

## Characteristics of cutaneous anthrax in Turkey

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### Abstract

**Background:** Incidence of anthrax is diminishing in developed countries; however, it remains a public health problem in developing countries, especially those whose main source of income is farming.

**Methodology:** Charts of patients hospitalized between 1992 and 2008 in the Infectious Diseases and Clinical Microbiology Department of Ankara Numune Education and Research Hospital were reviewed.

**Results:** Fifty-eight cases with cutaneous anthrax were reviewed. The mean age was 49.8, and 36.2% were female. The most common professions were farmers (62%), butchers (19%), and housewives (15%). The mean incubation period was eight days. Most cases (62%) were exposed to bacteria when butchering sick animals. Eighteen patients used an antibiotic before admission to hospital (31%). The predominantly affected sites were hands (39%) and fingers (29%), followed by forearms (12%), eyelids (7%) and necks (3%). All cases initially had painless ulcers with vesicles; dissemination of the lesion was seen in 27.5% of patients. Gram stain was positive in 11 cases; culture was positive in 7 cases for *Bacillus anthracis*. All patients except one were discharged and treated with penicillin and/or ciprofloxacin or imipenem. One patient with a disseminated lesion on the neck died even though a steroid was used with the antibiotic.

**Conclusions:** Cutaneous anthrax should be considered as a possible diagnosis in cases with a painless ulcer with vesicles, edema, and a history of exposure to animals or animal products. Despite previous antibiotic use, taking smears and cultures should be encouraged. Treatment with penicillin G or penicillin procain alone is effective for cases with cutaneous anthrax without severe edema and superinfection.

**Key words:** cutaneous anthrax, Turkey

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### Introduction

Anthrax is a zoonotic infection that presents in 3 forms: cutaneous, inhalational, and gastrointestinal. Caused by *Bacillus anthracis*, anthrax is an aerobic, spore-forming, gram-positive rod found throughout the world. [1]. Although anthrax is primarily an animal disease, humans can acquire anthrax by exposure to infected animals, animal products, or spores in the soil.

The clue to the diagnosis of cutaneous anthrax is the history and rapid development of a painless ulcer surrounded by a zone of edema. The diagnosis is confirmed by bacteriological examination of the lesion or isolation of *B. anthracis* from the infected ulcer or blood by culture. Anthrax has been well known for a long time in the eastern part of Turkey, where traditional animal husbandry is the primary occupation. In this study we evaluated the epidemiologic and clinical characteristics of 58 adult cutaneous anthrax cases, and reviewed the

therapeutic options in the perspective of very recent Centers for Disease Control (CDC) guidelines.

### Materials and Methods

The charts of patients who had been hospitalized between 1992 and 2008 were reviewed. All cases had been patients in the Infectious Diseases and Clinical Microbiology Department of the Numune Education and Research Hospital, which is one of the largest tertiary state hospitals in Ankara. Age, sex, profession, type of exposure, site of lesion, dissemination status, incubation period, antibiotic use of patients prior to admission, and choice of treatment were recorded. The diagnosis of patients was based upon the detailed history and clinical findings of patients and /or isolation of *B. anthracis* from a lesion by Gram staining and/or growth with the culture media. The patients had been treated with penicillin (G or procain) and/or ciprofloxacin.

**Figure 1.** Vesicles of cutaneous anthrax prior to eschar formation



The data were analysed by Stata 8.0 (USA). The categorical comparisons were done by Chi square test, and if the data were sparse by Fisher exact test. The p value was set as  $< 0.05$ .

## Results

Of the 58 cases with cutaneous anthrax, 21 (36.2%) were females, and the mean age was 49.8 years. The mean incubation period was eight days. The most common profession was farmer (62%) and 62% of the patients had the history of exposure to anthrax while butchering sick animals. The most common site of lesions was on the hands (39%). All 58 cases had painless ulcers with vesicles initially and sixteen of the patients' lesion showed dissemination with lymph node enlargement and/or cellulitis (Table 1). The ulcers and vesicles of all 58 patients resulted in a black eschar. Eighteen cases had secondary infections and/or severe edema. Superinfections were caused by *Staphylococcus aureus*, *Escherichia coli* and *Sphingomonas paucimobilis*. Ciprofloxacin or imipenem was added to the regimen for these cases according to susceptibility tests and treatment was prolonged up to four weeks.

We detected *B. anthracis* in 11 of the smear samples and had culture positivity in seven of the

patients. Eighteen of the patients had previous antibiotic use before admission. The previous use of an antibiotic had no effect on culture or smear positivity ( $p = 0.554$ ) (Table 2).

The mean duration of treatment was 11 days, excluding the case with *Sphingomonas paucimobilis* superinfection, who was treated for four weeks.

## Discussion

Anthrax is essentially a disease of grazing herbivorous animals. The most common form of the disease is cutaneous anthrax, which accounts for 95% of all cases [2]. All cases in our study were cutaneous anthrax.

Although the incidence of anthrax is diminishing in developed countries, it remains as a considerable public health problem in developing countries especially, those whose main source of income is farming, as in our cases (Table 1). Anthrax is still common among domestic farm animals and cutaneous anthrax is an endemic disease among people in the eastern part of Turkey where traditional animal husbandry is the primary occupation [3,4,5].

The disease is transmitted to humans by contact with sick animals or their products, such as wool, skin, meat, etc. Whereas industrial cases account for most of the cases in developed countries where there is no conventional exposure to infected animals or animal products, the spread of anthrax in developing countries occurs most frequently by direct contact [2].

All our cases had direct contact with either raw meat or a live animal. Infection from direct contact with raw meat is more common (90%) than infection from direct contact with wool (9%).

Diagnosis of cutaneous anthrax requires suspicion. The differential diagnosis of cutaneous anthrax includes brown recluse spider bite, ecthyma, accidental vaccinia, ulceroglandular tularemia, and necrotic herpes simplex. Cutaneous anthrax is painless, does not include rash, and results in a black eschar (Figure 1). Patients with cutaneous anthrax may have fever, extensive edema, and other systemic signs. The diagnosis is confirmed by bacteriological examination of the lesion or isolation of *B. anthracis* from the infected ulcer or from the blood culture. Gram stain and culture of the lesion are recommended; however, prior antibiotic treatment rapidly renders the infected site culture-negative for *B. anthracis*. Serologic testing and punch biopsy at the edge of the lesion, examined by silver staining

**Table 1.** Epidemiological characteristics of the patients

	N = 58 (%)
Mean age (min-max)	49.8 (18-73)
Females	21 (36.2)
Profession	
<i>Farmer</i>	36 (62)
<i>Butcher</i>	11 (18.9)
<i>Housewife</i>	9 (15)
<i>Carpenter</i>	2 (3)
Type of exposure	
<i>Butchering</i>	36 (62)
<i>Contact with raw meat</i>	16 (27)
<i>Contact with live animal</i>	6 (8)
Site of lesion	
<i>Hand</i>	23 (39)
<i>Finger</i>	17 (29)
<i>Forearm</i>	7 (12)
<i>Arm</i>	5 (8.6)
<i>Eyelid</i>	4 (6.8)
<i>Neck</i>	2 (3)
Dissemination	16 (27.5)

**Table 2.** The effect of pretreatment to the microbiological tests

	Positive microbiology		Negative microbiology	<i>p</i> value for the comparison of positive and negative results
	Smear <i>N</i> = 11	Culture <i>N</i> = 7		
Antibiotic use before admission ( <i>pen G, cipro, sulb-ampicillin</i> )	3	1	13	0.554
No antibiotic use before admission	8	6	31	

and immunohistochemical testing, are useful in diagnosing cutaneous anthrax in patients who have received antibiotic therapy. Detailed history and physical examination as well as smear and culture were used to detected lesions in our cases. Smears were stained by Gram, Giemsa and methylene blue. We demonstrated gram-positive encapsulated bacilli in only 11 out of 58 patients, and a positive culture was obtained in seven patients. Öncül *et al.* reported microbiological evidence for 26 of 32 patients [3]. Another group from Turkey reported that culture positivity in their study group was 38.5% and gram stain smears revealed *B. anthracis* in 64% of their cases [6].

As lesions usually become sterile within 24 to 48 hours with antibiotics, the cultures may not yield bacterial growth. Generally the low rate of microbiological diagnosis is contributed to previous antibiotic usage [1]. Since our institution is a tertiary hospital, the majority of the patients had been

referred from primary or secondary centers and therefore 18 of 58 patients used an antibiotic before admission. In our cases, however, there was no statistical difference between the rate of microbiological diagnosis of patients who received and didn't receive an antibiotic before admission (*p* = 0.554). In spite of this observation, taking smears and cultures should be encouraged in all cases.

PCR detection systems have been developed for *B. anthracis* but it will probably be some time before they become totally stand-alone and generally available for use in a non-specialist laboratory [7].

Dissemination of the lesion was detected in 27.5 % of the cases. These cases were accepted as severe cases. Two of these cases had previous surgical intervention due to compartment syndrome (Figure 2). During acute phase of the lesion, surgical intervention is not recommended if there is not absolute indication as it may lead to septicemia. In one patient, after isolation of *B. anthracis* from the

**Figure 2.** Cutaneous anthrax lesion disseminated after surgical intervention



infected ulcer, *Sphingomonas paucimobilis* was isolated from blood culture as an superinfection. Because the patient's physical and laboratory findings revealed sepsis, we switched the therapy from penicillin plus ciprofloxacin to imipenem. The medication was prolonged to four weeks because of dissemination of the cellulitis.

Penicillin G is still the drug of choice in the therapy of naturally occurring anthrax in most parts of the world [7]; however, in the last update from the Centers for Disease Control and Prevention, it was reported that even naturally occurring strains of *B. anthracis* may produce inducible cephalosporinases and penicillinases [8]. According to this guideline, ciprofloxacin and doxycycline have been recommended as first-line therapies for cases of inhalational anthrax. As for inhalational disease, intravenous therapy with a multidrug regimen is recommended for cutaneous anthrax with signs of systemic involvement, for extensive edema, or for lesions on the head and neck. In such cases monotherapy with penicillin is not currently recommended [2,8,9]. We treated 66% of the patients by penicillin procain only. However, it should be noted that these patients had neither secondary infection nor severe edema. Other studies from

Turkey also show the effectiveness of penicillin alone in the treatment of cutaneous anthrax [3,4]. Three of the studies from Turkey [3,4,10] reported no resistance to penicillin; however, resistance was reported in other studies [11,12]. Esel *et al.* reported the MIC(90) values of penicillin G, doxycycline, ciprofloxacin, gatifloxacin, and levofloxacin as 0.016, 0.03, 0.06, 0.06 and 0.12 mg/l, respectively [13].

Eighteen cases with secondary infection and/or severe edema were treated by penicillin and ciprofloxacin. One patient who died was treated not only with combined antibiotics but corticosteroid as well, as recommended by some experts for extensive edema or swelling of the head and neck region associated with cutaneous anthrax [8]. He was admitted to our clinic with a disseminated lesion on his neck and died of laryngeal edema.

The mean duration of treatment for our cases was 11 days. Although CDC recommends 60 days of therapy for cutaneous anthrax in case of simultaneous transmission by inhalation, all our cases except one cured, and there were no complications or recurrence of infection.

In conclusion, cutaneous anthrax is still a public health problem in Turkey. Cutaneous anthrax should be considered as a possible diagnosis in cases with a painless ulcer with vesicles, edema, and a history of exposure to animals or animal products. Treatment with penicillin G or penicillin procain alone is effective only for cases with cutaneous anthrax without severe edema, superinfection, and probability of inhalation.

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