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Candida Albicans Infection after Spinal Arthrodesis: Case Report and Literature Review

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1. Introduction

One of the most common complications after spinal surgery is surgical site infection (SSI). The incidence of SSI in instrumented spinal surgery ranges from 2% to 20% [1] impacting on patient morbidity and health care cost burden [2].

Staphylococcus aureus, followed by coagulase-negative Staphylococci, are the most frequent isolated pathogens found on cultural analysis [3,4].

Fungal spinal infections are uncommon and generally affect immunocompromised patients due to opportunistic fungi overgrowth such as Candida spp [5,6].

Candida Albicans is an opportunistic yeast which commonly colonizes the gastrointestinal tract, female reproductive tract, oral cavity and skin, being part of the healthy human microbiota [7,8].

It may overgrows due to reduction in host's immune system, stress or alterations in resident microbiota, leading to a wide range of infections [7] from superficial mucosal and dermal infection to disseminated infections, which can even involve the central nervous system (CNS) with high mortality rate[8,9].

Up to day, only few case reports and case series about Candida spondylodiscitis are described in literature. All the reported cases were collected in a recent systematic review [10] in which only two cases are related with the outbreak of this infection after spinal arthrodesis[11,12].

We are reporting a case of an healthy 58 year-old woman who underwent spinal fusion that complicated with C. Albicans infections, and the struggling efforts we made trying to eradicate it.

2. Case Presentation

A 58 year-old immunocompetent woman, active smoker (20 pack-year) and with no history of diabetes mellitus or obesity, was suffering from L5 left radicular pain for months. The MRI showed a synovial cyst compressing the left L5 nerve root with spinal instability (Figure 1). After failure of medical treatment, the patient underwent lumbar spine fusion. The surgery performed was a transforaminal interbody fusion (TLIF) with implantation of titanium cage (CONDUIT). The postoperative radiographs (Figure 2a) revealed a correct surgical outcome and the following hospital stay was regular. The patient remained afebrile for all the hospitalization. She was discharged home 3 days after surgery with complete remission of preoperative sciatic pain. The 30-day outcome was satisfactory, but two weeks later the patient had fever and lumbar swelling. She went to the Emergency Room where empiric antimicrobial therapy was started with amoxicillin- clavulanic acid (875-125 mg/8h) and Moxifloxacin (400 mg/d).

Two weeks later, the patient was readmitted to hospital because of back pain and persistent fever. Blood analysis showed an inflammatory syndrome. We performed contrast-enhanced MRI that revealed a fluid collection with peripherally contrast enhancement between the L4 spinous process and the suprafascial space. Eight weeks after the first surgery, the patient underwent surgical debridement with irrigation. The fluid collection was evacuated and intraoperative microbial samples were collected. After surgery the antimicrobial therapy was adapted, according to infectious disease specialists, with daptomycin 10 mg/kg/d and piperacillin-tazobactam 4 g/6h. Microbiological samples tested positive for multi- sensible Candida Albicans. A new multidisciplinary meeting, including infectious disease specialists, was carried out. We interrupted the antibacterial therapy and Caspofungin 50 mg/d was initiated.

The clinical and biochemical responses to antifungal therapy were good, with reduction of WBC count and PCR on laboratory tests and the scar remained clear.

Three weeks after the second surgery, a new contrast- enhanced MRI was performed because of fever and lumbar tenderness. The exam revealed that the fluid collection was decreased in size, compared to the previous exam, and new fluid collections with rim-enhancement were noted in a deeper layer, in close relationship with posterior fixation.

A new multidisciplinary meeting with infectious disease specialists was performed. Because of the relapsed infectious symptoms and the new onset of a more deeply location of the paraspinal abscess, we opted for a surgical remotion of the posterior fusion elements (screws and rods). The cage was not removed to avoid excessive spinal instability. Postoperative RX scan (Figure 2b) showed satisfactory results. The intraoperative microbiological cultures isolated again C. Albicans and Staphylococcus Epidermidis.

The antifungal therapy with Caspofungin was continued along the hospital stay and daptomycin was added in therapy as initially prescribed.

Since C. Albicans spondylodiscitis are rare events and mostly correlated with an hematogenous spread from another infectious site, we performed an echocardiography and a contrast enhancement chest- abdomen CT scan, which resulted negative for cardiac vegetations and for any hidden infectious sites.

After 4 weeks of antimicrobial therapy with Caspofungin and daptomycin, the therapy was switched to Fluconazole 600 mg/d and dalbavancin 500 mg/week and the patient was discharged home, afebrile and with progressive reduction of biological inflammatory markers on blood exams.

After an initial clinical wellness, the patient started again to have fever, back pain and presented wound dehiscence. On blood analysis we found a raise in inflammatory markers. A new contrast-enhanced MRI showed a paravertebral abscess to L4-L5 level 10-weeks after the second revision surgery.

Because of the persistence of the infection, despite the previous surgical treatment and the prolonged antifungal therapy, we performed new surgery with posterior debridement, irrigation and remotion of the implanted cage through an anterior retroperitoneal surgical route. The device was substituted with heterologous bone plugs. Candida Albicans was found again on cultures in 1 out of 5 intraoperative samples.

After surgery, dalbavancin was discontinued, we maintained fluconazole 600 mg/d and we added daptomycin 10 mg/kg/d as prescribed before. Postoperative lumbar CT (Figure 3) scan showed correct surgical outcome. The clinical response was good and the inflammatory markers on the blood exam progressively decreased. The good outcomes allowed us to switch daptomycin with linezolid per OS 1,2 g/d for two weeks and to reduce the dose of fluconazole from 600 mg/d to 400 mg/d.

The patient was discharged home with no sign or symptoms of infection with a dorsolumbar orthosis.

After three months from the last surgical revision, the infection was completely resolved, the scar remained clear and the clinical and radiological outcome (Figure 2c, Figure 4) was good without back pain or radiculopathies. Treatment flow-chart is resumed in Figure 5

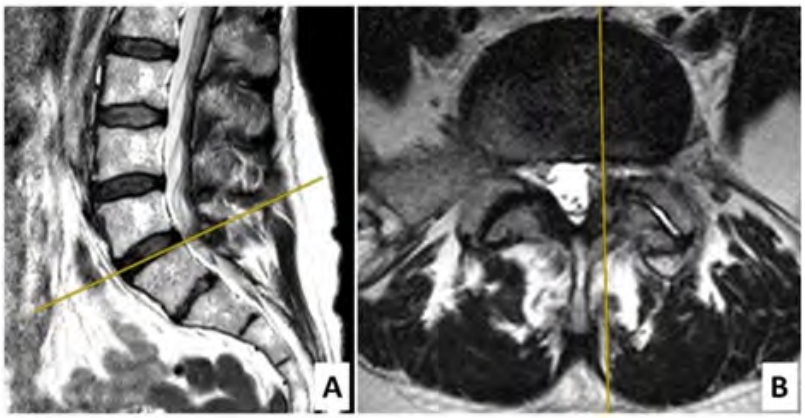

Figure 1: Lumbar MRI in sagittal view (A) and axial view (B) shows L4-L5 left synovial cyst compressing left L5 nerve root with spinal instability

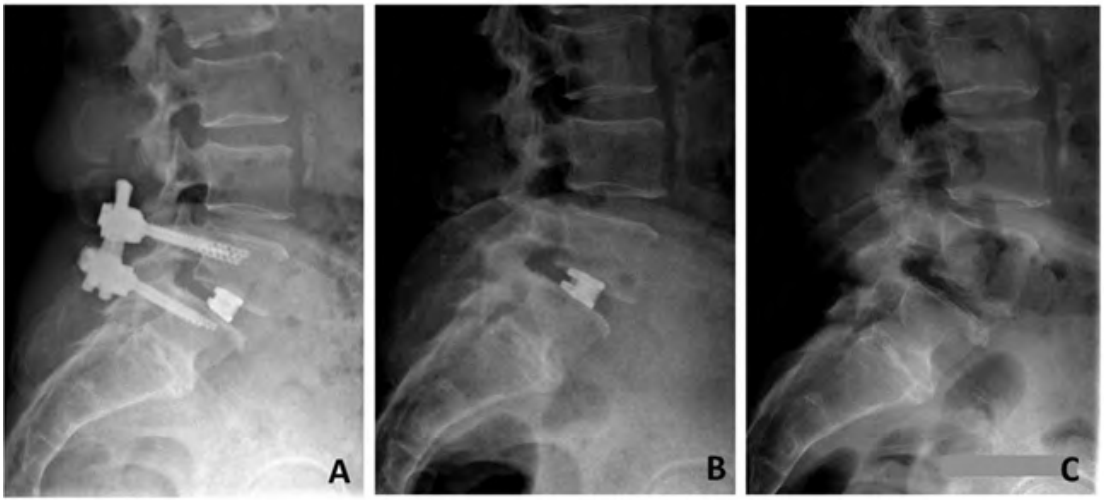

Figure 2: Post surgery RX scan after L4-L5 TLIF shows correct positioning of the pedicle screws with lordotic rods and itersomatic titanium cage (A). RX scan after the second revision surgery revealed no mobilization of the intersomatic cage after remotion of posterior hardware elements (B). The RX scan after 30 day from last surgery illustrate the correct placement of the implanted heterologous bone plug with initial L4-L5 interbody bone formation (C)

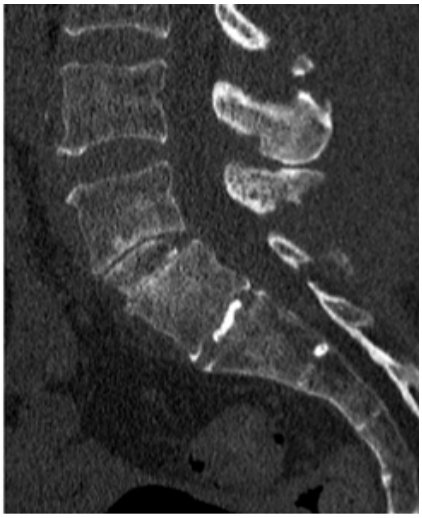

Figure 3: Correct positioning of the L4-L5 intersomatic heterologous bone plug after asportation of titanium intersomatic cage through an anterior retroperitoneal surgical route

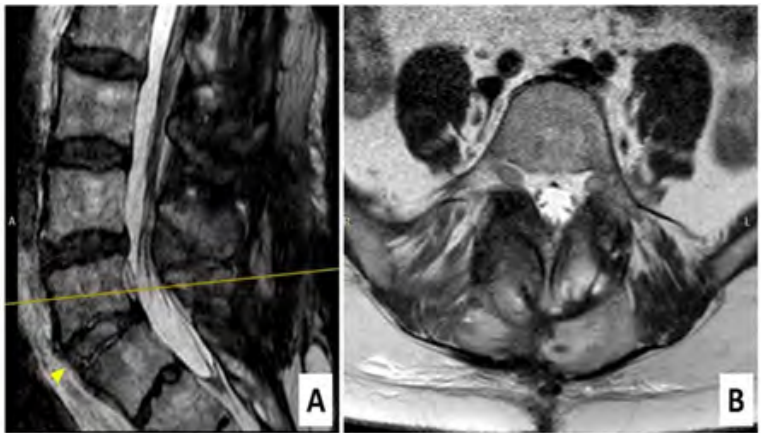

Figure 4: Lumbar MRI sagittal view (A) and axial view (B), three month after last surgery highlights the absence of fluid collection in the paraspinal soft tissues after the removal of the posterior hardware and the substitution of the intersomatic titanium cage with heterologous bone plug (yellow arrowhead)

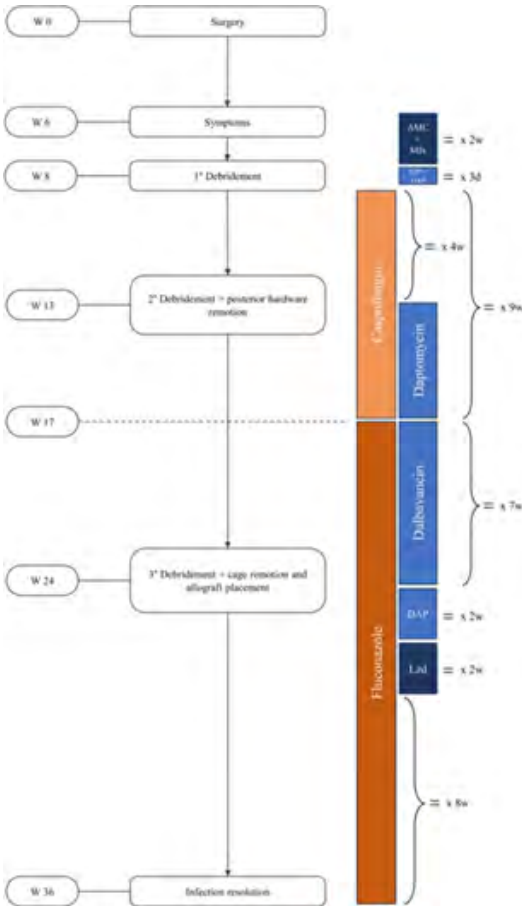

Figure 5: Treatment flow chart. Main events are in the central column. Time is expressed in weeks in the left column.

Antifungal and antibiotic therapy and their duration are shown on the left side of the chart, light color refer to a parental drug administration, whereas dark colors refer to orally delivered therapy. Abbreviations: AMC: Amoxicillin/clavulanic acid, Mfx : Moxifloxacin, TZP: Piperacillin/tazobactam, DAP: Daptomycin, Lzd: Linezolid, w: weeks, d: days

3. Discussion

Fungal infections of the spine are extremely rare. They can be primary or secondary to spinal surgery and can be caused by alteration in held immunity because of diabetes mellitus, chemotherapy, chronic corticosteroid use, or malnutrition [13,14]. The patient of this case did not have any of the above.

Candida-related spondylodiscitis may present with non- specific laboratory tests and absence of fever, so that fungal infection after spinal surgery are extremely difficult to identify not only because of their rarity [13]. In our case, the patient presented with fever and back pain after 7 weeks after surgery. This clinical picture led us to further investigations with radiological imaging.

Blecher et al. [11] reported a case of a C. parapsilosis infection developed after 4 months from receiving a XLIF at the L3-L4 level. Because of spinal instability the implants were removed and the spinal stabilization was achieved by a polymethyl-methacrylate (PMMA) spacer in the L3-L4-disc space and posterior spinal instrumentation from L2 to S1.

Wajchenberg et al. [12] described a case of a TLIF infected by C. parapsilosis 2.5 months after surgery. They removed the instrumentation after the first surgical debridement and irrigation failed. Spinal stabilization was made by intervertebral autograft and posterior instrumentation.

Our case can be considered as an early onset postoperative infection since the symptoms of infection developed within three months after the fusion surgery [15]. Current recommendations for early onset postoperative infection, suggest that surgical debridement and irrigation with long term antimicrobial therapy may be sufficient for their management [16,17]. The removal of any spinal instrumentation should not be recommended for early infection to avoid spinal destabilization [18,19].

For infection that occur after 3 month from instrumented spinal surgery, hardware removal is more necessary to achieve debridement in deep located sites and to reduce the chance of infection recurrence [20,21].

Despite our attempts to resolve the infection by keeping in the spinal instrumentation, the symptoms presented again, this can probably be explained by biofilm formation. C. Albicans biofilms are formed by densely packed cells, strongly adherent to a surface [7,22]. This ability confers C. Albicans a major virulence activity. In this case hardware removal was needed, even if spinal fusion wasn't achieved yet in our patient. The cage was replaced by an allograft. This method can be used to obtain bony fusion without an increase in postoperative infection rate [20].

We want to point out that the first microbiological samples tested negative for bacteria, unlike the second one, in which Staphylococcus Epidermidis was isolated. This can be explained by the antimicrobial therapy started in ER without any collection of cultural samples. After the first revision surgery, antibiotic therapy with daptomycin and piperacillin-tazobactam was started based on literature recommendations [23] considering the most probable bacterial etiology of the infection. The antibiotic therapy was replaced by antifungal therapy with Caspofungin and then with fluconazole once C. Albicans was identified on cultural examinations.

These drugs were initially effective against the pathogen identified, but 2 treatment failures occurred, requiring 3 revision surgeries.

4. Conclusions

This case illustrates how challenging the treatment of a postoperative spinal infection caused by C. Albicans can be. Long-term antifungal therapy and three debridement-irrigation surgery combined with implant removal and substitution with intervertebral allograft were necessary to resolve the infection.

Multidisciplinary coordination between surgeons and infectious disease specialists is extremely crucial to find the right therapeutic approach to overcome postoperative infections.

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