

# ***VIBRIO FLUVIALIS* – UNUSUAL CASE OF CELLULITIS LEADING TO SEPSIS**

## **ABSTRACT**

*Vibrio fluvialis*, an enteric, Gram negative bacterium commonly isolated from sewage/ sea water contaminated with human and animal's faeces. Infections with this unusual organism can cause cholera like bloody diarrhoea and also wound infection. *Vibrio fluvialis* causing skin infection and sepsis is uncommon with very few cases reported worldwide. It is an emerging pathogen with distinct features as compared to the other species of *Vibrio* group of bacteria in terms of high virulence and adaptability in hostile environments. Here is a case report of skin and soft tissue infection by *Vibrio fluvialis*, in a patient suffering from severe pedal oedema due to nephrotic syndrome and right lower limb deep vein thrombosis .

Case report: A young male, farmer, presented with ascites, pedal oedema, puffy face due to nephrotic syndrome. He developed skin and soft tissue infection resulted from skin atrophy and ulcer due to pedal

oedema as well as right limb deep vein thrombosis .He had high grade fever, leucocytosis, anaemia, hypoproteinaemia, right leg cellulites and features of sepsis requiring wound debridement .

Immunodeficiency and corticosteroids associated immunosuppression were absent in this patient.He was diagnosed with nephrotic syndrome due to minimal change disease.

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

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

## INTRODUCTION

*Vibrio fluvialis* is an emerging infectious disease-causing pathogen.<sup>[1]</sup> It is one of the pathogens posing potentially a serious threat to public health, due to multi-drug resistance and clinically challenging infections.<sup>[2]</sup>

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.<sup>[3]</sup> Water contaminated with animal, human faeces and sewage have been identified as potential sources of pathogenic bacteria.<sup>[4]</sup>

*Vibrio fluvialis* is an emerging pathogen of marine milieu, which flourishes when temperature (warm) and salinity favours its proliferation.<sup>[5]</sup> 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.<sup>[2]</sup> It has not just been found as a free living bacteria but also attached to various biotic and abiotic structures.<sup>[6]</sup> This complex property of forming biofilm contributes to its survival against environmental stressors.<sup>[6,7]</sup> 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.<sup>[7,8]</sup> 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.<sup>[8,9]</sup> Such state has been observed in many vibrio species including historically important human disease causing pathogens like *V.cholerae*, *V.parahemolyticus* and *V.vulnificus*.<sup>[9]</sup> 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 pathogenic to humans.<sup>[10]</sup> *V.fluvialis* related illnesses includes gastroenteritis, cellulitis and primary septicaemia.<sup>[11]</sup> 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.<sup>[11]</sup>

We are reporting an unusual case of young male having nephrotic syndrome, deep vein thrombosis of leg complicated by skin and soft tissue infection caused by *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 high grade fever associated with right lower limb pain and bullous skin lesions which later became necrotic ( Figure 1) . Patient was admitted with clinical diagnosis of nephrotic syndrome with cellulitis. He denied any recent and remote medical illnesses and past hospitalizations. He didn't have any addictions

The patient appeared sick on examination, was febrile with tachycardia, hypotension and tachypnoea. 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), 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 were 4.7 grams.

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 paraentral 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. Local site culture of the tissue showed gram negative rods on primary isolation (Figure 6) which was identified as *Vibrio fluvialis*; differentiated from other vibrio species, by the Vitek ID/AST GNB automated system. Organisms were 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 until day 10 (Figure 3-5). Dressing was done daily, and the wound healing was observed closely. There was significant reduction in the oedema 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.

**FIGURES 1 TO 5 : PROGRESSION OF SKIN LESION FROM BULLOUS TO NECROSIS AND POST DEBRIDEMENT.**

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**FIGURE 1&2: DAY 1-3: RAPID NECROSIS OF TISSUE.**





**FIGURE 3- DAY 4- PROGRESSION OF INFECTION**



**FIGURE 4: DAY 7 – GRANULATION TISSUE**



**FIGURE 5: DAY 10 - POST DEBRIDEMENT**



**FIGURE 6 : colonies on nutrient agar - round, translucent approximately 1-2 mm in diameter**

## 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.<sup>[12]</sup> Most of these infections are minor in nature but may progress to complicated infections leading to tissue necrosis and sepsis when other underlying risk factors are present such as diabetes mellitus and immunodeficient states.<sup>[12,13]</sup> 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, and patient may develop sepsis which can lead to death also.<sup>[13,14]</sup>

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 caused by this 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.<sup>[2]</sup> Among them, most important *vibrio spp* which causes skin and soft tissue infection which often require debridement and amputation are *Vibrio fluvialis* and *Vibrio vulnificus*. *V. fluvialis* is associated with gastroenteritis and cholera like illness and among extra-intestinal infections, it has also been found to cause haemorrhagic cellulitis, cerebritis, peritonitis and primary septicaemia.<sup>[15]</sup> 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 leading to obliterating vasculitis and vascular necrosis which requires tissue debridement.<sup>[15]</sup> *V. fluvialis* associated cellulitis can occur when an abraded area of skin is inoculated by bathing in marine waters where this bacterium thrives.<sup>[16]</sup> 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 of 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 with chronic illness or in an immunocompromised state. Majority of the cases required tissue debridement/amputation and inotropic support. 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<sup>R</sup>, 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.<sup>[15]</sup> Another case of 47 years old Asian fisherman 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.<sup>[16]</sup> 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 debridement, 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.H *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 mellitus and chronic kidney disease. 12 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.<sup>[17]</sup> In our case our patient denied exposure to sea water and marine life and he was vegetarian by diet, and the most possible exposure could have been from the water used for agricultural purposes contaminated with vibrio. Among other extraintestinal manifestations, it has also been found to cause ear infections as reported in Taiwan in 2012 by Chen, Ping-jen, *et al*, in a 40 year old female, who acquired the bacteria after swimming, and presented with purulent exudated otitis<sup>[18]</sup>.

These bacteria are thermostable and have hemolysin as virulent factor. It was found by Han *et al* that hemolysin from *V. fluvialis* forms pores in membranes of erythrocytes inducing osmotic lysis.<sup>[19]</sup> 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.<sup>[20]</sup>

Antimicrobial resistance is commonly reported in vibriospecies. 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*.<sup>[21]</sup>

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 in cases with high index of suspicion, though it is never a choice for empirical therapy for sepsis treatment guidelines.<sup>[22]</sup>

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**

It is highly recommended to suspect *Vibrio fluvialis* in cases of rapidly progressive skin and soft tissue infections leading to sepsis and haemodynamic instability in comorbid patients, and prompt initiation of appropriate antibiotics with debridement can be lifesaving.

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