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CASE REPORT

Major Amputation Needed to Treat Purulent Tenosynovitis and Necrotizing Fasciitis in a Patient with a Human Bite and Severe COVID-19

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Background: Peripheral human bite wounds are rarely serious and are typically treated medically, with the most complex cases requiring only minor amputation or excision of the infected site. There are few to no reports documenting the development of purulent tenosynovitis, necrotizing fasciitis, and osteomyelitis from these lesions. Major amputations are required only rarely in these cases.

Case Presentation: A 71-year-old woman presented with an uncontrolled infection following a self-inflicted bite wound to her left middle finger. A bacterial culture of the lesion revealed methicillin-resistant *Staphylococcus aureus* (MRSA). The infection could not be controlled with antibiotics or additional interventions, including debridement and minor amputation. She contracted severe COVID-19 while in the hospital which limited the available treatment options. In an attempt to control the infection, the patient ultimately underwent a major amputation of the distal left forearm. While recovering from the procedure, the patient succumbed to septic shock and cardiopulmonary arrest.

Conclusion: The unusual progression of this case may be attributed to the interventions required to treat acute COVID-19 as well as a variety of confounding factors. For example, vasopressors and steroids used to treat severely-ill patients compromise the local and systemic physiologic responses to acute bacterial infection. It is important to reconsider clinical expectations during the pandemic and intervene as early as possible to prevent ongoing damage and clinical deterioration.

Keywords: COVID-19, amputation, bite wound, necrotizing fasciitis, gangrene, purulent tenosynovitis, immunocompromised

Background

Human bites, a clinical rarity, oftentimes pose a significant threat of systemic infection transmission. Bite wounds mostly present with symptoms of inflammation and can very easily be overlooked as a wound from another cause. As many bite wounds can be puncture wounds and allow infection into deep tissue spaces, early diagnosis and management are paramount. Deep tissue infection, combined with poor vascular performance and other comorbidities is known to be a strong determinant of bad outcome however this has yet to be explored with a bite wound exacerbated by a Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoC-2) infection.

SARS-CoV-2, a beta coronavirus related to the viruses that cause Middle East Respiratory Syndrome and Severe Acute Respiratory Syndrome, is the etiologic agent of Coronavirus Disease-2019 (COVID-19). There are no published reports to date that describe exacerbations of human bite wounds by COVID-19 or its treatment. In this case, a self-inflicted bite wound progressed into purulent tenosynovitis followed by necrotizing fasciitis and avascular necrosis, ultimately requiring amputation of the distal forearm. The presentation and progression of this case are highly unusual as most cases of purulent tenosynovitis respond to antibiotics, debridement, and minor amputation. In this case, the

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infection progressed due to numerous confounding factors, including several that were directly associated with COVID-19 infection and its treatment.

Case Presentation

A 71-year-old Japanese woman with a past medical history of type 1 diabetes, end-stage renal disease, complete atrioventricular block, and previous myocardial infarction was admitted to the Gastroenterology service of our hospital for evaluation and treatment of acute loss of consciousness secondary to hypoglycemia. At the time of admission, she had a permanent pacemaker and was undergoing hemodialysis three times a week. The Orthopedics service was contacted to evaluate swelling, heat, and redness of her left hand due to a bite wound at the tip of her left middle finger that was self-inflicted during an episode of dementia. (Figure 1). A standard course of intravenous cefazolin (1g per day) was prescribed to treat presumptive cellulitis. The infection did not respond and progressed despite two full days of antibiotic treatment. Bacterial culture of the lesion revealed methicillin-resistant *Staphylococcus aureus* (MRSA). Upon physical exam, the patient displayed all four of Kanavel's cardinal signs of flexor tenosynovitis. Vancomycin infusion (trough value, 15–20 μg/mL) was initiated to treat the MRSA infection, together with wound debridement and a partial amputation at the distal interphalangeal joint. (Figure 1). Decompression of the median nerve was performed to relieve pressure resulting from a purulent abscess. While redness and swelling persisted after this procedure, the progression of the infection appeared to be somewhat reduced. While the antibiotic course of Vancomycin was continued, on day 5 the patient suddenly complained of abdominal pain, dark brown blood in the stool indicative of a gastrointestinal bleed, and developed signs consistent with systemic shock. Her initial systolic blood pressure reading was 60 mmHg which responded to acute administration of vasopressors. Laboratory data included an elevated white blood cell (WBC) count of 9890 per mm^3, together with increased serum levels of C-reactive protein (CRP; 259.7 mg/L) and creatinine (421.7 μmol/L) and reduced levels of sodium (132 mEq/L), blood glucose (2.6 mmol/L), and hemoglobin (8.2 g/dL). Findings from an abdominal computed tomography (CT) study resulted in a diagnosis of non-occlusive mesenteric ischemia; an emergency small bowel resection was performed. Tube feedings were initiated and continued for one week. Norepinephrine was added to her regiment to maintain blood pressure at levels necessary to sustain organ perfusion with a target mean arterial pressure of 70.

During her hospital stay, the patient was exposed to SARS-CoV-2 after extended close contact with an infected individual while undergoing dialysis. Her nasal swab test was positive for COVID-19 using a loop-mediated isothermal amplification assay. Four days after the positive test, she developed signs of acute pneumonia. Results of a chest

Figure 1 Clinical Progress Photographs during the initial stages of the infection following the wound. Photograph documenting self-inflicted bite wound in the tip of the left third digit (**A**). Photograph documenting necrosis of the third digit extending to the distal interphalangeal joint and swelling secondary to an abscess in the flexor tendon sheath as well as indications of heat and redness (**B**).

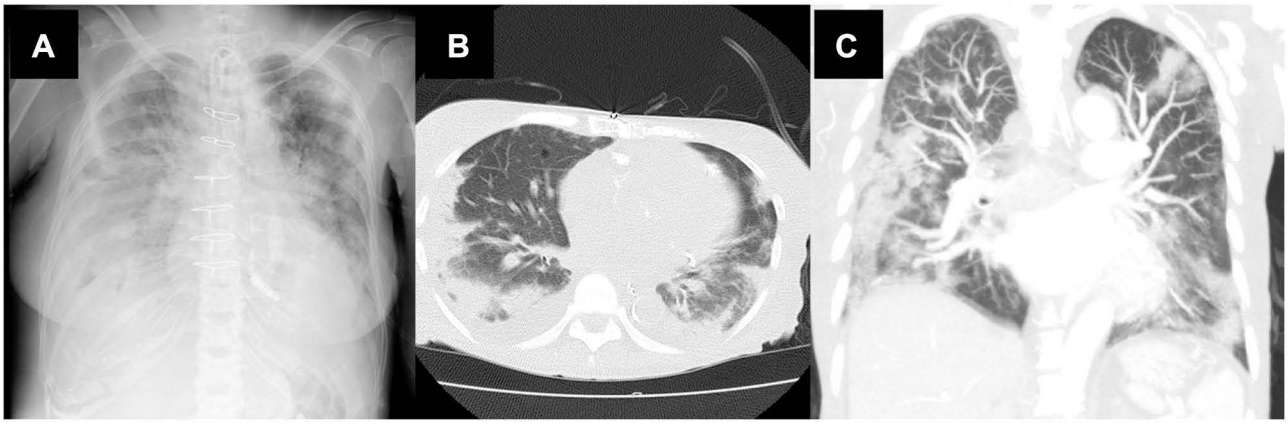

Figure 2 Radiographs and Computed Tomography of Lungs During COVID-19 Infection. Anteroposterior chest radiograph documenting pneumonia associated with SARS-CoV-2 infection (**A**). An axial CT scan revealed bilateral pleural effusions (**B**). A coronal CT scan revealed bilateral lung involvement and ground-glass opacities typically observed in patients diagnosed with COVID-19 (**C**).

radiograph and CT scan confirmed this diagnosis and revealed consolidation of the lungs as well as bilateral pleural effusions. (Figure 2). Antiviral treatment with favipiravir (200 mg orally twice per day) was initiated and the patient was transferred to the intensive care unit. This was in accordance with recommendations at the time of administration. The patient was hypervolemic with increased oxygen demand. Continuous hemodiafiltration was performed to avoid fluid overload.

Immediately before exposure to COVID-19, the patient developed clinical signs of necrotizing fasciitis. The infection had extended into the fascia and the surrounding musculature of her left hand. While emergency hand amputation was deemed necessary, the patient developed septic shock and required mechanical respiration due to a sudden increase in oxygen demand. High flow oxygen was administered continuously via the endotracheal tube, and her antiviral regimen was changed to remdesivir (100 mg intravenous once a day) together with intravenous hydrocortisone (200 mg/dose). Remdesivir was still under compassionate-use status at the time. While undergoing treatment for acute life-threatening events, the infection progressed to include the phalanges of the left middle finger, with bone necrosis visible on radiography. (Figure 3). Vancomycin (500 mg) was prescribed to manage the osteomyelitis and prevent its further spreading. The patient subsequently developed acute respiratory distress syndrome (ARDS). Although the patient's COVID-19 infection was under control after two weeks, she developed disseminated intravascular coagulation (DIC; score >4) which may have accelerated bacterial growth. As heparin was contraindicated in this case, ART-123, a recombinant and soluble form of thrombomodulin alpha was administered intravenously (12,800 U once per day for 3 days) to dissolve the systemic clots. The infection progressed to include necrosis of the entire third digit as well as the skin, fascia, and musculature up to the radio-carpal joint with signs of progressive invasion into the forearm (Figure 4). Unfortunately, COVID-associated hospital restrictions and shutdowns precluded further surgical treatment at this time.

The patient ultimately recovered from COVID-19. At two weeks after the initial diagnosis was made, the patient was weaned from mechanical ventilation and the endotracheal tube was withdrawn. Two weeks post-extubation, the patient completed the treatment for COVID-19 and had a negative SARS-CoV-2 antigen test. A major amputation at the distal third of the forearm was then performed. The tissues were debrided and lavaged completely during the procedure and all infected tissue was removed. Because the amputation site was proximal to her indwelling hemodialysis shunt, its replacement was discussed with vascular surgeons and nephrologists. The procedure revealed heavy calcification of the arteries of her left forearm with tortuosity and possible occlusions both proximal and distal to the shunt (Figure 5). The bruit and thrill detected in the shunt also suggested the possibility of distal hypoperfusion ischemic syndrome. Adequate skin flap coverage was achieved and the stump was closed; a follow-up radiographic study revealed no complications (Figure 6). The stump appeared to be healing well, one month later, the patient succumbed to septic shock and cardiopulmonary arrest.

Figure 3 Pre-operative anteroposterior radiographic image of the left hand. As shown in the image, the patient developed osteomyelitis through the basal phalanx and metaphysis.

Figure 4 Photographs documenting the progression of the later stage of the infection over four weeks. Shown are photographs documenting the progression from cellulitis, to purulent tenosynovitis, necrotizing fasciitis, and osteomyelitis. Within one month, the infection progressed from cellulitis (**A**) to necrosis of the entire finger, with the infection invading the musculature (**B**). Two weeks after the finger had fully necrosed (**C**), the infection had extended up to the radiocarpal joint (**D**).

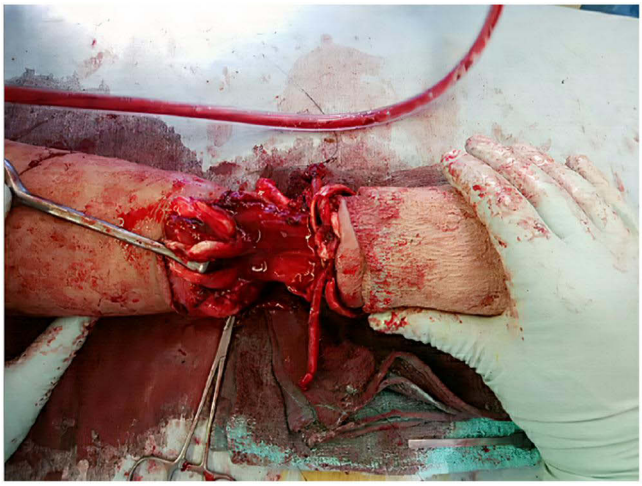

Figure 5 Perioperative photograph of Arterial calcification and tortuosity. Photograph during amputation surgery documenting heavy calcification and tortuous arteries with the possibility of occlusions in regions that were both proximal and distal to the dialysis shunt. Left, proximal to the torso; right, distal to the torso.

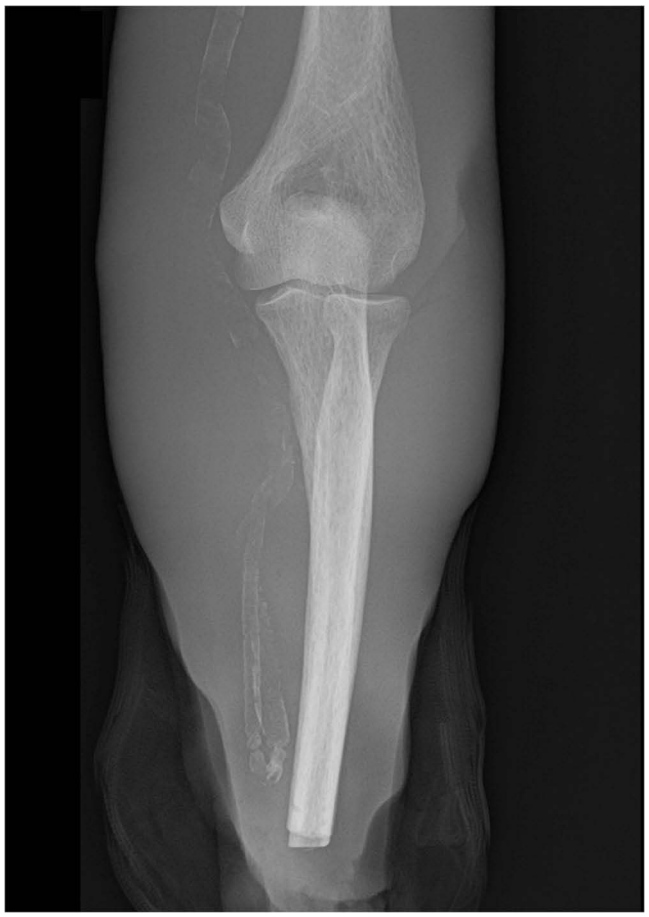

Figure 6 Radiograph of the left arm after amputation of the distal forearm. Amputation at the distal third of the forearm proximal to the dialysis shunt.

Discussion and Conclusions

The COVID-19 pandemic has presented numerous challenges to the healthcare systems in Japan and throughout the world. Among these issues, surgeries have been canceled due to outbreaks within hospitals. Similarly, patients diagnosed with COVID-19 have only limited access to emergency services and critical diagnostic devices including Magnetic

Resonance Imaging (MRI) scanners. While there is substantial ongoing research into the secondary health effects of COVID-19, the impact of this pandemic on orthopedic services has not been clearly established. This case features several of the many challenges faced by orthopedic surgeons when attempting to provide high-quality care to patients with complex co-morbidities who develop COVID-19.

As a first concern, we all recognize that immunocompromised patients may be susceptible to serious infections and the need to intervene early to prevent excessive and ongoing tissue damage.[1] Thus, while corticosteroids may be effective for COVID-19 as they limit the destruction associated with ongoing inflammation, the immunosuppressive effects of these drugs may result in increased susceptibility to bacterial infections.[2,3] In the case presented here, the uncontrolled growth of a skin infection that is typically amenable to treatment led to the necrosis of both muscle and bone. Furthermore, the major amputation that was ultimately required to prevent further infiltration and necrosis may have resulted in bacterial translocation and secondary systemic infection. Although we initially intended to address this complication with a minor amputation, this was not possible once the patient contracted COVID-19. In this case, surgery was delayed and the infection progressed significantly.

We also recognize that all physicians and surgeons need to adjust their expectations and also their protocols during the ongoing COVID-19 pandemic. This is perhaps most critical when addressing the concerns of complex patients. In many cases, infections may not be adequately controlled by standard methods and/or within the normally-anticipated timespan. Our report documented the case of a lesion at the distal end of the left third digit that progressed to purulent tenosynovitis that spread from the tenosynovium into the bones. To the best of our knowledge, this is the first report that documents this type of progression of what is typically a localized infection. While severe cases of purulent tenosynovitis may require digital or carpal amputation, there are no previous reports that document cases in which a forearm amputation was required.[4]

Numerous secondary effects caused by COVID-19 contributed to the outcome of this case. For example, protocols in place that were designed to limit the spread of COVID-19 played a large role in the development of this patient's treatment plan and anticipated timelines. There are numerous and varied hospital policies for patients diagnosed with COVID-19, most notably with respect to the use of hospital facilities and operating rooms. At our hospital, COVID-19-positive patients could not enter any of the operating rooms for at least two weeks after obtaining a confirmed negative result because of the high risk of disease transmission to anesthesiologists, surgeons, nurses, staff, and other patients. In this case, we believe that the infection was exacerbated by the combined effects of COVID-19 treatment as well as the circulatory disturbances and vasoconstriction resulting from the administration of norepinephrine. Norepinephrine is a catecholamine that stimulates the alpha-1-adrenoreceptor, thereby inducing peripheral vasoconstriction.[5] Our patient was treated with norepinephrine (1 g/mL) administered intravenously five times a day for a full one month to maintain adequate systemic blood pressure. Previous case reports suggest that the use of high-dose norepinephrine and similar inotropes can result in necrosis secondary to severe vasoconstriction and tissue hypoperfusion.[6] Close monitoring for ischemia should be maintained when inotropic agents are used; our case was a good example of this principle. As shown in Figure 4, the patient exhibited signs of hypoperfusion, notably, her fingers developed a white to purple hue. Likewise, the use of vasopressor drugs results in impaired regional circulation secondary to distal hypoperfusion ischemia syndrome from the shunt. This creates a scenario in which antibiotics may be unable to reach peripheral tissue and may result in poor perfusion and an increased vulnerability to ongoing infection.

This case illustrates the complexity of managing patients with multiple comorbidities as well as the challenges presented by the current pandemic, including lockdowns that limit access to healthcare, various hospital-based restrictions, and overload of the healthcare system due to lack of staff and personal protective equipment.[7] These challenges can exacerbate one another which will lead to even more extensive difficulties when treating these complex patients. Increased mortality rates and poor prognoses have been recognized in at least one study that focused on patients who underwent surgery while infected with SARS-CoV-2.[5] All physicians need to understand, plan, and prepare for the impact of COVID-19 and consider how pandemic conditions can alter the progression of even seemingly-unrelated diseases. For example, Liu and Zhang[9] reported that both COVID-19 and its treatment may have endovascular effects. Similarly, Makhoul et al[8] reported on a series of COVID-19 patients who required amputation of their extremities due to endovascular and coagulation disorders following ischemia and arterial occlusion. This case is the first report of a infection caused by a human bite that was exacerbated by COVID-19

and/or its treatment. In our case, ischemia secondary to vasoconstriction and coagulopathy most likely permitted the bacterial infection to spread up to the distal forearm and expedited the necrosis process. There was a particularly high risk associated with bacterial infiltration of the arteriovenous shunt in the left arm and thus the potential for systemic infection. Physicians will need to review the medical literature on an ongoing basis and proceed under the assumption that the presentation and progression of many otherwise controllable conditions may be varied and unanticipated in these patients. For example, while COVID-19 related coagulopathy presents in a fashion that is similar to DIC, recent evidence suggests that conventional treatments may not be effective and must be used in conjunction to other COVID-19 specific treatment.[9] Likewise, atherosclerosis and hypercoagulation have been linked with COVID-19 infection in the literature; these factors increase the risk of arterial occlusion and ischemia.[10] The use of vasopressors may exacerbate these effects by promoting necrosis of peripheral tissues and increasing the risk of infection. Likewise, patients with comorbidities are more susceptible to both vascular complications and the uncontrolled spread of the infection. Physicians need to treat small wounds carefully in patients with comorbidities and provide the same level of care as would be applied to larger wounds. This is critical to prevent the uncontrollable spread and the development of a life-threatening condition. This is especially important to consider now during the COVID-19 pandemic, given the complications associated with long-term COVID-19 treatment, including vasopressors, corticosteroids, and immuno-suppresive drugs. Collaboration between caregivers on primary care teams, ie, nurses, pressure ulcer care teams, and physiotherapists is also a critical factor in early diagnosis and treatment, especially in the age of COVID-19. Early diagnosis and treatment are critical for all patients who are at risk of contracting COVID-19; it is critical to recognize that these patients might ultimately be prevented from entering an operating room and thus face a limited number of treatment modalities. In the future, it might be helpful to prepare operating theaters or create temporary structures that are capable of handling COVID-19 patients to facilitate early diagnosis and treatment and improve patient outcomes and quality of life.

Abbreviations

COVID-19, Coronavirus disease-2019; MRSA, Methicillin-resistant *Staphylococcus aureus*; MERS, Middle East Respiratory Syndrome; SARS, Severe Acute Respiratory Syndrome; SARS-CoV-2, Severe Acute Respiratory Syndrome – Coronavirus – 2; WBC, White Blood Cell; CRP, C-reactive protein; CT, Computed Tomography; ARDS, Acute Respiratory distress syndrome; DIC, disseminated intravascular coagulation; MRI, Magnetic Resonance Imaging.

Data Sharing Statement

Data sharing does not apply to this article. No datasets were generated or analyzed during the current study.

Ethics Approval and Consent to Participate

This study was approved by the review board at our hospital and was performed in accordance with the Helsinki Declaration. The patient and/or next of kin provided informed consent for the study.

Consent to Publish

The patient next of kin provided informed verbal consent for publication including the use of clinical images and information as the patient was deceased prior to the writing of the article. Written confirmation of the consent is documented in our center's clinical records system. Institutional Approval was granted from the Saiseikai Yokohamashi Tobu Hospital ethics committee.

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Author Contributions

All authors made a significant contribution to the manuscript in areas such as the conception, acquisition of data, analysis, interpretation, drafting, revising, and critically reviewing the article. All authors gave final approval of the manuscript and the journal to be submitted and agreed to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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