female (61.9%). Gelaw and Asaminew presented three male cases with periorcular cutaneous anthrax with ages ranging from 25-45 years⁽¹¹⁾. In a study related to CA in Turkey, Baykam et al.,⁽¹⁸⁾ reported that the female/male ratio was 0.57 and the mean age was 49.8 years. In a study including patients with CA, Karahocagil et al.,⁽⁶⁾ stated that the female/male ratio was 0.85 and the mean age was 30.6 years. In our study, the female/male proportion was 1.85 and the mean age was 30.45 ± 14.29 . Our results about the average age of the study were similar to Tekinet als and Gelaw's results. Our result related to female/male proportion was higher than literature.

People are contaminated when the spores of bacillus anthracis enter the body by contact with infected animals or animal products⁽¹⁾. Therefore,

farm workers, butchers, veterinarians and shepherds have great risk since they are exposed to the source of infection⁽¹¹⁾. In addition, Karahocagil et al.⁽⁶⁾, stated that housewives (41.2%) and farmers (23.5%) commonly contracted the disease and Baykam et al.⁽¹⁸⁾ found that most cases of anthrax in humans were found in farmers (62%). In our study the occupations of our cases were as follows; housewife (50%), shepherd (25%), butcher (15%), other (10%). The largest infected group being housewives we consider that they are contaminated during the contact with infected meat in the kitchen. Baykam et al.⁽¹⁸⁾ stated that transmission was more common through raw meat (90%) however, Karahocagil et al.⁽⁶⁾ found the most common contact form in their study was with contact sick animals (50.6 %) In our study, all the cases had direct contact with raw meat or a live animal with the common form of contact was from cutting the meat into slices (40%)

In the literature, anthrax cases were common in the summer months^(6,13,19,20). In our study, the cases were observed in summer and autumn. Karahocagil et al.⁽⁶⁾, stated that periocular lesions rates comprised 25.4 % of all the CA. In their study, Baykam et al.⁽¹⁸⁾ found this to be 6.4%. Tekin et al.⁽¹³⁾ stated that periorbital lesions were more common in the right eye. In the series of three cases with periocular anthrax cases, Gelaw et al.⁽¹¹⁾ found that the right eye was affected in two cases. Our study only included patients with OA and similar to Tekin et al. study, we found that 60% of cases had lesions in the right eye.

As in many infectious diseases also in OA there is an increase in various inflammatory cells. In one study concerning to CA, in the 63.5% of cases the leukocyte was $> 10.000 \text{ mm}^3/\text{mL}$ and in the 67 % of cases, C-reactive protein (CRP) was $> 30 \text{ mg/L}$ ⁽⁶⁾. In our study, leukocyte and CRP were higher than the normal range.

Tekin et al.⁽¹³⁾ stated that their diagnosis of cases was based on the isolation of bacteria in 23.8% of the cases, detection of gram-positive bacilli in the direct examination of characteristic lesion material in 28.5% of the cases and from the characteristic appearance of the lesion in 47.7% of the cases. Irmak et al.⁽²¹⁾ reported that their diagnosis of cases was based on isolation of bacteria in 64% of the cases in their study. In the cases who were culture-negative and without bacilli in gram-staining, the diagnosis was based on the presence of characteristic clinical presentation with a history

of severe scarring formation, swelling, black eschar and positive response to the treatment⁽¹³⁾. In our paper, the diagnosis was made from the characteristic appearance and isolation of bacteria from the infected ulcer in 25% cases and the characteristic appearance of the lesion together with the patient's history and response to treatment in 75% cases. Our findings related to the rate of bacterial isolation were similar to those of Tekin et al's findings.

Penicillin G, ciprofloxacin and doxycycline are suggested as therapeutics for inhalation and cutaneous anthrax⁽²²⁾. In the treatment of anthrax, penicillin is the first choice for every age group⁽⁶⁾. The use of oral antibiotics has been stated to be adequate for anthrax presenting as malignant pustules⁽²⁰⁾. Tekin et al.⁽¹³⁾ stated that penicillin, ampicillin-sulbactam and ciprofloxacin were used in the treatment of their patients. In the study by Karahocagil et al.⁽⁶⁾ intramuscular penicillin was administered to eighty patients and oral amoxicillin given to five patients. In the same study, two patients with sepsis who underwent tracheostomy needed artificial ventilation due to a respiratory tract obstruction. In our series, sixteen patients with OA received intramuscular procaine penicillin (2x0.8 MU) for one week. Four patients who had small lesions received amoxicillin (2 x1000 mg/day). In addition, necrotic tissue was removed from the lesions then they were covered with gauze saturated with rivanol. Systemic corticosteroid (prednisolone 1-2 mg/kg/day for 4 days) and antihistaminic were administered to six patients with laryngeal and large facial-neck edema. Two patients with laryngeal edema were intubated and received ventilatory therapy.

In the literature, it has been reported that untreated cutaneous anthrax could determine life-threatening septicemia^(18,23). Karahocagil et al.⁽⁶⁾ reported that two patients died owing to sepsis. Baykam et al.⁽¹⁸⁾ stated that there was one fatality due to a disseminated neck and laryngeal edema. In the current study, all of the cases recovered. In addition, we found upper eyelid scar tissue due to necrosis in the 20% and ectropion in the 10% of cases. Yorston et al.⁽¹⁷⁾ stated that scar ectropion evolved in the 72.7% of their cases and this occurred in 47.7% of patients in the study by Tekin et al.⁽¹³⁾. David et al.⁽¹⁾ stated that ectropion and blindness did not afflicted their cases. In our study, Blindness were not developed similar to David et als study. Baykam et al.⁽¹⁸⁾ reported that the mean

duration of hospitalization was 11 days, whereas Karahocagil et al.⁽⁶⁾ stated that this duration was 7.9 days in patients with malignant pustules and 12.8 days in patients with malignant edema. Amraoui et al.⁽¹⁶⁾ reported a length of stay of about 7 days in the series of three cases related to anthrax of the eyelids. Finally, in the study by Soysal et al.,⁽¹⁴⁾ the stay in hospital was 10 days. In our case series, the mean of duration of hospitalization was 9.9 days as compatible with literature.

The low ratio of isolation of bacteria from the infected ulcer owing to technical limitation was the most limitation factor for this study.

Conclusion

Anthrax continues to be an endemic serious infectious disease in developing countries including Turkey. A diagnosis of Anthrax should be considered in patients with a periocular painless ulcer and having a relevant history of contact with infected animals or contaminated animal products. Early diagnosis and appropriate antibiotic treatment can facilitate recovery and prevent the development of eyelid complications. In this study, the low rate of eyelid complications may be due to early antibiotic treatment.

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