

Case study

VIBRIO FLUVIALIS– UNUSUAL CASE OF CELLULITIS LEADING TO SEPSIS

Comment [HG1]: *Vibrio fluvialis*– use scientific name

Comment [HG2]: After this, please add author's name, affiliation and corresponding author's name and address.

ABSTRACT

Vibrio fluvialis, an enteric, Gram-negative bacterium which can be isolated from dirty sewage/ sea water contaminated with human and animal's faeces. Infections with this unusual organism can cause cholera like bloody diarrhea and also wound infection. Here is a case report of skin and soft tissue infection due to *Vibrio fluvialis* in patient having severe pedal oedema due to nephrotic syndrome and right lower limb deep vein thrombosis.

Comment [HG3]: Rewrite this sentence. It's complex and at the same time meaning does not reveal properly. You can say; The objective of this case report is to analyse the skin and soft tissue infection caused by

Case report: A young male, farmer, presented having with ascites, pedal oedema, and puffy face due to nephrotic syndrome. He developed skin and soft tissue infection resulted from skin atrophy and ulcer due to pedal oedema and right limb deep vein thrombosis. He had high grade fever, leucocytosis, anaemia, hypoproteinemia, right leg cellulites and features of sepsis requiring wound debridement. He was not on steroids and was not immuno-deficient. He was diagnosed to have Nephrotic syndrome due to minimal change disease.

Comment [HG4]: Mention the age

Comment [HG5]: You're using a lot of due to. Please use appropriate synonyms

Comment [HG6]: The symptoms of skin and soft tissue infection were

Comment [HG7]: Degree?

Conclusion: *Vibrio fluvialis* infection can occur due to wound contaminated with sewage water resulting into life threatening skin and soft tissue infection and sepsis.

Comment [HG8]: Is it a disease?

Comment [HG9]: You did not mention anything about how you find that *V. fluvialis* is the causative agent of this infection? You did Koch's postulate? Or Isolate this pathogen from the infected tissues?

Key words: *Vibrio fluvialis* infection, skin and soft tissue infection, sepsis, Nephrotic-nephrotic syndrome

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INTRODUCTION

Vibrio fluvialis is an emerging infectious disease causing pathogen.^[1]

It is one of the pathogens posing potentially a serious threat to public health, due to multi-drug resistance and clinically challenging infections.^[2]

The emerging pathogenic species of many bacteria have been posing serious threat to public health. There is complex interaction between environmental factors and industrialized world. In developing nations like India, waterbodies are contaminated with sewage water, cattle manure, household and industrial waste effluents. These waterbodies serve as raw water sources to municipal water treatment systems.^[3] Water contaminated with animal, human faeces and sewage have been identified as potential sources of pathogenic bacteria.^[4]

Vibrio fluvialis is an emerging pathogen of marine milieu, which flourishes when temperature (warm) and salinity favours its proliferation.^[5] It has become medically important pathogen as it has been found to cause illnesses like cholera and rarely skin infections, which are very challenging for clinicians to treat.^[2] It has not just been found as a free living bacteria but also attached to various biotic and abiotic structures.^[6] This complex property of forming biofilm contributes to its survival against environmental stressors.^[6,7] As such *vibrio* species can survive for a long time and adapt well to common stressors encountered in natural ecosystem like lack of nutrients, by changing their cell physiology and morphology.^[7,8] There is a state called viable but non culturable (VBNC) where some bacterial species adapt strategies under stressful conditions from which these can recover themselves when optimal conditions are restored.^[8,9] Such state has been observed in many *vibrio* species including historically important human disease causing pathogens like *V. cholerae*, *V. parahaemolyticus* and *V. vulnificus*.^[9] Similar mechanism has been observed in this unusual and less studied pathogen, *V. fluvialis*, which can maintain its virulence under hostile conditions and still be

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pathogenic to humans.^[10] *V. fluvialis* related illnesses includes gastroenteritis, cellulitis and primary septicaemia.^[11] There have been identifiable host factors that can predispose to development of serious infection with this bacterium, which includes alcoholic liver disease, immunocompromised states like HIV/AIDS, diabetes, iron overload and primary immunodeficiencies.^[11]

We are reporting an unusual case of young male having nephrotic syndrome, deep vein thrombosis of leg and skin and soft tissue infection caused by *V. vibrio-fluvialis* leading to sepsis.

CASE REPORT

A 21 year- old male, farmer by occupation with no comorbidities presented with complaints of generalized abdominal pain with distension associated with facial puffiness and bilateral pedal edema since the past 2 months and recent onset of right lower limb pain with bullae initially and later becoming necrotic and associated with high grade fever. Patient was admitted with clinical diagnosis of nephrotic syndrome with cellulitis. He denied any history of addictions, prior hospitalizations and relevant past medical history.

The patient appeared sick on examination, was febrile had tachycardia, hypotension and tachypnea. He was cooperative, conscious and oriented to time, place and person. Pallor was observed, so was grade 3 pitting pedal oedema. There was moderate ascites with grade II splenomegaly and pleural effusion. His right lower limb was painful, discoloured and tense without regional lymphadenopathy. The cellulitis was rapidly progressive from mere swelling to formation of bullae and tissue necrosis within 24-36 hours (Figure 1 and 2).

On laboratory investigation, following were yielded - haemoglobin 11.4 g/dl, total count – 18000/cu.mm (93% neutrophils), ~~e~~Erythrocyte sedimentation rate – 90 mm/hr, C- reactive protein – 108 mg/dl, serum albumin 2.0 mg/dl. Urinalysis revealed foamy urine with specific gravity of 1.016, albumin 4+, and few fatty casts were seen on urine sediment. 24 hour urinary proteins was 4.7 grams.

Comment [HG13]: This sentence is not clear

His lipid profile was deranged with hypercholesterolemia and hypertriglyceridemia. Rest of the routine blood investigations including renal function tests were within normal. He was tested negative for HIV, hepatitis B, C and Syphilis. RT-PCR for COVID 19 was done and found negative. Haemoglobin electrophoresis was done and didn't reveal any hemoglobinopathy. Abdominal ultrasonography revealed mild splenomegaly and moderate ascites. Bilateral moderate pleural effusion was seen on chest x-ray and chest sonography. The right lower limb arterial and venous doppler was done which was suggestive of subcutaneous oedema with partial thrombosis of saphenous vein. ECG and 2-D Echocardiography was normal. Antinuclear antibody (ANA) test and ANA profile was unremarkable.

The total leukocyte counts raised to 30,000 /cu mm on day 3 of admission and patient had continuous high grade fever with hypotension. He had septic shock with metabolic acidosis. Empiric para-arterial antibiotic was started on admission which included linezolid and meropenem. Blood cultures were sent. Surgical debridement of the foot was done and tissue specimen was sent for culture. Blood cultures showed no growth until day 7 and was considered negative. Tissue culture showed gram negative rods identified as *V. ~~ibrio~~ fluvialis* sensitive to gentamicin and doxycycline. The antibiotics were switched as per antibiogram report. Patient was also given injectable human albumin 20% as infusion. He kept deteriorating with until day 10 (Figure 3-5). Dressing was done daily and the wound healing was observed closely. There was significant reduction in the edema and development of granulation tissue at the wound site by day 15. He recovered from septic shock and total leukocytes counts started falling (10,000 by day 17). He was discharged by day 25 after recovering from sepsis with healing wound.

Comment [HG14]: To where for what?

Comment [HG15]: You can add a figure with Gram-staining and other bacterial characterization tables or API kit figures.

Comment [HG16]: How did you identify? Better you explain a bit about the bacterial identification – i.e. colony morphology, biochemical tests



Figure 1&2 : day 1-3 :Rapid necrosis of tissue.

Comment [HG17]: Group all your figures into single figure, give a title (i.e. Infection stages of *Vibrio fluvialis*) and label the individual figures from A-E and write the signs and symptoms in the legend.

Comment [HG18]: Use arrow heads to show where actually the necrosis found?



Figure 3- day 4- progression of infection



Figure 4 : Day 7 – Granulation tissue



Figure 5:Day 10 - Post debridement

DISCUSSION

The skin and soft tissue infections are more commonly caused by Gram-positive organisms like staphylococci and streptococci which are part of skin and mucous membrane flora.^[12] Most of these infections are minor in nature but may progress to complicated infection leading to tissue necrosis and sepsis when other underlying risk factors are present such as diabetes mellitus and immunodeficient states.^[12,13] It becomes highly challenging to differentiate which of these patients require immediate and surgical management. The affected area becomes dysfunctional and depending on comorbidities the infection can progress rapidly, may develop sepsis which can lead to death ~~also~~.^[13,14]

Comment [HG19]: What is the point of saying this here? Because Vibrio is gram negative.

In case presented above, the patient was non-diabetic, non-alcoholic individual with nephrotic syndrome and peripheral venous thrombosis in right lower limb with secondary cellulitis by a rare unusual pathogen. *Vibrio* species are a rare cause of necrotizing soft-tissue infections and primary sepsis, which are likely to occur in patients with hepatic disease, diabetes, adrenal insufficiency, and immunocompromised conditions.^[2] Among them, most important ~~vibrio~~ *Vibrio* spp which causes skin and soft tissue infection which often require debridement and amputation are *Vibrio fluvialis* and *V. ~~ibrio~~ vulnificus*. *V. fluvialis* is associated with gastroenteritis and cholera like illness and among extra-intestinal infections, it has been found to cause haemorrhagic cellulitis, cerebritis, peritonitis and primary septicaemia.^[15] Acute gastroenteritis which rapidly progresses to shock in 4 to 24 hours, whereas cellulitis which rapidly causes local tissue necrosis associated with haemorrhagic bullae, further causing obliterating vasculitis and vascular necrosis requiring tissue debridement.^[15] *V. fluvialis* associated cellulitis can occur when an abraded area of skin is inoculated by bathing in marine waters where this bacteria thrives.^[16] As it has been documented that the prevalence of this bacteria is high in aquatic realm, the exposure to its infection in our patient could have been during farming practices where dipping feet in water is required.

Very few cases have been reported around the world, most have been from Asian and developing countries and having the history of exposure to marine environment and having chronic illness or in an immunocompromised state. Majority of the cases required tissue debridement/amputation and inotropic support. As in our case described above, patient had immunodeficient state with hypercoagulability due to loss of proteins in urine secondary to nephrotic syndrome. Huang Kuo-Chin and Wen-Wei Hsu R, reported a case of *vibrio fluvialis* in a 45-year-old male following exposure to brackish water causing haemorrhagic cellulitis and cerebritis which required amputation and causing death even after aggressive management.^[15] Another case of 47 years old Asian fisherman

Comment [HG20]: Things discussed in introduction seemed like repeated in discussion too. Avoid it.

reported by Tsai Yao-Hung et al in known case of Hepatitis B infection with exposure to sea water on an open wound who presented with swelling and bullae of lower limb, which progressed to tissue necrosis and an above knee amputation was performed to save the patient.^[16] Our patient had non haemorrhagic bullae on admission and which rapidly progressed to tissue necrosis and required debridement. We managed the sepsis in our patient aggressively with multiple tissue debridements, and timely initiation of tissue culture sensitive antibiotics, which perhaps helped in containment of the infection and controlling sepsis.

A retrospective study of 13 patients done by Tsai Y. *et al* on systemic vibrio infection presenting as necrotising fasciitis and Sepsis revealed that all of these patients had history of contact with sea water or raw sea food and all of them had one or other comorbid conditions like cirrhosis, ~~Diabetes-diabetes~~ mellitus and chronic kidney disease.¹² Twelve patients required tissue debridement or limb amputation with death in 5 patients. The risk factors identified for high mortality included low systolic blood pressure and leucopenia on admission.^[17] In our case our patient denied exposure to sea water and marine life and he was vegetarian by diet, and most possible exposure is from the water used for agricultural purposes contaminated with ~~vibrio~~ *Vibrio*.

These bacteria are thermostable and have hemolysin as virulent factor. It was found by Han et al. (year) that hemolysin from *V. fluvialis* forms pores in membranes of erythrocytes inducing osmotic lysis.^[18] Their strategies against starvation helps them survive for long term in sea water indicating that these species are endemic in marine environment and can infect marine hosts when conditions are favourable to them.^[19]

Antimicrobial resistance is commonly reported in ~~vibrio~~ *Vibrio* species. Culture report of this cited case had *V. fluvialis* resistant to meropenem, cephalosporins and other beta-lactams. The *V. fluvialis* species isolated from diarrheal patients in Kolkata were resistant to fluoroquinolones and beta-lactams. It was due to mutations of quinolone resistance-determining region (QRDR) of *gyrA*.^[20]

Comment [HG21]: Cite!

Comment [HG22]: What hosts? Fish?

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We treated our patient with doxycycline and gentamicin. The empirical antibiotic of choice can be debated as this pathogen has multiple resistance patterns. Injectable doxycycline 100 mg 12 hours apart has been recommended by Haq and Dayal (year) in cases with high index of suspicion, though it is never a choice for empirical therapy for sepsis treatment guidelines.^[21]

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This concise case report aims at providing knowledge regarding such emerging pathogens and diseases caused by them, as there is paucity of literature and reported cases about these pathogens. Also it highlights the importance of early debridement, early cultures and early introduction of appropriate antibiotics as per the sensitivity and supportive care will significantly reduce the mortality of patients.

CONCLUSION

V. ~~ibrio~~Fluvialis causing skin infection and sepsis is uncommon with very few cases reported worldwide. In cases of rapid progression of the symptoms leading to tissue necrosis and haemodynamic instability in comorbid patients, must consider and evaluate for Gram-negative sepsis due to such *~~vibrio~~Vibrio* species.

REFERENCES

Comment [HG26]: Your references need to be formatted in a particular style. THE journal name must be in italics. Check the scientific names to be in italics.

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