

***Vibrio alginolyticus* Cellulitis Following Coral Injury**

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Infections associated with marine activities, particularly work or recreation in salt water, present unique diagnostic challenges for the infectious disease practitioner. Those caused by halophilic, non-cholera *Vibrio* species are increasingly being recognized in clinical practice. They typically follow saltwater injuries, especially those associated with coral. Because these infections can be both severe and life-threatening, a consideration of halophilic *Vibrio* species in the differential diagnosis of marine-acquired infections is important. In this case report, we discuss the diagnosis and treatment of cellulitis in a patient with a Caribbean coral injury associated with *Vibrio alginolyticus* cellulitis.

CASE PRESENTATION

DR. THOMAS PATTERSON (*Fellow, Section of Infectious Diseases*): A 65-year-old man was admitted to the Yale–New Haven Hospital with cellulitis of his right leg. His past medical history was unremarkable, but he had recently traveled to St. Thomas, in the Caribbean. Two weeks prior to admission, while sailing there, he slipped on some rocks and injured his right calf. He did not return home but was seen by a local physician who recommended wound dressings; no antibiotics were prescribed. He remained in the Caribbean, but he did not further expose his injured leg to salt water. Approximately one week later, his right calf became erythematous, red, and warm to touch. He experienced no fever, chills, or sweats, but his leg became significantly more painful over the ensuing week. He returned home to Connecticut where he sought medical care because of leg pain and swelling. On presentation to the Yale–New Haven Hospital emergency room, he was afebrile and had a normal physical examination, except for an area of edematous cellulitis on his right calf. The cellulitis extended as far as his knee and was surrounded by erythema, with an area of central necrosis. Laboratory examination on admission revealed a total white blood cell count of 8,700 cells/mm³ with a normal differential count; routine chemistry values were within normal ranges.

A PHYSICIAN: Could you describe the circumstances surrounding the boating injury?

DR. PATTERSON: He was in salt water off St. Thomas, in the U.S. Virgin Islands. He slipped and crushed his leg between a coral reef and the boat.

DR. FRANK J. BIA (*Acting Chief, Section of Infectious Diseases*): A radiograph of the leg would be useful to exclude the possibility of retained coral or some other foreign body.

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Abbreviations: TCBS: thiosulfate-citrate-bile salts VP: Voges-Proskauer

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DR. PATTERSON: A radiograph of the leg was obtained on admission and revealed a small radio-dense object, most likely a piece of embedded coral. There was no soft-tissue gas detected.

So, we are presenting a 65-year-old man with a soft-tissue injury involving salt water and coral two weeks prior to admission. It has progressed to form a large area of cellulitis with central necrosis. Furthermore, a radiograph of the area has shown a retained foreign body.

DR. BIA: What potential causative organisms might we consider in a situation like this?

A PHYSICIAN: It seems to me that the possibilities are broad and very diverse. They include many bacterial species, in addition to mycobacteria and algae. Perhaps a biopsy of the area, including debridement of the foreign body and culture of the specimen, would be helpful.

A PHYSICIAN: Were any bullae present?

DR. PATTERSON: There were no bullae present at the time of admission, and he did not recall any vesicles or bullae earlier in the course of the illness.

DR. VINCENT T. ANDRIOLE: (*Professor of Medicine*): I agree that the differential diagnosis is diverse, but it should also include certain unusual fungi, which are endogenous to that area and fairly innocuous unless introduced by trauma.

I saw a Jamaican man who had an impressive case of chromomycosis caused by *Phialophora verrucosa*, resulting in a chronic infection which was very difficult to treat. It can cause this kind of cellulitis, as either a superficial or deep wound infection; however, it typically causes pedunculated verrucous lesions, which you did not describe in this patient.

DR. BIA: Is that organism found in fresh or salt water?

DR. ANDRIOLE: *P. verrucosa* is a soil organism, and infections have been reported mainly in farm workers from tropical areas. I do not know if he acquired his infection from water or from soil, while he was on the beach.

DR. PATTERSON: This infection was temporally related to the patient's coral injury. After the injury he was careful to keep the lesion bandaged and avoided both soil and saltwater contamination.

A PHYSICIAN: You must consider the possibility of a non-cholera vibrio infection, with particular consideration given to *Vibrio vulnificus*. *Vibrio vulnificus* infection is acquired in salt water and results in cellulitis; however, such infections usually progress rapidly and are more severe than what occurred in this patient.

Because of the broad differential diagnosis, I would debride and culture the tissue in an attempt to identify an organism. In addition, it might be helpful to alert the Microbiology Laboratory regarding the clinical possibilities, so that *Vibrio* species can be quickly identified.

DR. PATTERSON: On the night of admission he was taken for debridement of a large area of tissue. The excised tissue was sent to the Microbiology Laboratory for culture, and he was started on cephalothin, 1 g intravenously every eight hours, and gentamicin, 70 mg intravenously every eight hours.

A PHYSICIAN: Systemic symptoms would be more common with *Vibrio vulnificus* than some other possible organisms. Did he have systemic symptoms?

DR. PATTERSON: He was not systemically ill, but the infection was significant enough to require admission to the hospital. He underwent prompt surgical debridement both because of the obvious necrotic tissue and for identification of a retained foreign body.

Despite both antibiotic therapy and surgery, he did not improve. In fact, the area of necrosis continued to enlarge and erythema persisted. Three days after surgery, plans were made for additional debridement and the Infectious Disease service was asked to see the patient. At that time examination showed an erythematous, tender right calf with the surgical area now surrounded by necrosis and an edge of erythema. Cultures obtained at admission revealed a heavy growth of *Staphylococcus aureus* and a single colony of a gram-negative rod.

DR. BIA: We were interested in his possible *S. aureus* infection, but we also wanted to identify that gram-negative rod. We were actually concerned that it might be a non-cholera *Vibrio* species growing poorly on non-selective media.

DR. PATTERSON: That is correct. Our differential diagnosis at that point included *Vibrio vulnificus*, which would usually be associated with more systemic symptoms, and other non-cholera vibrios, such as *V. alginolyticus* and *V. parahaemolyticus*. The wound was again widely debrided. Antibiotic therapy was changed to doxycycline, 100 mg intravenously every 12 hours for two weeks, and cephalothin, 1 g intravenously every six hours for a total of ten days. The lesion slowly improved.

The organism was identified as *Vibrio alginolyticus* in the following manner. A gram stain revealed curved gram-negative rods indicative of a *Vibrio* species. Based upon its biochemical reactions, this organism was placed in a group which included *V. alginolyticus*, *V. parahaemolyticus*, and *V. vulnificus*. Additional tests were performed to differentiate between these three organisms. Fermentation testing with lactose, salicin, and L-arabinose was negative. Sucrose was fermented. The organism was resistant to colistin, ampicillin, cephalothin, and carbenicillin. A thiosulfate-citrate-bile salts (TCBS) agar was also inoculated, and large yellow colonies grew.

The sugar fermentation test results as well as the resistance to ampicillin and carbenicillin and the growth on TCBS were most consistent with *V. alginolyticus*; however, a negative Voges-Proskauer (VP) reaction and a positive citrate test were more consistent with *V. vulnificus*. Most other reactions were not.

V. parahaemolyticus could not totally be eliminated but was unlikely since only 1 percent ferment sucrose. Additional tests were performed at the Connecticut State Laboratory. The organism had positive reactions for nitrate reduction, catalase, and motility. Esculin was weakly hydrolyzed. The following sugars were not fermented: raffinose, dulcitol, xylose, glycerol, 10 percent lactose, and cellobiose. Acetate utilization was negative. The organism did not grow in 0 percent NaCl or 10 percent NaCl, but did grow in 3.5 percent NaCl and 7.0 percent NaCl. Also, contrary to our citrate test result, theirs was negative, which was more consistent with *V. alginolyticus*.

The final identification was *Vibrio* species most consistent with *V. alginolyticus*. *In vitro* testing showed the organism was susceptible to tetracycline, trimethoprim/sulfamethoxazole, chloramphenicol, and gentamicin. All subsequent wound cultures were negative.

A PHYSICIAN: Did he have osteomyelitis?

DR. PATTERSON: There was no evidence for osteomyelitis on his radiograph, but he eventually required skin grafting to the site of infection.

A PHYSICIAN: Did you have a tissue gram stain of the first necrotic tissue that had been removed?

DR. PATTERSON: No. *V. alginolyticus* is typically characterized as a curved, gram-negative rod which can be either filamentous or round and swollen at the ends, but no such organisms were noted, except in culture.

DR. BIA: I would like to point out that the initial culture contained a heavy growth of *S. aureus*, but on such non-selective media there was a single colony of the gram-negative organism. It was fortunate that the technician in the Microbiology Laboratory worked up that organism, because the antibiotic coverage the patient received initially was not adequate for *Vibrio* spp. I also want to emphasize that in examining the leg, even after debridement, the muscle appeared brown and dusky. In fact, it appeared as if there might be a component of myositis. We were concerned that infection had progressed on the initial antibiotic regimen despite surgery. It looked like more than a *S. aureus* infection.

DISCUSSION

Halophilic, non-cholera *Vibrio* species are increasingly recognized as important intestinal and extra-intestinal pathogens [1–4]. In the United States, this observation is probably related, in part, to increased consumption of raw or undercooked seafood and to increased recreational use of coastal and inland water areas, as well as to increased travel to tropical areas [3]. *V. alginolyticus* requires a halophilic environment to grow in the laboratory and requires sodium chloride to thrive in the natural environment as well [5]. The organism requires at least 0.5 percent sodium chloride and a temperature of at least 10°C. With those minimum requirements, however, it has been isolated from both salt water and brackish inland water. *V. alginolyticus* and other halophilic vibrios, including *V. parahaemolyticus* and *V. vulnificus*, have all been isolated from East Coastal waters [6–10]. Several cases of *V. alginolyticus* infection reported from Connecticut were acquired in Long Island Sound [5,9].

Halophilic vibrios grow well on nutrient or MacConkey's agar, but are best isolated using a vibrio-selective media such as thiosulfate-citrate-bile salt (TCBS) agar [3]. Selective media were not initially requested for culturing this patient's tissue specimen. It was fortunate that, despite the heavy growth of *S. aureus*, one colony of a gram-negative organism was identified.

In recent years, most of the attention given to the halophilic vibrios has been centered upon *Vibrio vulnificus* [11–14], an organism which should be included in the clinical and microbiological differential diagnosis of our patient's illness. The most striking difference between *V. vulnificus* and other halophilic vibrios is that *V. vulnificus* usually causes a serious or overwhelming illness, even though the initial presentation might simply be mild cellulitis following a saltwater injury to an extremity. Patients with *V. vulnificus* infection usually show a rapidly deteriorating course; the area of cellulitis quickly expands and evolves into necrotizing fasciitis, often complicated by sepsis [15]. Such infections have been reported to occur most commonly in patients with cirrhosis, iron-overload states, or underlying malignancies [11]. Often infection occurs after ingestion of raw seafood [12].

V. parahaemolyticus is another halophilic vibrio which most often causes gastrointestinal infections but can also present as cellulitis [8]. Clinical infections due to *V. parahaemolyticus* are usually less dramatic than the typical course for *V. vulnificus* and more closely resemble those caused by *V. alginolyticus*.

Cellulitis, otitis media, otitis externa, and conjunctivitis are the most common presentations of *V. alginolyticus* infections [2,3,5,16–18]; rarely, bacteremia has occurred in immunocompromised hosts [3]. The course of disease seen in our patient is typical for *V. alginolyticus* infection. Typically, *V. alginolyticus* is isolated from infections associated with necrotic lesions; however, the course is usually more indolent than that seen with *V. vulnificus* infections. *V. alginolyticus* ear infections, both otitis externa [16,18] and media [9], have been described in swimmers. One such patient acquired an infection after swimming in Long Island Sound [9]. Conjunctivitis has been associated with exposure to seashells; this infection occurs most commonly in fishmongers and fishermen [10]. One reported patient was a gardener who used seashells in his yard [17].

Soft-tissue infections are the most common infections caused by *V. alginolyticus*. Frequently the skin lesions occur after a saltwater injury, especially one involving coral [16]. The infections can range from a mild cellulitis, which usually has a component of necrosis, to a severe necrotizing fasciitis. In our patient the process remained localized, but he required repeated debridement of necrotic muscle. Skin grafting was also required, but this procedure is not uncommon when dealing with *V. alginolyticus* infections [2,5].

Howard et al. reviewed 18 cases of halophilic vibrio infections [2]. Only one was specifically identified as *V. alginolyticus*. Risk factors for such infections included underlying liver disease, corticosteroid use, and malignancy. Six of the 18 patients died, and three of the 18 required amputation of an extremity.

In that series, debridement seemed more crucial for effective therapy than antibiotic treatment. Pien et al. [16] reported eight *V. alginolyticus* infections; five were soft-tissue infections, and two were directly related to coral. Several patients improved with only debridement, local care, and either no antibiotics or antibiotic therapy to which the organism was resistant *in vitro* [16]. *V. alginolyticus* infection can be indolent, as it was in our patient, and it can even develop into a chronic infection [5].

Mixed bacterial infections which include *V. alginolyticus* have been described [5,10,16]. A plane crash survivor suffered immersion in Long Island Sound and had multiple water-associated organisms cultured from his wounds, including *V. alginolyticus* [9]. Several case reports describe both *S. aureus* and *V. alginolyticus* isolations from the same wound, as was seen in our patient [5,16].

Most strains of *V. alginolyticus* are susceptible to tetracyclines, as are most of the non-cholera *Vibrio* species; doxycycline and tetracycline are the drugs of choice for these infections. They should be instituted empirically if a vibrio infection is suspected [6]. *V. vulnificus* is often susceptible *in vitro* to many drugs, including penicillin, but clinical experience has shown penicillin and other beta-lactam antibiotics are less effective than the tetracyclines for treating vibrio infections [19]. The *V. alginolyticus* isolate from our patient was resistant to both penicillin and cephalothin. His lesion progressed despite surgery and antibiotic therapy with the antibiotic combination of cephalothin and gentamicin.

In summary, our patient developed an indolent, necrotic, skin infection after sustaining a coral injury in salt water. While early treatment with tetracyclines might have improved the therapeutic outcome, debridement of residual coral in conjunction with parenteral doxycycline therapy was crucial to eradicating his infection. *V. alginolyticus* and other halophilic vibrios present significant health risks which must be considered in the differential diagnosis of infections appearing after saltwater injuries associated with coral.

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