CASE REPORTS

CANDIDA ALBICANS INFECTION OF PROSTHETIC JOINTS

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Among complications of total joint arthroplasty, infection is of the most concern because it may be devastating and potentially lethal. The rate of prosthetic joint infection has remained relatively stable at 0.5% to 2.0% and most frequent organisms are Staphylococcus epidermidis and Staphylococcus aureus. Pugal arthritis following joint replacement surgery is particularly rare with only 17 previous cases reported in the English language literature. We describe three new cases of hip prostheses infected by Candida albicans. We expect that more such cases will be seen in the future, as immunosuppressed patients on steroids develop avascular necrosis of subarticular bone.

CASE REPORTS

Case 1. A 42-year-old woman with a renal transplant 20 years earlier was admitted for increasing right hip pain. Despite chronic rejection of her graft, adequate renal function was maintained with immunosuppressive drugs, including corticosteroids. There had been prior bilateral total hip and knee replacements for avascular necrosis. Nine years earlier she had revision of her right hip prosthesis for infection with S. aureus. For the past 8 years she complained of progressing right hip pain. Eight to 10 weeks prior to admission, the pain rapidly increased.

At admission she was afebrile and had limited range of motion of her right hip. White blood cell count was 7,300 with 80% polymorph neutrophils. Urine cultures were negative. Initial plain films demonstrated dislocation of the right hip prosthesis and lucency around the acetabular component suspicious of loosening (Fig 1). Scintigraphic arthrogram was normal and synovial fluid cultures were negative.

Fig 1: Frontal radiograph shows dislocation of the right hip prosthesis with lucency around a verticalized acetabular component suggestive of loosening (arrows).

At surgery, purulent material was identified in the joint. The prosthesis was removed and a Girdlestone procedure was performed. C albicans was the only pathogen growing from a culture of intraoperative specimens. Amphotericin B was begun at low dose because of her renal problem and gradually increased to 25 mg/day. Drainage from her hip persisted. Amphotericin B was continued to a total of 2 gm. In much later hip aspiration, C albicans was again identified. She subsequently died of end-stage renal disease before a revision arthroplasty was performed.

Case 2. A 67-year-old woman with long-standing rheumatoid arthritis had prior bilateral total knee and total hip arthroplasties. Seven years previously, she had a fracture distal to the tip of the femoral component of her left hip prosthesis requiring a long stem femoral prosthesis. Three years later the acetabular component of the left prosthesis was revised because of loosening.

She complained of drainage and pain from her left hip. On physical examination, she was afebrile with limited range of motion of her left hip. She was taking prednisone 15 mg/day for several years. White cell count was 10,300 with 93% polymorph neutrophils. Her erythrocyte sedimentation rate was 25 mm/hr. Urine cultures showed C albicans on few occasions. Plain radiographs showed lucency at the cement-bone interface of the femoral compo-
The left hip prosthesis was removed and the patient was given 6 weeks of intravenous vancomycin, but there was residual drainage from the wound. At further debridement, cultures from acetabular tissue and cement fragments grew *C. albicans*. The patient was then treated with amphotericin B 25 mg/day and ceftriaxone for 6 weeks.

After treatment, excessive polymorphs on frozen sections during left hip revision indicated persistent infection and cultures identified *S. epidermidis*. She improved on cephalazolin and was discharged on vancomycin. Fluconazole was also given because of the history of previous hip infection with *Candida* and recurrent urinary yeast infection. She died a year later from an unrelated condition.

**Case 3.** A 57-year-old alcoholic man has bilateral total hip prostheses for post-traumatic avascular necrosis of both femoral heads diagnosed 18 years earlier. Both hips have had multiple surgeries. The left hip was infected on four occasions, the last one being 10 years before the current admission. The right hip was infected three times, and a Girdlestone procedure was performed for the last episode 1 year earlier. Organisms involved include *S. aureus*, *S. epidermidis*, Group D *Streptococcus*, *Pseudomonas aeruginosa*, *Bacteroides fragilis*, and *Corynebacterium* species. The left hip was last revised 2 years previously because of loosening.

The patient presented with spontaneous drainage from the left hip for a week after complaining of pain for a year. He was afebrile. White cell count was 7,900 with 72% polymorph neutrophils. Erythrocyte sedimentation rate was 72 mm/hr. Plain radiographs were unremarkable. An arthrogram showed no signs of loosening, but the aspirate was sanguinous. Cultures of the synovial fluid were not conclusive. The prosthesis was removed and cultures of surgical specimens grew *P. aeruginosa*, *Enterobacter cloacae*, alpha Group D *Streptococcus* as well as *Bacillus* species. *C. albicans* was also identified. Vancomycin, imipenem, and fluconazole were started via a Hickman catheter. The postoperative course was uneventful. The patient returned a month later with recurrent drainage from his left hip. Cultures were positive for *S. epidermidis*. He responded well to debridement and methicillin and he was asymptomatic 6 months later.

**DISCUSSION**

Recently there has been an increase in invasive *Candida* infections, particularly in immunocompromised patients. In neonatal septic arthritis, *Candida* is as frequent as *Staphylococcus*. In Spain, *Candida* septic arthritis and osteomyelitis have become more frequent than staphylococcal disease in heroin abusers. *Candida* pyarthrosis is also part of a distinctive syndrome in intravenous drug abusers associated with multiple cutaneous abscesses and ocular manifestations. Risk factors known to be associated with fungal infection include indwelling catheter, the use of multiple antibiotics, hyperalimentation, immunosuppression, steroids, multiple surgeries, malignancy, malnutrition, cirrhosis, and intravenous drug abuse.
Fungal infection of a joint implant is rare. Including our three patients, only 20 cases of prosthetic joint fungal infections have been described in the English language literature. With two exceptions, all of these infections were caused by *Candida* species. *C. albicans* was the most frequent isolate occurring in 56% of cases. *C. parapsilosis* and *C. tropicalis* each accounted for about 22% of the remaining cases. Interestingly, 13 cases of fungal infection of joint prosthesis have been reported since 1988, which may indicate a trend similar to that in natural joints. This increase may simply reflect the rising number of joint arthroplasties, or the increasing number of patients with associated systemic illnesses or immunosuppressed status in whom this procedure is being done.

It was thought that most patients with prosthetic joint fungal infection have no predisposing condition other than the prosthesis itself. This was said to differ from the clinical setting of natural joint *Candida* infection. However, that review did omit a heroin abuser with a prosthetic joint infected by *Candida parapsilosis*. Four other cases have since been reported in patients chronically treated with corticosteroids. Our patients also had risk factors for fungal infection. Our first patient had several previous surgeries, including a renal transplant, and she was receiving immunosuppressive medication including steroids. The second had rheumatoid arthritis, she was treated with prednisone, and she also had multiple surgeries. The third patient had numerous previous surgeries and alcoholism. Including our patients, 11 of 20 (55%) had risk factors for fungal infection other than the simple joint replacement.

One quarter of patients with candidal periprosthetic joint infection had rheumatoid arthritis. The propensity of rheumatoid patients to become infected is well known. The pathogenesis of joint infections in rheumatoid arthritis is multifactorial, including decreased polymorphonuclear leukocyte chemotaxis, decreased phagocytosis, and decreased bactericidal activity of synovial fluid. Although patients with rheumatoid arthritis have four times the risk of any prosthetic joint infection as other patients, the number of cases of *Candida* infection is too small to draw further conclusions about predisposition.

In our patient with rheumatoid arthritis, bacterial infection preceded the fungal infection. A similar sequence was also observed in other reported cases. Use of antibiotics in bacterial arthritis may predispose to candidal infection. Preoperative antibiotic therapy has also been postulated to cause fungal infection.

Most fungal infections of prosthetic joints present as chronic indolent disease, as was the case for our patients. This makes the differential diagnosis from mechanical loosening difficult since both may present with local pain, no systemic signs and normal laboratory values.

The exact mechanism of candidal infection of prosthetic joints is not clear. Direct inoculation at the time of surgery has been proposed especially in patients without underlying risk factors. In most cases however, as in our three patients, there is a relatively long interval (mean: 14 months) between surgery and the occurrence of the candidal arthritis. This suggests a hematogenous route of infection from unrecognized candidemia as a more likely mechanism.

The diagnosis of *Candida* infection is not always readily made. The fungus is a saprophyte that may exist as a non-pathogenic or non-invasive colonizer of hospitalized patients. It is also a normal contaminant so its identification in synovial fluid culture may be disregarded unless the organism is identified on serial aspirations. It has been suggested that a definitive diagnosis be made by direct microscopic demonstration of the invasive fungus in the material from the site where cultures were obtained. The organism, however, is rarely identified on gram stains. Histologic evidence of invasive *Candida* however, was not present in any of the reported cases of prosthetic joint. In this setting, the diagnosis was made by positive culture from multiple joint aspirations or from a single aspiration in the proper clinical milieu. Culture from tissue specimen at the time of surgery may subsequently confirm the diagnosis.

Treatment remains controversial, and amphotericin B is still the most frequently used antibiotic. It has, however, many side effects including nausea, chills, hematological abnormalities, hepatic dysfunction, and nephrotoxicity. Ketoconazole, 5-flucytosine and fluconazole are less toxic, but experience with these drugs is limited. All reported cases required excision of the prosthesis. Only one patient had a new implant installed.

The rising number of joint arthroplasties and number of patients with systemic illnesses on which the procedure is being performed will contribute to a continuing increase of such opportunistic infections. Awareness of this complication is important since *Candida* infection may present insidiously and it may mimic mechanical failure. The outcome is generally poor. In patients at risk, search for the organism in synovial fluid aspirate or at the time of revision arthroplasty may allow for early recognition and treatment.
REFERENCES


EDITORIAL DISCUSSION

ORTHOPEDICS: Because Candida infections are relatively common in the urethra/bladder and in the vagina, do the authors feel that those infections in patients who are at risk (ie., rheumatoid arthritis, immunosuppressed) should be treated vigorously with fungicides to diminish risk of infection of the prosthesis?

Cardinal et al: Immunocompromised patients, especially those receiving steroids, are frequently colonized by Candida, mainly albicans, without candidiasis. A chronic prophylactic anti-fungal treatment in all patients is not practical, inasmuch as it may lead to colonization by multi-resistant Candida species such as Candida krusei or globata. When a candidiasis is documented in immunosuppressed patients, it should not be considered a benign condition, and more aggressive treatment should be given. Indwelling catheter and long-term antibiotics should be kept in mind as known risk factors for fungemia.

While transient candidiasis has been postulated as a mechanism for prosthetic joint fungal infection, it is frequently unrecognized and, therefore, difficult to treat. Our article focused on the need to search for fungi at the time of joint aspiration or revision arthroplasty in immunosuppressed patients, especially since fungal arthritis generally presents as an indolent process and may mimic mechanical failure.

ORTHOPEDICS: Why were so few attempts made to revise prosthetic joints infect-
ed with *Candida* after elimination of the fungus infection?

**Cardinal et al:** Of 20 patients treated for *Candida* infected prosthesis, all required resection. One had an unsuccessful limited debridement that eventually required excision of the prosthesis. One patient had a reimplantation 9 months after the infection and was well 2 years later. Another patient had an attempted reimplantation with resection and infection with the fungus. Five patients had an arthrodasis performed as a definitive treatment.

Reasons for the few cases of reimplanted hip prostheses are not clear. Although there is general agreement that treatment of fungal prosthesis joint infection requires resection of the prosthesis and long-term antifungal therapy, the duration of therapy is not precisely known. This creates uncertainty concerning the timing and eventual outcome of a new prosthesis, which may discourage surgeons, especially when they consider an underlying debilitating condition. One may also postulate that with the short follow up available (average: 14 months), there may have been reimplantations attempted after publication of these papers.

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**CHARCOT SPINAL ARTHROPATHY IN CONGENITAL INSENSITIVITY TO PAIN**

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Neuropathic joints can arise secondary to multiple etiologies. Charcot, in 1868, described neuropathic joints due to tabes dorsalis. Later, Morvan noted a series of cases with neuropathic joints and compromised sensation. Most of these patients had syringomyelia. Jordan, in 1936, first recognized the presence of neuropathic joints in diabetic patients. Diabetes mellitus is now recognized as the most common cause of neuropathic arthropathy. Estimates state that one of every 680 diabetic patients develops Charcot arthropathy at some site.

The incidence of spinal involvement has ranged from 6% to 21% in reported cases of Charcot arthropathy. Mitchell, reporting in 1831, noted a relationship between spinal cord lesions and arthropathies. In 1884, Kronig reported the first case of neuropathic spinal arthropathy. The reported causes of neuropathic spinal arthropathy include tabes dorsalis, syringomyelia, spinal cord tumors, traumatic spinal cord injury, acute transverse myelitis, and diabetes mellitus.

Congenital insensitivity to pain is a very rare cause of neuropathic arthropathy. In 1932, Dearborn reported a case of "congenital general pure analgesia." The report described a carnical worker calling himself the "Human Pin Cushion." Since that time, various authors have proposed theories to explain the cause of this disorder. To date, however, no single anatomic, physiologic, or pathologic entity has been identified as the cause of congenital insensitivity to pain.

In 1953, Petrie described the orthopaedic manifestations of congenital insensitivity to pain. Piazza et al, in 1988, reported a case of neuropathic spinal arthropathy in congenital insensitivity to pain. A 28-year-old woman with destruction at the L1-L2 interspace developed kyphosis and instability. She remained neurologically intact and was fused successfully with staged anterior and posterior procedures. Hegness recently reported the case of a 17-year-old girl who developed truncal asymmetry during pregnancy. A dense paraparesis developed 10 days after delivery. She had developed a Charcot spine at L3 and L4 with significant canal compromise. She underwent anterior decompression and stabilization of the spine after which she made a complete neurologic recovery. Two other cases of spinal arthropathy with congenital insensitivity to pain have appeared in literature.

We report the case of a 12-year-old girl with congenital insensitivity to pain and a neuropathic spine who suffered a progressive neurologic compromise secondary to her L4-5 lesion.

**CASE REPORT**

A 12-year-old girl initially presented in February 1990 with a neuropathic lumbar spine. Her medical history was significant for the diagnosis of congenital insensitivity to pain. The child was born at full term, complicated by maternal gestational diabetes. In the nursery, the family noted that the child did not cry when stimulated to encourage breathing. At 6 months of age, she was diagnosed with a problem perceiving pain. At that time she had fallen and hit her head, but did not respond to the injury. Since that time, she has sustained...