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Post viper bite *Pasteurella multocida* necrotizing fasciitis complicates with septicaemia and renal failure

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Abstract. Necrotizing fasciitis is a rare, severe and rapidly progressive life-threatening clinical disease which is commonly caused by streptococci. However, the disease caused by *Pasteurella multocida* is infrequently reported. Here, we report a rare case of a 85-year-old Malay man who developed septicaemia secondary to necrotizing fasciitis post viper bite. *P. multocida* was isolated from pus, tissue and blood cultures. A post viper bite was the only risk factor and to the best of our knowledge, this is the first reported case of *P. multocida* necrotizing fasciitis secondary to viper bite.

INTRODUCTION

Necrotizing fasciitis is a life-threatening, invasive, soft tissue infection which primarily involves the superficial fascia and subcutaneous tissue which results in loss of the cutaneous microcirculation and tissue. It is associated with widespread fascial necrosis with relatively sparing of the skin and underlying muscle (Dworkin *et al.*, 2009). Clinically, it manifests as local pain, fever, and systemic toxicity and is often fatal.

The common infective cause of necrotizing fasciitis is known to be streptococococci. *Pasteurella multocida*, a small, Gram-negative coccobacillus and often with bipolar staining is rarely being reported as the causative agent. It is a fastidious organism and can be found in the normal flora of the nasopharynx and gastrointestinal tract of both domestic (such as cats, dogs, and rabbits) and wild animals (such as snakes and monkeys) and birds. Human transmission generally occurs *via* animal bites and scratches and via exposure to animal secretions (Von *et al.*, 2007).

Elapid bites such as viper bites rarely cause secondary bacterial infection. The infections after envenomation have been due to a range of organisms which includes *Staphylococcus aureus* and *Escherichia coli* (Kerrigan, 1991; Garg *et al.*, 2009).

In a-five-year retrospective study from 2006 until 2010, 20% of the snake bites cases were due to viper bites. Of all viper bites, 27% of cases manifest as severe presentation which described as clinical evidence of systemic poisoning that potentially can be fatal. Wound infection secondary to venomous snake bites were uncommon which only contributed about 5% of cases (Chew *et al.*, 2011).

Here, we report a rare case of an elderly man who developed of the necrotizing fasciitis right hands as a result of secondary *P. multocida* infection whereby the viper bite as the only risk factor.

Case Report

A 85- year- old Malay man, no known medical illness, was referred to an orthopedic team for sudden and progressive right hand swelling and pain for three days. He also complained of inability to move his right wrist joint due to the swelling and pain. Further history discovered that he had a snake (viper) bite on the affected hand five days prior to admission.

No house hold pets or cattle around the residence of the patient and no contact with other animals had been described by the patient. Patient also had seen a general practitioner on the same day he was bitten. He was then given pain killer and had a wound dressing. No antibiotic was given.

During admission, he appeared pink, mildly dehydrated, in pain but not in respiratory distress. He had low grade fever (37.5°C), and transiently hypotensive but responded to fluid resuscitation. Local examination revealed tense swelling of proximal phalanges of right hand extended proximally to middle third of the forearm, accompanied with tenderness, warmth, shiny skin and inability to flex the wrist joint. However, the local circulation was still intact and good. Other systemic review was unremarkable. No anti venom was given.

Empirical antibiotic was antibiotic with ampicillin-sulbactam 1.5g twice daily was commenced immediately and given for 1 week. Two pairs of blood cultures were collected prior to antibiotic therapy. Incision and drainage (I&D) was performed under local anaesthesia within 24 hours of admission. About 50 cc of pus with slough was removed. Pus and tissue samples from debrided areas were sent for culture and sensitivity.

The initial full blood count showed normal total white cells count (10.4x 10^9/L). However, on the same day, his condition worsened, whereby he developed metabolic acidosis with acute renal injury secondary to septicaemic shock. His was transferred to ICU, whereby he was electively intubated for severe metabolic acidosis. Inotrope was started for circulatory support, several blood products were transfused to correct coagulopathy and he underwent hemodialysis for acute renal injury.

On day two of admission, the total white cells count was rapidly increased up to 21.6x 10^9/L. Patient had anaemia and worsened from 9.9 to 8.0x10^9/L.

Laboratory investigations also showed patient was dehydrated and on acute renal failure with high urea and creatinine levels with 26.1mmol/L and 361umol/L respectively. However, the sodium level was slightly low and potassium level was normal.

Two days later, after his condition was stabilized, wound debridement was done under general anesthesia. Intra-operatively, the wound was associated with deep intra-muscular abscess of extensor compartment muscle of the right forearm.

After surgical debridement, his general condition improved tremendously. The patient was successfully extubated two days later and transferred to orthopedic ward. He had no longer required renal dialysis as his renal function improved gradually.

Microbiological investigations

Cultures from pus, tissue and blood showed gram negative cocobacilli microscopically. The isolate was able to grow on blood agar, Mac Conkey agar and chocolate agar. The colonies were mucoid. On further identification by Vitek 2, *P. multocida* was identified with 98.5% detection rate.

The isolate was sensitive to all antibiotics tested by disc diffusion method which includes amikacin, ampicillin, augmentin, cefepime, cefoperazone, cefotaxime, ceftazidime, cefuroxime, ciprofloxacin, gentamicin, imipenam, meropenam, ertapenam, doripenam and tazocin.

Empirical intravenous ampicillin-sulbactam was changed to intravenous cefuroxime 750mg three times daily for 12 days. Wound healing progressed well and he was discharged home with proper wound care and physiotherapy of the hand. A month later, split skin graft was done to cover big wound area over patient's hand and forearm.

DISCUSSION

Necrotizing fasciitis (NF) is rarely caused by *P. multocida*. Generally, *P. multocida* commonly cause wound infection. However, under certain conditions, complication such as cellulitis, abscess, necrotizing fasciitis, sepsis or osteomyelitis can happen which had been reported previously.

More than 50% of NF cases were polymicrobial infection. Most commonly cultured organism, either as part of a polymicrobial organisms or monomicrobial infection, were streptococcal species followed by group A streptococcus (GAS) (Dworkin *et al.*, 2009). Polymicrobial necrotizing fasciitis is usually caused by enteric pathogens, whereas monomicrobial necrotizing fasciitis is usually due to skin flora (Ronald *et al.*, 1996).

Animal bites account for 1% of all emergency department visits, and mostly related to dog bites which account 80% of cases. In cat and dog bites *Pasteurella* species are the most common isolates and also often include *S. aureus*, *Bacteroides tectum*, and *Fusobacterium*, *Capnocytophaga*, and *Porphyromonas* species. In determining the route of administration of the antibiotics whether oral or parenteral, it will depend on several factors such as the depth and severity of the wound and also the time when the bite occurred (Steven *et al.*, 2005).

Infections related to animal bites are often polymicrobial, such as in dog bites, it is predominantly *Pasteurella* spp. and *Bacteroides* spp. The infection usually appear less than 12 hours after injury particularly if infected with *Pasteurella* spp. and in cases whereby the infected bites appear more than 24 h after the event, are likely to be infected mainly with staphylococci or anaerobes (Dryden, 2009). To the best of our knowledge, none of the post viper bites cases which complicates with NF have isolated *P. multocida*.

Specifically for snake bites cases, *S. aureus* (32%) has contributed the most followed by *E. coli* (15%). In contrast with other animal bites cases, monomicrobial infections were more frequent than polymicrobial infections (Garg *et al.*, 2009).

The possible risk factors have been described have more frequently occurred in diabetics, alcoholics, immunosuppressed patients, intravenous drug users, and patients with peripheral vascular disease (Ronald *et al.*, 1996; Morgan, 2010).

The pathogen will be introduced initially into the subcutaneous space which occurs via disruption of the overlying skin or by hematogenous spread from a distant site of infection. Tissue damage and systemic toxicity occur as result from the release of endogenous cytokines and bacterial toxins (Ronald *et al.*, 1996; Morgan, 2010).

Generally, the oral bacterial flora of various snakes and their venom has revealed a mixture of both aerobic and anaerobic bacterial species. Studies of the oral floral bacteriology of Chinese cobras, bamboo pit vipers, and Malayan pit vipers have yielded a various aerobic and anaerobic organisms, for instance coagulase-negative staphylococci, *Proteus* species, *Morganella morganii*, *Aeromonas hydrophila*, *Enterococcus faecalis*, and *Clostridium* species (Abrahamian & Goldstein, 2011).

In a study, venom and oropharyngeal swabs from Malayan pit vipers (*Calloselasma* rhodostoma) in southern Thailand and captive specimens in England were cultured. The result showed a wider range of organisms than their venoms, especially gut-related Gram negative rods such as *Enterobacter* spp. and *Pseudomonas* spp. and some staphylococci and clostridia (Theakston *et al.*, 1990). From our literature review, *P. multocida* has not been described to be part of normal flora in snakes. With regards to this case, we postulate that the possible source of *P. multocida* could be from the prey of the snake. The snake possibly had harbored *P. multocida* accidently from its prey, particularly rodents as the main source of its diet. Rats have been found to be colonized by *P. multocida* in its oropharynx with about 14% rate of colonization (Chen *et al.*, 2002).

The aim of therapy is to reduce mortality and morbidity as the major complication (Childers *et al.*, 2002). The gold standard in managing NF includes the administration of intravenous abroad-spectrum antibiotics

coverage, surgical debridement, and supportive care in an intensive care unit (Leitch *et al.*, 2000). Thus, in achieving this goal, early clinical suspicion and surgery are key to improving survival, and patients with NF need integrated multidisciplinary management, adjusted to the infecting organism(s), the site of infection, and the effects from any toxins produced (Morgan, 2010). With regards to *P. multocida*, antibiotics such as dicloxacillin, cephalexin, erythromycin, and clindamycin are less active for this particular organism. Cephalosporins mainly cefuroxime, cefotaxime, and ceftriaxone are effective against *P. multocida* (Steven *et al.*, 2005).

In terms of prognosis, no specific type of organism or family including *P. multocida* has been described previously to be associated with severity of the disease including the risk of progressing to septicaemia (Dworkin *et al.*, 2009).

In conclusion, *P. multocida* should be considered as one of pathogenic organism that causes secondary bacterial infection in patient post venomous snakes bites which can be fatal. Thus, prompt and accurate clinical assessment of skin and soft tissue infection is crucial in ensuring appropriate early management and improving prognostic rate.

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