Cutaneous Anthrax in Eastern Turkey

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Anthrax, caused by the spore-forming bacterium Bacillus anthracis, *is rarely seen in industrial nations but is common in developing countries. Cutaneous anthrax (CA), the most common form of the disease, accounts for 95% of cases and usually develops on exposed sites. This study reviews the clinical and laboratory findings of 21 patients diagnosed with CA during 2 separate epidemics in the Van region of Turkey. All patients had a history of direct contact with infected cattle. The patients, aged 1.5 to 64 years, included 13 females and 8 males. Of the patients, 9 were 15 years or younger. Skin lesions were localized on the hands and fingers in 15 patients, on the face in 3 patients, on the face and finger in 1 patient, on the chest and finger in 1 patient, and on the eyelid in 1 patient. Gram-positive bacillus were noted on Gram stains of material obtained from skin lesions in 2 patients. All but one patient was successfully treated with penicillin; the unresponsive patient was treated with cefuroxime and required plastic reconstructive surgery because of a skin defect on the eyelid.*

Anthrax is caused by the spore-forming bacterium *Bacillus anthracis*. Cutaneous anthrax (CA), the most common form of the disease, accounts for 95% of cases and usually develops on exposed sites.[1] Although a rare disease in developed countries, CA remains an occupational hazard for herdsmen and workers who have direct contact with infected animals or who process animal hides, hair, wool, and bone and bone products in developing parts of the world.[1,2] Epizootic and enzootic anthrax have long been a problem in Iran, Pakistan, Sudan, and Turkey. Consequently, animal products, particularly goat hair, imported from these areas are likely to be contaminated.[3] The cases of CA or those associated with anthrax complications have been reported previously from different regions of Turkey.[4-13] In this study, we review the clinical and laboratory findings of 21 cases of CA.

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Case Reports

This study included 21 cases of CA (Table) in the Van region in Eastern Turkey during two 1998 epidemics, one in September that included 8 cases (group 1) and another in July that included 13 cases (group 2). The patients in group 1 consisted of 2 neighboring families. There was a history of direct contact with a dying cow (presumably suffering from anthrax) and ingestion of meat from this animal. The patients in group 2 consisted of 3 neighboring families and 3 patients who were living in the same region. There was also a history of contact with a dying animal among all patients in group 2. Of the 21 patients, there were 13 females and 8 males. The patients ranged in age from 1.5 to 64 years; 9 patients were 15 years or younger.

In group 1 (Figure 1 through Figure 6), lesions were localized on the face in 3 cases (patients 1, 2, and 6), on the fingers in 3 other cases (patients 3, 5, and 7), on the chest and finger in 1 case (patient 4), and on the face and fingers in 1 case (patient 8). In group 2, the lesions were localized on the hands and/or fingers in all cases except for one (patient 21) where the lesion was on the eyelid.

Three of the 8 cases in group 1 (patients 1, 2, and 6) received treatment and follow-up care at Yüzüncü Yil University School of Medicine, and 5 cases (patients 3, 4, 5, 7, and 8) were treated in Van State Hospital. In group 2, all but one case (patient 21) were treated on an outpatient basis.

Routine blood analysis, peripheral blood smear, erythrocyte sedimentation rate, and blood culture analysis were performed in all patients in group 1. In addition, Gram staining and lesion cultures were performed in patients 1 and 2. Hemoglobin levels were

Clinical and Laboratory Findings of Patients With Cutaneous Anthrax*

Patient No./Sex	Age, years	Features and Localization of Lesions	Hemoglobin Level, g/dL	Leukocyte Count, /mm^3	Erythrocyte Sedimentation Rate, mm/h	Hospital Days
Group 1						
1/F	1.5	Black necrotic central eschar surrounded by hyperemia 2×1.5 cm in diameter on the left cheek and extensive edema on the left side of neck	10.9	19,500	26	7
2/F	3	Mildly necrotic central eschar surrounded by hyperemia and vesicles 2×3 cm in diameter on the inferior region of the chin and bilaterally extensive edema on the submandibular region	12.7	21,000	5	7
3/F	15	Necrotic lesion surrounded by hyperemia 2×1 cm in diameter on the dorsal face of the first finger of the left hand	12.5	8700	33	1
4/F	25	Necrotic lesion surrounded by hyperemia 3×8 cm in diameter, extensive edema on the dorsal face of the third finger of the left hand and an ulcer 0.5×0.5 cm in diameter on the left side of chest	13.2	12,100	40	1
5/F	27	Black necrotic central eschar surrounded by hyperemia 2×3 cm in diameter on the dorsal face of the middle phalanx of the third finger of the left hand	13.8	12,600	30	1
6/F	30	Papule 1×1 cm in diameter on the inferior of the left auricle and 2 lymphadenopathies approximately 2×1 cm in diameter in the same region	11.9	9100	23	—
7/F	35	Necrotic lesions surrounded by hyperemia 0.5×0.5 cm and 1.5×1.5 cm in diameters on the dorsal surface of the second and third fingers of the right hand, respectively	11.6	3100	30	1
8/M	40	Black necrotic central eschar surrounded by vesicles 2×2 cm in diameter on the anterior region of the left auricle and a lesion 0.5×1 cm in diameter on dorsal face of the third finger of the right hand	10.8	6300	24	1
Group 2†						
9/M	3		—	—	—	—
10/M	5		—	—	—	—
11/M	6		—	—	—	—
12/M	13		—	—	—	—
13/F	14		—	—	—	—
14/F	15	Lesions were localized	—	—	—	—
15/M	17	on the hands and/or fingers	—	—	—	—
16/F	17		—	—	—	—
17/F	17		—	—	—	—
18/M	19		—	—	—	—
19/M	27		—	—	—	—
20/F	55		—	—	—	—
21/F	64	Necrotic lesion 0.5×2 cm in diameter on the right lower eyelid and periorbital extensive edema	—	—	—	15

*M indicates male; F, female.
†Laboratory investigation could not be performed in group 2 patients.

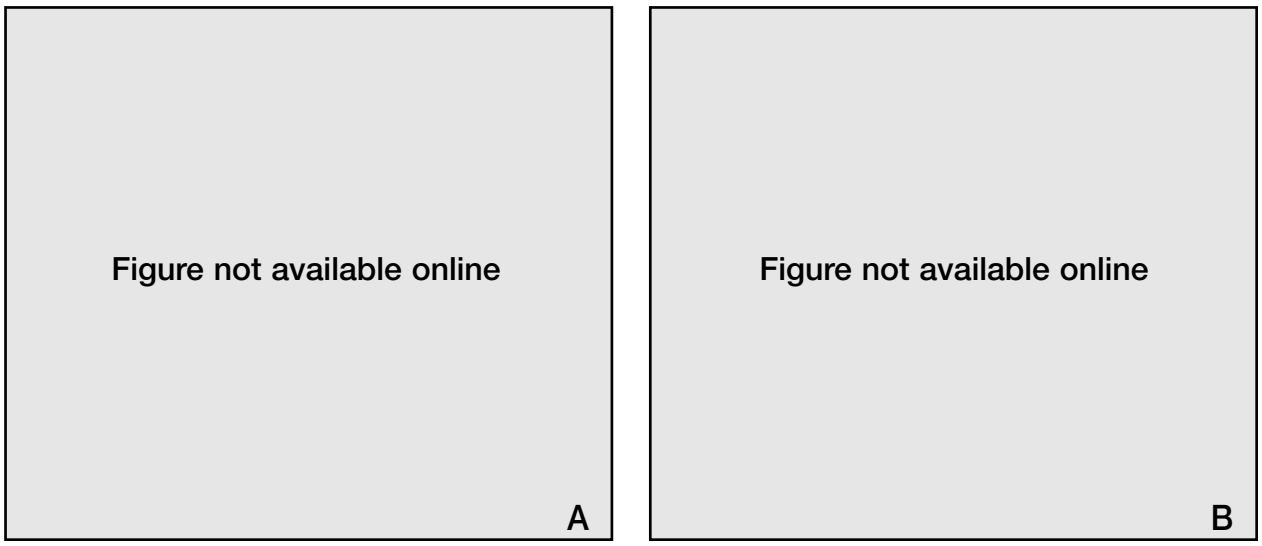

Figure 1. A black necrotic central eschar surrounded by hyperemia on the left cheek (A) and extensive edema on the left side of neck (B)(patient 1).

Figure 2. A mildly necrotic central eschar surrounded by hyperemia and vesicles 2×3 cm in diameter on the inferior region of chin (A) and bilateral extensive edema on the submandibular region (B)(patient 2).

normal in all patients studied. There was leukocytosis in 4 cases (patients 1, 2, 4, and 5), and the erythrocyte sedimentation rate was high in all cases except for patient 2. None of the patients had a positive blood culture. In 2 patients, cultures obtained from lesions were negative, but gram-positive bacillus were noted on Gram staining. Laboratory investigations could not be performed in the patients in group 2 because the state hospital had inadequate technical capabilities.

All patients, except for patient 21, were successfully treated with penicillin for 10 days. Patient 21 was unresponsive to penicillin but was successfully treated with cefuroxime sodium and with prednisolon (250 mg/d for 3 days) to treat severe periorbital edema.

Comment

Human cases of anthrax have been divided into 2 groups: agricultural or industrial. Agricultural cases result from direct contact with an animal dying from anthrax. Industrial cases result from contact with anthrax spores through contaminated raw materials such as hides, goat hair, wool, and bones that are used as part of a manufacturing process.[1,3] Person-to-person transmission does not occur.[3] In the highly agricultural region of Turkey, epidemic cases of human anthrax are usually caused by direct contact with

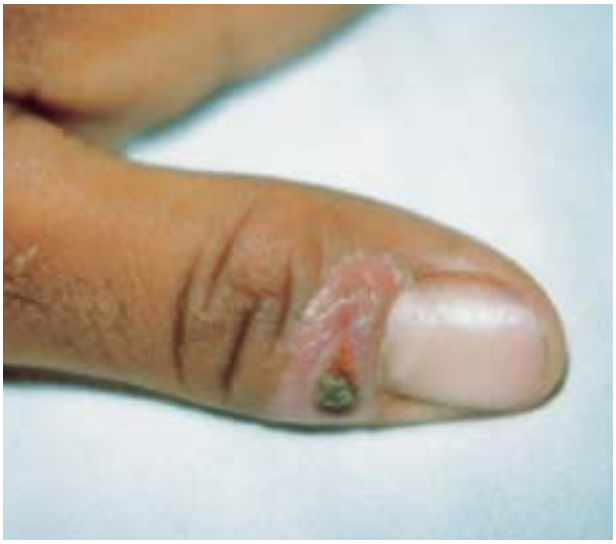

Figure 3. A necrotic lesion surrounded by hyperemia 2×1 cm in diameter on the dorsal face of the first finger of the left hand (patient 3).

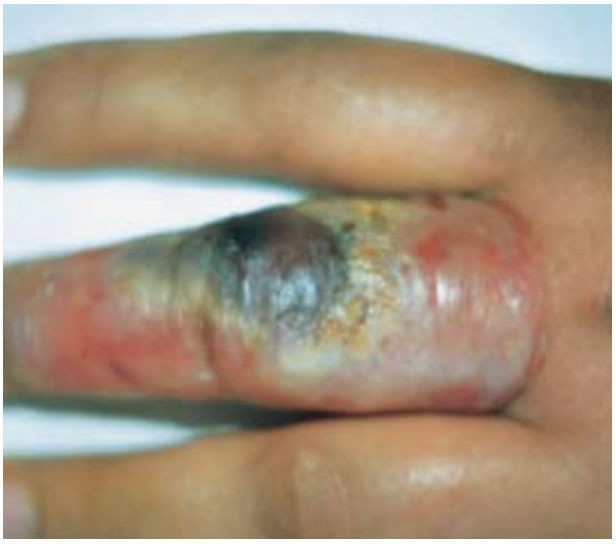

Figure 4. A necrotic lesion surrounded by hyperemia 3×8 cm in diameter with extensive edema on the dorsal face of the third finger of the left hand (patient 4).

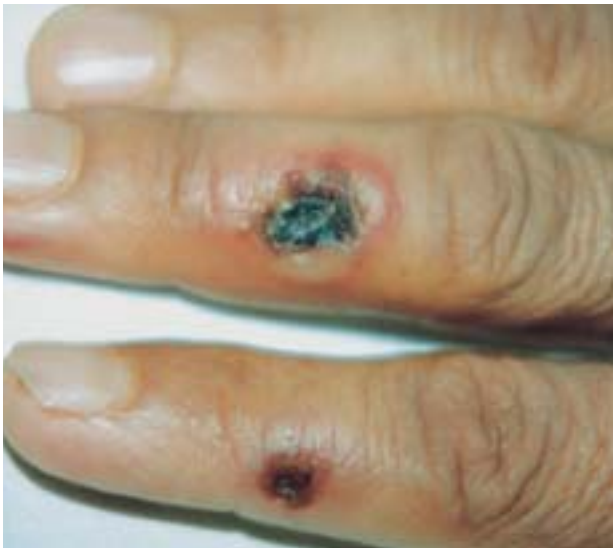

Figure 5. Necrotic lesions surrounded by hyperemia 0.5×0.5 cm and 1.5×1.5 cm in diameters on the dorsal surfaces of the second and third fingers of the right hand, respectively (patient 7).

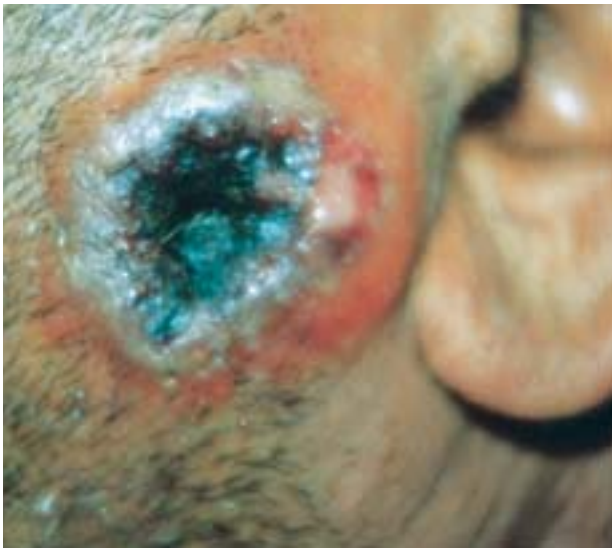

Figure 6. A black necrotic central eschar surrounded by vesicles 2×2 cm in diameter on the anterior region of the left auricle (patient 8).

animals infected with anthrax. This region experienced 3 prior epidemics of anthrax (mean 6–8 cases in each epidemic). In all past and present cases in our region, the disease occurred because of direct contact with infected or dead animals.

CA accounts for more than 95% of cases of anthrax.[1,3] Subcutaneously inoculated anthrax spores grow rapidly, producing organisms that release toxins, which account for the marked brawny edema and tissue necrosis.[3,14] The infection begins as a small papule that is often pruritic. The papule enlarges and, within 24 to 48 hours, develops into an ulcer surrounded by vesicles. A characteristic black necrotic central eschar develops later. Edema is often striking, particularly with facial lesions. More than 90% of cases occur on exposed areas such as the arms, hands, face, and neck.[3] In our series, the localization of lesions, which are painless, were on the face in 3 patients; on the face and finger in 1 patient, on the chest and finger in another patient, on the right eyelid in the last patient. The lesions were localized on the hands and/or fingers in the remaining 15 patients. In addition, extensive edema was noted in 3 patients with facial lesions

(patients 1, 2, and 21), which supports the findings in the current literature.

Aside from CA, there also have been reports of inhalation anthrax, hemorrhagic mediastinitis, septicemia, meningitis, and fatal meningoencephalitis.[3,15] In addition, oropharyngeal anthrax and gastrointestinal anthrax following ingestion of grossly contaminated undercooked meat have been reported.[3,15] In patients in group 1, there was a history of eating contaminated meat, although none had gastrointestinal system involvement because the contaminated meat was probably well cooked.

In the diagnosis of CA, anthrax bacilli are easily identified from Gram-stain smears and cultures of vesicular fluid.[3] Enzyme-linked immunosorbent assay and electrophoretic immunotransblot also are used in the diagnosis.[16] In 2 patients, cultures obtained from lesions were found negative, but gram-positive bacillus were noted on Gram staining. The differential diagnosis of CA includes bovine pustular stomatitis, plague, and tularemia.[3,14]

In the treatment of CA, local surgery is contraindicated. Although the first choice of drug is penicillin in antibiotic therapy, cases of penicillin resistant have been reported.[3,17,18] Erythromycin, tetracycline, and chloramphenicol are effective alternative drugs in penicillin-sensitive patients.[3] Doganay and Aydin[9] tested 22 *Bacillus anthracis* isolates for susceptibility to 27 antimicrobial agents by agar dilution. All isolates were sensitive to penicillin and did not produce β-lactamase. Although all isolates were sensitive to cefazolin, cephalothin, cephradine, and cefoperazone, resistance ratios differed with cefuroxime, cefotaxime, ceftizoxime, ceftriaxone, and ceftazidime.

Control of CA in humans ultimately depends upon control of the disease in animals. Animals dying of anthrax should be buried or cremated, and any person with possible exposure to anthrax should be vaccinated.[3] In industrialized countries, the zoonotic disease anthrax has been virtually eradicated because of effective public health measures such as animal vaccination and quality control of animal products. In developing countries, however, anthrax remains an occupational hazard for herdsmen and workers who have direct contact with infected animals or who process animal hides, hair, wool, and bone and bone products.[2]

REFERENCES

1. Mallon E, McKee PH. Extraordinary case report: cutaneous anthrax. *Am J Dermatopathol*. 1997;19:79-82.
2. Smego RA Jr, Gebrian B, Desmangels G. Cutaneous manifestations of anthrax in rural Haiti. *Clin Infect Dis*. 1998; 26:97-102.
3. LaForce FM. *Bacillus anthracis* (anthrax). In: Mandell GL, Douglas RG, Bennett JE, eds. *Principles and Practice of Infectious Diseases*. 3rd ed. New York, NY: Churchill Livingstone; 1990:1593-1595.
4. Doganay M, Kökkaya A, Hah MM. A review of 35 anthrax cases. *Mikrobiyoloji Bül*. 1983;17:1-10.
5. Doganay M, Almac A, Hanagasi R. Primary throat anthrax: a report of six cases. *Scand J Infect Dis*. 1986;18:415-419.
6. Doganay M, Bakir M, Dokmates I. A case of anthrax with toxaemic shock. *Br J Dermatol*. 1987;117:659-662.
7. Kutluk MT, Seçmeer G, Kanra G, et al. Cutaneous anthrax. *Cutis*. 1987;40:117-118.
8. Aksaray N, Cinaz P, Coskun U, et al. Cutaneous anthrax. *Trop Geogr Med*. 1990;42:168-171.
9. Doganay M, Aydin N. Antimicrobial susceptibility of *Bacillus anthracis*. *Scand J Infect Dis*. 1991;23:333-335.
10. Turnbull P, Doganay M, Lindeque PM, et al. Serology and anthrax in humans, livestock and Etosha National Park wildlife. *Epidemiol Infect*. 1992;108:299-313.
11. Doganay M, Aygen B, Inan M, et al. Temporal artery inflammation as a complication of anthrax. *J Infect*. 1994;28: 311-314.
12. Kocabas E, Alhan E, Aksaray N, et al. Dolayli endüstriyel temasa bagli çocukluk çagi deri sarbonu. *Çocuk Sagligi ve Hastaliklari Dergisi*. 1995;38:219-225.
13. Doganay M, Aygen B. Diagnosis: cutaneous anthrax. *Clin Infect Dis*. 1997;25:607,725.
14. Edwards MS. Anthrax. In: Feigen RD, Cherry JD, eds. *Textbook of Pediatric Infectious Diseases*. Philadelphia, Pa: WB Saunders Co; 1992:1045-1068.
15. Kwong KL, Que TL, Wong SN, et al. Fatal meningoencephalitis due to *Bacillus anthracis*. *J Paediatr Child Health*. 1997;33:539-541.
16. Harrison LH, Ezzell JW, Abshire TG, et al. Evaluation of serologic test for diagnosis of anthrax after an outbreak of cutaneous anthrax in Paraguay. *J Infect Dis*. 1989;160:706-710.
17. Bradaric N, Punda-Polic V. Cutaneous anthrax due to penicillin resistant *Bacillus anthracis* transmitted by an insect bite. *Lancet*. 1992;340:306-307.
18. Lalitha MK, Thomas MK. Penicillin resistance in *Bacillus anthracis*. *Lancet*. 1997;349:1522.