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Medical and surgical treatment of pyogenic spondylodiscitis

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Abstract. – *Background:* **Pyogenic vertebral osteomyelitis (PVO) represents approximately 2-7% of all cases of osteomyelitis. The approach to the treatment of PVO may be conservative, which includes antibiotic therapy and orthopaedic treatment, or surgical.**

Aim: **To overview conservative and surigical approaches to PVO.**

Methods: **A literature review was performed using the Pubmed database to identify studies published in the last 20 years, addressing the treatment of PVO.**

Results: Empirical antibiotic treatment of PVO, while waiting for the results of cultures or in culture-negative cases, should include broad spectrum agents in association with agents active on *Staphylococcus (S.) aureus.* Based on local epidemiological data, antibiotics active on methicillin resistant S. aureus (MRSA) should be included. Once an organism has been identified, antibiotics should be initially administered intravenously but the optimal duration of antimicrobial therapy is unclear. Studies have reported that the incidence of treatment failure was higher when i.v. therapy was administered for less than 4 weeks. Rifampin is widely used in the combination therapy of PVO, but no controlled trials are available to define weather this approach is beneficial. Many PVO need a surgical treatment and can represent a real challenge for the orthopaedic surgeon. Anterior and posterior cervical, thoracic, lumbar approaches and the relatives surgical strategies are reported in this review. Moreover, recently the mininvasive posterior stabilization have been proposed as a efficient alternative to open surgery in elderly with severe comorbidities. Possible advantages and limitations of this technique are also reported.

Conclusions: **Further research is needed in order to define the optimal duration of antibiotic therapy, and the benefits and limitations of open or mini-invasive surgical techniques.**

Key words:

Pyogenic vertebral osteomyelitis, Conservative treatment, Surgical treatment.

Introduction

Pyogenic vertebral osteomyelitis (PVO), or pyogenic spondylodiscitis, represents approximately 2-7% of all cases of osteomyelitis[1,2]; it involves the vertebral body and the disc space and it is caused by many types of microorganisms with the prevalence of *Staphylococcus (S.) aureus,* responsible of the majority of PVO[3].

Although PVO remains rare, its incidence is rising[4,5], due to an increasing population with predisposing factors such as advanced age, diabetes mellitus, chronic renal or liver disease, intravenous drug use, HIV infection, long-term steroid use, malignancy, chemotherapy, severe trauma, previous surgery. An other reason of the increased incidence is the availability of more effective diagnostic tools. A high index of suspicion for vertebral osteomyelitis is needed in patients presenting with unremitting back or neck pain and inconstant fever, to ensure prompt diagnosis and improved long-term outcomes[6].

Because of the non-specific nature of the symptoms at presentation, PVO is usually not recognized at an early stage, when treatment is most effective[7,8].

Early diagnosis is based on a high level of suspicion with emphasis on the following:

- Symptoms: fever, localized spinal pain with paravertebral muscle spasm, limitation of movement and evidence of neurological deficit;
- Risk factors: increased age, diabetes mellitus, rheumatoid arthritis, steroid use, ethanol abuse, immunosuppression, intravenous drug abuse (IVDA), infectious endocarditis, and history of recent surgical or invasive diagnostic spinal procedure[9-12];
- Imaging studies, with magnetic resonance imaging (MRI) to be considered the gold standard;

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- Research of distant infectious foci;
- Laboratory studies: blood cultures, C-reactive protein (CPR), ertithrocyte sedimentation rate (ESR), WBC count.

The treatment of spontaneous PVO is either conservative or surgical.

The goals of treatment are to eradicate infection, establish spinal stability, relieve pain, prevent or reverse neurologic deficits and prevent recurrence.

Conservative management consists of antimicrobial therapy and non-pharmacological treatments such as immobilization.

The spinal column should be immobilized[13] to prevent vertebral damage.

In order to establish an effective antibiotic treatment an accurate microbiological diagnosis is necessary. The choice of appropriate antibiotics should also take into account the pharmacological features of each drug.

Since PVO is mostly a hematogenous infection, blood cultures should be obtained as soon as the disease is suspected. Blood should be collected in three separate samples for cultures, if possible during fever spikes or chills. A percutaneous biopsy of the affected disc can be performed, also obtaining blood cultures routinely after the procedure[14]. This procedure is particularly useful when the previous tests are negative. The diagnostic yield of blood cultures ranges from 40% to 60%[6]. If the percutaneous biopsy is not diagnostic, an open surgical biopsy may be indicated[6].

Antimicrobial therapy

While waiting for the microbiological results, an empirical therapy can be started, covering for the commonest microorganisms such as *S. aureus* and Gram-negative rods, also taking into account the patient's risk factors[15] and the possible distant infectious foci. Some Authors believe that antimicrobial treatment should not be started until the organism is identified, except when clinical circumstances indicate otherwise, for instance in patients with neutropenia or severe sepsis[16].

Empirical treatment of PVO, while waiting for the results of cultures or in culture-negative cases, should include broad spectrum agents in association with agents active on *S. aureus*. Based on local epidemiological data, antibiotics active on methicillin-resistant *Staphylococcus aureus* (MRSA) should be included.

Once an organism has been identified, antibiotics should be initially administered intravenously but the optimal total duration of antimicrobial therapy is unclear. Most Authors recommend an initial treatment with intravenous antibiotics to reach adequate concentrations in necrotic bone[6]. Studies have reported that the percentage of treatment failure was higher when parenteral therapy was administered for less than 4 weeks[10,17]. After induction with parenteral antibiotics, oral therapy should be continued to complete treatment. Early oral switch is not recommended until endocarditis has been excluded[18]. A convenient cost-effective[19] option for the treatment of PVO is outpatient parenteral therapy, that can be proposed when the patient is stable, compliant with the therapy and when it is possible to reduce the number of daily administrations. However, specific data for PVO are limited[20].

The discontinuation of antibiotic therapy is decided taking into account clinical resolution and a gradual decrease of aspecific inflammation indexes such as ESR and CRP[21,22]. According to some Authors, a CRP weekly reduction of 50% represents a good marker of improvement[23]. Follow-up MRI may be unnecessary[16] and even misleading, since in some cases there may be an initial worsening of the images in spite of clinical and laboratory improvement[24]. An MRI during treatment and follow-up is useful only if there is no clinical or laboratory improvement or if an epidural abscess formation is suspected[25].

The choice of antibiotic depends on the causal pathogen and its sensitivity pattern. Also the ability of bone and disc penetration should be considered. Bone penetration of many antibiotics has been tested *in vivo* and *in vitro*[26,27], but because of the lack of standardized methodology, results are not always comparable[28].

With the available data we know that clindamycin, fluoroquinolones, macrolides, rifampicin, fusidic acid, metronidazole and linezolid reach good levels in bone tissue. Beta-lactam antibiotics and glycopeptides achieve moderate levels and aminoglycosides diffuse poorly into the bone[16].

Due to the relatively low vascularity in necrotic bone, areas of poor penetration and low oxygen tension result at the site of infection; this can compromise the activity of certain antimicrobials such as gentamicin and vancomycin[29,30].

Rifampin has a good tissue penetration index and is probably active on biofilm phenotypes. However, it should never be given as monothera-

py, due to the rapid development of resistance. Regimens including rifampin in combination with other antimicrobials are widely used in bone and joint infections; however, there are very few compelling data to support this strategy. In fact, the available data indicate that rifampin combination therapy is clinically effective in biofilm infections and in the presence of prosthetic implants[31]. No controlled trials are available to define weather combination therapy with rifampin is beneficial for the treatment of PVO.

Table I summarizes the suggested antibiotic regimens for the i.v. treatment of PVO. Suggestions are based on guidelines[32] and review of observational studies[6,33].

The main characteristic of antimicrobials used for the treatment of bone infections are listed below.

Beta-lactams have a moderate bone penetration. Nonetheless, the good tolerance and the high dosages achievable parenterally make them the first choice for the induction treatment of PVO caused by sensitive pathogens.

Clindamycin is a bacteriostatic antibiotic that has the major advantage of a higher bone penetration than beta-lactams, also in the presence of relatively low serum concentrations. Because of its good bioavailability and high levels in bone, clyndamycin is a convenient choice for oral switch therapy in patients who can be discharged[34].

Quinolones are widely used for the treatment of bone infections because they are active against a broad spectrum[35,36] of bacteria (including adherent bacteria), they penetrate macrophages and PMNCs[37,38] and reach effective bone concentration also with oral administration[38,39]. Quinolones can be also used for long periods since they have a favourable safety profile[34]. However, it should be considered that long antibiotic treatments are a well established risk factor for the development of resistant bacterial strains[40].

Rifampicin is peculiarly effective against bacterial biofilm and can kill phagocytosed bacteria penetrating white blood cells; it has also a good bone penetration[41]. Rifampicin should never be used in monotherapy because of the rapid development of resistance, but it can be used in combination therapy with beta-lactams[41-43], with quinolones[43-45] and with vancomycin, teicoplanin or minocycline for MRSA[30,46,47]. The commonest side effect is hepatic damage, so monitoring of liver function is recommended[34].

Fusidic acid has a good bone penetration[48,49] and a bactericidal activity against *S. aureus* but, like rifampicin, it causes the rapid development of resistance, so it should be used in combination therapy[49].

Glycopeptides are the first choice in infections caused by MRSA[34]. The use of vancomycin allows a more rapid killing of staphylococci than teicoplanin[50], but if it has a decreased activity in anaerobic conditions[29]. Vancomycin is more nephrotoxic[51,52] but more easily measurable in serum than teicoplanin[53]. Teicoplanin is more frequently associated with thrombocytopenia and neutropenia[54]. Vancomycin cannot be administrated once daily, whereas teicoplanin can be used for outpatient parental therapy[55-57].

Daptomycin is a new lipopeptide antibiotic, active on Gram-positive bacteria, useful in the treatment of MRSA osteomyelitis[32], even if it is FDA-approved only for adults with *S. aureus* bacteremia, right-sided infective endocarditis, and skin and soft tissues infections. It has a

Table I. Suggested antibiotic regimens for the i.v. treatment of PVO.

MSSA	Flucloxacillin 2 g q6h iv or equivalent anti-staphylococcal penicillin OR Ceftriaxone 2 g daily iv
MRSA	Vancomycin 15-20 mg/kg q12h-q8h iv aiming for pre-dose levels of 15-20 mg/L OR Teicoplanin 8-12 mg/kg daily iv after loading OR Daptomycin 6 mg/kg/day IV QD 6-10 mg/kg/day IV QD
Enterobacteriaceae	Ciprofloxacin 400 mg q12h iv or 750 mg q12h orally OR Ceftriaxone 2 g daily iv OR Meropenem 1 g q8h iv
Pseudomonas aeruginosa	Ceftazidime 2 g q8h iv+aminoglycosides OR Meropenem 1 g q8h iv+aminoglycosides OR Ciprofloxacin 400 mg q12h iv or 750 mg q12h orally OR combination of two different antibiotic classes
Streptococci	Benzylpenicillin 2.4 g q6h iv OR Ceftriaxone 2 g once daily iv
Enterococcus faecalis	Amoxicillin 2 g q6h iv + gentamicin 1 mg/kg q12h-q8h iv
Enterococcus faecium	Vancomycin 15 mg/kg q12h iv +gentamicin 1 mg/kg q12h-q8h iv
Anaerobes	Metronidazole 500 mg q8h iv OR Clindamycin 600 mg q6h i.v.

MRSA = methicillin-resistant *Staphylococcus aureus*

rapid bactericidal activity and there might be a possible cross resistance with vancomycin[58]. An interesting feature of daptomycin is its possible activity on biofilm infections[59]. Main adverse effects are elevation in creatinine phosphokinase (appeared in patient treated with the maximal doses), weakness, myalgia, renal failure[60]; eosinophilic pneumonia is rare[61]. Further studies on its bone penetration, safety in long-term treatments and effectiveness compared with glycopeptides are needed.

Trimethorim/sulfamethoxazole administrated orally in high doses can be an alternative for the treatment of MRSA infections. However, it is associated with adverse effects (hematologic and renal toxicity) that may limit its use in prolonged treatments[62].

Oral *minocycline* (with or without rifampicin) is effective in the treatment of MRSA bone infection[63,64]. It has a good bioavailability and it is frequently used when shifting from parentreral to oral therapy.

Quinupristin/dalfopristin is a parenteral antibiotic with bactericidal activity against *Enterococcus (E.) faecium*, including VRE[65,66] and *S. aureus*, including MRSA[67], it has no activity against *E. faecalis*. Quinupristin/dalfopristin administered three times daily by central infusion can cause myalgia, which may necessitate cessation of treatment[34].

Linezolid is an oxazolidinone antibiotic which inhibits bacterial protein synthesis and is active against Gram-positive organisms including VRE (*E. faecium* and *E. faecalis*) and MRSA[68]. There is no evidence of cross-resistance with other antibiotics. Although its good bone penetration and its complete oral bioavailability[69], linezolid is not approved for the treatment of osteomyelitis. The use of linezolid is limited by its potential hematologic toxicity (anemia, thrombocytopenia), especially during long-term treatments[70], and by its high cost.

Orthopedic conservative and surgical treatment

The treatment of pyogenic vertebral osteomyelitis (PVO) can represent a challenge for the spine surgeon[71]. The role of surgery in the management of PVO is firstly diagnostic: needle aspiration biopsy from the intervertebral disc space or vertebral bone usually confirms the clinical and/or radiographic suspicion of PVO, aids in differential diagnosis between infectious and non-infectious vertebral lesions, and identifies the specific etiologic agent of PVO. Percutaneous biopsy can be performed with either a thin needle or cutting needle under fluoroscopy or CT guidance. The surgical approach performing a biopsy is most often transpedicular, occasionally parapedicular or passing directly into the soft tissue masses. Sensitivity has been reported in different case series from a low of 30-50% to a high of 70-90%. However, these reports are based on small numbers of patients. As both culture and histology of biopsy specimens may be negative despite the presence of infection, open biopsy sampling should be performed when two times-repeated CT-guided biopsy samples or blood cultures do not identify the causative agent[13].

In the last two decades the treatment with more effective antimicrobial agents have promoted nonsurgical medical management of PVO, but have even allowed for more aggressive surgical procedures[2] when needed.

When there are no neurological deficits and no significant kyphotic deformity or instability, spinal infections can be managed without surgical intervention[3,72-74]. Discitis without structurally significant osteomyelitis that does not threaten nervous tissue may be treated with antibiotic medications alone[71]. Lumbar epidural abscess may be approached with a conservative treatment only if there is no evidence for cauda equina or conus dysfunction[71]. Spondylitis is commonly managed non-operatively, with intravenous culture-specific antibiotics for a minimum of 4 to 6 weeks and bracing[74,75]. Bed rest with low-molecular weight heparin treatment is needed for 3 to 4 weeks. Subsequently, a thoraco-lumbo-sacral orthosis or hard cervical collar should be worn for 1 to 3 months[76]. Immobilization with bracing is necessary for patient comfort and walking, to maintain spinal stability and to prevent deformity until bony ankylosis occurs on neuroimaging[13,77].

Spontaneous bony ankylosis, however, requires 6 to 24 months and may not take place at all[77]. This fusion, moreover, may be accompanied by narrowing of the foramina and kyphosis or listhesis[78]. Chronic mechanical back pain in non-surgically treated patients is attributable to both postinfection kyphosis and pseudarthrosis[75,77]. Even if the majority of PVOs responds to medical treatment, about 40% of patients suffering from PVO need surgical intervention[13,75,77,79,80]. In case of failure of prolonged medical manage-

ment, delayed treatment or complications as sepsis, neurologic impairment, or residual vertebral destruction leading to early or late spinal instability or segmental kyphosis with intractable pain, surgery is indicated[71-75,79-84]. The surgical indications should always be conditioned by the medical comorbidities of each patient[72]. The main goals of surgical treatment are maximal preservation of neurological function and healing of the infection with prevention of sepsis. These goals are obtained mainly by means of aggressive radical debridement and spinal stabilization[13,78,79,83]. Emergency decompression is indicated if complete paraplegia develops[16,81]. Cervical and thoracic epidural abscess should be treated by surgical decompression. Motor loss or cauda equina syndrome due to lumbar epidural abscess may require nerve root or spinal cord decompression surgery[16]. Surgical removal of a bone sequester or fixation material in case of postoperative PVO may be required.

If neurological deficit exists, decompression and instrumented spinal stabilization may be performed in the same procedure, even in the setting of acute pyogenic infection; on the contrary, if deformity and pain are present in a patient without neurological compromise, correction of deformity with placement of instrumentation may be delayed until the infection has been cleared with antimicrobial drugs[71,85] After the complete resolution of the vertebral infection, surgery may be needed to correct residual instability, kyphosis, and/or scoliosis[16] (Case illustration, Figure 1).

Nonetheless, the choice of surgical techniques and appropriate approaches, instrumentation and staging to treat PVO are still a matter of controversy[73,75,77,78,80,81,83]. Options include anterior or posterior approach, single-stage or two-stage surgery, with or without instrumentation[73], but the decision about the surgical approach and technique should be always guided by the determination of the state of neurological threat or mechanical instability[78]. A neurological injury requires prompt neural decompression with or without spinal arthrodesis, whereas mechanical instability requires arthrodesis. The decision whether to obtain spinal arthrodesis with spinal fixation or bed rest or rigid external bracing is determined by the degree of segmental instability[78].

Radical excision of all infected and necrotic disc and bony tissues and evacuation or drainage of paravertebral abscesses are mandatory for the permanent healing of PVO[13,73,79,86,91].

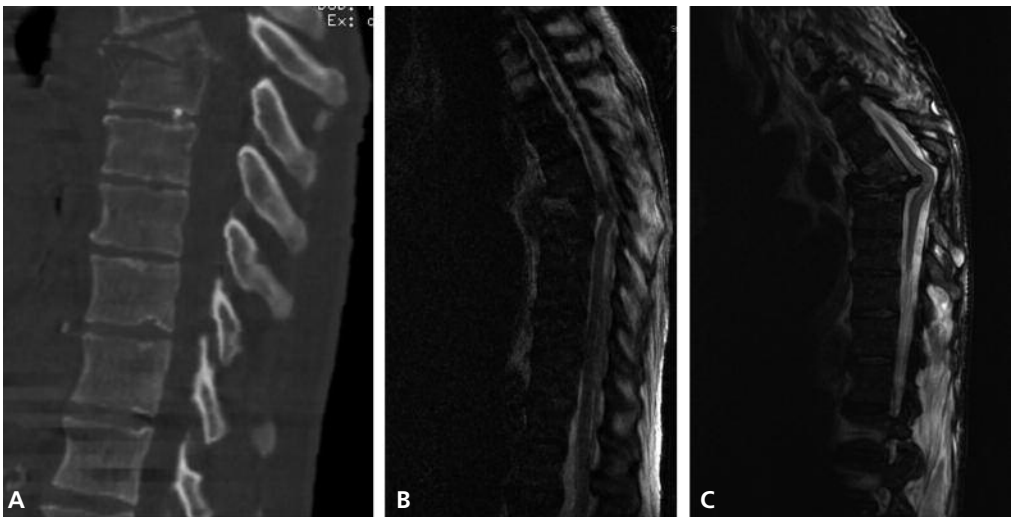

Figure 1. *Case illustration 1.* A 64-year-old male patient with diabetes and a 3-week history of back pain and low-grade fever was admitted with fever, mental confusion in a state of septicemia and progressive acute right monoplegia. Sagittal CT reconstruction *(A)* and T2-weighted MR image *(B)* of thoraco-lumbar spine at the time of presentation showed wedge-shaped collapse of T6 with spinal cord compression and bone destruction of the superior end plate of T7 and the extent of inflammatory changes of the disc space and a prevertebral abscess extended from T5 to T7 and an epidural abscesses from T6 to T12. Because of the wide extension of VO and the high risk for his general health condition, the patient underwent emergent posterior decompression with no internal fixation. Cultures were obtained during the operation. The patient was treated with postoperative intravenous antimicrobial drugs for *Staphylococcus aureus* and reported a significant improvement of neurological deficits. Postoperative MR image at 3-months follow-up *(C)* showed residual severe deformity in segmental kyphosis.

PVO predominantly involves the vascularized vertebral body and adjacent disc spaces (anterior and/or middle spinal column), with involvement of the posterior elements in only 5% of the cases[72,75,81]; thus, anterior surgical approach is most often used to allow direct access to the focus of infection for aggressive debridement[13,73,75,78,84]. Nevertheless, the involved area is exposed either from an anterior or posterior approach, depending on its localization and pathological features, and in all cases surgical debridement should be planned preoperatively by using appropriate imaging[13].

In the cervical spine, an abscess can be found in the anterior or posterior triangle of the neck or in the supraclavicular area, but sometimes it extends into the prevertebral fascia and into the mediastinum. Drainage of the abscess should be performed immediately via an extra-oral approach in case of airway compromise, but generally the approach is antero-lateral (Case illustration, Figure 2). The costotransversectomy approach is commonly used for drainage of abscesses in the high-thoracic spine; the approach to midthoracic spine is transthoracic from the right side, the thoracolumbar and upper lumbar spine is approached by a left-sided transdiaphragmatic-retroperitoneal exposure, and the lower lumbar spine *via* a standard retroperitoneal or transperitoneal approach. However, when an abscess extends posteriorly in the thoracolumbar region in a clinically unstable patient, a posterior approach should be preferred since an anterior approach would carry a high risk of morbidity and/or mortality. Paravertebral lumbar abscesses can be evacuated through a longitudinal incision laterally to the vertebral spinal processes. Psoas muscle abscesses are extraperitoneal and can be drained through the Petit triangle. Wound swabs and bioptic tissue samples should be obtained from infected areas; debridement can be considered complete when bleeding from vital well-vascularized cancellous bone, muscle, or fat tissues has been achieved and it should be followed by an extensive irrigation of the cavity with antibiotic solution[13].

Debridement and spondylodesis seem to be sufficient in cases without instability and severe deformity[16,75,82], combined with bed rest and bracing. When the defect created by the debridement leads to the loss of anterior column integrity with potential instability, especially in multi-segmental involvement, surgical reconstruction is necessary to maintain sagittal profile, prevent deformity or segmental collapses, and to achieve interbody fusion[77]. Laminectomy alone is contraindicated in PVO because it may increase spinal instability[13,77]. Laminectomy is indicated only for primary epidural abscess or granulation tissue causing neurocompression[77,87], but it should be followed by posterior stabilization, with or without staged anterior reconstruction[77,83]. Anterior decompression and fusion with strut grafting or titanium cages and single- or two-stage additional posterior instrumentation is the procedure of choice for PVO with a significant amount of bone destruction, complicated by neurologic deficit and severe instability[13,72,74,75,80,82]. The addition of posterior instrumentation provides better deformity correction, a faster rate of bony fusion and it does not appear to increase the risk of infection[74]. The posterior stabilization is obtained with internal fixation by means of monoaxial pedicle screw-rod system, which restore spinal alignment avoiding the communication with the anterior infection site.

After extensive anterior debridement, residual large defects can adversely affect spinal stability leading to long-term segmental kyphosis[79]. The gold standard for anterior column reconstruction is the use of structural bone grafting[82,85]. Among interbody grafts, iliac crest bone autograft is often the first choice[13,73,88]; vascularized rib graft has also been used with good success and fibula allograft is used in the cervical spine[71,78]. Allograft as an alternative of autogenous bone grafting can avoid the donor site morbidity[21] and shorten the operation time, even if the risk of disease transmission and immunological reaction for allografting should be considered[73,79]. Other methods for interbody fusion included bone cement and methylmethacrylate[73,78].

Even if tricortical iliac crest autograft with or without addition of anterior compression titanium plates commonly achieve a complete interbody fusion, long-term results have shown that this technique is associated with pseudarthrosis, graft collapse, and extrusion even in the presence of rigid posterior instrumentation[81]. An effective alternative to structural bone autograft for anterior support is the titanium mesh or PEEK cage[73,79,82,84]. Available in various diameters and heights, the cage can provide custom reconstruction of the anterior column defect. The fenestrations and its circular shape allow for containment of the morsellised autologous bone graft so that the cage can act as a bony conduit[81].

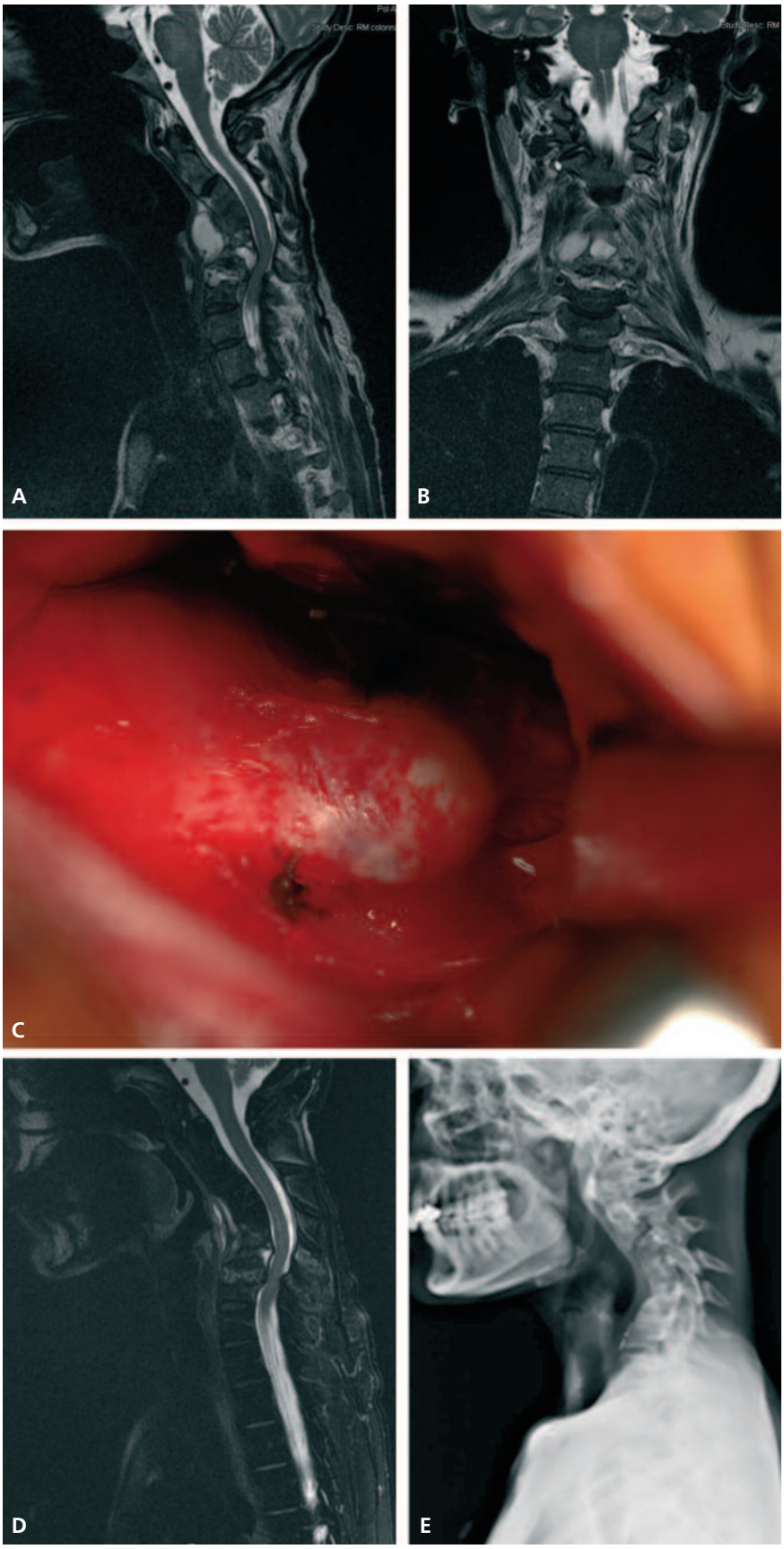

Figure 2. *Case illustration 2.* T2-weighted gadolinium-enhanced sagittal MR image *(A)* demonstrating C4-7 spondylodiscitis with a marked kyphotic deformity with apex in C5 compressing the cervical myelon. Two prevertebral abscesses formation, respectively median and right paramedian extended contiguously to carotid artery are concomitant at coronal MR image *(B)*. CT-guided needle biopsy samples and cultures from ultrasonography-guided thin needle aspiration of the abscesses identified *Candida albicans* as causative agents. The 58-year-old female patient underwent anterior debridement via left-sided antero-lateral approach *(C)* with microsurgical evacuation of cervical spondylodiscitis, drainage of prevertebral abscesses and careful irrigation in one setting. Postoperative sagittal MR image 15 days after surgery and intravenous antibiotic treatment *(D)* showing minimally decompressed myelon, evacuated disc spaces, but residual kyphosis and stenosis. Lateral cervical plain X-ray image 10 months after surgery *(E)* showing bony fusion of the involved vertebral bodies.

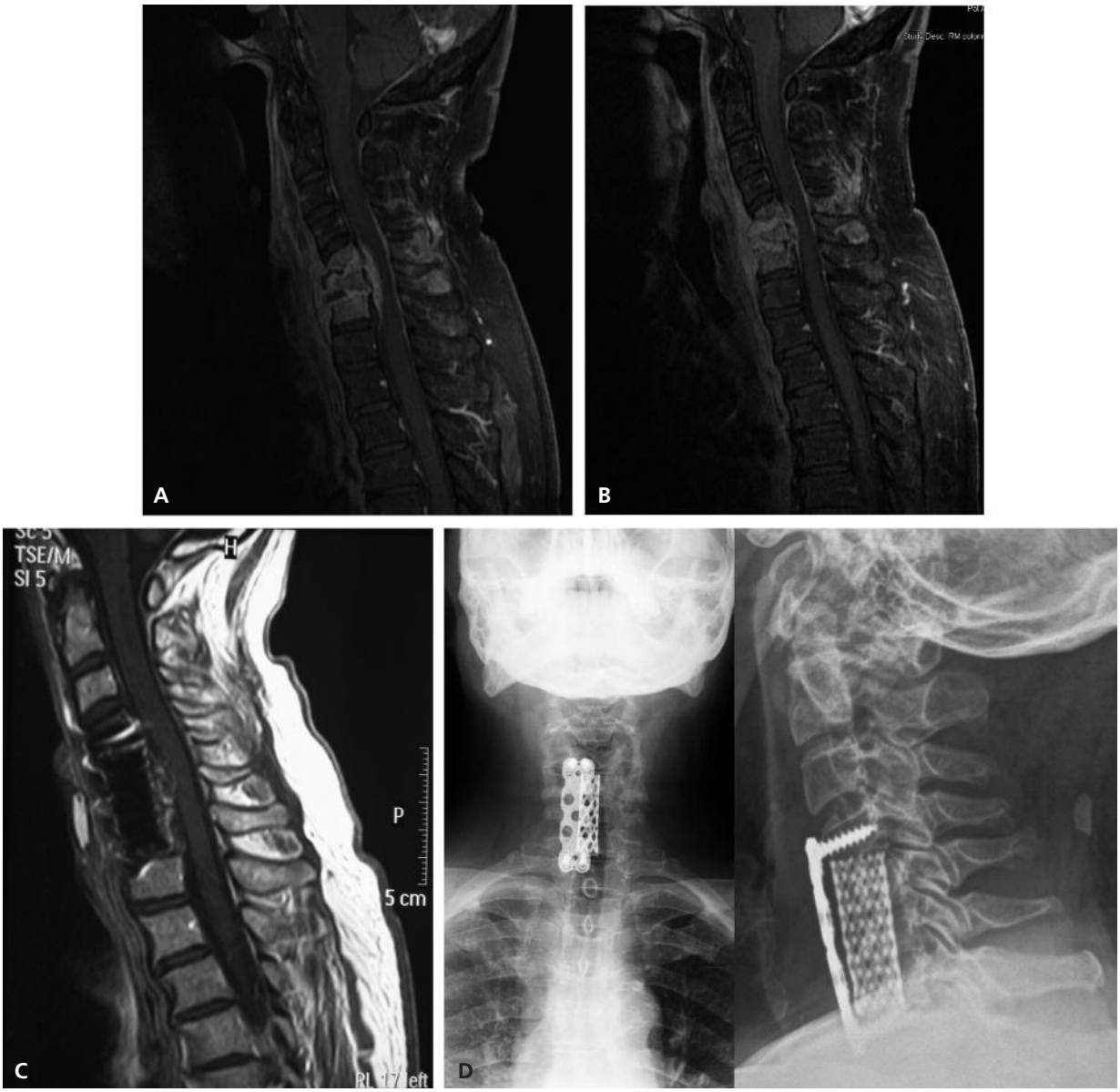

Figure 3. *Case illustration 3.* A 54-year-old man was admitted for fever, neck pain and mild neurological symptoms of myelopathy. Cervical spondylodiscitis was suspected on the basis of gadolinium-enhanced MR image and the diagnosis was confirmed by laboratory tests and blood cultures. T1-weighted sagittal MR image before *(A)* and after *(B)* 3-months of intravenous antibiotics drugs for spondylodiscitis from *Staphylococcus hominis* showed erosion and loss of height of C5, C6, C7, pathological high-signal of the involved vertebral bodies and correspondent disc spaces, a retropharyngeal abscess formation with partial regression of epidural abscess leading to myelon compression at C5-C7 level. This patient underwent anterior debridement and partial resection of the vertebral bodies C5, 6, 7 via an antero-lateral approach; then spinal cord decompression and fusion C5-C7 using a titanium mesh cage filled with iliac crest autograft and titanium plating were performed. Postoperative sagittal MR image *(C)* 6 months after surgery and plain X-ray image *(D)* of the cervical spine at 1-year follow-up showed decompressed myelon, regression of the soft-tissue swelling around the involved vertebrae and solid bone fusion.

When cage is combined with rigid anterior and/or posterior instrumentation in a single-stage procedure, this technique ensures immediate stability with marked neurological amelioration, maintenance or correction of sagittal alignment avoiding graft collapse and, moreover, it decreases morbidity from donor site[75,79,81,82,90] (Case illustration, Figure 3).

The metal selection for the implant should also be considered[71]. In infected areas, titanium and titanium alloys are superior to stainless steel implants; firstly titanium reduces the formation of a

pseudocapsule and biofilm that could facilitate bacterial adhesion and proliferation; moreover, the porous nature of titanium facilitates soft-tissue attachment and the delivery of adequate concentrations of antimicrobial drugs. Third, titanium produces less artifact on the MR imaging[71,73,80] needed during the follow-up.

Some controversy exist whether anterior and posterior approaches should be performed as single or multiple stage procedures[72,82,90]. Two-stage surgery allows a shorter operation time, less blood loss, and it is safer for patients with poor general health conditions as compared to one stage operation[90]. However, the trend is, nowadays, to treat sick patients affected by persistent or complicated septic PVO with one-stage combined surgical approach including anterior debridement, instrumented reconstruction with autogenous bone graft and cage with or without anterior plates, plus posterior traditional open or minimally invasive pedicle screw fixation[73,75,80]. Simultaneous anterior and posterior approaches does not predispose patients to recurrent infection if compared to staged procedures and it results in shorter hospital stay, lower rate of complications, earlier mobilization and a less troubled compliance of the patient since he undergoes only one operation and one anesthesia[72,73,80,81,83]. Surgical intervention with instrumentation can relieve pain, improve sagittal balance and neurologic function and it finally results in an early mobilization and faster rehabilitation, which is of considerable importance in an usually old patient population[73,79,80,81,91]. However, among different options the final decision should be made on the basis of the experience of the surgeons and the general health condition of the patients[73].

The reported recurrence rate of infection after non-surgical treatment ranged from 0% to 25%[77,78,81], while recurrence rates of 2% to 18% have been noted after the surgical treatment of PVO in the antibiotic era[75,77,92]. These data suggest that the surgical implants did not interfere with the reactivity against the infection[73]. However, occasional recurrence of infection at the site of surgical stabilization is one of the most feared complications because of the potential dislocation of spinal instrumentation (Case illustration, Figure 4).

Other complications in surgical treatment of PVO are graft dislodgements or extrusion or hardware failures with or without nerve root compression, dislocation or settling of the cage, vertebral osteoporotic fractures, persistence of infection at the site of debridement, nerve root lesions, infection developed at an adjacent level to the interbody fusion, pseudarthrosis, wound infections, hematomas[73,78,79]. The most common complications after not instrumented surgical treatment include loss of kyphosis correction ranging from 3° to 12°, olisthesis, pseudarthrosis, and spinal stenosis[73,81]. Surgical combined procedures are associated with considerable morbidity in up to 11% of all patients, correlated to potential risk of lesion of major vessels such as the aorta, vena cava and the azygos system[74]. Therefore, in the last years minimal invasive surgery has been reported as an useful and efficient option especially in elderly patients, also because of severe comorbidities and a high risk of thromboembolism correlated to immobilization[13,74]. Video-assisted thoracoscopic surgery debridement and instrumentation over multiple levels can be achieved with minimal invasiveness, but this procedure is still technically demanding and special instruments are needed[93]. Also percutaneous transpedicular discectomy and drainage has been described especially in the management of early stages of uncomplicated PVO, obtaining infection local control and an immediate relief of pain when the kyphotic deformity is not structured yet; it is contraindicated in advanced infections wherein excessive neurocompression or extensive bony destruction have developed[94]. A percutanous dorsal pedicle screw-rod fixation is increasingly performed in case of thoraco-lumbar PVO with no neurological deficit in order to avoid prolonged immobilization and to overcome the potential complications of a dorsoventral open surgery. Minimally invasive instrumentation seems to be theoretically in contrast with the current management of PVO, in according to which a complete debris resection is mandatory for the healing of infection. However, in case of PVO with no instability nor neurological deficits needing decompression, a minimally invasive pedicle screw-rod system fixed to non-infected bone of the adjacent vertebral levels acts as an effective internal fixation that can ensure posterior bridging "bypassing" the site of infection, with a significant reduction of intraoperative complications and good short and mid-term outcomes in terms of spontaneous bony fusion and spinal stability, comparable with combined anterior and posterior open surgery[74]. Further reports including larger series and continuing long-term follow-up examinations are necessary in order to define benefits and limitations of mini-invasive surgical technique (Case illustration, Figure 5).

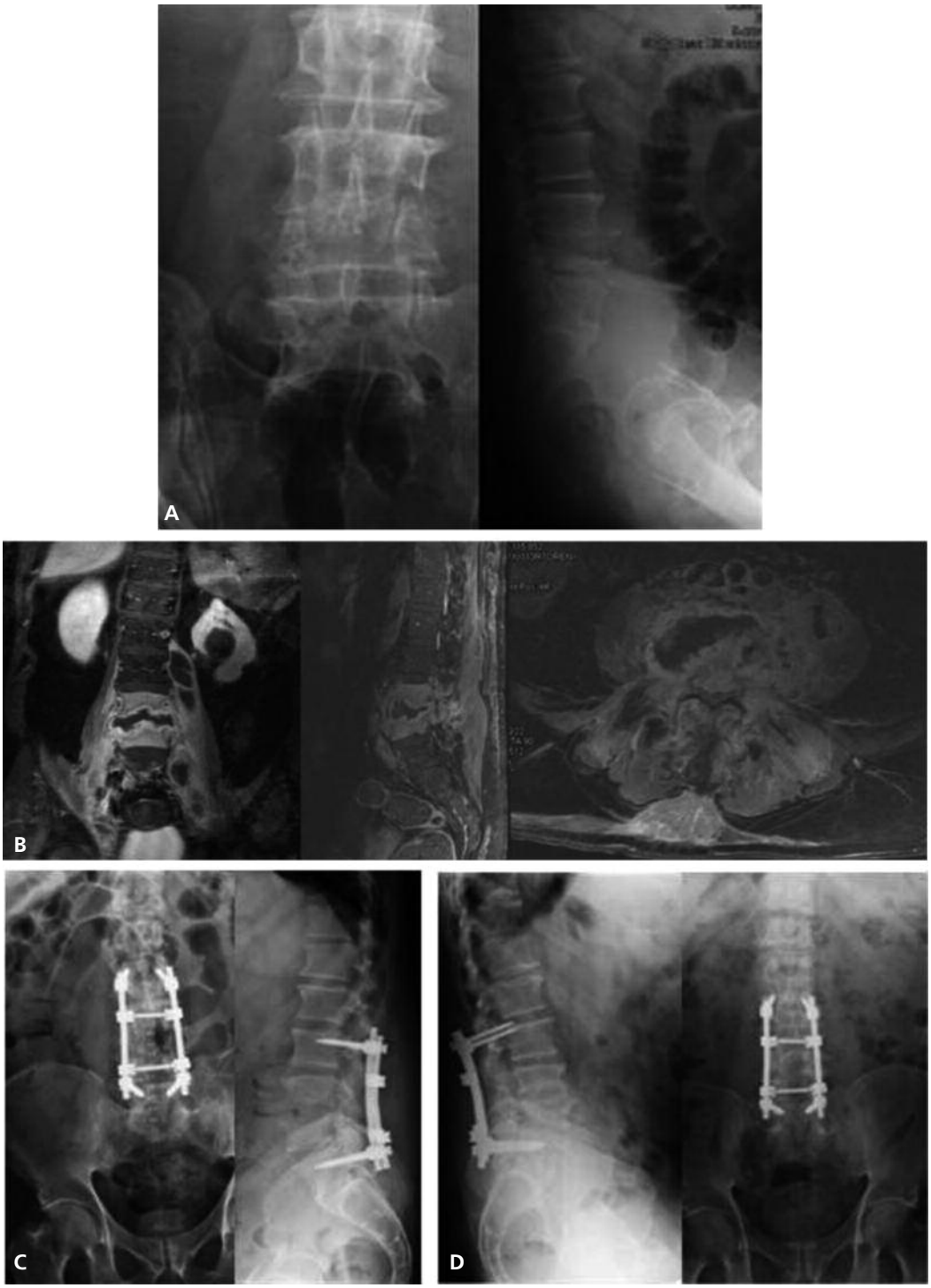

Figure 4. *Case illustration 4.* A 63-year-old man presented with low-back pain and pain in his lower extremities. Plain X-ray film *(A)* was performed in suspicion of osteoporotic fracture, but it showed narrowing of the intervertebral disc space L4-L5 with sclerosis of contiguous end plates of the two adjacent vertebrae. Gadolinium-enhanced MR image *(B)* demonstrated spondylodiscitis at L4-5 with epidural abscess formation and wide bilateral psoas muscle and paravertebral abscesses. Because of his critical general health conditions, the patient underwent posterior aggressive debridement, wide decompression and stabilization with pedicle screw-rod system fixed at L2 and L5, as documented at the 6-months postoperative X-ray *(C)*. Cultures were obtained during the operation, and the causative organism was identified as *Staphylococcus epidermidis,* for which the patient was treated with specific antibiotics for 3 months. The patient was re-admitted 2-year after surgery referring acute low back pain and plain X-ray *(D)*.

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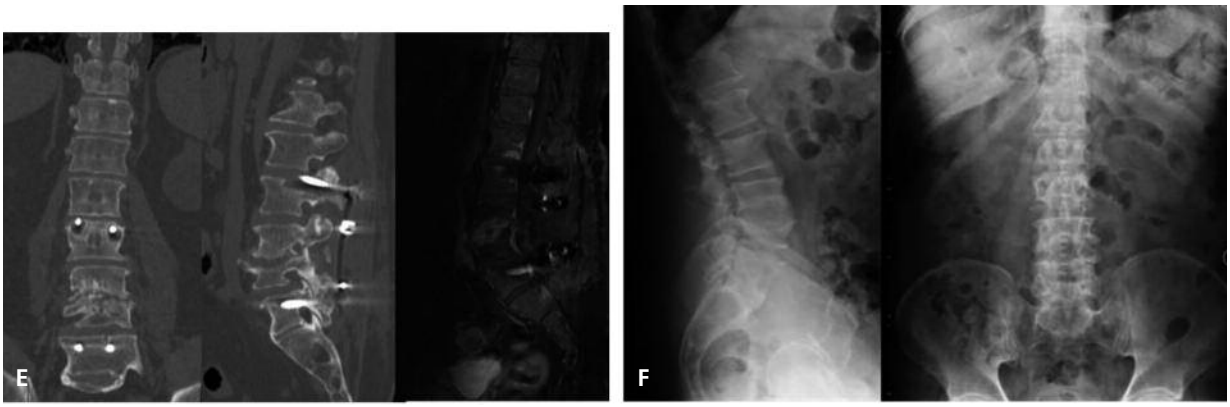

Figure 4 cont'd. CT reconstruction and MR image *(E)* showed absence of bony fusion, partial dislocation of instrumentation and recurrence of the spinal infection. This was treated by posterior debridement and complete removal of the implanted material. Because of the lack of severe deformity and neurological symptoms, only antibiotic therapy, bed rest and lumbar orthesis were indicated for 3-months after surgery; the 3-months postoperative X-ray image *(F)* showed initial bony fusion and maintenance of the correct alignment of lumbar spine.

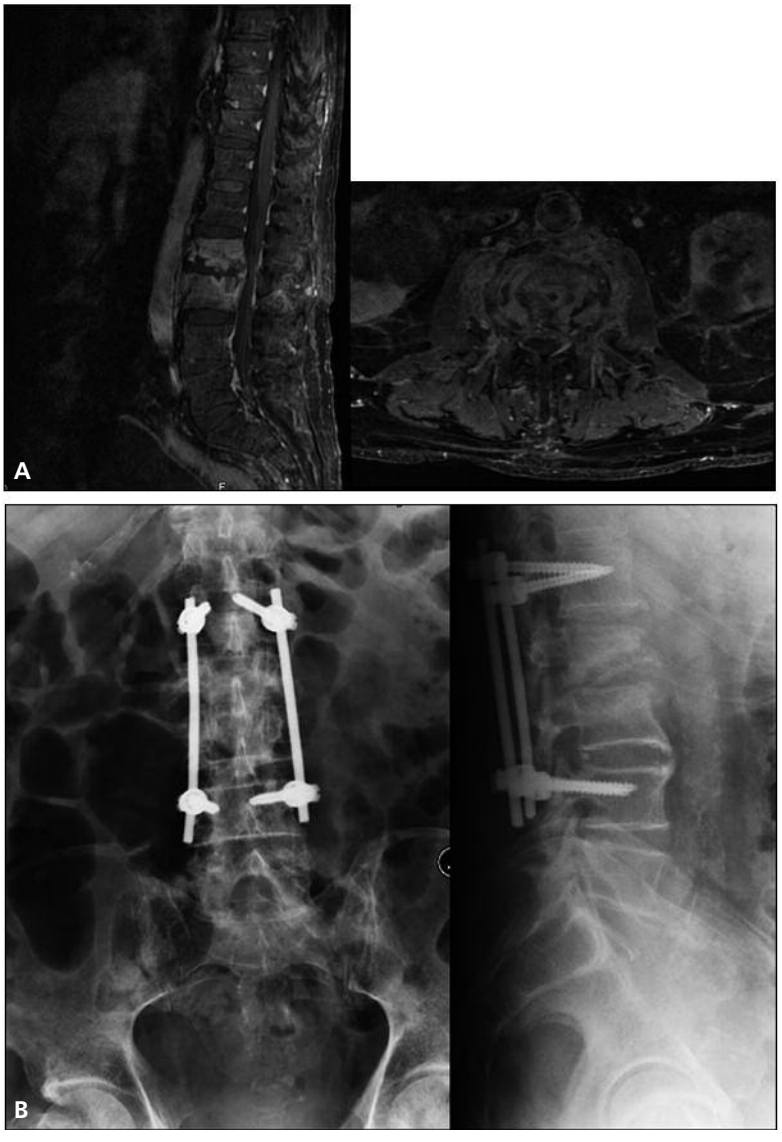

Figure 5. *Case illustration 5.* Preoperative sagittal and axial T1-weighted gadolinium-enhanced MR image *(A)* demonstrating typical features of VO with irregular end plates bony erosion and contrast enhancement in L2 and L3, in the epidural space leading to marked spinal cord compression and in the paravertebral soft tissue. The 79-year-old patient underwent spondylodesis with minimally invasive percutaneous posterior instrumentation fixed in L1 and L4. Posterior decompression and debridement were performed and *Staphylococcus epidermidis* was isolated as the causative agent. Postoperative X-ray *(B)* demonstrates correct alignment of pedicle screws and rods.

References

1) Tyrrell PN, Cassar-Pullicino VN, McCall IW. Spinal infections. Eur Radiol 1999; 9: 1066-1077.
2) Stabler A, Reiser MF. Imaging of spinal infection. Radiol Clin North Am 2001; 39: 115-135.
3) Pintado-García V. Espondilitis infecciosa Enferm Infecc Microbiol Clin 2008; 26: 510-517.
4) Cottle L, Riordan T. Infectious spondylodiscitis. J Infect 2008; 56: 401-412.
5) Carragee EJ. Pyogenic vertebral osteomyelitis. J Bone Joint Surg Am 1997; 79: 874-880.
6) Gouliouris T, Aliyu S, Brown N. J Antimicrob Chemother 2010; 65: 11-24.
7) Mampalam TJ, Rosegay H, Andrews BT. Nonoperative treatment of spinal epidural infections. J Neurosurg 1989; 71: 208-210.
8) Verner EF, Musher DM. Spinal epidural abscess. Med Clin North Am 1995; 69: 375-384.
9) Lestini WF, Bell GR. Spinal infections: patient evaluation. Semin Spine Surg 1990; 2: 244-256.
10) Eismont FJ, Bohlman HH, Soni PL, Goldberg VM, Freehafer AA. Pyogenic and fungal vertebral osteomyelitis with paralysis. J Bone Joint Surg Am 1983; 65: 19-29.
11) Friedman JA, Maher CO, Quast LM, McClelland RL, Ebersold MJ. Spontaneous disc space infections in adults. Surg Neurol 2002; 57: 81-86.
12) Osenbach RK, Hitchon PW, Menezes AH. Diagnosis and management of pyogenic vertebral osteomyelitis in adults. Surg Neurol 1990; 33: 266-275.
13) Quinones-Hinojosa A, Jun P, Jacobs R, Rosenberg WS, Weinstein PR. General principles in the medical and surgical management of spinal infections: a multidisciplinary approach. Neurosurg Focus 2004; 17: E1.
14) Cherasse A, Martin D, Tavernier C, Maillefert JF. Are blood cultures performed after disco-vertebral biopsy useful in patients with pyogenic infective spondylitis? Rheumatology (Oxford) 2003; 42: 913.
15) Ozuna RM, Delamarter RB. Pyogenic vertebral osteomyelitis and postsurgical disc space infections. Orthop Clin North Am 1996; 27: 87-94.
16) Grados F, Lescure FX, Senneville E, Flipo RM, Schmit JL, Fardellone P. Suggestions for managing pyogenic (non-tuberculous) discitis in adults. Joint Bone Spine 2007; 74: 133-139.
17) Sapico FL, Montgomerie JZ. Pyogenic vertebral osteomyelitis: report of nine cases and review of the literature. Rev Infect Dis 1979; 1: 754-776.
18) Pigrau C, Almirante B, Flores X, Falco V, Rodríguez D, Gasser I, Villanueva C, Pahissa A. Spontaneous pyogenic vertebral osteomyelitis and endocarditis: incidence, risk factors, and outcome. Am J Med 2005; 118: 1287.
19) Nathwani D, Barlow GD, Ajdukiewicz K, Gray K, Morrison J, Clift B, France AJ, Davey P. Cost-minimization analysis and audit of antibiotic management of bone and joint infections with ambulatory teicoplanin, in-patient care or outpatient oral linezolid therapy. J Antimicrob Chemother 2003; 51: 391-396.
20) Tice AD, Hoaglund PA, Shoultz DA. Outcomes of osteomyelitis among patients treated with outpatient parenteral antimicrobial therapy. Am J Med 2003; 114: 723-728.
21) Legrand E, Flipo RM, Guggenbuhl P, Masson C, Maillefert JF, Soubrier M, Noël E, Saraux A, Di Fazano CS, Sibilia J, Goupille P, Chevalie X, Cantagrel A,Conrozier T, Ravaud P, Lioté F. Rheumatology Network Organization. Management of nontuberculous infectious discitis. Treatments used in 110 patients admitted to 12 teaching hospitals in France. Joint Bone Spine 2001; 68: 504-509.
22) McHenry MC, Easley KA, Locker GA. Vertebral osteomyelitis: long-term outcome for 253 patients from 7 Cleveland-area hospitals. Clin Infect Dis 2002; 34: 1342-1350.
23) Legrand E, Massin P, Levasseur R. Stratégie diagnostique et principes thérapeutiques au cours des spondylodiscites infectieuses bactériennes. Rev Rhum 2006; 73: 373-379.
24) Kowalski TJ, Berbari EF, Huddleston PM, Steckelberg JM, Osmon DR. Do follow up imaging examinations provide useful prognostic information in patients with spine infection? Clin Infect Dis 2006; 43: 172-179.
25) Sendi P, Bregenzer T, Zimmerli W. Spinal epidural abscess in clinical practice. QJM 2008; 101: 1-12.
26) Cunha BA, Gossling HR, Pasternak HS, Nightingale CH, Quintiliani R. The penetration characteristics of cefazolin, cephalothin and cephradine into bone in patients undergoing total hip replacement. J Bone Joint Surg Am 1977; 59: 856-860.
27) Summersgill JT, Schupp LG, Raff M J. Comparative penetration of metronidazole, clindamycin, chloramphenicol, cefoxitin, ticaricillin and moxalactam into bone. Antimicrob Agents Chemother 1982; 21: 601-603.
28) Landersdorfer CB, Bulitta JB, Kinzig M, Holzgrabe U, Sörgel F. Penetration of antibacterials into bone: pharmacokinetic, pharmacodynamic and bioanalytical considerations. Clin Pharmacokinet 2009; 48: 89-124.
29) Norden CW, Shaffer M. Treatment of experimental chronic osteomyelitis due to Staphylococcus aureus with vancomycin and rifampicin. J Infect Dis 1983; 147: 352-357.
30) Verklin R M, Mandell G L. Alteration of effectiveness of antibiotics by anaerobiosis. J Lab Clin Med 1976; 89: 65-71.
31) Forrest GN, Tamura K. Rifampin combination therapy for non-mycobacterial infections. Clin Microbiol Rev 2010; 23: 14-34.
32) Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, Kaplan SL, Karchmer AW,

Levine DP, Murray BE, J Rybak M, Talan DA, Chambers HF. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis 2011; 52: 285-292.

33) Skaf GS, Domloj NT, Fehlings MG, Bouclaous CH, Sabbagh AS, Kanafani ZA, Kanj SS. Pyogenic PVO: an overview. J Infect Public Health 2010; 3: 5-16.

34) Darley E, MacGowan A. Antibiotic treatment of Gram-positive bone and joint infections. J Antimicrob Chemother 2004; 53: 928-935.

35) Giammarellou H. Activity of quinolones against Gram-positive cocci: clinical features. Drugs 1995; 49: 58-66.

36) Rissing JP. Antimicrobial therapy for chronic osteomyelitis in adults: role of the quinolones. Clin Infect Dis 1997; 25: 1327-1333.

37) Hooper J A, Wood A J J. Fluoroquinolone antimicrobial agents. N Engl J Med 1991; 324: 384-394.

38) Desplaces N, Acar J F. New quinolones in the treatment of joint and bone infections. Rev Infect Dis 1988; 10: 179-183.

39) Metallidis S, Topsis D, Nikolaidis J, Alexiadou E, Lazaraki G, Grovaris L, Theodoridou A, Nikolaidis P. Penetration of moxifloxacin and levofloxacin into cancellous and cortical bone in patients undergoing total hip arthroplasty. J Chemother 2007; 19: 682-687.

40) Tacconelli E. Antimicrobial use: risk driver of multidrug resistant microorganisms in healthcare settings. Curr Opin Infect Dis 2009; 22: 352-358.

41) Zimmerli W, Widmer A, Blatter M, Frei R, Ochsner PE. Role of rifampicin for treatment of orthopaedic implant-related staphylococcal infections. JAMA 1998; 279: 1537-1541.

42) Norden C W. Experimental osteomyelitis. Therapeutic trials with rifampicin alone and in combination with gentamicin, sisomycin and cephalothin. J Infect Dis 1975; 132: 493-499.

43) Widmer AF, Gaechter A, Ochsner PE. Antimicrobial treatment of orthopaedic implant-related infections with rifampicin combinations. Clin Infect Dis 1992; 14: 1251-1253.

44) Drancourt M, Stein A, Argenson JN, Zannier A, Curvale G, Raoult D. Oral rifampicin plus ofloxacin for treatment of Staphylococcus-infected orthopaedic implants. Antimicrob Agents Chemother 1993; 37: 1214-1218.

45) Drancourt M, Stein A, Argenson JN, Roiron R, Groulier P, Raoult D. Oral treatment of Staphylococcus spp. infected orthopaedic implants with fusidic acid or ofloxacin in combination with rifampicin. J Antimicrob Chemother 1997; 39: 235-240.

46) Clumeck N, Marcelis L, Amiri-Lamraski MH, Gordts B. Treatment of severe staphylococcal infections with a rifampicin-minocycline association. J Antimicrob Chemother 1984; 13: 17-22.

47) Yzerman EPF, Boelens HAM, Vogl M, Verbrugh HA. Efficacy and safety of teicoplanin plus rifampicin in the treatment of bacteraemic infections caused by Staphylococcus aureus. J Antimicrob Chemother 1998; 42: 233-239.

48) Chater EH, Flynn J. Fucidin levels in osteomyelitis. J Irish Med Assoc 1972; 65: 506-508.

49) Lautenbach EEG, Robinson RG, Koornhof HJ. Serum and tissue concentrations of sodium fusidate in patients with chronic osteomyelitis and in normal volunteers. S Afr J Surg 1975; 13: 21-32.

50) Bailey EM, Ryback MJ, Kaatz GW. Comparative effect of protein binding on the killing activities of teicoplanin and vancomycin. Antimicrob Agents Chemother 1991; 35: 1089-1092.

51) Wood M. The comparative efficacy and safety of teicoplanin and vancomycin. J Antimicrob Chemother 1996; 37: 209-22.

52) Lemaire X, Loiez C, Valette M, Migaud H, Dubreuil L, Yazdanpanah Y, Senneville E. Wood MJ. Comparative safety of teicoplanin and vancomycin. J Chemother 2000; 12: 21-25.

53) Lemaire X, Loiez C, Valette M, Migaud H, Dubreuil L, Yazdanpanah Y, Senneville E. Comparison of vancomycin and teicoplanin trough serum levels in patients with infected orthopedic devices: new data for old therapies. J Infect Chemother 2011;17: 370-374.

54) Wilson APR,Grüneberg RN. Safety. In Teicoplanin: The First Decade. The Medicine Group (Education) Ltd, Abingdon, Oxfordshire, UK, 1997, p. 143.

55) Graninger W, Wenisch C, Wiesinger E, Menschik M, Karimi J, Presterl E. Experience with outpatient intravenous teicoplanin therapy for chronic osteomyelitis. Eur J Clin Microbiol Infect Dis 1995; 14: 643-647.

56) Davey PG, Rowley DR, Phillips G. Teicoplaninhome therapy for prosthetic joint infections. Eur J Surg 1992; 567: 23-25.

57) Greenberg RN. Treatment of bone, joint and vascularaccess-associated Gram-positive bacterial infections with teicoplanin. Antimicrob Agents Chemother 1990; 34: 2392-2397.

58) Boucher HW, Sakoulas G. Perspectives on daptomycin resistance with emphasis on resistance in Staphylococcus aureus. Clin Infect Dis 2007; 45: 601-608.

59) Leite B, Gomes F, Teixeira P, Souza C, Pizzolitto E, Oliveira R. In vitro activity of daptomycin, linezolid and rifampicin on Staphylococcus epidermidis biofilms. Curr Microbiol 2011; 63: 313-317.

60) Arbeit RD, Maki D, Tally FP, Campanaro E, Eisenstein BI. The safety and efficacy of daptomycin for the treatment of complicated skin and skin-structure infections. Clin Infect Dis 2004; 38: 1673-1681.

61) Miller BA, Gray A, Leblanc TW, Sexton DJ, Martin AR, Slama TG. Acute eosinophilic pneumonia secondary to daptomycin: a report of three cases. Clin Infect Dis 2010; 50: 63-68.

62) Stein A, Bataille JF, Drancourt M, Curvale G, Argenson JN, Groulier P, Raoult D. Ambulatory treatment of multidrug-resistant Staphylococcus aureus-infected orthopaedic implants with high dose oral co-trimoxazole (trimethoprim-sulfamethoxazole). Antimicrob Agents Chemother 1998; 42: 3086-3091.

63) Qadri SM, Halim M, Ueno Y, Saldin H. Susceptibility of methicillin-resistant Staphylococcus aureus to minocycline and other antimicrobials. Chemotherapy 1994; 40: 26-29.

64) Yuk JH, Dignani MC, Harris RL, Bradshaw MW, Williams TW Jr. Minocycline as an alternative antistaphylococcal agent. Rev Infect Dis 1991; 13: 1023-1024.

65) Summers M, Misenhimer GR, Anthony SJ. Vancomycin-resistant Enterococcus faecium osteomyelitis: successful treatment with quinupristin-dalfopristin. South Med J 2001; 94: 353-355.

66) Reyzelman AM, Van Gils CC, Hardin TC, Vayser DJ, Harkless LB. Vancomycin- resistant enterococci osteomyelitis in the foot. A case report. J Am Podiatr Med Ass 1997; 87: 434-437.

67) Allington DR, Rivey MP. Quinupristin/dalfopristin: a therapeutic review. Clin Ther 2001; 23: 24-44.

68) Zurenko GE, Gibson JK, Shinabarger DL, Aristoff PA, Ford CW, Tarpley WG. Oxazolidinones: a new class of antibacterials. Curr Opin Pharmacol 2001; 1: 470-476.

69) Stolle LB, Plock N, Joukhadar C, Arpi M, Emmertsen KJ, Buerger C, Riegels-Nielsen P, Kloft C. Pharmacokinetics of linezolid in bone tissue investigated by in vivo microdialysis. Scand J Infect Dis 2008; 40: 24-29.

70) Gould FK. Linezolid: safety and efficacy in special populations. J Antimicrob Chemother 2011; 66: 3-6.

71) Hsieh PC, Wienecke RJ, O'Shaughnessy BA, Koski TR, Ondra SL. Surgical strategies for vertebral osteomyelitis and epidural abscess. Neurosurg Focus 2004; 17: E4.

72) Ogden AT, Kaiser MG. Single-stage debridement and instrumentation for pyogenic spinal infections. Neurosurg Focus 2004; 17: E5.

73) Chen WH, Jiang LS, Dai LY. Surgical treatment of pyogenic vertebral osteomyelitis with spinal instrumentation. Eur Spine J 2007; 16: 1307-1316.

74) Deininger MH, Unfried MI, Vougioukas VI, Hubbe U. Minimally invasive dorsal percutaneous spondylodesis for the treatment of adult pyogenic PVO. Acta Neurochir (Wien) 2009; 151: 1451-1457.

75) Kuklo TR, Potter BK, Bell RS, Moquin RR, Rosner MK. Single-stage treatment of pyogenic spinal infection with titanium mesh cages. J Spinal Disord Tech 2006; 19: 376-382.

76) Veillard E, Guggenbuhl P, Morcet N, Meadeb J, Bello S, Perdriger A, Chalès G. Prompt regression of paravertebral and epidural abscesses in patients with pyogenic discitis. Sixteen cases evaluated using magnetic resonance imaging. Joint Bone Spine 2000; 67: 219-227.

77) Hadjipavlou AG, Mader JT, Necessary JT, Muffoletto AJ. Hematogenous pyogenic spinal infections and their surgical management. Spine 2000; 25: 1668-1679.

78) Lee MC, Wang MY, Fessler RG, Liauw J, Kim DH. Instrumentation in patients with spinal infection. Neurosurg Focus 2004 15; 17: E7.

79) Ruf M, Stoltze D, Merk HR, Ames M, Harms J. Treatment of vertebral osteomyelitis by radical debridement and stabilization using titanium mesh cages. Spine 2007; 32: E275-280.

80) Korovessis P, Repantis T, Iliopoulos P, Hadjipavlou A. Beneficial influence of titanium mesh cage on infection healing and spinal reconstruction in hematogenous septic spondylitis: a retrospective analysis of surgical outcome of twenty-five consecutive cases and review of literature. Spine (Phila Pa 1976) 2008; 33: E759-767.

81) Korovessis P, Petsinis G, Koureas G, Iliopoulos P, Zacharatos S. Anterior surgery with insertion of titanium mesh cage and posterior instrumented fusion performed sequentially on the same day under one anesthesia for septic spondylitis of thoracolumbar spine: is the use of titanium mesh cages safe? Spine 2006; 31: 1014-1019.

82) Strowitzki M, Vastmans J, Vogel M, Jaksche H. Complex 360°- reconstruction and stabilization of the cervical spine due to osteomyelitis. Eur Spine J 2011; 2: S248-252.

83) Acosta FL Jr, Chin CT, Quiñones-Hinojosa A, Ames CP, Weinstein PR, Chou D. Diagnosis and management of adult pyogenic osteomyelitis of the cervical spine. Neurosurg Focus 2004; 17: E2.

84) Pee YH, Park JD, Choi YG, Lee SH. Anterior debridement and fusion followed by posterior pedicle screw fixation in pyogenic PVO: autologous iliac bone strut versus cage. J Neurosurg Spine 2008; 8: 405-412.

85) Przybylski GJ, Sharan AD. Single-stage autogenous bone grafting and internal fixation in the surgical management of pyogenic discitis and vertebral osteomyelitis. J Neurosurg (Spine) 2001; 94: 1-7.

86) Fayazi AH, Ludwig SC, Dabbah M, Bryan Butler R, Gelb DE. Preliminary results of staged anterior debridement and reconstruction using titanium mesh cages in the treatment of thoracolumbar vertebral osteomyelitis. Spine J 2004; 4: 388-395.

87) Rath SA, Neff U, Schneider O, Richter HP. Neurosurgical management of thoracic and lumbar vertebral osteomyelitis and discitis in adults: A review of 43 consecutive surgically treated patients. Neurosurgery 1996; 38: 926-933.

88) Dimar JR, Carreon LY, Glassman SD, Campbell MJ, Hartman MJ, Johnson JR. Treatment of pyogenic vertebral osteomyelitis with anterior debridement and fusion followed by delayed posterior spinal fusion. Spine 2004; 29: 326-332.

89) Banwart JC, Asher MA, Hassanein RS. Iliac crest bone graft harvest donor site morbidity. A statistical evaluation. Spine 1995; 20: 1055-1060.

90) Fukuta S, Miyamoto K, Masuda T, Hosoe H, Kodama H, Nishimoto H, Sakaeda H, Shimizu K. Two-stage (posterior and anterior) surgical treatment using posterior spinal instrumentation for pyogenic and tuberculotic spondylitis. Spine 2003; 28: 302-308.

91) Chang WC, Tsou HK, Kao TH, Yang MY, Shen CC. Successful treatment of extended epidural abscess and long segment osteomyelitis: a case report and review of the literature. Surg Neurol 2008; 69: 117-120.

92) Fang D, Cheung KMC, Dos Remedios IDM, et al. Pyogenic vertebral osteomyelitis: Treatment by anterior spinal debridement and fusion. J Spinal Disord 1994; 7: 173-180.

93) Muckley T, Schutz T, Schmidt MH, Potulski M, Buhren V, Beisse R. The role of thoracoscopic spinal surgery in the management of pyogenic vertebral osteomyelitis. Spine 2004; 29: 227-233.

94) Hadjipavlou AG, Katonis PK, Gaitanis IN, Muffoletto AJ, Tzermiadianos MN, Crow W. Percutaneous transpedicular discectomy and drainage in pyogenic PVO. Eur Spine J 2004; 13: 707-713.