

CHAPTER 1

Skin and Soft Tissue Infections

Case 1.1 Soft tissue infection following traumatic aquatic exposure

In early September 2010, a 7-year-old boy suffered a laceration injury to the left calf during a recreational boat ride on a coastal river. He was brought to the emergency room (ER) within 2 hours of this accident, after initial cleansing first aid with saline in the field.

The wound was noted to be severe and deep, and was described as “partial degloving” by the ER physician. The boy’s vital signs were stable. Due to the nature of the wound, an orthopedic surgeon was consulted and the patient was taken to surgery within 2 hours for wound washout and closure. X-rays of the leg showed no fractures.

Cefazolin and gentamicin were given preoperatively. The patient received 34 stitches to close the large (>10 cm) complex left calf laceration injury after extensive washout. No cultures were done.

One day later, infectious diseases consult was sought for outpatient oral antibiotic recommendations, in anticipation of discharge home later that day.

The boy’s past medical history was unremarkable, except for hospital admission for symptoms of nausea and vomiting 1 year earlier, and ear tubes placed 1.5 years earlier.

His examination was unremarkable except for superficial abrasions on the lower abdomen and right upper arm, and the deep (now sutured) left calf laceration. Temperature was 100.5 °F, but other vital signs were stable.

A combination of trimethoprim/sulfamethoxazole and cefuroxime was recommended as oral antibiotics, and the patient was then discharged to outpatient follow-up.

Six days after discharge from the hospital, he was readmitted because of wound infection. He had failed to take the prescribed antibiotics because of severe nausea.

At surgery, no frank pus was found but serous old blood and drainage were noted. A swab of this drainage was stained and cultured.

Cases in Clinical Infectious Disease Practice: Obtaining a Good History from the Patient Remains the Cornerstone of an Accurate Clinical Diagnosis: Lessons Learned in Many Years of Clinical Practice, First Edition. Okechukwu Ekenna.

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The infectious diseases consultant was called (after surgery) to help with additional recommendations. He added ceftriaxone to the vancomycin already prescribed. Examination of the patient the next day found him to be comfortable, afebrile, and eating breakfast. His temperature was normal (97.8 °F). The abdominal skin abrasions were healing, but the left calf was wrapped up following the surgical incision and debridement (I&D) the day before.

Basic laboratory findings were normal (white blood cell [WBC] count was 7300/ μ L, platelet count 401,000/ μ L, and creatinine 0.5 mg/dL).

The gram stain of the serous fluid from the wound showed rare WBCs and no organisms. Twenty-four hours later, the culture was reported positive for a gram-negative rod (GNR).

The left calf wound was clean when inspected on day 4 post surgery (Fig. 1.1a).

- *What are the likely organisms in this patient (differential diagnoses) and why?*

The GNR was found to be oxidase positive, beta-hemolytic on sheep blood agar (BA), and the subculture showed luxuriant growth on all three agar media (BA, chocolate BA, and MacConkey agar) within 24 hours (Fig. 1.1b). It was noted later to be resistant to penicillin/ampicillin-like agents, including carbapenems, but sensitive to second- and third-generation cephalosporins, quinolones, and trimethoprim/sulfamethoxazole, as well as tetracyclines and aminoglycosides.

- *What is your new diagnosis?*

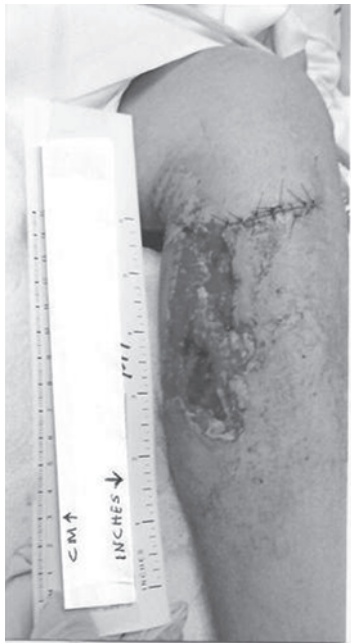


Figure 1.1a Left calf wound on day 4 post surgery (reproduced with permission). (See insert for color information)



Figure 1.1b Luxuriant growth of gram-negative rod on blood agar medium in 24 hours, and comparative growth of the same organism on BA, chocolate BA, and MacConkey agar. (*See insert for color information*)



Figure 1.1c Photo taken in March 2011, 6 months after the injury: healed left calf post skin grafting (reproduced with permission).

The patient was discharged 6 days later to outpatient follow-up on intravenous ceftriaxone after a peripherally inserted central catheter (PICC line) was placed.

Two months later he was doing very well, and underwent plastic surgical repair of the calf laceration (Fig. 1.1c).

- *What were the clues to the diagnosis?*

Case discussion

First, the injury occurred while boating on a river, in possibly brackish water (coastal river). Gram-negative organisms are common and likely to contaminate the wound with such a severe laceration injury. The organism grew rapidly on all three culture media used (BA, Choc BA, and MAC). It was oxidase positive, non-lactose fermenting, mucoid, and beta-hemolytic on sheep BA. It did not require high salt concentration to grow, making certain *Vibrio* organisms (those that need high, 6.5% salt concentration) unlikely. The sensitivity pattern is also useful (see earlier). The organism turned out to be sensitive to the two agents originally recommended (trimethoprim/sulfamethoxazole and cefuroxime). The child was unable to take the antibiotics because of persistent nausea.

Differential diagnosis

Our differential diagnoses at the onset were *Aeromonas* or *Pleisiomonas*, more likely than *Vibrio*, because of the fresh water or brackish water environment where the injury occurred. The luxuriant growth in all three media was in keeping with the differential diagnoses chosen.

- *Final diagnosis: Aeromonas hydrophila*

Some data from the literature on *Aeromonas* are shown in Table 1.1a and given below.

Sites of isolation of *Aeromonas* (environmental reservoirs) [2]

- Fresh water
- Estuarine (brackish) water

Table 1.1a Organisms associated with soft tissue infection following water exposure.

Organisms	Exposure	Clinical syndromes
<i>Aeromonas</i> spp*	Fresh water	Rapidly developing infection associated with fever; sepsis
<i>Edwardsiella tarda</i> *	Fresh water	Cellulitis, occasionally fulminant infection with bacteremia
<i>Erysipelothrix rhusiopathiae</i>	Puncture wounds from shrimp, crabs, and fish	Indolent localized cutaneous eruption; erysipeloid
<i>Vibrio vulnificus</i> *	Salt or brackish water	Rapidly progressive necrotizing infection; bullous cellulitis; sepsis
<i>Mycobacterium marinum</i>	Salt or fresh water including fish tanks	Indolent infection; papules progressing to shallow ulcers; ascending lesions may resemble sporotrichosis

*Infection associated with patients with underlying liver disease, iron overload syndromes, and cancer; infections in these high-risk groups are particularly fulminant [1].

Reproduced with permission of UpToDate from Baddour [1].

- Surface water, especially recreational
- Drinking water, including treated, well, and bottled
- Polluted waters
- Waste water effluent sludge

The organism grows at a range of temperatures from 0 °C to 42 °C.

Characterization and classification of *Aeromonas* [2]

- Aeromonads are ubiquitous inhabitants of fresh and brackish water.
- They have also been recovered from chlorinated tap water, including hospital water supplies.
- They occasionally cause soft tissue infections and sepsis in immunocompromised hosts and increasingly have been associated with diarrheal disease.
- Because of recent phylogenetic studies, *Aeromonas* species have been moved from the family Vibrionaceae to a new family, the Aeromonadaceae.

Microbiologic identification of *Aeromonas* [2,3]

- Oxidase-positive, polar flagella, glucose fermenter, facultative anaerobic GNR.
- Resistant to the vibriostatic agent O/129, and unable to grow in 6.5% NaCl.
- Hemolysis is variable but most are beta-hemolytic on BA media.
- There are a few useful standard biochemical tests (*A. hydrophila* is catalase positive and motile, converts nitrate to nitrite, and is urease negative).

Antimicrobial susceptibility tests of motile *Aeromonas* spp [2]

- Most strains are resistant to penicillin, ampicillin, carbenicillin, and ticarcillin.
- Most are susceptible to second- and third-generation cephalosporins, aminoglycosides, (carbapenems), chloramphenicol, tetracyclines, trimethoprim/sulfamethoxazole (TMP-SMX), and fluoroquinolones. In the case presented here, the *Aeromonas* was resistant to carbapenems, ampicillin, and first-generation cephalosporins.
- Higher resistance patterns (to TMP-SMX, tetracycline, and some extended-spectrum cephalosporins) have been found in Taiwan and Spain.
- Therapy with ampicillin or first-generation cephalosporins is not appropriate.

Lessons learned from this case

- Think of wound contamination with any complex laceration injury.
- Culture of the wound is critical before antibiotics are prescribed.
- No complete closure of wound, especially when environmental contamination is known or anticipated, as in this case.
- The patient should be advised to take the antibiotics or report if there are problems, so adjustments may be made. The patient in this case did not take the prescribed antibiotics because of nausea.
- Inspect wounds regularly for signs of inflammation or infection (pus, redness, pain, swelling, induration, or drainage).

- Think of the epidemiology (type of injury, environment, place, and season of the year) of the injury, and likely organisms expected in the given circumstances

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Case 1.2 Soft tissue infection of the hand and wrist in an 81-year-old man

An 81-year-old Caucasian male was seen for soft tissue infection of the right hand and wrist.

Infectious diseases (ID) consult was sought on 3/4/09 because of a severe hand and wrist wound following surgery. This patient had extensive flexor tenosynovectomy of the right wrist and drainage of abscess of the palm, plus carpal tunnel release 16 days earlier on 2/16/09.

He had been seen 6 weeks earlier in January elsewhere because of swelling of the right thumb several days after a shrimp fin puncture injury to his thumb. Following computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound studies, he had been started on antibiotics without improvement in the swelling of the thumb. When he began to develop cellulitis of the right arm, he was referred to the orthopedic surgeon for further management. Initially, steroid injection to the right wrist was tried, along with oral clarithromycin, but these treatments did not help the swelling. Incision and debridement was therefore done on 2/16/09. At surgery, thick white, purulent material (pus) was obtained, and sent for culture.

The significant finding in the review of systems was severe pain in the wrist, but no fever.

Past medical history and underlying diseases included the following: Atrial fibrillation, for which he had been on Coumadin (warfarin) for years. He had easy bruising (and may have bled into the wrist?). He had bladder stone removed 2–3 months earlier through cystoscopy. He also had exploratory laparotomy several years earlier, including lysis of adhesions. He had significant generalized arthritis

and coronary artery disease (CAD), with coronary artery bypass graft (CABG) surgery more than 3 years earlier, plus cardiac stents 4 years previously. Other underlying diseases included hypertension, gout, and sleep apnea (he was on home continuous positive airway pressure – CPAP).

He was retired after working for many years in the construction business. He stopped smoking 40 years earlier, and stopped drinking alcohol 2 years before the office visit. He had no allergies.

On examination, he was alert, oriented, pleasant, and in no acute distress. The vital signs were as follows: blood pressure (BP) 148/78, respiratory rate (RR) 18, heart rate (HR) 78, temperature 98.6 °F; height 5'9"; weight 197 pounds.

Head and neck exam was significant for partial dentures with extensive dental work and bridges. No adenopathy was noted. The heart exam showed irregularly irregular heartbeat consistent with atrial fibrillation. The chest showed a healed thin median sternal scar from previous CABG surgery. The rest of the exam other than the extremities showed nothing significant. The upper extremities showed ecchymotic skin changes in the forearms; the right forearm, wrist, and proximal palm surgical site is shown in Fig. 1.2a. The radial artery was palpable.

- *What are the possible differential diagnoses based on the history and physical exam so far?*
- *What would be your recommendation to the orthopedic surgeon at this time?*

A preliminary result of the 2/16/09 wound culture was available, but final confirmation of the organism and sensitivity was still pending.

The ID consultant suggested a limited I&D of the ballotable bulge in the wrist, to resolve whether a hematoma, seroma or pus was present. Additional cultures would also be obtained.

Additional I&D was done the next day (3/5/09) and the patient was subsequently seen in the office 10 days after the initial office visit, 9 days after the second surgery.

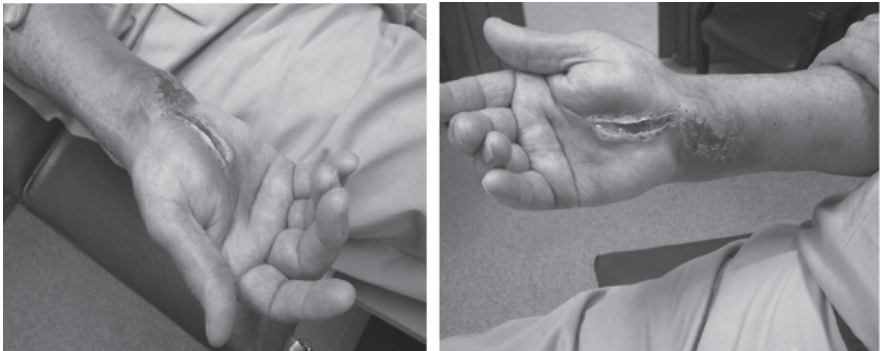


Figure 1.2a A large bulge of purplish bruised area is noted in the right wrist, along with the surgical incision in the hand. Photo was taken on 3/4/09 (reproduced with permission). (*See insert for color information*)

Initial laboratory findings

The histopathology of the 2/16/09 flexor tenosynovium from the right wrist was described as showing: "severe acute and chronic tenosynovitis with fibrin deposition, reactive and degenerative changes; rare giant cells with focal polarizable material and noncaseating granuloma."

- *How does this pathology report influence your preliminary diagnosis?*

Photographs of the right wrist were taken during follow-up visits 10 days, and 10 weeks, respectively, after the initial office visit on 3/4/09 (Fig. 1.2b).

The initial culture of tissue obtained on 2/16/09 was reported positive for acid-fast bacilli (AFB) on 2/26/09 (10 days later), and sent off for final identification or confirmation and antimicrobial sensitivity to a reference laboratory.

- *Final diagnosis: Mycobacterium marinum infection of right wrist*

The diagnosis was confirmed on 3/17/09, 1 month after the initial surgery and culture, by DNA probe and high performance liquid chromatography (HPLC).

The susceptibility test was available 18 days later, on 4/4/09. The organism was sensitive to all the six tested agents, including clarithromycin and trimethoprim/sulfamethoxazole, the two drugs which the patient was given as treatment. It was also sensitive to minocycline, doxycycline, ethambutol, and rifampin. Antimicrobial treatment duration was about 5 months, ending in August 2009.

Case discussion

This patient had *Mycobacterium marinum* infection in his right hand and wrist following a puncture injury from a shrimp fin that occurred when he was handling and cleaning shrimp. Initially, it was just a localized swelling of the thumb that was managed like a routine puncture wound. By the time he was seen by the ID

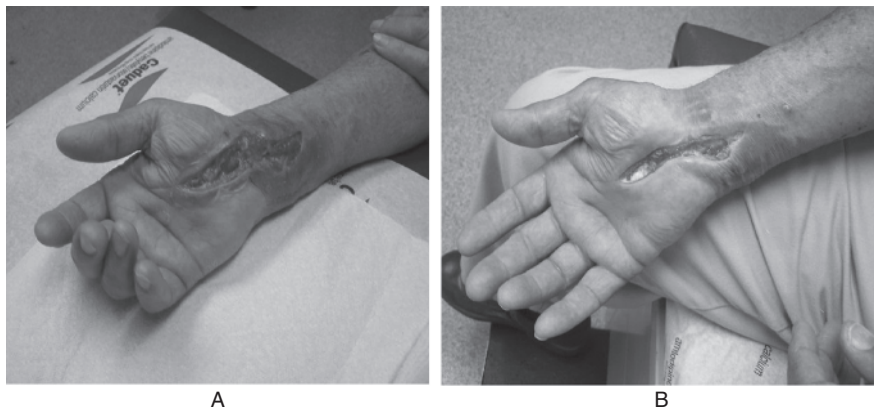


Figure 1.2b A. Photo taken on 3/14/09, 9 days after the second surgery. B. 10 weeks later, on 5/21/09 (reproduced with permission).

physician, he had been on clarithromycin for 3–4 weeks, and had been referred to the orthopedic surgeon who suspected a mycobacterial infection. However, the earlier treatment included, in addition to antibiotics, steroid injection in the wrist because of severe pain. The infection had spread to involve the hand and wrist, and included cellulitis of the forearm. All through these symptoms, fever was not an issue for the patient; pain and swelling were the paramount complaints. At incision and debridement (flexor tenosynovectomy) of the right wrist on 2/16/09, thick whitish pus was noted and cultured for routine as well as AFB and fungal cultures. All the initial stains were negative. However, 10 days later, an organism was cultured that was AFB positive. By the time of the office visit on 3/4/09, mycobacterial infection was the working diagnosis. The bulge in the wrist was opened up the next day, on 3/5/09, but that culture was negative. This patient was on warfarin, and may have also bled into the wrist area.

Mycobacterium marinum was suspected, based on the epidemiology (shrimp fin puncture injury, initial indolent infection, and AFB-positive growth in 10 days) of the wound and injury. Trimethoprim/sulfamethoxazole was therefore added on 3/6/09 to the clarithromycin that the patient was already taking. That choice was made based on knowledge of the local susceptibility pattern of this organism. As it turned out several weeks later, the *M. marinum* was sensitive to all six antimicrobial agents tested: clarithromycin, trimethoprim/sulfamethoxazole, minocycline, doxycycline, ethambutol, and rifampin.

The patient received the two-drug regimen of clarithromycin and trimethoprim/sulfamethoxazole from March to August, for 5 months altogether, and clarithromycin for slightly longer. The wound took so long to heal completely not because of bacterial persistence but because of the large size of the wound, two extensive surgical procedures, in a patient on warfarin therapy, and with other co-morbidities. He healed eventually without any plastic surgical procedures, but needed extended outpatient wound care 2–3 times a week. He was seen in the office at 3–6-weekly intervals, with the final visit 4 months after completion of antimicrobial therapy, and complete wound healing (Fig. 1.2c).

Non-tuberculous mycobacterial (NTM) infections

Currently, there are more than 120 species of mycobacteria classified under non-tuberculous mycobacteria (NTM) [1]. This group of mycobacteria is composed of species other than the *M. tuberculosis* complex, and had previous group names that included atypical mycobacteria and mycobacteria other than *M. tuberculosis* (MOTT) [1].

The classification of mycobacteria remains quite complex and continues to evolve, with advancement in culture and molecular techniques that have identified previously unknown organisms [1,2]. In the past, many of these organisms were either not recognized or were dismissed as laboratory contaminants. The



Figure 1.2c Healed right hand and wrist wound. Photo was taken on 12/18/09, 4 months after completion of antimicrobial therapy. The healing occurred without plastic surgery (reproduced with permission).

NTM are typically found in the environment, and have been recovered from surface water, including tap water and biofilms, soil, domestic and wild animals, as well as food and milk products [1,2].

Mycobacteria can be classified by their growth rate or whether they produce pigment [1,2]. The slowly growing mycobacteria require more than 7 days to reach maturity, while the intermediately growing NTM (e.g. *M. marinum* and *M. goodii*) require 7–10 days to reach maturity. *M. marinum* grows optimally at room temperature, 28–30 °C [1,3].

Clinicians are, however, more familiar with the clinical syndromes produced by these mycobacteria. There are four distinct common clinical syndromes caused by NTM [1,2].

- Progressive pulmonary disease (bronchiectasis or chronic obstructive pulmonary disease [COPD]: *M. avium complex* [MAC], *M. kansasii*, and *M. abscessus*; especially in older adults).
- Superficial lymphadenitis (especially cervical in children caused by MAC, *M. scrofulaceum*, and *M. tuberculosis* in TB endemic areas).
- Disseminated disease (severely immunocompromised patients: HIV and non-HIV patients) [4].
- Skin and soft tissue infection (typically as a consequence of direct inoculation, as in our patient).

Mycobacterium marinum has in the past been recognized as causing soft tissue infections termed “swimming pool” and “fish tank” granuloma [1]. These

designations reflect the type of activities those that acquired the infection were engaged in [5]. Skin break or inoculation precedes the infection, which typically follows within 2–3 weeks of contact or injury. The typical patient is otherwise healthy. Inoculation of the organism occurs through skin abrasion or punctures, and contact with saltwater fish, shrimp, or fins contaminated with *M. marinum*. The infection can sometimes present like sporotrichosis, with papules and nodules, but may produce more complicated wounds, as occurred in our patient. Antimicrobial treatment should take into account the local organism susceptibility, if available from the hospital or state health department laboratory.

Treatment typically includes two drugs, given for a minimum of 3 months [1]. Interestingly, an orthopedic group from Hong Kong reporting on *M. marinum* infection of the hand and wrist emphasized the importance of biopsy and debridement in managing patients with deep-seated infection [6]. In their review, they note that delay in diagnosis is common, because this is often an indolent infection. Often, the physician fails to elicit a history of aquatic exposure, and there is a lack of clinical suspicion, at least initially. A review of a large number of *M. marinum* infections was reported from France in 2002 [5]. Many of the reported cases had “fish tank” exposure, with most infections occurring in the upper limb.

Lessons learned from this case

- A good history and relevant epidemiology remain crucial in making a timely and accurate diagnosis of infectious diseases, including soft tissue infections such as mycobacterial infections.
- The injury from a marine crustacean (shrimp fin puncture) was a clue to the likely organism to expect in this wound infection.
- Appropriate cultures must be obtained, if an accurate diagnosis is to be made. If you do not think of the possibility, then the appropriate cultures (AFB) will not be done.
- Typically, appropriate mycobacterial cultures will require tissue obtained during surgical incision and debridement.
- Steroid injection, given for severe pain, was likely unhelpful and would be contraindicated in this case. I suspect it was done because the patient was not responding “fast enough” to the clarithromycin started earlier.
- Mycobacterial infections typically respond slowly, as with many indolent infections. Patience is therefore needed in the treatment of such infections.
- Often, a two-drug regimen is used, as in this instance, to prevent resistance during prolonged therapy.
- Treatment is typically prolonged: 3–4 months is usual, if there are no complications or underlying immunosuppression. With immunosuppression, treatment is even longer.

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The next four cases deal with severe beta-hemolytic streptococcal soft tissue infections.

Case 1.3 A 41-year-old Caucasian female with right arm swelling

A 41-year-old Caucasian female was admitted on 1/2/10, with acute swelling of the right arm and elbow. One day before admission she had complained of sore throat, followed by significant nausea and vomiting, up to 10 times in less than 24 hours. She awoke the next morning with redness and swelling of the right elbow. Within hours, the swelling had spread to involve areas below and above the elbow. A temperature of 103 °F was noted, in association with chills. She came to the emergency room, where she was medicated for nausea and vomiting, and admitted.

The review of systems was positive for sore throat starting the day before admission, fever and chills on the day of admission, and severe nausea and vomiting (10× in 24 hours) starting the day before and continuing up to the admission. On the day of admission, a rapid, severe, and extensive swelling of the right arm was noted.

The past medical history was significant for a previous swelling of the right elbow 2 years earlier without cellulitis. The symptoms resolved in 7 days. She had documented hypertension for several years and three C-sections 6, 10, and 15 years earlier. She did not drink alcohol, and had not smoked in 20 years. She was allergic to penicillin (rash).

Two days after admission, on January 4, infectious diseases consult was placed for assistance with the severe arm cellulitis, with bursa swelling of the right elbow.

The epidemiologic history was significant for the following: the patient's 10-year-old daughter had tonsillitis 7 days before the patient became ill with sore throat. By this time the daughter had recovered after antibiotic therapy. Her husband was also ill with a similar sore throat in the week between the daughter's illness and the patient's. Furthermore, she had cut her right index finger distal phalanx with a kitchen knife 8 days before her illness. Pus had developed a few days later, but the finger was now healed, with residual skin peeling but no streaking up the arm. They had two house dogs aged 3 and 9 years. She was a school teacher of 12–13-year-old children but school was out at Christmas, at the onset of the illnesses.

On examination, she was alert, oriented, not in acute distress, but worried. The vital signs were as follows: BP 95/52, RR 16, HR 70, temperature 100 °F (up to 103.2 °F the night before); height 5'6" and weight 160 pounds. The throat showed only slight redness of the oropharynx, but no pus. The heart, lung, and abdominal examinations were normal. Lymph nodes were not palpably enlarged. The right elbow was puffy and fluctuant, and there was tenderness involving the whole arm while the index finger was scabbed, reflecting the healing knife cut injury. Other extremities and the neurologic exam were normal. A photograph of the right arm taken on 1/6/10, 4 days after admission, is shown in Fig. 1.3a.

Laboratory findings showed the following complete blood count parameters and basic chemistries (sodium/potassium, glucose, BUN/creatinine, respectively) on the following days.

- On 1/2/10: white blood cells (WBC) 21.1, 12.3/36.2, mean corpuscular volume (MCV) 81.9, platelet 190 (diff: 89p 7L 4 M). Chemistries: 134/2.7, 125, 19/0.9
- On 1/3/10: WBC 18.4, 10.9/33.5, MCV 82.9, platelet 195 (83p 4b 6L 6M 1meta). Chemistries: 137/2.4, 104, 16/0.8
- On 1/4/10: WBC 14.4, 11.4/35.4, MCV 83.9, platelet 142 (55p 34b 7L 3M 1Eo). Chemistries: 136/4.1, 98, 14/0.8

Blood cultures on 1/2/10 and 1/4/10 were negative while plain x-ray of the right arm and elbow showed only soft tissue swelling.

Hospital course, procedures, and follow-up

A very limited incision and drainage procedure of the right elbow was done on 1/4/10. The photographs taken 2 days later on 1/6/10 (Fig. 1.3b) suggested a



Figure 1.3a Swelling of the right arm, elbow, and hand, reflecting cellulitis. Compare the left hand without swelling. Photos taken on 1/6/10 (reproduced with permission). (*See insert for color information*)

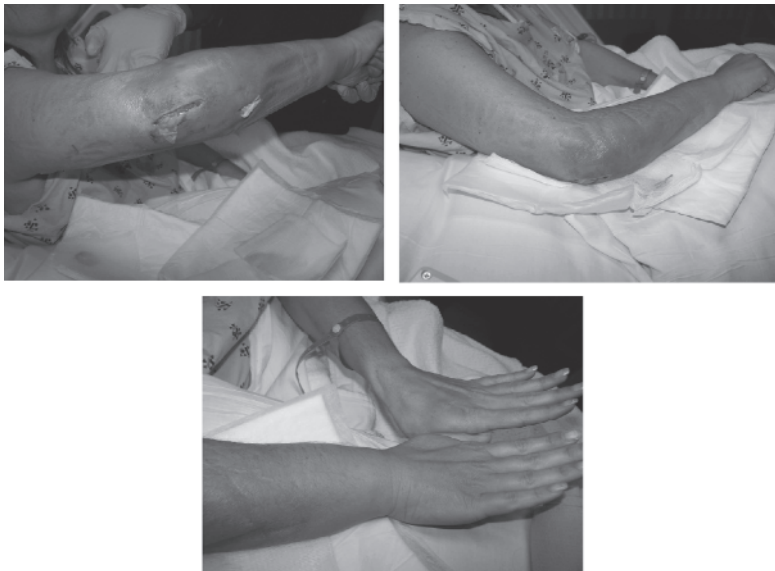


Figure 1.3b Photographs taken on 1/10/10, 2 days after the second surgery: markedly improved arm swelling (reproduced with permission).

need for further debridement. The patient was therefore taken back to surgery on 1/8/10 for a more extensive debridement. Two days later, there was a marked reduction in the arm swelling, reflected in the photographs taken on 10/1/10, 2 days after the second surgical debridement. The initial gram stain of pus obtained from the elbow on 1/4/10 showed 2+ (moderate) WBCs, but no organisms seen. Cultures from the elbow drainage on 1/4/10 and 1/7/10 were positive for group A beta-hemolytic *Streptococcus* (*S. pyogenes*).

Because of the history of penicillin allergy, the patient received a variety of other antibiotics that included daptomycin initially, and was discharged on 11/1/10 on a combination of oral clindamycin and levofloxacin. She continued to receive outpatient wound care till March 2010, 2 months after discharge from the hospital.

Comments

- This patient had inadequate surgical drainage initially, and so extended and prolonged inpatient and outpatient care continued till March 2010, 2 months after the hospital discharge.
- More detailed discussion will follow later after presentation of other cases.

Case 1.4 A 24-year-old female with fever and arm swelling

A 24-year old Caucasian female was admitted through the emergency room (ER) in late August 2009 because of swelling of the left elbow area.

Infectious diseases consult was sought 3 days later on 8/31/09 because of continued high fever, pain, and swelling of the arm.

The past medical history was significant for “crack cocaine” and other substance abuse, including oxycontin, and “crystal meth” (methamphetamine). She had failed a previous drug rehab treatment 2 years earlier. She had a history of anxiety and depression, asthma, hypertension, gastroesophageal reflux disease, and previous genital herpes infection. She had smoked a pack of cigarettes a day for 10 years and had no known drug allergies.

Epidemiologically important is that the patient had injected “crack cocaine” dissolved in water into her left arm (antecubital area) about 1 week before admission. Progressively worsening pain had been noted in the left elbow over the 3–4 days prior to admission.

On examination, she was alert, depressed, but not in acute distress. Her vital signs on 8/31/09 were as follows: BP 106/75, RR 16, HR 90, temperature 99.0 °F; height 5'8", and weight 136 pounds. The maximum temperature on 8/29/09, 1 day after admission, was 104 °F. Head and neck examination showed thrush while the heart, lung, and abdominal exams were unremarkable. She had tender

left axillary adenopathy, but no other abnormal lymph node enlargements. The rest of the skin (other than the left arm) was healthy looking, except for tattoos. The neurologic exam was significant for a depressed affect, but no focal findings.

Hospital course, laboratory findings, and follow-up

The initial I&D of the left arm done on 8/28/09 was limited. The cultures obtained showed mixed organisms that included the following: group C *Streptococcus*, *Streptococcus mitis/oralis*, as well as diphtheroids. Additional I&Ds were done on 8/31/09, with obtained specimens showing a pure culture of group C *Streptococcus*. HIV serology was negative, as was serology for acute hepatitis A, B, and C. She was hospitalized from 8/28 to 9/5/09, a total of 8 days, before discharge to outpatient wound care and follow-up on oral amoxicillin/clavulanate and levofloxacin.

Comments

She was seen in the office 19 days after admission (9/16/09), with the wounds almost healed. She failed to show up for her scheduled final visit 2 months later.

I spoke to the patient by telephone nearly 6 years later in 2015. She was still struggling with aspects of drug addiction, but was well.

It is thought that she acquired her infection through injection drug use under unsterile conditions (crack cocaine or oxycontin dissolved in water). She required about three surgical debridement procedures before discharge from the hospital. Initial ultrasound examination of the arm on 8/28/09 suggested heterogeneous hypoechoic abscess or hematoma within the antecubitus. MRI 2 days later confirmed the presence of superficial perivascular and subcutaneous abscesses plus diffuse edema and enhancement consistent with cellulitis of the whole left arm.

Case 1.5 A 72-year-old male with necrotic soft tissue elbow infection

A 72-year-old black male was admitted with severe right arm and elbow cellulitis. He had been hospitalized for 9 days (1/26–2/5/10), and then transferred to a rehab center on 2/5/10.

Infectious diseases consult was placed on 2/16/10 to address the cause of the prolonged necrotizing fasciitis, unresolved after two previous radical debridement and fasciotomy procedures on 1/28 and 2/1/10.

Recent past history and epidemiology included the following: the patient had fallen at home, and was admitted and worked up for stroke and coronary artery disease during the admission of 1/2–1/4/10. He had three stents placed at that time. It was not clear how long he had lain on the floor after the fall. He was

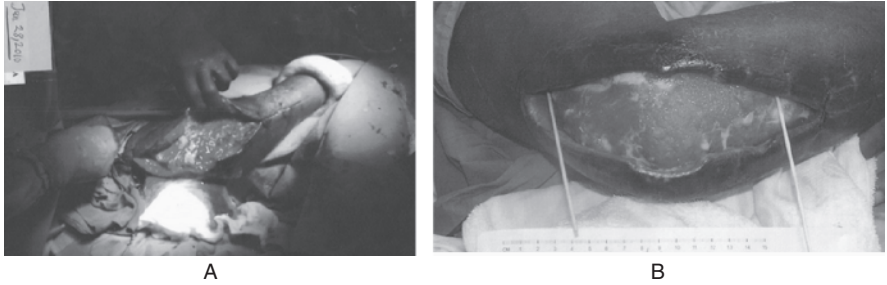


Figure 1.5a A. Photo taken at surgery on 1/28/10. B. Right elbow on 2/16/10, 19 days after the initial surgery (reproduced with permission).

readmitted from 1/7 to 1/18/10 with right arm cellulitis. Group A *Streptococcus* was cultured; clindamycin was prescribed, but it is uncertain how well the medication was taken by the patient. The third admission was on 1/26/10, this time for necrotizing fasciitis of the right arm and elbow.

Past medical history and other underlying diseases included type 2 diabetes mellitus, with cataracts and left eye blindness; degenerative joint disease (osteoarthritis); coronary artery disease with three stents placed 5–6 weeks earlier, and previous coronary artery bypass graft (CABG) surgery $\times 3$. He had a recent stroke with left-sided weakness and paresis. He also had chronic kidney disease, with a creatinine value of 1.8 mg/dL.

On examination, he was alert and oriented. His vision was poor (fuzzy). His vital signs were as follows: BP 129/60, RR 18, HR 87, temperature 98.1 °F. His height was 5'6" and weight 238 pounds. He had poor vision of the right eye with cataract, and loss of the left eye. He was edentulous. The heart, lung, and abdomen showed nothing significant while the chest showed a median sternal scar from previous CABG surgery. The upper extremities showed changes of osteoarthritis of the hands, loss of interosseous muscles of the left hand, and a slight weakness of the left arm, consistent with the stroke. The right arm showed a large open wound, up to 9 inches or more in length, as shown in Fig. 1.5a(B), taken on 2/16/10.

Comments

- The likely initial problem in the right arm was an abrasion suffered following a fall at home in early January, 2010. This may not have been readily apparent during the initial 1/2–1/4/10 admission. That hospitalization addressed primarily the stroke and CAD problems.
- Abscess was cultured on 1/7/10 when the patient was readmitted from 1/7 to 1/18/10 for cellulitis. However, he was inadequately treated until the admission on 1/26/10, during which period he had two I&Ds on 1/28 and 2/1/10.
- This patient was subsequently admitted to the hospital rehabilitation center from 2/5 to 2/25/10, and was discharged home on oral amoxicillin

and levofloxacin. He received hyperbaric oxygen therapy as part of the management of his arm wound infection during this admission.

- On 3/11/10, he was seen in the office with a wound VAC attached; the wound was still incompletely healed at that time, but was very clean. The antibiotics were discontinued 10 days later.

Case 1.6 A 37-year-old man with severe body aches and fever

A 37-year-old Caucasian male was admitted on 6/6/01 with severe headache, fever up to 100.5 °F, and confusion. CT scan of the head was normal. Lumbar puncture was attempted, but was unsuccessful, probably because of three previous back surgeries and distorted anatomy of the lumbar area. The WBC count was 12.1; the liver panel was normal, but throat culture was positive for group A *Streptococcus*. He was treated with levofloxacin and methylprednisolone, and discharged home on 6/8/2001, improved, on tapering steroids.

Two days after discharge home on 6/8/01, he developed new-onset fever and chills, generalized and severe body aches that became progressively worse, involving especially the right upper, right lower, and left lower extremities as well as the abdomen and back. He had no sore throat or cough at this time, and did not have a stiff neck or confusion. One day later, on 6/11/01, he was readmitted to the hospital.

The epidemiologic history showed that he had been covered with hundreds of gnats, especially on exposed legs, elbows and arms, after extended yard work 4 days prior to the initial admission on 6/6/01. Outpatient medications received by the patient were unknown.

On 6/12/01, one day after the second admission on 6/11/01, infectious diseases consult was sought for “septicemia.”

The past medical history was significant for three back surgeries between 1984 and 1997, and hypertension. He was married, with a 15-month-old healthy son. He had a desk job, but spent a lot of time outdoors, including gardening. He had smoked one and a half packs of cigarettes per day for 20 years and was allergic to codeine (urinary retention).

On examination on 6/12/01, he was alert, apprehensive, and dyspneic. The vital signs were as follows: BP 136/66, RR 26, HR 99, temperature 102.3 °F; height 5'9" and weight 200 pounds. The head, neck, heart, back, lymph nodes, and genital examinations were unremarkable. Lungs showed left basal crepitations while the abdomen was distended, with active bowel sounds, but was non-tender. There was tense swelling of the right arm, from the biceps and triceps area to the elbow, with some blisters on the inner wrist and near the elbow. The right lower extremity showed tense swelling involving the thigh and calf, down to the foot. There were minimal changes in the left upper and left lower extremity.

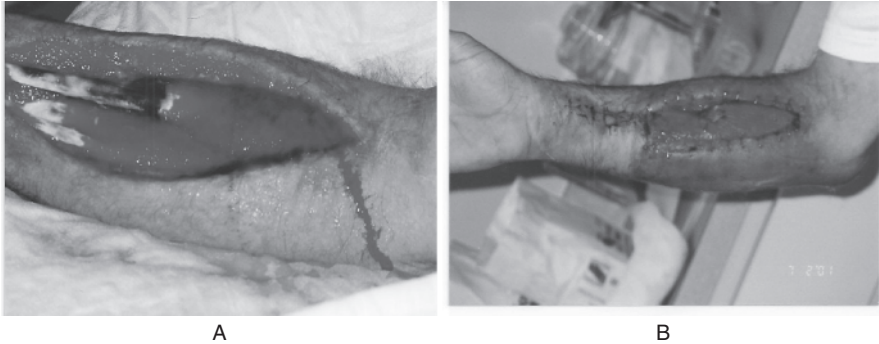


Figure 1.6a Right forearm: A. Day 15 post admission, after several debridements (note necrotic tendon). B. Day 21 of hospitalization: initial plastic surgery. Photos were taken on 6/26 (A) and 7/2/01 (B) (reproduced with permission). (See insert for color information)

The skin showed signs of livedo reticularis, consistent with vasoconstriction or poor circulation (patient was, however, not on pressor agents at the time). Faint peripheral pulses were noted on the left foot. The neurologic exam was positive for brisk deep tendon reflexes in the lower extremities. He was generally weak, apprehensive, and able to move all extremities.

Comments and postscript

The patient was hospitalized from 6/11/01 to 7/2/01, and discharged to outpatient follow-up on day 21 following admission. He had at least four surgical debridement and fasciotomy procedures on the following days: 6/12, 6/14, 6/19, and 6/22/01 (Fig. 1.6a). Additional skin grafting/plastic surgery would be done in the outpatient setting later, to ensure closure of the multiple wounds in all four extremities. While hospitalized, he received various antimicrobial agents that included, initially, piperacillin/tazobactam and clindamycin. He was subsequently discharged home on oral amoxicillin and ciprofloxacin. He had additional plastic surgery procedures in the outpatient setting and was completely healed when seen in the office 10 weeks later (Fig. 1.6b). A chest x-ray obtained on 8/23/01 showed complete clearance of the left-sided pneumonia and effusion. By the time of that office visit, he had been back to work (desk job) for several weeks.

The characteristics of the four patients with severe beta-hemolytic *Streptococcus* infection are shown in comparative detail in Table 1.6a.

Case discussion of the four beta-hemolytic *Streptococcus* infections

All four patients with beta-hemolytic *Streptococcus* infections presented here had severe illnesses that required either prolonged hospitalization or prolonged

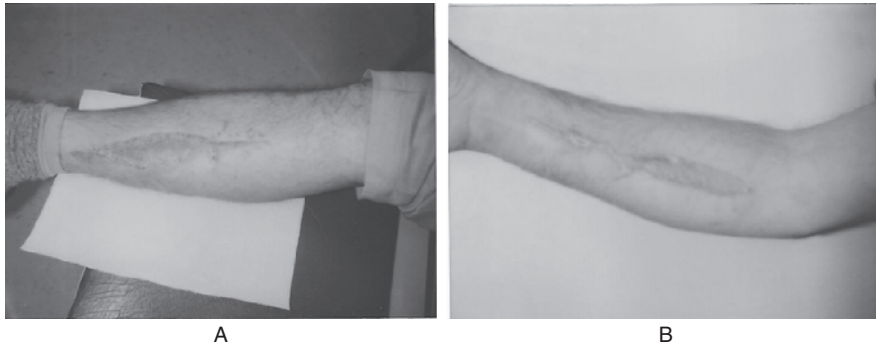


Figure 1.6b Photos taken on 8/23/01. Office visit 10 weeks after hospital admission. A. Healed right leg. B. Healed right arm wounds following skin grafts (reproduced with permission).

outpatient follow-up for wound care. They all also had multiple surgical debridement (at least 3× in each case) before the infection could be brought under control. Three cases were due to group A *Streptococcus*, while one case (case #1.4) was due to group C *Streptococcus* infection. The first and third cases were due to group A *Streptococcus* (*S. pyogenes*); the second case was due to group C *Streptococcus*. All of these streptococci are beta-hemolytic. The underlying pathogenesis in each case was some form of trauma: cut, abrasion or penetrating injury, or injection (as in the case of patient #1.4, who was an IV drug abuser). Patient no. 3 (case #1.5) had fallen after a stroke and likely lay on the floor for an extended period of time at home with a skin abrasion. His skin trauma or injury was missed, or inadequately cared for during the initial admission, because there was more concern at the time for the stroke and possible vascular event that may have led to the stroke. He had three coronary stents placed during the January 2–4, 2010 admission. He was readmitted 3 days later with right arm cellulitis, at which time *S. pyogenes* was cultured. He then had the first of three surgical incision and drainage or fasciotomy procedures in that arm. The third admission on 1/26/10 was for necrotizing fasciitis of that same arm.

The fourth patient (case #1.6) had group A streptococcal myonecrosis (gangrenous myositis), a different and more devastating clinical syndrome. This patient had multiple, extensive surgical debridement or fasciotomies during the second admission to the hospital and a prolonged second hospital stay of 21 days. He had severe body aches and systemic symptoms. Group A *Streptococcus* was cultured from the throat, blood, and wound (arm and leg). His was a more virulent disease with a higher mortality than the preceding three cases. All of the four presented patients survived.

The characteristics of the four cases of severe beta-hemolytic streptococcal soft tissue infections presented here have been summarized in Table 1.6a. All of these cases (except case #1.5 which occurred following a stroke) presented acutely

Table 1.6a Characterization of patients with severe beta-hemolytic streptococcal soft tissue infections.

Characteristic	Case #1.3 Admitted 1/2/10	Case #1.4 Admitted 8/28/09	Case #1.5 Admitted × 3: 1/2, 1/7, and 1/26/10	Case #1.6 Admitted × 2: 6/6 and 6/11/01
Age/sex	41 year C/F	24 year C/F	72 year B/M	37 year C/M
Site of infection	Right elbow	Left elbow	Right elbow	Right arm, right leg, and left leg
Maximum temperature (°F)	103.2	104	98.9	102.3
Days of symptoms before admission	1–2 days	3–4 days	1 day before initial admission; 3 days before second admission	4 days before 6/6/01 admission; 1 day before readmission on 6/11/01
Symptoms experienced	Sore throat, pain + swelling right elbow, N/V, and fever	Severe pain left elbow, and fever	Abrasion, pain, abscess, and swelling R elbow	Severe body aches, fever, and confusion
Duration of hospitalization	9 days	8 days	11 days	21 days
Number of surgical procedures and type	2x: incision and debridement	3x: incision and debridement	3x: incision and debridement, and fasciotomy	>4x: incision and debridement, or fasciotomy
Duration of outpatient follow-up	>2 months	19 days	>2 months	>2 months
Epidemiology of infection	Daughter and husband with sore throat; cut right index finger 10 days PTA	IV drug abuse: crack cocaine injection	Abrasion right arm following a fall; inadequate initial I&D, and treatment	Hundreds of gnats on exposed skin after extended yard work; presumably skin abrasions
Underlying diseases	Hypertension, allergy to penicillin	Substance abuse, GERD, and hypertension	DM type II, CAD, CABG surgery, CVA, CKD, and DJD	Hypertension, 3 back surgeries, and smoker

(continued)

Table 1.6a (Continued)

Characteristic	Case #1.3 Admitted 1/2/10	Case #1.4 Admitted 8/28/09	Case #1.5 Admitted × 3: 1/2, 1/7, and 1/26/10	Case #1.6 Admitted × 2: 6/6 and 6/11/01
Organism isolated	Group A <i>Streptococcus</i>	Group C <i>Streptococcus</i>	Group A <i>Streptococcus</i>	Group A <i>Streptococcus</i>
Other laboratory findings	WBC 21.0; blood cultures negative	WBC 12.9; blood cultures negative	WBC 9.7; blood culture not done	Blood cultures × 3 + for GAS; wound and throat cultures + for GAS; CPK 3166 (elevated)
Clinical syndrome	Severe cellulitis	Necrotizing fasciitis	Necrotizing fasciitis	Gangrenous myositis (myonecrosis)
Complications	Prolonged outpatient wound care	Extensive I&D above and below left elbow	3 hospital admissions, and 3 I&Ds	>4 extensive I&Ds and fasciotomy; left lower lung pneumonia and effusion; skin graftings
Antimicrobial therapy	Daptomycin, clindamycin, and levofloxacin	Ceftriaxone, amoxicillin/clavulanic acid, and levofloxacin	Vancomycin, amoxicillin, clindamycin, and levofloxacin	Piperacillin/tazobactam, clindamycin; amoxicillin and ciprofloxacin
Outcome: survived/died	Survived	Survived	Survived	Survived

B, black; C, Caucasian; CABG, coronary artery bypass graft; CAD, coronary artery disease; CKD, chronic kidney disease; CPK, creatine phosphokinase; CVA, cerebrovascular accident; DJD, degenerative joint disease; DM, diabetes mellitus; GAS, group A *Streptococcus*; GERD, gastroesophageal reflux disease; I&D, incision and debridement; M/F, male/female; NV, nausea/vomiting; PTA, prior to admission; WBC, white blood cell count.

(within days) with systemic symptoms that included high fever, body aches, and pain. All patients required multiple surgical debridement or fasciotomy procedures and prolonged inpatient or outpatient follow-up wound care management, in order to accomplish wound healing. The multiple antimicrobial agents used were a reflection of the severity of the patients' illnesses, and the desire on the part of the clinicians to find the "best" regimen.

Most beta-hemolytic streptococci are sensitive to most of the antimicrobials available, other than macrolides, e.g. erythromycin [1]. The isolates in all of our four patients were sensitive to the agents used for treatment. This group of organisms has maintained a relatively predictable susceptibility. The major toxicities caused by the beta-hemolytic streptococci are typically due to toxin production and other virulent factors, and not to any high level of antimicrobial resistance. Stevens and Bryant have outlined some of the virulent factors and other pathogenic mechanisms of disease caused by group A *Streptococcus* [2].

Adequate surgical debridement appears to be very important in achieving a more rapid healing, while inadequate debridement often led to prolonged hospitalization and wound healing.

In humans, the two most common sites of group A *Streptococcus* (GAS) infection are the skin and the upper respiratory tract. The intact skin usually presents an effective barrier to colonization or infection with GAS. However, infection is facilitated when there is skin damage [3], as was the case in all of the four patients described above. Because drainage of the abscesses and necrotic tissue was initially inadequate in all four patients, the duration of illness was prolonged, requiring additional surgical procedures. The patient with gangrenous myositis (myonecrosis) (case #1.6) had a more virulent disease, typically associated with a higher mortality. He was the only patient who had a positive blood culture, in addition to positive GAS cultures in wound tissue, and earlier in the throat as well. The differential diagnoses of GAS infections involving muscle and fascia have been summarized by Stevens and Baddour [4].

Lessons learned from these cases

- The typical severe beta-hemolytic streptococcal soft tissue infection presents acutely (within days), with systemic symptoms of fever, body aches, pain, and swelling.
- The source of most soft tissue infections is typically a breach in the skin by a variety of mechanisms, as was the case in all four patients presented here.
- Adequate drainage of skin abscess or necrosis is a crucial part of the management of severe beta-hemolytic streptococcal soft tissue skin infections.
- Delay in incision and drainage or incomplete drainage will likely lead to prolonged hospitalization or extended outpatient therapy.

- Antimicrobial therapy alone is often not sufficient to achieve successful treatment of severe soft tissue infections.
- The injury or damage caused by this group of organisms is usually not due to their high level of antimicrobial resistance, but to virulent factors that they produce, host factors, and type of treatment available to a patient.

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