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Vibrio mimicus: A rare wound infection in a patient with neuroendocrine tumor of the humerus

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Abstract
Introduction: Non-cholera *Vibrio* spp. can cause intestinal and extraintestinal infections. Wound infection with *V. mimicus* is rare and has not been previously documented to occur following orthopedic surgery.
Case presentation: A 61-year-old female with poorly differentiated large cell neuroendocrine tumor of the proximal humerus diagnosed in 2023. Patient underwent left humerus tumor resection and intramedullary nailing. On follow-up, tumor girth was increasing, and wound was healing. The patient was started on radiotherapy followed by chemotherapy. At 2.5 months postop, wound was draining and *V. mimicus* was identified from cultures; she was started on antibiotics.
Conclusions: *Vibrio* spp. associated infections are expected to increase worldwide, especially in the context of higher temperatures and ongoing global warming. This case raises concern about water contamination as a source of wound infection.

Keywords: *Vibrio*, wound infection, orthopedics surgery, neuroendocrine tumor

Introduction
*Vibrio*s are gram-negative rod-shaped organisms that include over 100 identified species, 12 of which been isolated from humans (Baker, brehm). The latter are aquatic bacteria that inhabit a wide variety of warm estuarine and marine environments (Brehm). The number of *Vibrio* strains isolated from human infections increase during summer months as reported by CDC (Newton, weis).
General categorization of *Vibrio* spp. include toxin-producing serogroups O1 and O139 of *V. cholera*. Ingestion through water or food can cause endemic and epidemic cholera, a severe acute secretory diarrheal illness. However, non-cholera *Vibrio* spp. are halophilic species associated with variable range of gastroenteritis, wound infections and septicemia; they are transmitted through traumatic exposure to contaminated sea or brackfish water, or consumption of raw/undercooked seafood (Dechet, Araj).
A couple of non-cholera *Vibrio* spp., such as *V. albensis* and *V. fluvialis* have been previously reported from our medical center as causes of non-gastrointestinal infection (Araj, Ghazal, Usta). To the best of our knowledge, there has been no previous reports on *V. mimicus* infection following orthopedics surgery. Thus, the theme of this first case presentation.

Case presentation
A 61-year-old female known to have liver cirrhosis secondary to hepatitis C infection, though not on treatment, in addition to hepatosplenomegaly and history of chronic anemia and thrombocytopenia. She presented in September 2023 for chronic left upper extremity pain that worsened 1 month prior to presentation. She reported severe pain that starts at the shoulder and radiates distally, necessitating immobilization and became refractory to pain medications. She denies an incident of fall or trauma, but reports history of pallor, fatigue and 10 kilograms weight loss over the preceding year. On physical examination, she was tender to palpation of the humerus with limited shoulder range of motion and decreased biceps flexion strength and decreased left hand grip strength.
Investigation was initiated by hematology/oncology team to rule out multiple myeloma, lymphoma or an underlying metastatic disease. Blood tests showed normal tests, without evidence of multiple myeloma. Xray of the humerus showed large lytic lesion eroding humerus diaphysis (Figure 1).

MRI revealed proximal humerus large lytic ovoid lesion of bright intensity on T_2 (Figures 2). Ct guided biopsy of lesion was performed; histology revealed large cells with hyperchromatic nuclei arranged in small lobules with moderate nuclear atypia. Pathology showed poorly differentiated carcinoma with positive CD56 and pancytokeratin markers but negative CK7, CK20, TTF1, CD99, and P40 markers; consistent with large cell neuroendocrine tumor. Positron emission tomography (PET) scan performed to identify a primary origin did not reveal a metastatic disease and showed a large ill-defined expansile lesion in left proximal humerus 8.5cm*8.9cm*7.8 cm with large extraosseous soft tissue component (Figure 3).

Discussion between medical team and the patient/family yielded a decision to proceed with surgical intervention. Preoperative laboratory tests showed elevated prothrombin time (PPT) 17.5, normal partial thomboplastin time (PTT) 32.9, hemoglobin 8.6/hematocrit 26 and platelet count 61900. Patient underwent left humerus tumor resection and intramedullary nailing, as seen in Figure 4. Intraoperatively, partial resection of the lesion was performed and yielded around 500cc of bloody jelly like material. Patient had a smooth in-hospital course having tolerated procedure well and received 2 platelet transfusions, 2 fresh frozen plasma, and 3 packed red blood cells transfusions. Wound was clean and had healed nicely on follow-up when sutures were removed. Pathology, previously taken intraoperatively, showed large cell neuroendocrine tumor.

The wound was healing but patient was still in pain from increase in tumor girth. Radiotherapy was discussed with patient for local control and started at 6 weeks postoperatively. However, on follow-up at 7 weeks, hematoma was noted under the skin; it was drained and was noticed to be abutting the necrotic tumor. At 8 weeks, patient was started on chemotherapy regimen: etoposide and cisplatin. At 2.5 months postop, wound was still draining despite less than before and specimens were taken in clinic setting.

In this case, the culture collected from this patient were submitted to the clinical microbiology laboratory for bacterial, mycobacterial and fungal cultures. *Vibrio mimicus* was recovered and identified by Matrix-Assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF) system (Bruker Daltonik, GmbH, Bremen, Germany). Antimicrobial susceptibility testing was done based on CDC recommendation which include testing for: chloramphenicol, ampicillin, trimethoprim sulfamethoxazole, tetracycline and nalidixic acid (CDC). The strain was susceptible to all the tested agents. As such patient was started on Augmentin and her regimen of chemotherapy treatment was resumed.

Discussion

This case report discloses a case of a surgical wound infected with *Vibrio mimicus*, an unusual organism that has not been previously reported in a patient with neuroendocrine tumor nor to cause wound infections following orthopedics surgery.

Neuroendocrine tumors (NETs) are a heterogenous family of neoplasms that originate from cells belonging to the neuroendocrine system. Skeletal system involvement in patients with NETs is usually secondary to metastatic disease with the latter being a rare and late event (Sultana). This case report is unprecedented because our patient did not have a focus of primary NET with secondary metastasis but the tumor was solely identified in bone (humerus).

V. mimicus was first identified in 1983 as a separate species (Tarcero). Similar to other *Vibrio* spp. *V. mimicus* inhabits marine water and can be found in fresh water as well. Several studies have identified high temperature, water salinity and dissolved oxygen as environmental factors that increase the abundance of *Vibrio* species in aquatic habitat (robles). Among the currently described species, the most frequent strains associated with human illnesses are *V. cholera*, *V. vulnificus* and *V. parahaemolyticus* (baker, janda).

Ingestion of food contaminated with the *V. mimicus* results in severe diarrhea and gastroenteritis similar to the foodborne outbreaks that happened in Chiang Mai, Thailand and Washington State, USA (kay, chitov). Additionally, *V. mimicus* is also an uncommon cause of acute otitis media and wound infections after exposure to contaminated water (Blake, kay, yang). In addition, *V. mimicus* has been previously isolated from few patients following surgical intervention, though none of which had underwent an orthopedic surgery. In 2009, Skandalos *et al.* reported-on identification of *V. mimicus* from the wound of a mycotic abdominal aortic aneurysm in a patient who had a 1-week history of gastroenteritis (Skandalos). Yang *et al.* reported a polymicrobial infection of a burn wound following a firework explosion accident including *V. mimicus* and *Aeromonas hydrophilia* (yang).

V. mimicus is an unknown cause of wound infection following orthopedic surgery; nonetheless, wound infected with other *Vibrio* spp. has been reported. *Vibrio harveyi* was previously reported to cause wound infection following traumatic leg amputation after a motorboat propeller injury in the Mediterranean Sea and as a cause of wound infection of an 11-year-old girl attacked by a shark (Brehm, Pavia). The 'flesh eating bacterium' *Vibrio vulnificus* is the most virulent *Vibrio* spp and has been reported to cause cellulitis, invasive rapidly spreading infections of the extremities, necrotizing fasciitis and can also cause compartment syndrome (Hui, Inoue, zaghi).

Previous studies showed that all clinical and environmental *V. mimicus* isolates possessed virulence associated genes encoding toxins, such as hemolysin (VMH) which is different and at times a more important pathogenic factor than the cholera toxin, and can result in pathogenesis leading to wound infections (Shinoda). Hemolysin induces the creation of membranous pores in erythrocyte membranes causing hemolytic activity, also increases levels of adenosine triphosphate (ATP) and cyclic adenosine monophosphate (cAMP) thus increasing fluid accumulation which may explain increased continuous drainage at wound site in our patient (Li).

Factors involved in the spread of *V. mimicus* infections include poor hygiene and inadequate sanitary conditions secondary to human activities and water contamination (Igbinosa, Usta). Unlike foodborne *Vibrio* infections, prevention of wound exposure to *Vibrios* may not be practical because wounds are exposed to marine and saltwater contaminated with these species and present in hospital and community water and wastewater (blake, Mavhungu).

A couple of studies from our institution have reported on human infection with *Vibrio* spp. Ascribed to contaminated water in Lebanon. There are also several reports about wells

and underground water in Lebanon being contaminated by wastewater (zaatity). Increased groundwater salinity secondary to delayed rainy season and to mixing with sea water can possibly contribute to increase pathogen concentration and in turn human infection rates as in this report (Usta). Hence, in light of high fatality rates associated with wound infections secondary to *Vibrio* spp., early aggressive antimicrobial treatment remains crucial especially considering the recent increase in antimicrobial resistance against different *Vibrio* spp (Bier, Lee). In our case, the recovered *V. mimicus* showed uniform susceptibility to all tested antimicrobial agents; thus, making the treatment used effective to eradicate the infection.

Fig 1: Xray of left humerus preoperatively showing large lytic lesion eroding the proximal humeral diaphysis with wide zone of transition and sparing of the humeral head and neck that extends for 7.7 cm craniocaudally with a large ill-defined soft tissue mass and extension and is highly suggestive of malignant bone lesion, possibly metastatic.

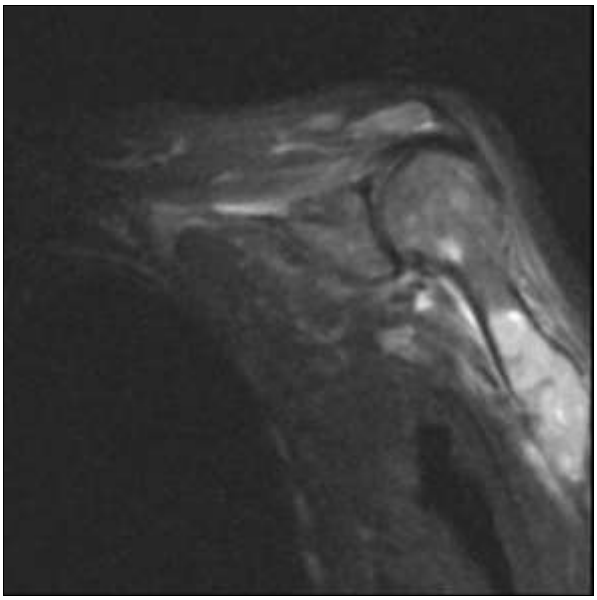

Fig 2: MRI of left humerus preoperatively showing large lytic lesion eroding the proximal humeral diaphysis with wide zone of transition and extending into the soft tissue of high intensity on T_2-weighted image; highly suggestive of malignant bone lesion, possibly metastatic.

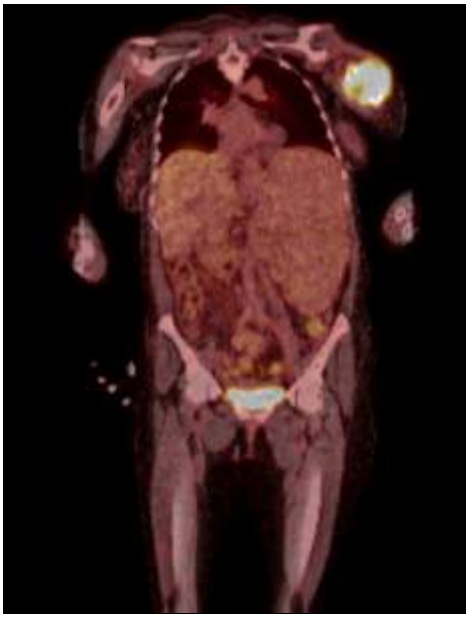

Fig 3: Positron emission tomography (PET) scan showing large ill-defined radiotracer avid expansile lesion in the left humerus with a large extraosseous soft tissue component 8.5 x 8.9 x7.8 cm in size, appears to be malignant.

Fig 4: Xray of left humerus postoperatively showing fixation with a long intramedullary nail and screws in good position and the proximal and distal fragments aligned in addition to large defect at the proximal to mid humeral shaft from aggressive tumor and post resection with significant cortical irregularity at the edges of both remnants of the humerus.

Conclusion

We report the first human infection with *V. mimicus* following orthopedic surgery and resection of neuroendocrine tumor of the bone. *Vibrio* spp. associated

infections are expected to increase worldwide especially in the context of higher temperatures and ongoing global warming. The relatively infrequent number of reported cases of infection with this organism may be due to underreporting or underdiagnosis. As such, this case suggests that physicians and microbiologists should be aware of variety of possible organisms to cause wound infections. It also raises the concern that water in the city of Beirut is a potential cause of infectious pathogens that contributes to morbidity and mortality in the absence of supervision and good sanitation, and the need for proper plan for water safety in this country.

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