

# A Rare Clinical Presentation and Outcome of Cutaneous Anthrax: Toxemic Shock: Case Report

## Toksemik Şok: Kutanöz Şarbonun Nadir Bir Klinik Şekli ve Sonucu

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**ABSTRACT** Clinical presentation of cutaneous anthrax may be severe and complicated in some cases. Twenty-two cases with cutaneous anthrax were monitored between 2002 and 2008; of those two cases had toxemic shock. The lesion was localized on the anterior neck in the first case and on the right arm in the second case. In addition, both cases had an extensive edema extending from the lesion to the chest. Low systolic blood pressure (<90 mmHg), apathy and toxemic appearance, leukocytosis, hypoalbuminemia and hyponatremia were common findings in both cases. Intravenous fluid, fresh plasma replacement and penicillin G therapy were administered. One case required dopamine infusion for the restoration of shock. Crusts and other necrotic tissues on the right arm in the second case were removed surgically and were grafted. Toxemic shock is a rare complication of cutaneous anthrax and it is life threatening. Physicians working in the endemic area should be aware of this severe form.

**Key Words:** Anthrax; complications

**ÖZET** Kutanöz şarbonun klinik seyri bazı olgularda ağır ve komplike olabilmektedir. 2002 ile 2008 yılları arasında izlenen 22 kutanöz şarbon olgusundan 2'sinde toksik şok gözlemlendi. Birinci olguda lezyon boyun anteriorunda, ikincisinde ise sağ kolda lokalizeydi. Olguların her ikisinde de lezyondan göğüse yayılan ödem mevcuttu. Ek olarak düşük sistolik kan basıncı (<90 mmHg), apati ve toksemik görünüm, lökositöz, hypoalbuminemi ve hiponatremi her iki olguda da gözlenen ortak bulgularlardı. Hastaların tedavi rejimi intravenöz sıvı, taze donmuş plazma ve penisilin G uygulamasından oluşuyordu. Bir olguda şok tedavisi için dopamin infüzyonu gerekli oldu. İkinci olguda sağ koldaki krut ve diğer nekrotik dokular debride edilerek greft uygulandı. Toksik şok kutanöz şarbonun nadir ve hayatı tehdit eden bir komplikasyondur. Endemik bölgelerde çalışan klinisyenler bu ağır tabloya yönelik olarak uyanık olmalıdırlar.

**Anahtar Kelimeler:** Şarbon; komplikasyonlar

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**A**nthrax is usually a disease of herbivores and only incidentally develops in humans. Humans usually acquire anthrax directly or indirectly from infected animals. The main route of transmission is contact with or inhalation of *Bacillus anthracis* spores. Human cases may involve agricultural, industrial and environmental-disease or biological warfare related disease.<sup>1,2</sup> Although anthrax is an unrecognized disease in western countries, it is still endemic in some parts of the world such as Middle East, Central Asia and Africa.<sup>1-4</sup> With the September 11 attack, anthrax has become a re-emerging disease in western countries.<sup>5,6</sup>

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The disease occurs primarily in three forms, which are cutaneous, respiratory and gastrointestinal. Sepsis and meningitis may rarely develop after the lymphohematogenous spread of *B. anthracis* from a primary lesion. Cutaneous anthrax accounts for 95% of human cases globally. Data from the pre-antibiotic and vaccine days indicated that 10-40% of untreated cutaneous anthrax cases might be expected to result in death. With the treatment, less than 1% of untreated cutaneous anthrax cases are supposed to be fatal. Clinical picture varies from mild to severe form. Cutaneous anthrax can be self-limiting and lesions resolve without complications or scarring in 80-90% of cases with treatment. Extensive edema and toxemic shock can develop. This clinical form is potentially life-threatening and a very rare complication of cutaneous anthrax.<sup>1-3,7</sup>

Twenty-two cases with cutaneous anthrax were diagnosed and treated between 2002 and 2008. Only 2 cases were diagnosed with toxemic shock. In this paper, the clinical presentations, lab-

oratory findings, and therapeutic features of the two cases with toxemic shock that developed as a complication of cutaneous anthrax were presented.

## CASE REPORTS

### CASE 1

A 30 year-old male patient who had a history of carrying unprocessed dead animal skin, was admitted to the emergency room with a lesion that appeared on the neck three days ago. On the first examination body temperature, pulse, respiratory rate and blood pressure were 36°C, 142/minute, 20/minute, and 70/40 mmHg, respectively. There was a vesicle of 0.5 cm in diameter on the left side of the anterior neck, with an extensive erythema and non-pitting edema starting from the neck and extending to the shoulders including arms and the entire chest. Intravenous fluid replacement from a central venous catheter and penicillin G 4x3 million units/day were initiated. Blood pressure and central venous blood pressure were low despite intravenous fluid infusion and the blood glucose level was high. Dopamine and insulin

**TABLE 1:** Laboratory findings of two cases with toxemic shock at initial examination and on the 3<sup>rd</sup> day of therapy.

	Case 1		Case 2	
	Initial visit	3rd day of therapy	Initial visit	3rd day of therapy
WBC/mm <sup>3</sup>	25700	39600	26210	26770
Neutrophils %	88	90	85.7	86.4
Platelet count x10 <sup>9</sup> /mm <sup>3</sup>	251	138	293	247
Hematocrit %	54.1	54.3	56.1	44.9
Sodium mmol/l	127	125	121	126
Potassium mmol/l	4.6	5.8	4.9	6.3
Chloride mmol/l	98	90	85	90
Creatinine mg/dl	1.5	1.1	2.2	1.2
AST iu/l	28	80	67	82
ALT iu/l	33	34	98	64
Alkaline phosphatase iu/l	75	125	ND	166
Albumin g/dl	2.2	2.1	2.1	ND
CRP mg/l	ND	ND	179	50.3
Blood glucose mg/dl	323	136	256	138
Gram positive bacilli from the lesion	+	-	-	-
Positive culture for <i>B. anthracis</i> from the lesion	-	-	+	-
Positive culture for <i>B. anthracis</i> from the blood	-	-	-	-
Anti-PA Ig G (µg/ml, 14 <sup>th</sup> - 21 <sup>st</sup> day)	10.59 - 13.26		ND	
Anti-LF Ig G (µg/ml, 14 <sup>th</sup> - 21 <sup>st</sup> day I)	214.26 - 817.60		ND	

ALT: Alanine aminotransferase; AST: Aspartam aminotransferase; CRP: C-reactive protein; Anti-LF: Antibody against lethal factor; ND: Not done; Anti-PA: Antibody against protective antigen; WBC: White blood cell.

infusion were added to the treatment regimen. Hyponatremia and hypoproteinemia were significant findings of the laboratory analysis (Table 1).

Gram positive, encapsulated bacilli were detected on the microscopic examination of the material obtained from the lesion. However, cultures obtained from the lesion and blood were negative.

On the fourth day of therapy, edema began to resolve and blood pressure was measured 90/60 mmHg. On the other hand, sodium and chloride levels were still lower than normal limits. Hereon, fresh frozen plasma and 0.9% NaCl solution were administered.

Penicillin was stopped on the 7<sup>th</sup> day of therapy. Hyponatremia and hypoproteinemia continued. Moreover, vomiting and visual hallucination occurred. The patient was administered 250 ml 3% NaCl solution because the serum sodium level was lower than 120 mEq/l.

The general condition of the patient worsened on the 10<sup>th</sup> day of therapy. Blood pressure was low again and the patient had fever. The central venous catheter tip and blood cultures were positive for methicillin sensitive *Staphylococcus aureus*. Intravenous cefazolin was initiated and was continued for 12 days. Edema completely resolved on the 22<sup>nd</sup> day of the disease.

## CASE 2

A 44-year-old male patient (a herdsman who had carried a cattle carcass ten days ago) was admitted with extensive edema and bullous lesions on the right arm. On physical examination, the patient had an apathetic and toxic appearance. Body temperature, pulse, respiratory rate, and blood pressure were 36.2 °C, 84/minute, 32/minute, and 90/70 mmHg, respectively. There was an extensive, non-pitting edema and erythema starting from the right hand and extending to the shoulder and the right chest. Many hemorrhagic bullous lesions (6x8 cm in diameter and less) were present on the forearm and dorsal site of his hand (Figure 1). The results of the initial laboratory analysis were shown in Table 1. The gram stain of the lesion was negative, but the culture was positive for *Bacillus anthracis*.



**FIGURE 1:** Widespread hyperemia, hemorrhagic bullae on the right arm and an extensive edema starting from the right arm extending to the axilla and the lateral chest wall.

(See for colored form <http://tipbilimleri.turkiyeklinikleri.com/>)

Upon clinical diagnosis of severe cutaneous anthrax and extensive edema, intravenous fluid infusion and penicillin G 20 million units divided into four doses were initiated. Fresh frozen plasma was also infused due to hypoproteinemia.

Edema and inflammatory reaction on the arm and chest increased despite antibiotic therapy. Body temperature continued between 36-36.5 °C. The creatinine level returned to normal limits within a short time. However, sodium and albumin levels started to rise after the 7<sup>th</sup> day of therapy.

Antibiotic therapy was continued for 5 days and then was stopped. Edema started to resolve on the 10<sup>th</sup> day of the disease. In the second week of the disease, the bullous lesions were dried, and the color returned to black. A typical black eschar developed (Figure 2). On the 22<sup>nd</sup> day, crusts and other necrotic tissues on the right arm were re-



**FIGURE 2:** The 17<sup>th</sup> day of the disease. Occurrence of black eschar.  
(See for colored form <http://tipbilimleri.turkiyeklinikleri.com/>)



**FIGURE 3:** The 22<sup>nd</sup> day of the disease. Surgical removal of the eschar.  
(See for colored form <http://tipbilimleri.turkiyeklinikleri.com/>)



**FIGURE 4:** After grafting.  
(See for colored form <http://tipbilimleri.turkiyeklinikleri.com/>)

moved surgically (Figure 3). In the 6<sup>th</sup> week, the wound was grafted (Figure 4).

## DISCUSSION

Anthrax is an endemic zoonosis in Turkey, particularly in the eastern part. The incidence of the disease in Turkey has been decreasing with economic

and social changes, strict animal vaccination programs and education of farmers.<sup>2,4</sup> According to the report of the Turkish Ministry of Health, 320 human cases were notified in 2005 in Turkey. Almost all of the cases reported until today were cutaneous anthrax. Other clinical forms of anthrax, such as sepsis, meningitis, throat anthrax and intestinal anthrax were also reported as few cases previously.<sup>2,8-12</sup> Although anthrax occurs throughout the year in Turkey, the majority of cases occur in late summer and autumn, which are the driest and hottest seasons.<sup>2,4</sup>

A well-developed anthrax lesion could be easily recognized by a physician familiar to the condition. Unfortunately, a limited number of physicians are familiar with the clinical picture nowadays. The lesions are generally seen on the exposed area of the body; mostly on the face, neck, hands and wrist. While cutaneous lesions are usually single, sometimes two or more lesions may be present.<sup>1-3,7-9,11</sup> In our case group, a single lesion was present in 18 patients and 2 lesions in 4 patients. Lesions were localized on the hands and the arms in 20 cases, on the neck in 1 case and on the face in 1 case.

Airway obstruction by compression on the trachea from edematous swelling around the neck, toxemic shock due to massive edema, sepsis, meningitis, temporal artery inflammation, deep tissue necrosis and secondary infection, deep scar tissue are all reported complications of cutaneous anthrax.<sup>1-3,9,11</sup> In our clinical experience, only 3 cases including the presented two cases were diagnosed with toxemic shock due to massive edema. One case was reported previously.<sup>12</sup> Main clinical and laboratory characteristics of the two cases were hypotension, low body temperature, tachycardia, tachypnea, mental changes, leukocytosis with neutrophilia, hyponatremia, increased aspartam aminotransferase (AST), alanine aminotransferase (ALT) and glucose levels, and decreased albumin level. Therapy may include volume replacement including fresh plasma and antibiotic administration. Steroid and dopamine may be also given.

Penicillin G is still the drug of choice. Additionally, doxycycline or ciprofloxacin are currently

the best alternatives in the treatment of naturally occurring anthrax. In the World Health Organization (WHO) Guidelines, intramuscular procaine penicillin, oral amoxicillin or penicillin V are recommended for the treatment of mild uncomplicated cases with cutaneous anthrax. Intravenous penicillin G is recommended in cutaneous anthrax with extensive edema.<sup>1,13</sup>

The appropriate duration of treatment is controversial. *B. anthracis* can not be isolated from cutaneous lesions 24 to 48 hours after an effective antibiotic administration. Although the current WHO Guidelines suggest 3-5 days (may be 3-7 days) of antimicrobial therapy for uncomplicated cutaneous anthrax, there is no controlled clinical study regarding the duration of treatment in cutaneous anthrax. Antibiotic treatment does not influence the progress of the lesion, or other toxin-related systemic damage. Early treatment will limit the size of the lesion but it will not alter the evolutionary stages. For this reason, early diag-

nosis and early initiation of therapy are very important. In our opinion, the duration of therapy may be 3-5 (may be 7) days in uncomplicated cutaneous anthrax.

In summary, cutaneous anthrax may be mild or severe, and sometimes leads to severe complications. Toxic shock is a life threatening complication of cutaneous anthrax. Hypotension, hypoproteinemia, hyponatremia and hyperglycemia are prominent findings of the patients with toxic shock. Early supportive treatment for those complications with appropriate antimicrobial therapy could be life saving. Physicians working in the endemic area for anthrax should be aware of this clinical form.

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