CASE REPORT

Septic arthritis and subsequent fatal septic shock caused by *Vibrio vulnificus* infection

Amir Emamifar,¹ Rikke Asmussen Andreassen,¹ Nanna Skaarup Andersen,²
Inger Marie Jensen Hansen²

¹Department of Rheumatology, University Hospital of Odense, Svendborg Hospital, Svendborg, Denmark

²Department of Clinical Microbiology, University Hospital of Odense, Svendborg Hospital, Odense, Denmark

Correspondence to

Dr Amir Emamifar,
emamifar_amir@yahoo.com.au

Accepted 23 September 2015

SUMMARY

Vibrio vulnificus is a rare but potential fatal bacterium that can cause severe infections. Wound infections, primary sepsis and gastroenteritis are the most common clinical features. Septic arthritis caused by *V. vulnificus* is an atypical presentation that has been reported in only two case reports; however, it has not been previously noted in Denmark. The authors report a case of septic arthritis caused by *V. vulnificus* in an immunocompromised patient. The disease progressed to severe sepsis and subsequent death within 10 h of admission.

BACKGROUND

Vibrio vulnificus is a Gram-negative halophilic (salt-requiring) bacillus ubiquitous in estuarine waters of temperate zones and, in warm summer months, as far north as Denmark. *V. vulnificus* may cause serious, life-threatening infection resulting from consumption of raw or undercooked seafood, especially shell fish, or exposing an open wound to contaminated coastal water.¹ Common clinical manifestations are severe distinctive soft tissue infection, including cellulitis with ecchymosis and bullae and/or septicæmia, rather than gastroenteritis.² Furthermore, atypical involvement of other organs, for instance, brain membrane, the peritoneum, endometrium, lung and eye as well as joints, has been infrequently reported in previous studies.^{1–3} Immunocompromised patients and patients suffering from a chronic disease, especially chronic liver disease, have a higher risk of severe infection by this organism.⁴ The clinical picture of primary sepsis is often abrupt onset of chills, fever and nausea, and a deteriorating haemodynamic state, with a mortality rate >50%, including those in whom hypotension developed.^{1,4}

V. vulnificus is diagnosed by laboratory evaluations including cultures of blood, stools and tissue. A previous report by Klontz *et al*⁵ showed that the mortality rate following antibiotic therapy would be lower if treatment started within the first 24 h. As a consequence, appropriate antibiotic therapy should be initiated immediately, if there is a suspicion of infection with *V. vulnificus*. In the event of skin involvement, imminent surgical evaluation is important; debridement of all devitalised tissue or, if necessary, amputation, may be lifesaving. During the summer of 2006, wound infection in bathers was reported in several European countries.⁶

We report a case of a patient, over 80 years of age, with a history of multiple myeloma and colon

cancer, who, in 2006, presented with septic arthritis of the right elbow and subsequent septic shock caused by *V. vulnificus*. The patient died within 10 h of hospital admission and 20 h of symptom onset.

CASE PRESENTATION

In late September 2006, at 19.30, a patient over 80 years of age presented to the emergency department of Svendborg Hospital, Denmark, with a history of acute, severe pain in the right arm and leg. The pain had started in the morning and increased gradually during the day. We did not find any signs of necrotising fasciitis, such as haemorrhagic bullae, subcutaneous bleeding, purpura, necrosis and gangrene. There was no recent history of eating seafood or bathing in the ocean. One year prior to this, the patient was diagnosed with rectum cancer, which was successfully treated by surgical resection of the rectum. In that same year, the patient was also diagnosed with idiopathic thrombocytopenic purpura (ITP) and monoclonal gammopathy of undetermined significance-IgA type (MGUS). These conditions were treated with Zoledronic acid injection once monthly and prednisolone. MGUS transferred into multiple myeloma 3 months later. The multiple myeloma was treated with melphalan 14 mg/day orally and prednisolone 100 mg in repetitive courses of 4 days duration followed by 4 weeks of rest. Two days before admission, the patient stopped the second of these courses. Tapering of prednisolone was still ongoing (75 mg/day at this point in time).

The patient was a farmer and lived on a very small island (area: 1.9 km²) in the Region of Southern Denmark. The farm was located very close to the coast. Although exposure to seawater prior to presenting symptoms was not positively recalled, it was highly probable. There was no history of cigarette smoking or consuming alcohol.

On admission, the patient was awake, alert and oriented with the following vital signs: temperature 36.7°C, blood pressure 117/61 mm Hg, pulse rate 78 bpm and respiratory rate 18 breaths/min. Initially, the right elbow was very painful and the movement of the elbow was described to be normal, but within a few hours, a 30° limitation of extension was found as well as redness and swelling. We did not find any skin lesion over the affected joint. Abdominal examination showed no sign of hepatomegaly. There were no other positive findings on the physical examination.

CrossMark

To cite: Emamifar A, Asmussen Andreassen R, Skaarup Andersen N, *et al*. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-212014

INVESTIGATIONS

Initial laboratory evaluation revealed haemoglobin of 6.9 mmol/L (normal range: 8.0–11.0 mmol/L), leukocytes 7.7×10^9 /L (normal range: $3.0\text{--}10.0 \times 10^9$ /L), myelocytes 0.31×10^9 /L (normal range: $<0.05 \times 10^9$ /L), metamyelocytes 0.31×10^9 /L (normal range: $>0.05 \times 10^9$ /L), thrombocytes 113×10^9 /L (normal range: $120\text{--}400 \times 10^9$ /L), calcium 1.15 mmol/L (normal range: 1.19–1.29 mmol/L), C reactive protein 117 mg/L (normal range: <10 mg/L), alanine aminotransferase 26 U/L (normal range: 10–45 U/L), alkaline phosphatases 40 U/L (normal range: 10–45 U/L), γ -glutamyltransferase 26 U/L (normal range: 15–115 U/L), serum albumin 33 mmol/L (normal range: 22–27 mmol/L) and total bilirubin 29 μ mol/L (normal range <20 μ mol/L). Aspiration of synovial fluid from the right elbow joint showed elevated levels of nucleated cells, leukocytes 840×10^6 /L (normal range: $<200 \times 10^6$ /L). Blood (2 blood collection sets of 2 bottles with 10 mL in each) and synovial fluid were sent to the department of clinical microbiology for Gram stain, culture and susceptibility testing. The synovial fluid's Gram stain visualised numerous Gram-negative rod-shaped bacteria.

Six hours after hospitalisation, the patient's haemodynamics became unstable. The blood pressure fell to 60/30 mm Hg and the patient became febrile with a rectal temperature of 39.3°C. Accordingly, there was difficult and rapid respiration with weak and increased peripheral pulses. Under these circumstances, the patient was admitted to the intensive care unit with a clinical diagnosis of septic shock, and further evaluation was performed. Arterial blood analysis showed metabolic acidosis (pH 7.27, pCO₂ 37.5 mm Hg, pO₂ 43.5 mm Hg, HCO₃ 17 mm Hg). d-Dimer test was performed due to suspicion of pulmonary emboli and the result was negative. Radiographs of the chest were unremarkable.

DIFFERENTIAL DIAGNOSIS

A patient with a red and warm swollen joint is highly suggestive of septic arthritis. Other possible conditions are necrotising fasciitis, erysipelas and deep vein thrombosis, as well as trauma.

TREATMENT

Empiric antibiotic therapy with intravenous cefuroxime 750 mg three times a day was initiated immediately after the joint puncture was performed. Tramadol 50 mg every 8 h was prescribed to reduce the pain. After admission to the intensive care unit, treatment with oxygen, fluid resuscitation and daily dose of dalteparin 25,000 anti-Xa was started. Owing to the patient's general condition, deterioration and insufficient response to the initial therapy, cefuroxime was discontinued and replaced with intravenous meropenem 1 g three times a day. In addition, dobutamine 3–10 mL/h was initiated to support blood pressure.

OUTCOME AND FOLLOW-UP

Four hours after starting treatment with meropenem, cardiopulmonary arrest occurred. Early resuscitation was started, however, it was unsuccessful. Results of microbiological findings revealed the presence of *V. vulnificus* in 4 of 4 bottles of blood culture and in the joint culture. Antimicrobial susceptibility testing of blood and joint fluid demonstrated that the bacterium was resistant to cefuroxime and susceptible to meropenem (table 1).

DISCUSSION

V. vulnificus is a rare, Gram-negative bacterium that can cause serious infection, including primary sepsis, in patients with

Table 1 Results of antimicrobial susceptibility testing

Antimicrobial susceptibility test results	
Penicillin	R
Erythromycin	S
Ampicillin	R
Gentamicin	S
Ciprofloxacin	S
Cefuroxime	R
Meropenem	S

R, resistant; S, susceptible.

underlying diseases. The mortality rate is higher than 50% in the presence of sepsis. In these patients, presenting features include: fever, haemodynamic instability and possible subsequent death.^{1 7 8} Patients presenting with gastrointestinal symptoms or wound infections have a comparatively lower risk of mortality.¹ A previous study by Shapiro *et al*⁹ showed that the mortality rate among cases with wound infection and gastroenteritis, are 17% and 9%, respectively. Gastroenteritis syndrome caused by *V. vulnificus* presents with abdominal pain and other accompanying symptoms such as nausea, vomiting and diarrhoea.¹

Diagnosis can be made by careful history-taking, physical examinations and laboratory evaluation, including cultures of blood, tissue and stools. Radiological findings are usually non-specific, however, these findings may help to exclude other conditions.^{1 7 8 10} The most common microbiological agents of soft tissue and septic arthritis are *Staphylococcus aureus* and *Streptococcus pyogenes* (also known as group A *Streptococcus*, GAS), susceptible under normal conditions to cefuroxime.^{7 11 12} In the case presented, there was no history of bathing in the ocean or consuming raw or undercooked seafood, and the lesion at the elbow did not present with the characteristics of *V. vulnificus* infection, therefore the initial empiric treatment with cefuroxime was, even in hindsight, rational.

It is important to diagnose sepsis immediately, since delay in initiation of appropriate antibiotic therapy may cause higher mortality.^{5 8 10} *V. vulnificus* is typically susceptible to a wide range of antibiotics. Treatment recommendations for Vibrio infections include tetracyclines (doxycycline, tetracycline), fluoroquinolones (ciprofloxacin, levofloxacin), third-generation cephalosporins (cefotaxime, ceftazidime, ceftriaxone), aminoglycosides (amikacin, apramycin, gentamicin, streptomycin) and folate pathway inhibitors (trimethoprim-sulfamethoxazole).^{1 10 13} The US Centres for Disease Control and Prevention (CDC) suggests treatment of *V. vulnificus* infections in adults to include doxycycline (100 mg orally/intravenously every 12 h for 7–14 days) plus a third-generation cephalosporin (eg, ceftazidime 1–2 g intravenously/intramuscularly every 8 h), although they state that monotherapy regimens employing a fluoroquinolone have been reported to be at least as effective in an animal model as combination drug regimens with doxycycline and a cephalosporin.⁸ Northern Europe does not follow the same tradition of empiric combination therapy regimes when treating *V. vulnificus*. In Denmark, a single agent regime using fluoroquinolone is usually considered sufficient as empiric treatment of *V. vulnificus*. Depending on the severity of the infection, a combination with an aminoglycoside could be considered, but, to the best of our knowledge, there are no joint European or even Danish recommendations. In patients presenting with severe soft tissue infection, surgical intervention should be considered, whereas

Table 2 Characteristics of septic arthritis caused by *Vibrio vulnificus*; review of previous cases together with our case^{3 15}

	Age, years	Alcohol/tobacco	Location of infection	Medical history	History of eating seafood or bathing in the ocean	Outcome
Case 1 (present case)	>80	No	Right elbow	Rectum cancer Multiple myeloma	No	Expired due to septic shock
Case 2	59	Alcohol 10/15 g/day 2 packs/day	Right wrist	Hypertension Diabetes Gout	Yes	Expired due to septic shock
Case 3	9	No	Right knee	β-Thalassaemia major Chronic haemosiderosis	Yes	Expired due to septic shock

antibiotic therapy alone is not usually effective.^{1 8} *V. vulnificus* can be significantly prevented by not consuming undercooked or raw seafood, especially oysters, and avoiding exposure of open wounds to coastal waters.^{7 8}

Only a few cases of *V. vulnificus* have been reported in Denmark.^{10 14} A previous study by Dalsgaard *et al*¹⁴ described that, of 11 patients diagnosed with *V. vulnificus* infection in Denmark, 4 presented with primary sepsis and 9 patients, including the 4 with primary sepsis, presented with wound infection. None of the patients had gastrointestinal symptoms. One of the patients died because of severe sepsis. Exposure to coastal waters during a warm summer was the only source of contamination. Johnson *et al*³ and Kuo *et al*¹⁵ reported two different cases of *V. vulnificus* presenting with septic arthritis as an atypical manifestation (table 2). Both patients were immunocompromised and initially presented with septic arthritis.

We report a rare case of septic arthritis that, as an atypical manifestation caused by *V. vulnificus*, in <10 h after admission to the hospital, progressed to severe sepsis and subsequent death. In conclusion, infection with *V. vulnificus* as a differential diagnosis of septic arthritis should be taken into consideration, especially during a warm summer. Precise patient history with attention to recently consumed food, exposure to coastal waters and immunocompromised hosts, especially those with cirrhosis or underlying liver disease, may lead to the diagnosis. To the

best of our knowledge, there are only two reports in the English literature, of *V. vulnificus* causing septic arthritis.

Contributors IMJH made a substantial contribution to the conception of the work. IMJH and NSA were involved in diagnosis and management of the patient. IMJH, AE, RAA and NSA were involved in data collection and interpretation and in drafting and reviewing the manuscript. IMJH, AE, RAA and NSA gave final approval of the version to be published.

Competing interests None declared.

Patient consent Not obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Horseman MA, Surani S. A comprehensive review of *Vibrio vulnificus*: an important cause of severe sepsis and skin and soft-tissue infection. *Int J Infect Dis* 2011;15:157–66.
- 2 Daniels NA. *Vibrio vulnificus* oysters: pearls and perils. *Clin Infect Dis* 2011;52:788–92.
- 3 Johnson RW, Arnett FC. A fatal case of *Vibrio vulnificus* presenting as septic arthritis. *Arch Intern Med* 2001;161:2616–18.
- 4 Linkous DA, Oliver JD. Pathogenesis of *Vibrio vulnificus*. *FEMS Microbiol Lett* 1999;174:207–14.
- 5 Klontz KC, Lieb S, Schreiber M, *et al*. Syndromes of *Vibrio vulnificus* infections. Clinical and epidemiologic features in Florida cases, 1981–1987. *Ann Intern Med* 1988;109:318–23.
- 6 Andersson Y, Ekdahl K. Wound infections due to *Vibrio cholerae* in Sweden after swimming in the Baltic Sea, summer 2006. *Euro Surveill* 2006;11:E060803.2.
- 7 Bross MH, Soch K, Morales R, *et al*. *Vibrio vulnificus* infection: diagnosis and treatment. *Am Fam Physician* 2007;76:539–44.
- 8 Centers for Disease Control and Prevention. *Vibrio* illness (vibriosis). 2013. . <http://www.cdc.gov/vibrio/vibriov.html> (accessed 30 Jun).
- 9 Shapiro RL, Altekruze S, Hutwagner L, *et al*. The role of Gulf Coast oysters harvested in warmer months in *Vibrio vulnificus* infections in the United States, 1988–1996. *Vibrio Working Group. J Infect Dis* 1998;178:752–9.
- 10 Theede K, Pfeiffer P, Skovbjerg H. Septic shock after exposure to *Vibrio vulnificus*. *Ugeskr Laeger* 2008;170:1849.
- 11 Vinh DC, Embil JM. Rapidly progressive soft tissue infections. *Lancet Infect Dis* 2005;5:501–13.
- 12 Swartz MN, Pasternack MS. Cellulitis and subcutaneous tissue infections. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Bennett, and Dolin: principles and practice of infectious diseases*. 6th edn. Philadelphia, PA: Elsevier Churchill Livingstone, 2005:1172–94.
- 13 Daniels NA, Shafae A. A review of pathogenic vibrio infections for clinicians. *Infect Med* 2000;17:665–85.
- 14 Dalsgaard A, Frimodt-Møller N, Bruun B, *et al*. Clinical manifestations and molecular epidemiology of *Vibrio vulnificus* infections in Denmark. *Eur J Clin Microbiol Infect Dis* 1996;15:227–32.
- 15 Kuo CH, Dai ZK, Wu JR, *et al*. Septic arthritis as the initial manifestation of fatal *Vibrio vulnificus* septicemia in a patient with thalassemia and iron overload. *Pediatr Blood Cancer* 2009;53:1156–8.

Learning points

- ▶ *Vibrio vulnificus* is a rare cause of septic arthritis and subsequent sepsis.
- ▶ Immediate joint puncture should be performed before starting antibiotic treatment.
- ▶ Precise patient history and characteristic skin lesions in combination with cultures of blood, tissue, stools and joint fluid, if there is suspicion of septic arthritis, can lead to diagnosis.
- ▶ Antibiotic therapy should be initiated immediately.
- ▶ In the event of skin involvement, imminent surgical evaluation is important.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow