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A Case Report of Pneumococcal Septic Arthritis Following a Respiratory and Gastrointestinal Prodrome with Accompanying Literature Review

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ABSTRACT

We report an uncommon case of septic arthritis of the ankle from a *Streptococcus pneumoniae* infection and provide an update of the literature reported since 2002. A 58-year-old female presented to the hospital with right ankle pain and an inability to bear weight. She reported a history of productive cough, vomiting, diarrhea, and subjective fevers 4 days earlier. Streptococcus pneumonia was identified in her ankle aspirate, and she was treated urgently with operative incision and debridement, followed by postoperative intravenous antibiotics. At her 7-week follow-up, she demonstrated complete resolution of symptoms and near-complete recovery of range of motion. This case demonstrates the importance of early identification, as the majority of patients recover fully with prompt treatment. The literature review included 44 cases of pneumococcal septic arthritis and found that the knee was the most commonly affected joint, followed by the shoulder and ankle. Blood cultures were positive for *S. pneumoniae* in 27 of 38 adults (71%) and 4 of 6 children (67%). Comorbid conditions were present in 32 of 38 adults (84%) and 4 of 7 children (57%), the most frequent of which were alcoholism and osteoarthritis in adults and malignancy or immunosuppression in children. Additionally, roughly half of included adults had an extra-articular focus of pneumococcal disease, most frequently pneumonia. Operative treatment was undertaken in 32 of 38 adults (84%) and all 7 children. Of adults with data available, 24 of 33 (73%) recovered with complete joint function, compared with 5 of 7 children (71%).

Septic arthritis is a medical emergency because of its significant morbidity, disability, and mortality and accounts for ~16,000 emergency department visits each year (1,2). The complications of untreated septic arthritis are devastating and include joint destruction, ankylosis, avascular necrosis, and spread of the infection to adjacent bone and nerve tissue (3,4). The mainstay of treatment for septic arthritis involves removing the purulent source of infection, either surgically or through arthrocentesis, and medical management based on empiric and targeted antibiotics (5).

Staphylococcus aureus is the most common organism implicated in septic arthritis, with an overall prevalence of 30% to 50% of all septic arthritis cases, followed by *Streptococcus pyogenes* (6,7). *Streptococcus pneumoniae* is an uncommon cause of septic arthritis, accounting for 2% to 4% of all cases (5,8,9). More often than not, patients who develop pneumococcal septic arthritis have an underlying comorbid condition, with some reports quoting rates as high as 85% in patients >2 years old (10). Herein, we present a case of pneumococcal septic arthritis in an otherwise healthy adult female. The authors are aware of 1 major literature review pertaining to pneumococcal septic arthritis that was published in 2003 by Ross et al (10) and reviews of cases before 2002. The purpose of the current report is to present a literature review of all reported cases from 2002 to the present to elucidate the demographics, presentation, treatment, and outcomes of pneumococcal septic arthritis. The secondary aim of this review is to compare these variables to those reported in comprehensive literature reviews of cases before 2002.

Case Report

A 58-year-old female with a history of intermittent alcohol use and a 20-pack-year smoking history presented to the hospital with a 4-day history of cough productive of sputum, vomiting, diarrhea, and subjective fevers. The patient reported an initial a cough, followed by vomiting and diarrhea 2 days later. Four days after the onset of her symptoms,

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she began to have significant right ankle pain with an inability to bear weight. She denied any preceding trauma. Upon presentation, she was afebrile with complete resolution of her respiratory and gastrointestinal symptoms despite ongoing subjective fevers.

Examination demonstrated mild erythema on the anteromedial aspect of the right ankle with significantly swelling. The right ankle was warm to touch and very painful with range of motion (ROM). No other joints were noted to be painful with ROM. The remainder of the physical exam was unremarkable.

In hospital, she was found to have elevated C-reactive protein of 297 mg/dL and a white blood cell (WBC) count of 16.8×10^9/L, with the differential demonstrating mostly neutrophils at 15×10^9/L. Aspiration of the right ankle yielded a thick yellow fluid. Gram stain of the right ankle aspirate found many pus cells and occasional Gram-positive cocci. The pathogen was identified as *S. pneumoniae*, susceptible to levofloxacin and penicillin (penicillin minimum inhibitory concentration ≤0.03 mg/L). To rule out seeding from an underlying bacteremia, a blood culture was performed, which showed no growth after 5 days.

The patient was taken to the operating room for an incision and debridement (arthrotomy and washout). Perioperatively, the patient received 2 g of cefazolin routinely every 8 hours. After application of an intraoperative tourniquet, an anterior midline approach between the malleoli was taken. The extensor retinaculum was incised in line with the skin incision. Incision into the joint capsule was followed by copious pussy joint effluent. The frank pus was aspirated for microbiology. A limited anterior synovectomy was also done and sent for microbiology. Intraoperative tissue cultures from the right ankle isolated *S. pneumoniae*. The joint was copiously irrigated with 3 liters of saline, with fluid running clear. 1 g of vancomycin was inserted into the wound followed by appropriate wound closure by layers. There were no intraoperative complications, and the patient was transferred back to the recovery room in stable condition.

Postoperatively, a peripherally inserted central catheter was placed, and antibiotic management was determined by the infectious diseases service at our hospital. The patient was started on ceftriaxone 2 g every 24 hours as the cefazolin was discontinued.

Chest X-ray obtained before surgical intervention demonstrated right middle lobe collapse. Given reports of a chronic hoarse voice, the differential included lung cancer in addition to atelectasis secondary to mucous plugging or other etiology. A postoperative chest computed tomography (CT) scan with contrast confirmed partial collapse of the right middle lobe and subsegmental atelectasis of the lung bases. The scan found no gross central obstructing mass. A follow-up chest X-ray 2 weeks after surgery found resolution of the previously described right middle lobe collapse and right lower lobe atelectasis. A follow-up chest CT 3 months postoperatively demonstrated near-complete resolution of the right middle and right lower lobe atelectasis.

The patient was discharged from hospital afebrile with stable vital signs on the fourth day postoperatively. The patient was seen in the outpatient clinic at 2 and 7 weeks postoperatively. At 2 weeks, her ROM in the affected joint was dorsiflexion to 5° and plantarflexion to 30°. She continued to feel well at 7 weeks, with complete resolution of her ankle pain and normal ambulation. Her ROM at 7 weeks was dorsiflexion to 5° and plantarflexion to 40° in the affected ankle, with no neurovascular compromise noted.

Literature Review

Methods

A literature review was conducted by keyword search of 3 databases (Pubmed, Embase, and MEDLINE) from publication date January 2001 to June 16, 2018. Keywords used included "pneumoc*", "Strep pneum*", and "septic arthritis." Additional searches included joints of the body by name. This search intentionally included duplicate articles that were a part of a 2003 review (10). These articles were manually excluded to ensure no missed cases. The references of key articles were also screened to ensure that no cases in the relevant time period were missed.

Results

From our search, we identified 18 articles that fit our inclusion criteria (7,10–27). The clinical characteristics of 45 cases of pneumococcal septic arthritis reported since 2002, including the above case, are summarized in Table 1. From the data provided, the mean age of adult patients was 61 ± 15.5 years, and the mean age of children with pneumococcal septic arthritis was 6 ± 6.3 years. Pneumococcal septic arthritis was reported more frequently in men (21 of 38, 55%) and boys (4 of 7, 57%) compared with women (17 of 38, 45%) and girls (3 of 7, 43%). There were few reported cases of recent trauma to the affected joint in adults (5 of 38, 13%), and no children reported recent trauma before infection. From the data available, 12 of 16 adults (75%) and 3 of 4 children (75%) presented with a temperature >38.0°C. Three of 29 adults (10%) and 2 of 7 children (29%) reported antecedent upper respiratory infections before the joint infections.

Laboratory values were inconsistently reported in the literature. From the available data, the mean serum leukocyte count was 15.0 ± 5.8×10^9/L in adults (n = 13) and 19.0 ± 6.3×10^9/L in children (n = 4). Mean C-reactive protein levels were 138.0 ± 131.3 mg/dL in adults (n = 11) and 37.1 ± 45.4 mg/dL in children (n = 5). Gram staining of joint fluid showed *S. pneumoniae* in 9 of 15 adults (60%) and the 1 child reported. Cultures of joint fluid for *S. pneumoniae* were positive in 35 of 38 adults (92%) and 6 of 6 children (100%). The mean WBC count in joint fluid was 184.2×10^9/L (n = 9); however, 7 patients were described as having elevated joint fluid WBC counts without values provided (12,25). Blood cultures grew *S. pneumoniae* in 27 of 38 adults (71%) and 4 of 6 children (67%).

The most commonly involved joint in both adults (45%) and children (50%) was the knee (Table 2). Other commonly affected joints in adults were the shoulder (10.4%), ankle (10.4%), wrist (10.4%), and hip (8.9%). Other commonly affected joints in children were the elbow (37.5%) and lumbar spine (12.5%). Polyarticular disease occurred in 16 of 38 adults (42%) and 1 of 7 children (14%). Pneumococcal septic arthritis involving a prosthetic joint occurred in 5 of 38 adults (13%).

Table 1
Demographic and clinical characteristics of pneumococcal septic arthritis patients (n = 38 adult; n = 7 children)

Finding or Characteristic	Adults, n/N (%)	Children, n/N (%)
Sex		
Male	21/38 (55)	4/7 (57)
Female	17/38 (45)	3/7 (43)
Recent upper respiratory tract infection	3/29 (10)	2/7 (29)
Antecedent trauma	5/38 (13)	0/7 (0)
Temperature >38°C	12/16 (75)	3/4 (75)
Prosthetic joint	5/38 (13)	0/7 (0)
Polyarticular infection	16/38 (42)	1/7 (14)
Extra-articular infection	18/38 (47)	0/7 (0)
Pneumonia	10/38 (26)	
Meningitis	3/38 (8)	
Endocarditis	1/38 (3)	
Other	7/38 (18)	
Bacteremia	27/38 (71)	4/6 (67)
Without extra-articular infection	14/38 (37)	4/6 (67)
With extra-articular infection	13/38 (34)	0/6 (0)
Mortality	4/38 (10)	0/7 (0)
Monoarticular infection	3/38 (8)	
Polyarticular infection	1/38 (3)	
WBC count >11 × 10^9 cells/L	10/13 (77)	3/4 (75)
Positive joint fluid *S. pneumoniae* results		
Gram stain	9/15 (60)	1/1 (100)
Culture	35/38 (92)	6/6 (100)

Table 2
Joint involvement in pneumococcal septic arthritis cases (n = 38 adults; n = 7 children)

Affected Joint	Adults, n (%)	Children, n (%)
Knee	30 (45.0)	4 (50.0)
Hip	6 (8.9)	0 (0)
Shoulder	7 (10.4)	0 (0)
Ankle	7 (10.4)	0 (0)
Elbow	3 (4.4)	3 (37.5)
Wrist	7 (10.4)	0 (0)
Sternoclavicular	1 (1.5)	0 (0)
Metatarsophalangeal	2 (3.0)	0 (0)
Acromioclavicular	1 (1.5)	0 (0)
Cervical spine	1 (1.5)	0 (0)
Lumbar spine	1 (1.5)	1 (12.5)
Costovertebral	1 (1.5)	0 (0)
Total	67	8

Comorbid conditions and risk factors were defined in accordance with the review by Ross et al (10). These conditions and factors were present in 32 of 38 adults (84%) and 4 of 7 children (57%) (Table 3). Major risk factors in adults included alcoholism (29%), osteoarthritis (16%), heart failure (16%), smoking (16%), and vaccination status (10%). Risk factors in children included malignancy (43%), immunosuppression treatment (43%), bone marrow transplant (43%), chronic graft versus host disease (43%), total-body irradiation (43%), prematurity (14%), and functional asplenia (14%).

Roughly half of the adults with pneumococcal septic arthritis had an underlying focus of pneumococcal disease (18 of 38, 47%). Eight patients (21%) had pneumonia, and 1 patient (2.6%) each had meningitis, endocarditis, soft tissue infection, pericarditis with positive pericardial fluid cultures, peritonitis, gingivitis, empyema, and sinusitis. Three adult patients had >1 extra-articular sites of infection, with 2 patients (5%) having pneumonia and meningitis and 1 patient (2.6%) having paraspinal and epidural abscesses. No children with pneumococcal septic arthritis had any underlying focus of pneumococcal disease.

Table 3
Comorbid conditions and risk factors in pneumococcal septic arthritis patients (N = 38 adults; n = 7 children)

Comorbid Conditions and Risk Factors	Adults, n (%)	Children, n (%)
Alcoholism	11 (29)	0 (0)
Osteoarthritis	6 (16)	0 (0)
Heart failure	6 (16)	0 (0)
Smoking	6 (16)	0 (0)
Unvaccinated	4 (10)	0 (0)
Renal failure	3 (8)	0 (0)
Malignancy	3 (8)	3 (43)
Multiple myeloma	3 (8)	0 (0)
Chronic obstructive pulmonary disease	3 (8)	0 (0)
Rheumatoid arthritis	3 (8)	0 (0)
Cocaine abuse	2 (5)	0 (0)
Cirrhosis	2 (5)	0 (0)
Hypertension	2 (5)	0 (0)
Immunosuppression treatment	2 (5)	3 (43)
Obesity	2 (5)	0 (0)
Splenectomy/functional asplenia	1 (3)	1 (14)
Hepatitis C	1 (3)	0 (0)
Diabetes mellitus	1 (3)	0 (0)
Bone marrow transplant	1 (3)	3 (43)
Aseptic necrosis of hip	1 (3)	0 (0)
Chronic graft versus host disease	1 (3)	3 (43)
Intravenous drug use	1 (3)	0 (0)
Recent prosthetic joint infection	1 (3)	0 (0)
Prematurity	0 (0)	1 (14)
Total body irradiation	0 (0)	3 (43)
Miscellaneous*	12 (32)	0 (0)
None (otherwise healthy)	6 (16)	3 (43)

*Miscellaneous conditions included dyslipidemia, hyperlipidemia, gastric bypass surgery, previous myocardial infarction, gastroesophageal reflux disease, diverticulosis, partial nephrectomy, seizure disorder, monoclonal gammopathy of undetermined significance, immunoglobulin M deficiency, and gout (1 patient each [2.6%]).

From the available data of adults treated for pneumococcal septic arthritis, patients were treated with intravenous antibiotics for an average of 33.2 days followed by oral antibiotics for an average of 32.4 days. Two patients were treated with intravenous antibiotics for an unknown duration, 1 patient was treated with arthroscopic draining and intravenous antibiotics for 10 days but had a recurrence of the infection 8 months later, 1 patient was lost to follow-up, and 4 patients died (these patients were excluded from the calculation of therapy duration). Ten patients (26%) were treated with operative incision and draining, 13 (34%) with arthrocentesis, 9 (24%) with arthroscopic drainage, and 6 (16%) nonoperatively. Five of the 7 children with pneumococcal septic arthritis were treated with intravenous antibiotics for an average of 19.6 days followed by oral antibiotics for an average of 18.7 days. Two children had complicated hospital courses requiring extensive intravenous and oral antibiotic administration, and 1 child was put on indefinite oral antibiotics (they were left out of the calculations for duration of therapy). Three children (43%) were treated with an operative incision and drainage, 2 (29%) with arthrocentesis, and 2 (29%) with arthroscopic drainage.

Functional outcomes for adults with pneumococcal septic arthritis were available for 33 (87%) of 38 patients. Of those with available data, 24 (73%) of 33 adults had complete recovery with full return of joint function; 3 (9%) recovered but with decreased range of motion in the joint; 1 (2.6%) recovered with mild joint pain with weightbearing, and 1 (2.6%) recovered without any pain but inability to ambulate. Of the 33 adults with available data, 4 (12%) died as a result of their infection. Complete recovery with full return of joint function occurred in 5 (71%) of 7 children with pneumococcal septic arthritis; 2 (29%) of the 7 recovered with limited joint mobility. There were no mortalities among the children.

Discussion

In our review, we found that males were affected slightly more often compared with females (55% versus 45%); however, Ispahani et al (28) reported that slightly more women were affected (14 of 25, 56%). The distribution between sexes shows only slight variations and may be due to sample size and chance alone. The most commonly affected joint in adults was the knee (45%), followed by the shoulder (10.4%), ankle (10.4%), and wrist (10.4%). Similarly, Ross et al (10) found that the knee was the most commonly affected joint (35 of 108, 32%); they reported fewer instances of wrist infections (2 of 108, 2%). Interestingly, Kennedy et al (29) found that in all cases of native joint septic arthritis, the shoulder was slightly more common than the knee (21.4% versus 21%, respectively), followed by small joints of the hand (14.9%). In children, we found that the most commonly affected joint was the knee (50%) followed by the elbow (37.5%). This is in contention with other reports showing that the hip is the most commonly affected joint, followed by the knee, shoulder, elbow, and ankle (4,10). Moreover, in 80% of all cases of pediatric septic arthritis, the hips, knees, and ankles are most commonly affected (30). Because of our small sample sizes, it is possible that the distribution of affected joints may have been altered. The higher proportion of polyarticular disease observed with *S. pneumoniae* infection may be related to the greater frequency of bacteremia among patients with pneumococcal septic arthritis (10). In our literature review, we found that 71% of adults with pneumococcal septic arthritis had positive blood cultures, compared with reports from all cases of septic arthritis, which showed positive blood culture values ranging from 24% to 33% (31,32). This is consistent with findings from Ross et al (10) that showed an incidence of bacteremia of 70.5% (n = 74 of 105) in pneumococcal septic arthritis.

Risk Factors and Etiology

Alcoholism is an important risk factor for the acquisition of adult pneumococcal arthritis, with a prevalence of 29% in our review. Alcohol decreases pulmonary macrophage phagocytosis, disrupts surfactant biochemistry, alters the levels of inflammatory cytokines, and potentiates the virulence of *S. pneumoniae*, culminating in an increased risk for the host (33–35). Smoking, heart failure, osteoarthritis, and lack of vaccination were other risk factors for infection. Smoking hinders the immune system by compromising the antibacterial functions of many WBCs, increasing host susceptibility to bacterial infection (36). Similarly, the increased levels of circulating cytokines and metabolic disturbances associated with cardiovascular disease may alter the body's immunomodulatory properties and predispose the host to infection (37). Likewise, as damaged joints are a nidus for infection, especially in the presence of bacteremia, osteoarthritis predisposes patients to pneumococcal arthritis. In a study comparing patients with invasive pneumococcal disease, osteoarthritis was an important risk factor for the development of septic arthritis (38). Vaccine status is another important consideration. Nagel et al (39) found that in vaccinated arthritic patients, pneumococcal infections were reduced by 45% compared with nonvaccinated patients. Unvaccinated patients accounted for 10% of cases in our review and represent a potential population to further decrease infection rates. Previous reports have documented rheumatoid arthritis (RA) as a major risk factor for pneumococcal arthritis, with upwards of 22% of pneumococcal arthritis patients having a diagnosis of RA (10). The inflammatory immune response and immunosuppressive therapies aimed at curtailing the disease leave patients prone to infection (40,41). Our review showed RA to be less of a risk factor for pneumococcal arthritis compared with the report by Ross et al (10).

Septic arthritis is an uncommon complication of pneumococcal bacteremia and may not be associated with an extra-articular foci of infection (42,43). A damaged joint is susceptible to hematogenous seeding of infection that is believed to arise from transient bacteremia from a mucous membrane source (10). In our review, less than half (47%) of the patients had an underlying pneumococcal infection, which is consistent with the previous review and other literature (10,19).

Treatment

The management of pneumococcal septic arthritis is dependent on the hemodynamic stability of the patient, the serotype, and antibiotic susceptibilities and involves both surgical and medical management. Incision and drainage (I&D) is an effective treatment for septic arthritis, as it removes purulent material from the joint space and decreases the intra-articular microbial load to a level unachievable with arthrocentesis alone (44). A retrospective cohort study over an 8-year period found that half of patients with septic arthritis of the shoulder or hip eventually required surgical intervention, suggesting that I&D should be a part of the initial protocol (45).

I&D can be performed openly via arthrotomy or arthroscopically, depending on which joint is infected and surgeon preference. Arthroscopy is an appropriate treatment for native joint septic arthritis, as it is minimally invasive and allows for a closed system with high intraarticular pressures to thoroughly irrigate the joint (46,47). Several studies have argued for the importance of arthroscopic evaluation followed by the removal of purulent material from the joint, especially given the low risk of arthroscopy and the high risk of joint sepsis (48–50). Although aspiration is able to remove purulent material, arthroscopy allows the surgeon to confirm the complete removal of said material and to assess the joint for other pathology that may require treatment. Johns and colleagues (47,51) found that in adult and pediatric patients with native knee septic arthritis, arthroscopic treatment was preferred, as it resulted in less repeat surgical irrigations. They also found that children were able to bear weight and range their knees earlier with arthroscopic treatment, whereas adults had significantly greater long-term ROM. Likewise, arthroscopic management of septic arthritis in very young children and for the wrist has been indicated as safe and effective, resulting in fewer operations and shorter hospital stays (52,53). Arthrotomy, however, is the best procedure to eradicate bacteria deeply embedded in a joint and for loculations; it is especially helpful for drainage of shoulders and hips. Böhler et al (54) found open arthrotomy to be superior to arthroscopy for septic arthritis of the shoulder. The preferred management for ankle and elbow septic arthritis has not been determined owing to the paucity of literature (55). In a systematic review involving a total of 15 ankles, arthroscopic treatment of septic arthritis demonstrated outcomes similar to arthrotomy; however, further research is needed (56).

Surgical management of septic arthritis allows for the most accurate joint staging, which is important to accurately tailor treatments. Boffeli and Thompson (57) came up with a treatment guideline, adapted from 2 case series studies (49,50), for the management of septic arthritis (Table 4). What is important in the proposed treatment plan is that the decision for repeat surgery should be decided by clinical judgment and laboratory results. Furthermore, it is important to be cautious with the debridement of tissue, as excessive debridement may destroy the natural barrier the synovium provides, whereas insufficient debridement may leave residual infected tissue (58). If the response to treatment is inadequate, it is necessary to consider that the causative organism may be incorrect, an alternative foci of infection may be present, or that antibiotic therapy may be insufficient (57).

The medical management for septic arthritis involves a short course of intravenous antibiotics (2 to 4 weeks), followed by the administration of oral antibiotics (3 to 4 weeks) (10,59). The choice of antibiotics and the duration of therapy is based on the organism's resistance profile and patient factors, with no one regimen showing superiority over another (59–61). The prognosis of pneumococcal arthritis is favorable, with >90% of patients regaining normal joint function (10,62). In comparison, *S. aureus* septic arthritis patients often have poor functional outcomes, with residual joint damage and deficits in mobility (32,63). Full recovery without any residual joint damage was seen in 73% of adults and 71% of children in our study, similar to what is quoted in the literature.

In conclusion, *S. pneumoniae* is an uncommon pathogen in septic arthritis and accounts for 3% to 10% of all cases of septic arthritis annually. Although it is common for pneumococcal arthritis to occur as an isolated disorder, alcoholism and osteoarthritis are important risk factors. Treatment for pneumococcal arthritis involves both intravenous and oral antibiotics and possible surgical intervention. Despite the rarity of *S. pneumoniae* septic arthritis, early identification is important, as the majority of patients recover fully with prompt treatment.

Table 4
Stage-based surgical treatment protocol

Stage	Surgical Treatment
I	Single arthroscopic irrigation with minimal debridement
II	Irrigation and debridement plus local synovectomy and fibrinectomy; may need to repeat procedure if clinical signs point to uncleared infection
III	Multiple irrigation and debridement procedures plus adhesion resection and partial to subtotal synovectomy
IV	Arthrotomy with multiple irrigations and debridements required plus removal of loose fragments and curettage of erosions or cysts

NOTE. The treatment algorithm was derived from the typical treatments necessary to successfully treat patients in 2 retrospective case series studies (49,50).

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