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CLINICAL RECORD

Fatal cutaneous anthrax in a heroin user

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Abstract

Background and objective: Cutaneous anthrax usually has a mortality rate of less than 1 per cent. However, since December 2009 there have been more than 13 deaths in the UK due to anthrax-contaminated heroin. We therefore wish to raise clinical awareness of this treatable disease.

Case report: We describe the case of a heroin user with an equivocal presentation of cellulitis in the neck. Within 36 hours, this led to death due to cutaneous anthrax.

Conclusion: Whilst cutaneous anthrax remains rare, this case report aims to raise awareness of the fact that the symptoms and signs of this condition in intravenous drug users may not always fit the typical picture.

Key words: Anthrax; Skin; Heroin; Drug Abuse, Intravenous

Introduction

In the past, cases of cutaneous anthrax in heroin users were very rare, except for an outbreak in 2000 in Norway.[1] However, since December 2009 the number of UK cases of cutaneous anthrax in intravenous (IV) drug users has risen steeply. In Scotland alone, more than 47 users have been admitted to hospital, of whom 13 died; this is a mortality rate of 27 per cent, and is much higher than the previous rate of less than 1 per cent.[1,2]

This report presents a case of cutaneous anthrax in an IV drug user, emphasises the potential causes of non-diagnosis, and reiterates the protocol for managing this condition.

Case report

A 29-year-old man presented to hospital with a three-day history of swelling of the right side of his neck after injecting heroin into his right external jugular vein. The patient reported increased swelling causing stiffness and pain on swallowing. There was no history of previous neck infection, respiratory distress, stridor, neurological symptoms, weakness, nausea or vomiting.

On examination, the patient was pyrexial. The oral cavity and oropharynx were normal, with a centrally positioned uvula. No discrete masses were found in the anterior triangle. The swelling was sited over the right posterior triangle of the neck, and was firm, erythematous and non-pulsatile (Figure 1). There was cellulitis of the right anterior chest wall, with decreased air entry on auscultation of the right anterior apex. Oxygen saturation was 93 per cent on air. On flexible nasoendoscopy, a bulge was noted in the pharyngeal wall, with no exudate. After a full general examination, no other abnormalities were noted.

The initial differential diagnosis was abscess or cellulitis.

Following a difficult IV cannulation, the patient was started on IV flucloxacillin 1 g 6-hourly, with a view to radiological investigation if there was no response.

Twelve hours later, the patient started to deteriorate, complaining of neck tightness and a tender abdomen. He had developed acute renal failure and had raised levels of inflammatory markers. A central venous cannula and a urinary catheter were inserted.

Due to the patient's rapid decline, we sought advice from the infectious diseases team. The clinical impression was that of necrotising fasciitis or cutaneous anthrax. Following advice from the microbiology team, the antibiotic regime was changed to IV ciprofloxacin 500 mg 12-hourly, IV clindamycin 900 mg 8-hourly and IV flucloxacillin 2 g 6-hourly. The patient was isolated in a side room. A sweep test for necrotising fasciitis was performed, with a negative result. Tissue fluid was sent for urgent Gram staining, which confirmed the diagnosis of anthrax. The patient was deemed too unstable for imaging at this stage.

The patient suddenly deteriorated, with signs of airway obstruction. Respiratory arrest ensued and he was intubated. This was followed by cardiac arrest, with asystole. Attempts at resuscitation using manual cardiopulmonary resuscitation, adrenaline and atropine were unsuccessful, and he was certified dead.

Discussion

Anthrax was first noted in the Bible, in the Book of Exodus, more than 3000 years ago, as the fifth plague affecting livestock in Egypt.[3] It is an acute infectious disease caused by the spore-forming bacteria *Bacillus anthracis*. The Gram-positive bacillus is found in spores in the soil. It is usually a zoonotic disease found in herbivores. Human infection is acquired and spread through contact with infected animals, animal products or by intentional actions. Approximately 95 per cent of human anthrax is cutaneous, 4 per cent is respiratory and 1 per cent is intestinal.[4]

Bacillus anthracis has three main virulent factors: (1) lethal factor, which causes pro-apoptotic activity in

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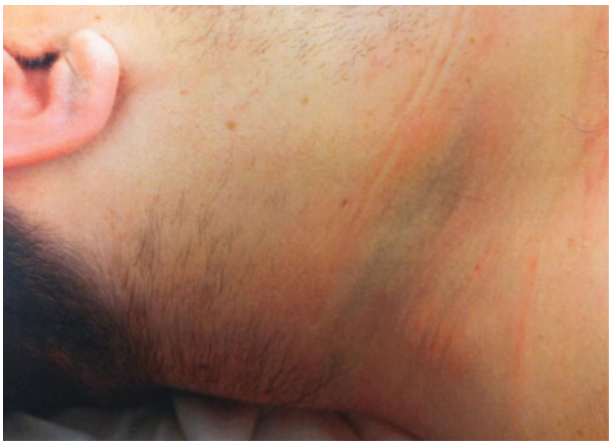

FIG. 1
The patient's right posterior triangle. Note the generalised oedema and erythema, with no sign of a black eschar or necrotic area suggestive of cutaneous anthrax.

macrophages, disrupts neutrophil chemotaxis and causes cytokine release from lymphocytes; (2) oedema factor, which causes tissue oedema; and (3) capsular polypeptide antigen, which creates a tough, antiphagocytotic coating.[2,3] Cutaneous anthrax usually starts as a painless, pruritic, raised lesion that increases in size over 48 hours to form an ulcer with an oedematous 'halo'. The exudate within the ulcer usually contains the anthrax bacilli.[2] This progresses to form a black eschar within 10 days, which lasts for 1 to 2 weeks before separating and scarring.

The main complications of anthrax are respiratory distress and asphyxiation if the lesion affects the neck. The other key complication is haematogenous dissemination, which occurs in 5–10 per cent of untreated cases.

Mortality is less than 1 per cent if the disease is diagnosed and treated early, with a 10–14 day course of either ciprofloxacin 500 mg or doxycycline 100 mg twice daily.[2] Anthrax immunoglobulin vaccine may ameliorate the condition if administered early; however, if it is dispensed after the onset of severe sepsis, the prognosis remains poor.[1]

Opioid-mediated immunosuppression in IV drug users is well recognised.[5] Studies have shown that IV drug users experience distinctively different types of infections and are more likely to have more severe infections, compared with a control population.[5] Additionally, although heroin addicts have decreased immune competency, this is further exacerbated by heroin withdrawal.[6] Withdrawal or abstinence from chronic morphine use for even 24 hours causes a significant decrease in lymphocytes in non-human primates.[7] As mentioned earlier, lethal factor induces cytokine release in lymphocytes during anthrax infection. Heroin-mediated and heroin withdrawal induced immunosuppression also specifically decrease the lymphocyte count. Paradoxically, whilst heroin, a short-acting opioid, appears to depress the immune system, methadone, a longer-acting opioid, modulates the immune system causing hyperactivation (following previous heroin-related inhibition).[8] The immuno-restorative effect of methadone is thus a potential key factor in the treatment of concurrent infections and heroin withdrawal.[8] Methadone should perhaps be administered within the first 24 hours of heroin cessation to prevent withdrawal-induced immunosuppression. Some of these factors may account for the missing features of cutaneous anthrax not seen in our case or the previously reported Scottish cases.

The other possible reasons for our patient's misdiagnosis at initial presentation may be the clinical appearance and progression of condition. A black eschar is usually the pathognomonic sign of anthrax.[9] However, no evidence of a black eschar or necrotic area was seen in our patient, nor in the recent Scottish cases.[1,9] All these reported patients did however have generalised, excessive oedema around their injection site. Furthermore, all these recent anthrax cases have had non-specific systemic features. The appearance of tachycardia, increased fluid requirements, coagulopathy, bleeding around the injection site and renal impairment seem to correlate with a clinical decline and poor prognosis.[1]

The presented case highlights the fact that cutaneous anthrax in IV drug users does not present in the classical fashion. Healthcare workers need to be aware of this so as not to miss any future cases. Accordingly, the clinical algorithm produced by Health Protection Scotland should be followed, with the addition of methadone replacement within the first 12–24 hours of presentation, to provide patients with effective treatment.[1]

- **About 95 per cent of anthrax cases are cutaneous; a black eschar is pathognomonic**
- **Mortality is less than 1 per cent if diagnosed and treated early**
- **In intravenous drug users, cutaneous anthrax does not present classically due to immunosuppression**
- **In such cases, cellulitis may indicate anthrax, and high-dose antibiotics must be started immediately**
- **Methadone should also be given, and immunoglobulin vaccine considered**

Cutaneous anthrax remains a rare differential diagnosis in IV drug users with serious infection. However, the presented case highlights the importance of improving clinical awareness within the National Health Service, especially if there are further instances of contaminated heroin in circulation. Rapid, accurate diagnosis and treatment are paramount in order to avoid further mortality.

Conclusion

Chronic heroin use and heroin withdrawal induces immunosuppression and may delay or modify the typical clinical signs of certain infections. Consequently, cellulitis in heroin users may indicate anthrax, and high-dose antibiotics must be started immediately. Methadone replacement should also be instigated and immunoglobulin vaccine administration considered.

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