

Original Article

Suspected cutaneous anthrax in rural areas

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Abstract

Introduction: Cutaneous anthrax (CA), a zoonotic infectious disease is an important endemic public health disease in rural areas around the world, accounting for 95% of anthrax cases.

Methodology: Fifty patients with CA were diagnosed by the presence of characteristic skin lesions and positive response to treatment. Twenty-nine patients had been treated with oral ciprofloxacin or doxycyclin for 14 days and 21 patients had been treated with intramuscular procaine penicillin for 7 days. The demographic risk factors, characteristics and treatment of CA in rural areas were evaluated. The responses to two different systemic medications were compared using χ^2 test.

Results: Twenty-two males and 28 females were included in this study. The predominant skin lesions were black eschar, ulcer and swelling of the skin. The predilection sites were the hand and fingers. The most common route of contamination for both male and female patients was handling raw meat. The most common occupation was housewife for female patients and animal industry for male patients. The patients under ciprofloxacin or doxycyclin administration responded better to treatment; pain at lesion site and new lesions at the time of treatment were significantly lower. Secondary infection appeared to be higher in patients under procaine penicillin administration, although this difference was not statistically significant.

Conclusions: In rural areas that lack medical facilities with diagnostic tools, in the presence of black eschar, rapid diagnosis and treatment of CA is essential. The administration of a broad-spectrum antibiotic is recommended as the first line treatment of suspected CA.

Key words: anthrax; cutaneous anthrax; rural areas.

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Introduction

Anthrax, a zoonotic infectious disease caused by an aerobic, Gram-positive, endosporeforming bacterium as *Bacillus anthracis* is an important endemic public health disease encountered in countries of the Americas, Australasia, Africa and Europe [1,2]. Anthrax is an illness of animal husbandry, disseminated during the slaughtering and skinning of affected animals, the feeding of infected meat, and processing of livestock products. Although anthrax manifests with respiratory and gastrointestinal sign, cutaneous anthrax (CA) is reported to account for 95% of anthrax cases [3-5]. In rural areas, where traditional animal husbandry is the primary occupation, anthrax has been well-known.. In this study, we evaluated demographic risk factors, characteristics and treatment of CA in a rural area in Turkey.

Methodology

Fifty patients with CA were included in this study. CA was diagnosed by the presence of characteristic skin lesions such as severe swelling and black eschar, typical

anamnesis and positive response to therapy. The age, sex, occupation, way of exposure, kind of animal, duration of incubation, site, type and number of lesions, presence of pain, accompanying lymphadenopathy, drug usage of patients prior to admission and positive reaction to therapy were recorded. In one group, 23 patients aged older than 18 years had been treated with oral ciprofloxacin 500–750 mg oral every 12 h for 14 days and six patients less than 18 years old were treated with doxycyclin 2×100mg/day oral) for 2 weeks. In the other group, 21 patients had been treated with intramuscular procaine penicillin 2×800,000 units for 7 days. The patients were followed up for complications by phone calls and outpatient visits. Patients who were unresponsive to ciprofloxacin treatment after 3 days of oral administration, unresponsive to procaine penicillin treatment after 3 days of intramuscular administration and the patients without a certain diagnosis based on physical examination findings and characteristic lesions were excluded from the study. The study was conducted according to the principles of the Declaration of

Helsinki and was approved by the local medical ethical committee. (IRB #122/11).

Results

A total of 50 patients with a diagnosis of CA were assessed. Clinical characteristics and demographic risk factors of the CA patients are summarized in Table 1. The study group comprised 22(44%) males and 28 (56%) females, with an age range of 14–63 years and a mean age of 31.8 ± 17 years. The incubation period for the disease varied between 1 and 8 days (mean 5.3 ± 1.3). Characteristic lesions and anamnesis were the sole diagnostic criteria in all cases. The most common initial

skin lesions were black eschar, ulcer and edema of the skin. The most common area in which the lesions appeared was the hand and fingers (94%). Seventy-four percent of ill animals with which patients had contact were cattle. The most common way of contamination was handling raw meat, for both males and females of all ages. The most common occupation was housewife for females and the animal industry for males. Male patients with multiple lesions were more likely to have lymphadenopathy than were patients with a solitary lesion. Nine (18%) patients were under 18 years of age. Some of their clinical features, demographic risk factors and characteristics differed from adults.

Table 1. Clinical characteristics, demographic risk factors and outcomes of the 50 patients with cutaneous anthrax.

Clinical features, demographic risk factors, and characteristics	n (%)		n (%) Total
	Ciprofloxacin/doxycycline (p.o)	Procaine penicillin (i.m)	
Number of patients	29	21	50
Age			
< 18 age	6 (20.6)	3 (14.2)	9 (18)
≥ 18 age	23 (79.4)	18 (85.7)	41 (92)
Occupation			
Housewife	13 (44.8)	14 (66.6)	27 (54)
Butcher	3 (10.3)	none	3 (6)
Shepherd	1 (3.4)	1 (4.7)	2 (4)
Child	5 (17.2)	2 (9.5)	7 (14)
Veterinarian	1 (3.4)	1 (4.7)	2 (4)
Animal husbandry	4 (13.8)	3 (14.2)	7 (14)
Field work (harvesting crops)	2 (6.9)	none	2 (4)
Exposure process			
Handling raw meat	14 (48.3)	16 (76.1)	30 (60)
Milking ill cows, sheep, goats	2 (6.9)	1 (4.7)	3 (6)
Processing hair/wool	3 (10.3)	none	3 (6)
Harvesting crops	3 (10.3)	none	3 (6)
Slaughtering ill cows, sheep, goats	6 (20.7)	4 (19)	10 (20)
Type of animal			
Cattle	20 (69)	17 (80.9)	37 (74)
Sheep	7 (24.1)	3 (14.2)	10 (20)
Goats	2 (6.9)	1 (4.7)	3 (6)
Sites of lesions			
Hand	23 (79.3)	17 (80.9)	40 (80)
Finger	4 (13.7)	3 (14.2)	7 (14)
Eyelid	1 (3.4)	none	1 (2)
Forearm	1 (3.4)	1 (4.7)	2 (4)
Number of lesions			
Solitary	13 (44.8)	5 (23.8)	18 (36)
Multiple	16 (55.2)	16 (76.1)	32 (64)
Presenting predominant type of lesion			
Vesicles	1 (3.4)	none	1 (2)
Blisters	2 (6.9)	1 (4.7)	3 (6)
Cutaneous ulcer	9 (31)	4 (19)	13 (26)
Black eschar	11 (37.9)	15 (71.4)	26 (52)
Swelling	6 (20.7)	1 (4.7)	14 (28)
Presence of pain at lesion site	4 (13.7)	2 (9.5)	6 (12)
Lymphadenopathy	7 (24.1)	3 (14.2)	10 (20)

In one group, treatment consisted of ciprofloxacin administered daily, and complete resolution was seen in 96.5% of cases at the second week of treatment. In the other group, treatment consisted of intramuscular procaine penicillin administered two times a day for 7 days, and complete resolution was seen in 76.1% of cases at the first week of treatment. The comparison between two treatment groups are shown in Table 2.

Discussion

Anthrax is still important in developing countries where the major sources of livelihood are dependent on agriculture and livestock. The disease does, however, continue to be a health problem in a number of developed countries [4-8].

In the majority, there was a history of contact with an infected animal or animal products. People are usually exposed to infectious anthrax agent while harvesting crops, butchering/slaughtering animals, processing/handling meat, cutting meat and skinning [2-7]. Our study demonstrated a similar time pattern as reported in the literature, with the majority of the cases occurring in summer and autumn [9]. Similar to previous studies, exposed skin sites such as the hands, forearms and fingers were mostly affected following a minor abrasion [2,10,11].

Nine patients were younger than 18 years of age. Seven of nine patients did not have a professional job, but all the boys helped their parents in animal husbandry and field work, while all the girls helped their parents in handling raw meat. One of the boys was a shepherd while one of the girls was a housewife. Most common sites of lesions were fingers. The most

common presenting type of lesion was black eschar, similar to what is seen in adults. The most common route of contamination did not differ from adults, and in this population was handling raw meat.

Differential diagnosis is essential for CA; if a patient has a painless pustule, ulcer, black eschar or edema and a history involving contact with domestic animals, one must consider CA. The diagnosis is established by observing the anthrax agent in gram stain or isolating the *bacillus anthracis* in culture, or by serological and molecular methods such as polymerase chain reaction or enzyme linked immunosorbent assay [12]. The differential diagnosis of CA includes ecthyma, pox disease, brown recluse spider bite, accidental vaccinia, necrotic herpes simplex and ulceroglandular tularemia. In particular, pox disease and staphylococcus infection may resemble the clinical characteristics of CA; both have a dark hemorrhagic crust and surrounding edema and erythema at the center of the lesions [3,13-14]. After evaluating all lesions in detail as mentioned above, we diagnosed these cases as suspected cutaneous anthrax.

All of the patients enrolled in our study resided in a rural district, far from the city center. In the local medical center, there was no access to diagnostic tools such as culture or serology to confirm the diagnosis of CA and the patients refused to go to the city center for further evaluation, thus diagnosis of all patients was made through history and detailed physical examination. People were afraid of losing their animals according to the ‘National Protection and Fight Guidelines Against Anthrax,’ so they preferred to conceal the disease even when they had the opportunity

Table 2. Comparison of 29 patients with cutaneous anthrax under oral administration of ciprofloxacin/doxycycline and 21 patients with cutaneous anthrax under intramuscular procaine penicillin administration.

	n (%) Ciprofloxacin/doxycycline (p.o)	n (%) Procaine penicillin (i.m)	n (%) total	P value
Number of patients	29	21	50	
Antibiotic use prior to admission	none	none	none	
Response to treatment	28 (96.5)	16 (76.1)	44 (88)	0.02
Pain at lesion site during treatment	1 (3.4)	5 (23.8)	6 (12)	0.02
Painful lymphadenopathy during treatment	1 (3.4)	3 (14.2)	4 (8)	0.16
Loss of edema at lesion site after one week of treatment	14 (48.2)	14 (66.6)	28 (56)	0.19
New lesion after the first day of treatment	1 (3.4)	5 (23.8)	6 (12)	0.02
Secondary infection	1 (3.4)	4 (19)	5 (10)	0.06

* Considered statistically significant when P < 0.05.

to obtain more sophisticated medical help and treatment in the city center.

While in general, the disease occurs equally in women and men in rural areas [2,6-7], in this study it was more common in females, especially in housewives. This was similar to the findings in another study in a rural area [15]. In contrast, CA was more common in males in several studies conducted in central regions of our country [16,17]. The reason for this may be the fact that the female population observed in this study generally work harder than men, spending more time on animal husbandry and housework, owing to local customs and traditions. Most of the patients included in this study were in their fourth decade in age.

There are differences between the findings of this study and the findings reported on CA in urban areas. Similar to other findings in rural areas, in urban areas the lesions are also mostly located on the hands, and the most common way of contamination is handling animal products, the most common occupation is being a housewife, and black eschar formation is the most common clinical sign [16,17]. On the other hand, there were more different exposure routes in rural areas, such as processing hair/wool and harvesting crops. The response to the treatment was lower due to secondary infection in bad hygienic conditions, and there was a higher frequency of multiple lesions [16,17]. According to this study, patients in the pediatric age group are observed in rural areas, perhaps because children in rural areas participate in daily work that exposes them to *Bacillus anthracis* more than children in urban areas would. On the other hand, a higher frequency of male patients were reported in urban areas [16,17] and this may be due to the lower prevalence of women as housewives in cities.

The gold standard in the diagnosis of CA is the positive culture of bacillus. On the other hand, positive cultures are seen in less than 65% of patients [3,4]. A study on 85 patients with anthrax infection reported the existence of positive cultures in only 12.9% of patients with confirmed clinical anthrax disease [6]. Another study [18] observed positive cultures in 30.4% of anthrax patients and gram staining in 34.8% of patients with anthrax, while Denk et al. found positive cultures in only 10.7% of patients [2]. In a recent study, the existence of the typical lesion was the sole diagnostic criterion in 77.6% of CA patients, similar to our study [19]. As can be seen from the data published in the literature, the percentage of positive cultures is lower than expected and hence, it can be inferred that patient history and the skin examination are most important for the diagnosis of CA in rural areas far from the city

center. On the other hand, having no access to diagnostic tools such as microbiological or immunological tests is the major limitation of our study in terms of confirming the diagnosis.

None of our cases had been treated with antimicrobials before being admitted to our hospital. Since topical therapy is not useful in CA, two recommended systemic treatment regimens were preferred: Ciprofloxacin 500–750 mg oral every 12 h or Doxycyclin 2×100mg/day oral for 2 weeks, and intramuscular procaine penicillin administered two times a day for 7 days [5,18–22]. According to most authors, the optimal duration of therapy is 3–5 days for uncomplicated CA and 10–14 days for systemic anthrax [5,18–22]. Oral antimicrobial therapy was administered for 14 days and intramuscular antimicrobial therapy was administered for 7 days, since some of the patients stated that they would not have the chance to revisit the clinic for follow-up. The diagnosis of the included cases were based only on history and clinical examination; and no diagnostic tool such as microbiological, immunological or histological tests were utilized. Therefore, the term "suspected cutaneous anthrax cases" was used according to WHO Anthrax Guidelines [23].

One patient under ciprofloxacin administration and four patients under penicillin administration had purulence after the onset of therapy. In addition, one patient under penicillin treatment needed surgical debridement. Since purulence is exclusively seen in secondary nonanthrax infections, these patients were considered to have secondary infections [22]. Secondary infection seemed to be more frequent in patients under penicillin administration, although this was not statistically significant. Therefore, patients under ciprofloxacin or doxycyclin administration had better responses to treatment. The pain at lesion sites and new lesions at the time of treatment were also significantly lower in the ciprofloxacin group.

Despite an apparent decline in CA cases worldwide, one can still see CA cases in rural areas [23-27]. Immediate identification of the signs and symptoms of CA is fundamental. On the other hand, in rural areas far from city centers, most of the medical facilities do not have the means to detect the infectious agent by Gram stain or isolation of *Bacillus anthracis* in culture or by serological and molecular methods. Therefore, in rural areas that lack medical facilities with diagnostic tools, the administration of a broad-spectrum antibiotic as the first line treatment of suspected CA is recommended. It is a safe and effective treatment regimen against many microorganisms, including the *Bacillus anthracis*, as well as the bacteriae responsible for the diseases in the

differential diagnosis such as infections of the urinary, respiratory, gastrointestinal tracts, bones and joints. [28].

Conclusions

In rural areas that lack medical facilities with diagnostic tools, immediate identification of the signs and symptoms of CA is fundamental to successful treatment outcome. The administration of a broad-spectrum antibiotic is recommended as the first line treatment of suspected CA.

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