CASE REPORT

Heroin-associated anthrax with minimal morbidity

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Accepted 21 February 2017

SUMMARY

In 2010, during an outbreak of anthrax affecting people who inject drugs, a heroin user aged 37 years presented with soft tissue infection. He subsequently was found to have anthrax. We describe his management and the difficulty in distinguishing anthrax from non-anthrax lesions. His full recovery, despite an overall mortality of 30% for injectional anthrax, demonstrates that some heroin-related anthrax cases can be managed predominately with oral antibiotics and minimal surgical intervention.

BACKGROUND

In 2010, there was an outbreak of anthrax affecting people who inject drugs (PWID) in Scotland. Published descriptions of cases from this outbreak are skewed towards patients with severe disease and substantial mortality requiring extensive and disfiguring surgery and concurrent therapy with multiple intravenous antibiotics. This case illustrates the other end of the spectrum of presentation of anthrax with mild disease, minimal morbidity and complete recovery managed predominantly with oral antibiotics in the community. The case also illustrates the difficulty in distinguishing injectional anthrax (IA) from cutaneous anthrax (CA) and other soft tissue infections seen in PWID when using clinical appearance alone and highlights the role of molecular testing by PCR in confirming the diagnosis of anthrax. Additionally, this report is the first to provide a photographic record of the anthrax lesion at presentation and at resolution.

CASE PRESENTATION

We describe the case of a heroin user aged 37 years who presented to his GP practice during the 2010 IA outbreak with an isolated area of soft tissue infection of the lower left leg. The patient had chronic hepatitis C and was on methadone but still injecting heroin. He was initially seen by the practice nurse and the lesion was swabbed prior to antibiotics and dressed without GP involvement. At that point, there was no clinical suspicion of anthrax. The local microbiology laboratory sent the swab for anthrax PCR. Within a week, the result returned PCR-positive for anthrax, but the patient declined review by GP or referral to an infection specialist for admission and intravenous antibiotics. Oral antibiotic treatment was therefore prescribed with flucloxacillin 500 mg and penicillin V 500 mg both four times daily and contact with the practice nurse was maintained for wound dressing. Venepuncture was attempted but unsuccessful due to poor venous access. Six days after his initial contact with the practice nurse, the patient

attended for inpatient management. The lesion appearance remained static during that period. He gave a 2-week history of a left leg lesion intermittently discharging pus. The history of injecting into this area was unclear, but the patient did describe hiding heroin in his sock prior to the onset of his symptoms at the area where the lesion subsequently developed. At the point of hospital admission, there was a 5 cm by 5 cm fluctuant swelling on the anterolateral aspect of the left lower leg (figure 1). He was afebrile with no signs of sepsis.

INVESTIGATIONS

As the presentation with soft tissue infection in an injecting drug user met the Health Protection Scotland (HPS) National Anthrax Outbreak Control Team criteria for testing for anthrax,¹ the leg swab taken by the practice nurse was sent to the Rare and Imported Pathogens Laboratory (RIPL) where PCR testing for anthrax was performed. The swab was positive for all three *Bacillus anthracis* genes (*lef*, *capA*, *bagC*).

After admission to hospital routine blood tests were taken (table 1).

Blood cultures taken on admission to hospital (after 6 days of oral antibiotic treatment) were negative after 5 days of incubation using the BacT/ALERT system (bioMérieux). Peripheral blood tested positive for *B. anthracis* by PCR and serology taken 2–3 weeks after the lesion initially appeared was also positive for anthrax (antiprotective antigen IgG antibodies and antilethal factor IgG antibodies detected).

Prolonged culture of the swab using conventional culture media failed to grow *B. anthracis* but did grow anaerobes (*Fingoldia magna* and *Prevotella oralis*).

Repeat swabs taken on hospital admission and again 2 months after discharge from hospital were culture and PCR negative for *B. anthracis*.

Figure 1 Left lower leg lesion seen on admission in 2010 demonstrating raised, fluctuant, 5x5 cm swelling with surrounding golden crusting resembling impetigo.

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To cite: Black H, Chapman A, Inverarity D, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-218316

Table 1 Routine blood tests during inpatient stay.

Test (units)	Day 6 16 February 2010	Day 7 17 February 2010	Day 8 18 February 2010	Day 9 19 February 2010	Day 10 20 February 10	Day 12 22 February 10	Day 13 23 February 2010
Haemoglobin (g/L)	12.4	12.9	12.4	13.8	12.9	13.8	13.8
Platelets ($\times 10^9/L$)	364	311	175	299	304	352	373
White cell count ($\times 10^9/L$)	12.1	11.1	8.9	11.5	10.8	12.5	12.5
Neutrophils ($\times 10^9/L$)	7.5	7.0	5.5	8.0	6.2	7.3	7.0
Haematocrit (L/L)	0.385	0.407	0.385	0.429	0.407	0.426	0.421
APTT (s)	0.9	NT	NT	NT	NT	NT	NT
INR	1.0	NT	NT	NT	NT	NT	NT
Fibrinogen (g/L)	3.2	NT	NT	NT	NT	NT	NT
Urea (mmol/L)	2.2	3.6	4.0	2.8	1.1	2.6	4.0
Creatinine ($\mu\text{mol/L}$)	60	77	76	72	71	74	77
Chloride (mmol/L)	101	105	109	109	111	101	101
Bicarbonate (mmol/L)	23	24	16	22	19	23	25
ALT (U/L)	25	24	NT	22	18	22	26
Alk Phos (U/L)	135	133	NT	121	110	125	121
Bilirubin ($\mu\text{mol/L}$)	6	8	NT	7	5	4	5
Albumin (g/L)	41	36	NT	39	37	40	44
CRP (mg/L)	14	12	10	10	13	28	20

NT, not tested.

DIFFERENTIAL DIAGNOSIS

The appearance of the leg lesion was consistent with soft tissue infection related to heroin injecting and the possible involvement of *Staphylococcus aureus*, β haemolytic streptococci and anaerobes such as *Clostridia* species were considered. Indeed, the golden crusting around the perimeter of the lesion had an appearance like impetigo suggesting *S. aureus* infection.

Additionally, this case could represent either IA or CA. The lesion has some features compatible with CA. It could be described as a papule in appearance with local oedema and there were golden vesicles evident which have been described with CA. However, there was notable absence of necrotic eschar when the lesion was assessed between days 10 and 14 into illness by an infectious disease consultant physician.

TREATMENT

When the positive leg swab PCR result confirmed a diagnosis of anthrax, the patient initially received oral flucloxacillin and penicillin V. When he continued to decline hospital admission and there was no clinical improvement, antibiotic treatment was altered to oral ciprofloxacin (750 mg two times per day) and clindamycin (450 mg four times daily) in an attempt to treat *B. anthracis* infection effectively, treat other possible concurrent bacterial infecting pathogens and maximise compliance with treatment.

Once inpatient management began, he was started on intravenous antibiotics and reviewed by a surgeon as to the feasibility of attaining source control through debridement of the affected area. He underwent excision of the lesion under general anaesthetic the day following admission. The surgical team excised back to healthy tissue; muscle appeared healthy and haemostasis was secured. The area was dressed with Kaltostat and Jelonet and bandaged with crepe bandages. Postoperatively, he was managed with intravenous flucloxacillin 1 g, benzylpenicillin 1.2 g and clindamycin 450 mg, all four times daily.

OUTCOME AND FOLLOW-UP

His recovery was uneventful and on day 4 postoperatively, he was switched to an oral combination of amoxicillin (1 g three

times daily), clindamycin (450 mg four times daily), ciprofloxacin (750 mg two times per day) and metronidazole (500 mg three times daily). These were planned for a further 14 days on discharge. The GP Practice Nurse was contacted to continue wound dressings in the community.

Following discharge, he was reviewed on the ward after 8 days. The appearance of his leg was static but as he had significant diarrhoea, clindamycin was discontinued. Two months following discharge, a repeat swab of the area (taken in the community) yielded no growth and *B. anthracis* was not detectable by culture or PCR.

The patient had no further contact with health services for 4 years when he represented with a right leg abscess associated with heroin injection (figure 2) which resembled the previous anthrax lesion but grew methicillin-susceptible *S. aureus*. The previous anthrax lesion of the left leg had healed with scarring (figure 3).

DISCUSSION

Before the European outbreak of IA in 2009/2010, there was only one reported case of anthrax infection in a drug user.² During this outbreak, there were 119 cases classed as anthrax cases—47 confirmed, 35 probable and 37 possible. Fourteen patients died (13 confirmed and 1 probable). They were all heroin users.³ Sporadic cases of IA have occurred since the outbreak was declared over.^{4 5}

The majority of IA cases described previously feature serious soft tissue infection with significant tissue oedema. This case demonstrates that milder cases of heroin-related anthrax soft tissue infection occur with little biochemical or haematological derangement and full recovery with minimal morbidity. The diagnosis of anthrax could easily have been missed if the initial swab had not been sent for anthrax PCR.

The patient's swab was PCR-positive for anthrax but culture-negative. It is possible that, as anthrax lesions are mainly toxin-driven, there were few bacilli at the site of the lesion and the bacterial load on the swab was insufficient to grow by direct plating. Another possible explanation, although there was nothing to indicate this in the discussed case, is that later in the

Figure 2 New right lower leg lesion prompting re-presentation in 2014. Although this closely resembles the previous anthrax lesion, it grew methicillin-susceptible *Staphylococcus aureus* and was negative for anthrax by PCR.

Figure 3 Original left lower leg lesion seen in 2014 demonstrating healing with scarring.

outbreak, there was more awareness of IA among the PWIDs and some individuals had managed to source and use non-prescription amoxicillin to self-medicate which may have influenced the ability to culture anthrax.

In terms of classification, the clear differentiation between CA and IA can be difficult. As stated, the lesion in this case had certain features which would potentially be compatible with CA—papular in appearance, local oedema and golden vesicles. Despite the latter being described with CA, they have been seen both in other local IA cases⁴ and described in IA by other investigators.⁷ The notable absence of necrotic eschar in PWID anthrax has been considered to be more characteristic of IA than CA.¹⁰ However, even confirmed IA cases encompass a spectrum of presentations including mild soft tissue infections such as this. This is a contrast to published reports which can over-represent the severe end of the spectrum of patients requiring critical care support and extensive surgical debridement.

Clinical management guidelines written during the 2009/2010 outbreak advocate aggressive management with multiple intravenous antibiotics, but this patient's initial management, out of necessity rather than clinical choice, was predominantly with oral antibiotics.

Antibiotic selection included flucloxacillin, metronidazole, benzylpenicillin and clindamycin. This is in keeping with standard empirical treatment for PWID with soft tissue infections in central Scotland because of outbreaks of polymicrobial severe infection involving Clostridial species, *Streptococcus pyogenes* and *S. aureus*. In this case, specifically flucloxacillin was selected in view of the yellow crusting suggesting possible impetigo (usually due to *S. aureus*) and metronidazole was added as anaerobes were grown from the initial swab. The use of flucloxacillin and metronidazole was also advised by HPS anthrax clinical management guidance.¹

Most described cases of soft tissue IA have required surgery with significant debridement and removal of tissue. Although this initial lesion was incised, very little diseased material was identified and removed and the lesion healed well (figure 3). Wound dressings were primarily managed by the practice nurse in the community. Extensive debridement and amputation were not required.

The minority of local IA cases required aggressive surgery, and two patients required no surgery in a local review of cases.⁴ Jallali *et al*⁷ report two further IA cases in London who also required no surgical intervention.

Although initial guidance from HPS was 'to excise affected skin with a >2 cm margin, remove any areas of subdermal fat that appeared altered and to widely excise any needle track identified in muscle', later in the outbreak some surgeons felt this was not necessary in all cases, going on to recommend a more cautious approach as there were concerns that the high mortality being seen in some centres may relate to the radical debridement approach with postoperative haemorrhage that was more difficult to control.⁷

Previous published images of the soft tissue manifestations of IA have been much more severe and disfiguring⁷⁻⁹ which again may be misleading, suggesting that heroin-related anthrax is only associated with severe soft tissue infection.

Some non-antimicrobial agents have activity against anthrax toxins.¹⁰ The patient was not on any of these drugs at presentation, nor were they used in subsequent management and do not explain the milder presentation.

This case was among 47 confirmed cases during the IA outbreak. A review of clinical cases looking at 27 other cases (16 survivors vs 11 non-survivors)⁶ demonstrated features that were

Learning points

- ▶ Distinguishing anthrax from non-anthrax soft tissue infection in addition to clearly differentiating injectional anthrax from cutaneous anthrax is extremely difficult, but crucial, as it may influence the management approach.
- ▶ Anthrax PCR should be performed on appropriate samples from any people who inject drugs where there is a suspicion of anthrax infection such as during an outbreak.
- ▶ Oral antibiotics have a role in anthrax cases with no systemic upset and mild soft tissue infection.
- ▶ Significant surgical intervention is not always required to achieve full resolution of heroin-related anthrax.
- ▶ Recovery from heroin-related anthrax is possible with minimal residual disability, despite being a disease with a high overall mortality.

more common in non-survivors were generalised symptoms on presentation (such as confusion or malaise), sepsis at presentation and need for vasopressors, mechanical ventilation or intensive care unit (ICU) admission. There was no difference found in the requirement for surgery between survivors and non-survivors. Five survivors did not require surgery at all with two requiring antibiotics only and being discharged within 1–2 days. The patient described in this case was systemically well with no sepsis, had minimal debridement and a short admission with antibiotics but no vasopressors, mechanical ventilation or ICU admission.

Overall, this case is useful to illustrate how difficult it is to make a diagnosis of anthrax in a heroin user by clinical appearance alone, let alone definitively distinguish between CA and IA. This case supports evidence that an aggressive approach in terms of intravenous antibiotics and surgical intervention is not always required. Clinical parameters, including mild soft tissue appearance and lack of systemic features and knowledge of the

route of anthrax exposure, may help to identify patients who may recover with a more conservative approach.

Acknowledgements Dr Andrew Todd and Dr Beth White, Department of Infectious Diseases, Monklands Hospital, Airdrie, UK. Dr Tim Brooks, Rare and Imported Pathogens Laboratory (RIPL), Public Health England, Porton Down, UK.

Contributors DI and SS were involved in the patients initial presentation. AC, HB and DI were involved in the readmission. DI and HB produced the case report and discussion.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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