A Rare Case of Neisseria animaloris Hand Infection and Associated Nonhealing Wound

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Neisseria animaloris is a rare pathogen in humans primarily associated with dog and cat bites. Fourteen cases have been documented in the literature related to the difficulty in identifying this bacterium in the laboratory. We present a patient case demonstrating a prolonged treatment course, which is often seen as the result of misdiagnosis, and subsequent nonhealing wound requiring multiple surgeries and eventual wide excision with staged graft coverage. We discuss the clinical course, laboratory identification techniques, surgical treatment, and patient outcome.

Case Report

A 57-year-old man presented to our clinic for evaluation of a left wrist wound in 2015. The wound began in 2014, several months before his initial clinic visit, as a nonhealing blister on the volar and ulnar aspect of the wrist. At that time, the patient lived in a rural area in a trailer with wolves, dogs, and stray cats, all of which he cared for, among other rodents and snakes which infested his living space. He had reported receiving numerous animal bites, mostly while trying to break up fights between the wolves and dogs, but he was unable to recount a specific inciting bite. His medical history was notable for facial pustular rosacea, for which he was observed by an outside dermatology clinic, as well as chronic alcohol abuse. Otherwise, his medical history was not concerning for immunosuppressive medications, smoking, peripheral vascular disease, or other processes that may have increased his susceptibility to rare infections.

He was initially seen in a rural clinic and treated for cellulitis with a course of doxycycline and metronidazole, with an unknown duration of antibiotics. He subsequently presented to the university emergency department for a nonhealing wound despite receiving antibiotic treatment. At that time, the patient lived in a rural area in a trailer with wolves, dogs, and stray cats, all of which he cared for, among other rodents and snakes which infested his living space. He had reported receiving numerous animal bites, mostly while trying to break up fights between the wolves and dogs, but he was unable to recount a specific inciting bite. His medical history was notable for facial pustular rosacea, for which he was observed by an outside dermatology clinic, as well as chronic alcohol abuse. Otherwise, his medical history was not concerning for immunosuppressive medications, smoking, peripheral vascular disease, or other processes that may have increased his susceptibility to rare infections.

He was referred to our clinic from the emergency department and underwent surgical biopsy by the senior author (M.S.M.) in November 2015. Surgical specimens were sent for
pathology and culture and returned with no malignant or pathologic lesion (nonspecific reactive histology noted). However, the specimens demonstrated Neisseria, which was neither meningitidis nor gonorrhea species, but was otherwise unable to be identified. The patient was given oral amoxicillin-clavulanate (875/125 mg twice daily) and oral clindamycin (300 mg 3 times daily) after surgery for broad-spectrum coverage. Four weeks after the initial biopsy, the patient had persistent wound drainage and infection and underwent repeat irrigation and debridement. Cultures again showed rare growth of an unknown strain of Neisseria species. He was subsequently referred to an infectious disease specialist for further antibiotic therapy. Antibacterial susceptibility was not performed on the surgical Neisseria specimens because this is not routine in our laboratory. The infectious disease specialist suspected Neisseria canis infection and gave the patient a 2-week course of oral moxifloxacin (400 mg daily).

The patient was unable to tolerate the full course of moxifloxacin because of medication side effects (agitation and paranoia), but clinically the patient demonstrated improvement in the infection over the following 6 months. He was then lost to follow-up until 2 years later. In 2018, the patient presented to the university dermatology specialty clinic for a continued nonhealing wrist wound on the volar and ulnar aspect of the left wrist (Fig. 1). He was diagnosed with botryomycosis at that time based on punch biopsy performed by dermatology in clinic, which resulted in anacanthotic squamous proliferation with suppurative inflammation, favored to be reactive tissue adjacent to wound or infection. The patient was again subsequently referred to our hand surgery clinic.

Upon reevaluation in our hand clinic, a plan was made for extensive wound debridement with subsequent tissue coverage. He underwent debridement of the wound measuring 4 × 7 cm, down to flexor carpi ulnaris tendon and ulna periosteum. Although a deep nidus was noted deep to the flexor carpi ulnaris, there was no evidence of periosteal abscess or osteomyelitis. Integra dermal regeneration template (Integra Life Sciences, Plainsboro, NJ) was placed as wound coverage with an overlying cotton bolster, with plans for staged skin graft (Fig. 2). The patient’s cultures and pathology were then observed closely, as well. Surgical pathology demonstrated multiple dermal microabscesses with Splendore–Hoeppli phenomenon suggestive of bacterial infection without positive staining (Fig. 3). Pathology was negative for carcinoma. In collaboration with an infectious disease specialist consultation, the tissue was sent for 16S ribosomal sequencing to subtype the Neisseria species that was demonstrated on culture. Ultimately, N animaloris was identified in tissue using the 16S ribosomal sequencing. Specific primers for fungi and mycobacteria did not demonstrate the presence of these organisms. Culture results of the surgical specimens were also positive for Staphylococcus epidermidis resistant to ampicillin, thought to represent coinfection. Multiple cultures for acid-fast bacilli and fungal pathogens were sent and were negative, whereas N animaloris was the only pathogen repeatedly cultured from tissue. The isolate was sent for susceptibility testing, but it grew in insufficient quantities to run susceptibilities. A literature search was performed by an infectious disease specialist, who suggested that the organism is typically susceptible to amoxicillin-clavulanate. The patient was prescribed amoxicillin-clavulanate (875/125 mg twice daily) after surgery for 4 weeks, and the duration was subsequently extended by the infectious disease provider based on clinical examination findings concerning for incomplete eradication of infection as well as the chronicity of the wound. An additional 4 weeks of amoxicillin-clavulanate was prescribed, for a total of 8 weeks of antibiotic treatment after surgery.

The patient returned to the operating room 4 weeks after the initial 2-layer skin regeneration system placement for staged split-thickness skin grafting. At the time of the skin graft, the Integra
Neisseria is recognized as a major pathogen associated with dog and cat bites; however, the species is often unknown.5,6 Neisseria animaloris is rare cause of infection related to dog and cat bites, but this rarity may be related to misdiagnosis. Misdiagnosis was initially thought to result from poor growth in the laboratory; however, Heydecke et al1 demonstrated growth on blood and chocolate agar within 2 days of incubation in ambient air. They postulated, therefore, that the difficulty with diagnosing this pathogen is instead with identification in the laboratory setting, rather than growth in the laboratory setting.1

Heydecke et al1 reported that a yellow-white colony grown on blood or chocolate agar, in addition to a negative spot indole test, can allow differentiation of N. animaloris and Pasteurella species.1 In addition, the Biolog system (Biolog, Hayward, CA) for microbial identification and production of arginine dihydrolase can be used to confirm diagnosis.1,2 Using this method of identification, no molecular techniques are required, and if an on-site laboratory offers the test, the results can return in hours.1 If available, the 16S ribosomal sequencing can also be used to confirm the Neisseria species, as was done in our case report.2 Ribosomal sequencing results are typically available in 1 to 2 days if an on-site laboratory offers the test, and if the test is sent to an outside laboratory, results are available in 1 to 2 weeks.

Identifying the pathogen and species can help guide antibiotic treatment accurately, to reduce rates of wound nonhealing as well as resistance to antibiotics. Available literature recommends treatment of N animaloris with amoxicillin-clavulanate.1,1 Heydecke et al1 examined antibiotic resistance and sensitivity of the organism and found that the organism is resistant to penicillin, oxacillin, cefuroxime, and gentamicin. The organism was susceptible to amoxicillin, imipenem, and ciprofloxacin.1 Cefotaxime was not studied. The patient in our report received multiple rounds of multiple antibiotics, eventually receiving amoxicillin-clavulanate once the diagnosis of N animaloris had been made.

Delay in diagnosis and inappropriate antibiotic treatment can contribute to chronic wounds. Heydecke et al1 reviewed the cases of 11 patients with N animaloris, only 3 of whom demonstrated complete wound healing at the time of their last visit with their physician. The 3 who demonstrated complete wound healing did so at 2 to 8 weeks. The current patient demonstrated a nonhealing wound over the course of 4 years, which eventually required a skin graft. The 3 who demonstrated complete wound healing did so at 2 to 8 weeks. The current patient demonstrated a nonhealing wound over the course of 4 years, which eventually required a skin graft. The patient in our report also developed botryomycosis and the Splendore–Hoeppli phenomenon, which, to our knowledge, has not been documented previously in relation to N animaloris. Biopsy performed by dermatology demonstrated botryomycosis, a rare cutaneous swelling due to chronic bacterial infection, which often evolves to ulcers or chronic sinuses.1 Botryomycosis is seen more often in immunocompromised patients but has also been documented in the literature in immunocompetent patients.1 Literature supports an extended course of antibiotics as well as surgical intervention for optimal treatment of botryomycosis.1 In addition, the Splendore–Hoeppli phenomenon is demonstrated on pathology by a pathogen surrounded by radiating eosinophilic material, caused by an immune reaction depositing antigen–antibody complexes.1 This is a nonspecific phenomenon, because it can occur with fungus, bacteria, and parasites; however, in the patient in this report, given the history of positive Neisseria culture with an inability to identify the species, it was thought to represent bacterial infection without positive staining.1 In the case presented, botryomycosis and the Splendore–Hoeppli phenomenon aided in the diagnosis of infection and our ability to rule out neoplasm or autoimmune pathology. These findings can prompt further testing, such as 16S ribosomal sequencing.

Early diagnosis and appropriately guided antibiotic treatment provide the best likelihood of resolution of N animaloris infection. When diagnosis and guided antibiotics are delayed, chronic nonhealing wounds can result, requiring multiple surgical interventions as presented in this case. Surgical intervention is rarely necessary in the early stages of infection. However, as chronic nonhealing wounds develop, surgery has a more critical role in the treatment of this pathogen. Early identification and appropriately guided antibiotics increase the likelihood of resolution of infection without surgical intervention. Identification methods presented in this report should be employed in the laboratory for culturing samples from dog and cat bites, especially in the case of a nonhealing wound, for possible N animaloris infection. In addition, extended antibiotic therapy should be considered, given the long duration often required for eradication of infection.

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