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A 35-Year-Old American Man With Fatigue and a Neck Lesion

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Clinical Presentation

History

A 35-year-old Caucasian male presents to a clinic in the United States with fatigue and a rash on his neck that started as a papule 2 days earlier. The lesion is non-pruritic, but it is associated with significant non-painful swelling and a pressure sensation in the neck. There is no history of fever, but the patient reports at least one episode of diaphoresis with mild confusion and headache.

The patient recalls a break in the skin at the site of the lesion 3 days before while shaving and is sure that he has not been bitten by an insect. He has had no contact with animals and no foreign travel within the previous year.

He had come to the clinic 24 hours earlier with similar symptoms. After blood cultures were obtained, he was given one dose of a first-generation cephalosporin and discharged on a ten-day oral course. He returns because of worsening malaise and neck swelling associated with mild difficulty breathing.

The past medical history is unremarkable. The patient is a postal worker by profession.

Clinical Findings

Examination reveals a 2 cm irregularly shaped, indurated non-tender patch on the left anterior neck with mild overlying erythema and several 2 to 3 mm vesicles. The main lesion has a 6 mm shallow ulceration. There is massive neck oedema making lymph nodes difficult to assess (see Fig. 21.1). His neck circumference had increased from 57 cm at baseline to a peak of 81 cm. Temperature is 36.9°C (98.4°F), pulse 118 bpm, blood pressure 138/90 mmHg and respiratory rate 20 breath cycles per minute. The remainder of the initial physical examination is normal.

• **Fig. 21.1** Papulovesicular lesion with extensive neck oedema 2 days after the onset of a small papule.

Investigations

Full blood count, Na^+, K^+, Cl^- HCO_3, BUN, creatinine and random glucose are normal except for a mildly elevated haemoglobin at 18.7 g/dL (reference range: 13.0–18.0 g/dL).

Questions

1. What are the distinguishing features of this lesion that help narrow down your differential diagnosis?
2. What investigations need to be performed to establish early diagnosis and appropriate treatment?

Discussion

A 35-year-old male postal worker presents to a clinic in the United States with a papulovesicular lesion on his neck associated with massive neck swelling. There is no fever but diaphoresis is present. The patient's condition is worsening despite antibiotic therapy with an oral cephalosporin.

Answer to Question 1

What Are the Distinguishing Features of This Lesion that Help Narrow Down Your Differential Diagnosis?

The differential diagnosis of an ulcerative skin lesion with concomitant massive soft tissue swelling and systemic symptoms depends on the epidemiological setting and the individual exposure; it includes bacterial ecthyma *(Streptococcus pyogenes, Staphylococcus aureus),* rickettsial diseases, necrotic arachnidism (bite by brown recluse spider), rat-bite fevers *Streptococcus moniliformis* and *(Spirillum minus),* ulceroglandular tularaemia and bubonic plague.

At the time of the patient's presentation, the United States was in the process of investigating a possible event of bioterrorism. Therefore the most important, though overall rare, diagnosis to consider was cutaneous anthrax.

There may be few distinguishing features at the time of presentation, depending on the age of the lesion. Although it is commonly known that cutaneous anthrax is manifested by a central black eschar, this is not seen until approximately a week after inoculation. The anthrax lesion begins as a painless papule that lasts 1 to 2 days before becoming a vesicle that later ruptures. It then develops the classic necrotic central ulcer and may be surrounded by smaller peripheral vesicles. Therefore a patient may present with a non-specific localized papulovesicular eruption. Key associated findings include a preceding history of a break in the skin at the affected site, the presence of systemic symptoms such as malaise and headache and extensive, non-tender oedema. Fever and leukocytosis may not be present. In parts of the world where anthrax is endemic, zoonotic exposure to infected animals or contaminated animal products is important to establish, whereas exposure from a bioterrorism act may not be immediately apparent.

Answer to Question 2

What Investigations Need to be Performed to Establish Early Diagnosis and Appropriate Treatment?

Aspirate of fluid from the skin lesion should be sent for Gram stain, culture and susceptibilities along with blood cultures in patients with systemic symptoms regardless of fever status. In the absence of preceding antimicrobial therapy, numerous Gram-positive rods in high concentration will grow within 24 hours. Empirical antibacterial treatment with a quinolone or doxycycline should be instituted while awaiting microbiological results. Because negative cultures do not exclude anthrax, full-thickness punch biopsy from the vesicle and the eschar should be obtained, fixed in 10% buffered formalin and sent to a specialized laboratory for nucleic acid amplification and immunohistochemical (IHC) staining to detect *Bacillus anthracis* antigens. Serum should also be tested for antibodies to the protective antigen at baseline and 4 weeks later.

The Case Continued…

Blood cultures taken at the first clinic visit grew gram-positive rods. Gram stain and culture of the skin lesion obtained at the second visit were negative for *B. anthracis.* The patient was admitted and received intravenous levofloxacin and ampicillin-sulbactam and recovered. Stains for bacteria and IHC of the skin biopsy performed at a reference laboratory showed abundant bacilli in the dermis and the presence of *B. anthracis* antigens, respectively. Serology revealed that antibody to protective antigen was present in convalescent serum.

The patient was exposed during his occupation as a postal worker, handling contaminated mail. Overall, 22 cases were identified, of which 11 presented with cutaneous anthrax, and a further 11 fell ill with the inhalational form. Five people died; all deaths occurred secondary to inhalational anthrax.

SUMMARY BOX

Anthrax

Anthrax is caused by *B. anthracis,* a Gram-positive rod that forms spores under certain environmental conditions. It is primarily a zoonotic disease affecting domestic and wild herbivores. Anthrax remains endemic in animals worldwide, most importantly in Asia, Africa and South-eastern Australia, as well as parts of the southern and western United States. Humans usually acquire the infection when they are exposed to infected animals or animal products, but anthrax has also been used as an agent of bioterrorism. In the developed world, cases usually tend to be sporadic. In resource-limited countries anthrax remains a relevant public health problem and large outbreaks can occasionally occur.

Depending on the route of entry, *B. anthracis* can cause cutaneous, gastrointestinal or inhalational disease. Cutaneous anthrax is the most common form worldwide, accounting for 95% of all human cases. Although only a small percentage develop systemic disease, it can be lethal if not treated quickly.

The clinical marker lesion is a painless central ulcer with vesicles and extensive surrounding oedema, but the initial lesion will appear as a non-specific papulovesicular eruption.

History includes recent exposure to infected animals or contaminated animal products, unless the setting is a bioterrorism event, a previous break in the skin at the affected site and the presence of systemic symptoms in disseminated disease. A high index of suspicion is critical to the diagnosis. Differential diagnosis of cutaneous anthrax depends on the setting and the individual exposures; it includes bacterial ecthyma, rickettsial diseases, rat-bite fevers, necrotic arachnidism, ulceroglandular tularaemia and bubonic plague.

Gram stain and culture of affected fluids (blood, skin lesion aspirate, pleural fluid) and paired serological testing for antibodies to protective antigen remain the cornerstone of diagnosis. However, negative cultures do not exclude anthrax. In cutaneous anthrax, full-thickness punch biopsy from the vesicle and eschar should be fixed and sent to a specialized laboratory for PCR and immunohistochemical staining. Empirical antibacterial treatment with a quinolone or doxycycline should be instituted while awaiting results for limited cutaneous infection. When disseminated infection or other forms of anthrax are suspected, multi-drug therapy that includes those with CNS penetration should be used.

Although 7 to 10 days of antibiotic treatment are usually sufficient in cutaneous anthrax, up to 60 days of antibiotics are needed in inhalational disease because of the possibility of retained ungerminated spores in the lungs. Prevention of anthrax involves either prevention of exposure in occupational settings or immunization. In the setting of a suspected bioterrorism event, those at risk of exposure should receive a 60-day course of postexposure prophylaxis with oral antibiotics.

Further Reading

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