Pseudomonas aeruginosa infections of cartilaginous structures

Nikolaos G. Almyroudis, Laura A. Clarke, Veronica T. Tucci, John N. Greene, Albert L. Vincent

Division of Infectious Diseases, Roswell Park Cancer Institute, Elm & Carlton Streets, Buffalo, NY 14263; Department of Psychiatry, New York University Medical Center, 560 1st Ave., New York, NY 10016; Division of Infectious Diseases and International Medicine, Department of Internal Medicine, University of South Florida College of Medicine, 12901 Bruce B. Downs Blvd., Tampa, FL 33612-4799; Division of Infectious and Tropical Medicine, H. Lee Moffitt Cancer and Research Institute, 12902 Magnolia Dr. Tampa FL 33612-9497, USA

Background: Pseudomonas aeruginosa is a gram negative facultative anaerobe and well-documented scourge of immunocompromised patient populations.

Objective: To study the prevalence and predisposing conditions for Pseudomonas aeruginosa infections of cartilaginous structures.

Method and results: We conducted an exhaustive search of the current literature using PubMed, Ovid, and Google Scholar. The various clinical entities of pseudomonal chondritis are discussed with respect to their epidemiology, clinical manifestations, diagnosis, and treatment.

Keywords: Auricular chondritis cartilage, costochondritis, invasive otitis, malignant otitis externa, pseudomonas aeruginosa, puncture wounds, pyogenic sacroiliitis.
factors, *P. aeruginosa* selectively infects certain cartilages. Local anatomic characteristics also underlie these tropisms. Risk factors for developing *P. aeruginosa* cartilage infections are summarized in Table 1 (see Discussion). Major sites of infection include fibrocartilaginous joints of intravenous drug users, cartilaginous regions of the foot in puncture wounds, auricular chondritis, perichondritis, and malignant external otitis. *P. aeruginosa* infections in more unusual sites such as nasal septum are also discussed in this review. Because septic arthritis is primarily an infection of the synovial membrane and surrounding fluid, that topic is omitted here. Antibiotic therapy and resistance have recently been reviewed by Cunha [9] and by Harris [10].

**Infections of the sternoclavicular, sternochondral, and costochondral joints**

Synchondroses are cartilaginous joints where hyaline cartilage is interposed between the articulating bones. Most ossify, becoming synostosis. Three exceptions are the sternoclavicular, sternochondral, and costochondral joints. The sternoclavicular joint consists of bone surfaces separated by a fibrocartilaginous disc, creating two synovium-lined articular cavities. The sternochondral and costochondral joints bear capsules of fibrous and synovial layers. These joints are supplied by the thoracic branch of the axillary artery.

Risk factors for infections include illicit IV drug use [11], median sternotomy, and osteomyelitis of the sternum. Bone involvement may arise from infected beast implants, subclavian central venous catheters or may complicate crushing injuries [12, 13]. Intravenous drug use leads to hematogenous seeding of joints, especially by *P. aeruginosa* and *Serratia*. Among IV drug users, the sternoclavicular joint is more susceptible than the sternochondral joint.

The course of costochondritis is usually subacute and the diagnosis may be pursued over the course of several months after the onset of symptoms. A prominent complaint is chest discomfort or pain over the affected joints. Usually, there is persistent fever, sometimes accompanied by weight loss and malaise. Sternoclavicular pyarthrosis is indicated by a pain in the neck or shoulder or one accompanying motion of the ipsilateral arm. Physical findings include erythema, swelling, and tenderness over the affected joints. Leukocytosis is variable, but the erythrocyte sedimentation rate (ESR) is typically elevated.

The diagnostic role of arthrocentesis in costochondritis is limited. In one exceptional case series, synovial biopsy demonstrated the causative agent in all cases reviewed [14]. Plain radiographs may be unremarkable or show a variety of abnormalities such as demineralization, lytic lesions, or periosteal elevation of the ribs [15]. Computerized tomography, which displays swollen soft tissue, is more useful in the early recognition of sternoarticular sepsis than is conventional X-ray [14]. Frequent findings are periosteal elevation of the clavicular head, rib, or sternum [16]. A tumor-like mass in the chest wall can easily be confused with a neoplasm [17]. Treatment consists of 6 weeks of intravenous antibiotics with antipseudomonal coverage. Contiguous bone involvement is an indication for surgical debridement.

**Infections of the symphysis pubis**

The symphysis pubis comprises two layers of hyaline cartilage separated by fibrocartilage. As in some other joints, pseudomonal infection has been described primarily in IV drug users [18, 19], but may also complicate pelvic surgery [20, 21].

Patients with infection of the symphysis pubis present with suprapubic, groin, or hip pain that is exacerbated by walking and that may simulate a hip infection. There is usually no leukocytosis, but an elevated ESR is the rule. Because initial radiographs are usually normal, a series of X-rays is needed to document erosion of the symphysis pubis and widening of the pubic rami [20]. Bone scans are usually positive. A definitive diagnosis is made by needle aspiration or by biopsy and cultures. Biopsy is necessary to differentiate pubic symphysis infections from osteitis pubis, a non-infectious, self-limited condition following pelvic surgery or trauma [22]. Antibiotic treatment should exceed four weeks and local debridement may not be necessary.

**Infections of the vertebrae and intervertebral disc**

Infections of these fibrocartilaginous discs have been described as complications of genitourinary surgery or urinary tract infections. The lumbosacral spine is most frequently affected, reflecting the common venous drainage of the spine and pelvis through Batson’s plexis. Among IV drug users the cervical spine is preferentially involved [7].

Several investigators have proposed that *Pseudomonas* disseminates from broken fragments
Infections of the sacroiliac joints

The sacroiliac joint consists of opposed hyaline cartilage between the sacrum and the ilium, with fibrocartilage superimposed in the superior position and surrounded by synovial membrane. Infections of the sacroiliac joints are rare, accounting for only 1%-2% of all cases of septic arthritis [25]. Pyogenic sacroilitis can be a complication of pelvic surgery or a consequence of IV drug use [26].

Patients may complain of pain over the sacroiliac joints, in the buttock, or in the anterior thigh, or one that is exacerbated by weight bearing. Because any motion of the spine irritates the sacroiliac joints, these patients tend to lie still in bed. The onset is usually acute and febrile. A positive straight leg-raising test may mislead the clinician to a diagnosis of lumbar disc pathology [26, 27]. The ESR is almost always elevated and notably, the blood cultures are frequently positive. Early plain radiographs of the sacroiliac joints are usually normal. Computerized tomography scans show widening of the joint space, subchondral bone changes, and swelling or abscess of the adjacent tissues. Magnetic resonance imaging with gadolinium-DTPA offers even greater sensitivity. Bone scans are usually positive. Intravenous antibiotics must be continued for at least 4 to 6 weeks. Miskew et al. [28] developed a reproducible method for obtaining culture specimens.

Invasive external otitis

“Malignant”, “necrotizing”, or “invasive” external otitis is an aggressive, life-threatening infection of the external auditory canal [29, 30]. Although some other bacteria have been implicated, P. aeruginosa is the usual culprit. Rather than remaining localized in the superficial skin overlying the external auditory canal, the organism invades and inflames the underlying cartilage and may extend into the adjacent bone at the base of the skull. Most patients with invasive disease are diabetics or immunocompromised, primarily by neutropenia. The majority of diabetics are type 2 with microvascular disease. Uncontrolled hyperglycemia, however, is apparently insignificant and diabetic ketoacidosis is absent in most cases [31, 32]. Infection is often initiated by self-inflicted or iatrogenic trauma to the external auditory canal [30]. Aural irrigation with water may heighten the risk of infection [33].

Otalgia around the ear and mastoid is the most prominent complaint. Purulent otorrhoea without fever or weight loss is typical [32]. Inflammation may extend to the pinna and a few patients will report hearing loss. Following temporal or basal osteomyelitis, neurodeficits may arise from the 7th and 9th-12th cranial nerves. On physical examination the external auditory canal is erythematous, edematous, and to a variable degree, obstructed by pus and debris. Pain is elicited by gentle traction of the pinna or upon mastication. Hallmarks of infection are the purulent discharge, the granulation tissue in the external auditory canal, and, in particular, a headache that defies treatment and is disproportionate to the balance of the clinical picture [34]. Leukocytosis is unlikely but the ESR is elevated, often over 100 mm/hr and is useful in following the response to treatment. Cultures of the external auditory canal and surgical specimens reveal the causative agent. Magnetic resonance imaging is superior to computerized tomography scan in demonstrating extension of disease [35, 36]. Technetium-99 is more sensitive in detecting early bone involvement, while gallium-67 single photon emission computerized tomography is useful in monitoring the response to treatment [37]. Malignant external otitis has a high mortality rate and cranial nerve deficits carry an especially poor prognosis. Extension to the temporomandibular joint may also be fatal [38]. Early
recognition and aggressive treatment is crucial. Surgical debridement should be accompanied by high doses of antipseudomonal antibiotics, four weeks in limited disease and 6-8 weeks in more advanced cases. Relapses may occur, usually within three months, but as long as 12 months after completion of antibiotics.

Auricular chondritis

The pinna of the ear is a fold of hyaline cartilage covered by a thin layer of skin. Once exposed or injured, the cartilaginous component becomes remarkably susceptible to infection. *P. aeruginosa* colonizes the cutaneous burn after the end of the first week and later invades both viable and necrotic underlying cartilage. *P. aeruginosa* is the most frequent cause of auricular chondritis (83-95% of cases), followed by *Staphylococcus* (55-56%), *Proteus* (20%), and other gram-negative bacteria [39]. The incidence of auricular chondritis in burn patients has decreased with the development of more effective topical antiseptics. As a consequence of high ear piercing, however, the frequency of perichondritis/auricular chondritis is rising [40-43]. Being avascular, the traversed cartilage is more prone to infection than is the lower fatty lobule. Organisms are injected directly into the cartilage by the piercing instrument, by the gun, or later, when newly compromised ears are exposed to water. The employees of cosmetic shops and earring kiosks are often poorly trained and use benzalkonium chloride, an inadequate preparatory agent [44]. *Staphylococcus* and *Streptococcus* are the most common organisms incriminated, but *P. aeruginosa* has been reported by various authors [40, 42, 45]. Perichondritis of auricular cartilage may also be caused by acupuncture [46].

Auricular chondritis manifests as dull ear pain that is refractory to analgesics, with erythema, edema, and extreme tenderness on palpation. The inflammatory process typically spares the lobule. Onset is usually 3-5 weeks after the burn or perforation. Crucial factors in prevention of chondritis are avoidance of pressure on burned ears and prompt topical control of local *Pseudomonas* infection [39]. Left untreated, the infection may progress to abscess, with necrosis of the cartilage and cosmetic deformity [40, 42, 45]. Treatment at this stage includes surgical drainage, debridement and antibiotics with antipseudomonal coverage. Coverage should continue for at least four weeks in limited disease and 6-8 weeks or longer for more extensive involvement. Cranial nerve involvement indicates a protracted course of treatment. Surgical reconstruction has been reviewed by Margulis et al. [47].

Foot puncture wounds and osteochondritis

*Pseudomonas aeruginosa* is the organism most commonly recovered from puncture wounds of the foot [48]. These wounds may lead to soft tissue infections, cellulitis, osteochondritis, osteomyelitis, or septic arthritis. Nails are the most frequent offenders but needles, wood, and glass are also dangerous [49]. Of 44 nondiabetic children admitted for puncture wounds of the foot, the most frequent pathogens in soft tissue infections were *Staphylococcus* aureus (54%) and *S. epidermidis* (19%), followed by *P. aeruginosa* (16%). In bone, however, the usual isolate was *P. aeruginosa* (86%), followed by *S. aureus* and *Streptococcus* spp [50, 51]. In a series of diabetic adult patients, Lavery et al. [52] found *P. aeruginosa* to be the most common pathogen in bone infections (36%), but in only 18% of soft tissue infections. Colonizing the humid inner sole of sneakers, *P. aeruginosa* may contaminate nails before entering the foot [51, 53, 54]. Pseudomonal osteochondritis is more common among those wearing sneakers than those wearing leather shoes [50, 55]. It occurs largely in children [56] because they are behaviorally more prone to puncture wounds [57] and because their feet are more cartilaginous than are those of adults [58]. Following infection, radiographs show premature closure of cartilage growth plates, joint space narrowing, and cyst formation. Systemic signs and symptoms such as fever may be absent, and the WBC count is typically normal, but the ESR is elevated. Local findings include moderate erythema, swelling, pain, and tenderness to deep palpation [49, 50]. Technetium bone scan is usually diagnostic. Magnetic resonance imaging can provide definitive diagnosis and the more precise anatomic localization necessary for surgical intervention [59]. If symptoms occur within one week, debridement and aggressive intravenous antibiotic treatment are imperative [48]. Intravenous antipseudomonal coverage [60] should be maintained for at least one week and up to six weeks for bone involvement. Oral antibiotic therapy for one to two weeks has also been successful [61]. Ciprofloxacin is the treatment of choice for plantar puncture wounds [62].
Complications in children include recurrence, chronic pain, and deformities that require sequestrecomies, angular osteotomies, and leg-lengthening procedures [63]. Cases taken lightly may lead to litigation [64].

**Infections of the nasal septum**

*P. aeruginosa* infections of the nasal septum have been described in burn wounds involving the nose, as a complication of elective rhinoplasty or other facial surgery, and in severely malnourished infants [65-70]. Although rare, infections of the nose may necessitate cartilage debridement and lead to cosmetic deformity. Ciprofloxacin resistance was reported by Pennekamp et al. [69].

**Hip joint**

Meek et al. [71] reported a single case of pseudomonal chondrolysis of the hip joint in a child who did well after a subtotal synovectomy and a prolonged course of antibiotics.

**Discussion and conclusion**

*Pseudomonas aeruginosa* tends to infect the cartilaginous structures of the body, often in patients with an underlying immune deficiency or comorbid illness. Diabetes mellitus is associated with invasive otitis externa, while burn patients are at special risk of auricular chondritis. Infections in otherwise healthy patients are provoked by piercing wounds into the upper pinna of the ear of adolescents and nail puncture wounds into the feet of children, especially those wearing sneakers colonized by the organism. Infections of the cartilaginous structures of the axial skeleton have become increasingly common during the last three decades with the rise of illicit IV drug use [4]. When *Pseudomonas* is allowed access to the circulation, certain joints are placed at special risk of chondritis (Table 1). Contamination may arise from the moist skin of the groin when addicts access their femoral vessels. Lemon water used to dissolve heroin powder enhances the growth of *P. aeruginosa* [72]. Moreover, opioids impair immune function, placing

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<th>Table 1. Risk factors for <em>pseudomonas aeruginosa</em> infections in cartilaginous structures.</th>
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abusers at higher risk of infectious diseases [73]. Samples of street heroin have antibacterial activity against S. aureus and Bacillus cereus, but none against P. aeruginosa [74].

The physical proximity of organisms resident on the mucosa or on moist surfaces of the skin is a key factor in the pathogenesis of auricular chondritis and septal infections. S. aureus often colonizes these same sites and is otherwise equally as aggressive, but is less likely to attack cartilage. Microanatomy may also play a role. Cartilage has more extracellular substance than do cellular tissues and, in contrast to the neighboring bone, its matrix is not vascularized. Nutrients and blood components are supplied by diffusion from the capillaries of the fibrous perichondrium. Cartilage is, therefore, less accessible to both antibiotics and to neutrophils, a major component of the immune defense against P. aeruginosa.

Physicians should be aware of pseudomonal chondritis as a clinical entity. Upon finding a pseudomonal bacteremia, the clinician should pursue the possibility of joint involvement. In patients presenting with pain or swelling over cartilaginous joints, Pseudomonas should be remembered in the differential diagnosis. Unrecognized infections may become difficult to manage and necessitate surgical removal of bone and cartilage.

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