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ABSTRACT

Vertebral osteomyelitis (VO) is a disease that responds well to conservative treatment and antibiotherapy if diagnosed in an early stage. Due to the prolonged onset of this pathology, many cases are diagnosed in mid or late stages and require surgery. The surgical treatment is not yet standardized and may only mean decompression of the infectious outbreak without stabilization, or surgical decompression associated with stabilization.

Using only bone grafts for surgery or stabilizing the spine through segmental posterior and/or anterior instrumentation is accompanied by many controversies.

In this review, we focus on demonstrating that combining a well-conducted antibiotherapy with thorough debridement of the necrotic areas and using metal implants for spinal stabilization lowers the infection rates, provides an early pain-free mobilization of the patient and reduces hospitalization costs.

1. INTRODUCTION

Vertebral osteomyelitis (also called osteodiscitis) is an acute or chronic infection of the spine with direct iatrogenic or indirect (hematogenous) inoculation. It is a rare infection concentrated in the spine, the cases being so rare that only 2-4% of all bone infections are attributed to this disease. Vertebral osteomyelitis attacks the intervertebral disc and the two adjacent vertebrae, causing the destruction of the intervertebral space. The prognosis of the disease depends on several factors: the place where the infection is concentrated in the spine, the time elapsed between the initial onset and the treatment used, but also the approach used to treat the disease (1,5).

Historically we will cover the treatments applied to vertebral osteomyelitis over the years. The first measures taken were bed rest and symptomatic medication.

Laminectomy was the first attempt at surgical treatment, but it brought poor results in the approach to the anterior spine, and the

Keywords

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main complication was postoperative instability (2, 11).

In 1911, Albee introduced a posterior bone fusion technique, but this was abandoned due to postoperative kyphosis (6).

Hodgson and Stock introduced the approach technique of the infectious outbreak, which directly resolves the infection and preserves the integrity of the anterior spine, preventing postoperative kyphosis (10).

After the introduction in the 1970s by Roy Camille of the vertebral fixation technique with transpedicular screws and rods, it became a standard in the surgical treatment of vertebral osteomyelitis (5, 8).

MATERIALS AND METHODS

For accomplishing this review, we enlisted a throughout research of database from "PubMed", "Scopus", "Web of science" using key words as "vertebral osteomyelitis", "spinal infection", "osteodiscitis", "spinal stabilization" and "spine surgery". Of the many existing studies, we reviewed 35 studies independent of time and date and from which we concluded this review, comparing different methods of treatment in vertebral osteomyelitis.

RESULTS

ETIOLOGY AND PATHOPHYSIOLOGY

The source of the infection was found in only 40% of cases and was represented by urinary tract infections, soft tissue, respiratory, intestinal, dental infections, endocarditis and penetrating trauma. The etiology of vertebral osteomyelitis consists of infections with *Staphylococcus aureus*, *Streptococcus*, *Mycobacterium tuberculosis*, etc.

The study by Nolla JM et al shows that acute VO affects mostly elderly patients with associated comorbidities. (27)

Most cases of osteodiscitis occur due to the inoculation of bacteria by hematogenous at the level of the intervertebral disc. Dermal inoculation is also present. The most common bacterial cause is *Staphylococcus Aureus* (32-67%). Occasionally, coagulase-negative staphylococci may be a cause with or without epidural involvement. Gram-negative organisms, such as *Escherichia coli* (21%), often from a urinary tract source are the second most commonly identified cause of infection.

Pseudomonas sp. are associated with approximately 6% of cases and should indicate a history of environmental water exposure or intravenous drug use (20).

In their study, Patzakis and coworkers included a 78 % of the patients as intravenous drug users and found *S. aureus* at a low prevalence as the main bacteria (17%), while *Pseudomonas aeruginosa* was the predominant etiologic agent (38%) (29).

Spinal infections lead to a spectrum of diseases with a varied clinical presentation. Vertebral infection usually results from bacterial insemination of the vertebral disc, which then spreads to adjacent vertebrae (vertebral osteomyelitis). A muscular abscess is frequently present in the paravertebral muscles. In 17% of cases, the infection at the disc level migrates into the epidural space, resulting in the epidural abscess. Its timely identification is essential, as 1 in 4 patients with this condition quickly develop paralysis (26).

Several studies describe the vertebral level involved and describe the following incidence of affection: lumbar spine (58%), thoracic spine (30%) and cervical spine (11%) (34, 28, 2, 26, 17). Vertebral defects were found in multiple levels, 6% were reported with continuous character and 3% reported with skipping multifocal involvement. A large number of multifocal involvement was reported in iv drug abusers (29).

SYMPTOMS. CLINICAL EVALUATION

A detailed neurological examination is essential for any patient suspected of having vertebral osteomyelitis. Objective neurological signs are rare, but when present can range from mild (radicular pain corresponding to a nerve root injury), moderate (motor weakness, sensory loss, urinary or intestinal dysfunction), to severe (paralysis).

In the presence of an abnormal neurological examination, the presence of a possible epidural abscess should be investigated, because the delay of the diagnosis can lead to the permanence of the deficit.

The accentuation of the neurological signs indicates the progression of the infection in the epidural space and the damage of the nerve roots or the compression of the spinal cord.

According to numerous studies, many patients present an insidious onset and unspecific symptomatology (neck or back pain, fever, painful

flexion/extension of the back and/or neurological deficits). Early diagnosis of this disease is important, but not always possible as 30-70% of the patients do not show signs of prior infection (5) and a delay of 2 to 6 months from the starting symptomatology to the diagnosis of this disease has been reported. (1, 11)

Local clinical examination, represented by the point of sensitivity to palpation can differentiate vertebral osteomyelitis from other differential diagnoses. There are no pathognomonic signs or symptoms to indicate the presence of this condition. A normal clinical examination does not rule out presence diagnosis of vertebral osteomyelitis. The classic triad consisting of fever, back pain and neurological deficit is specific to this condition. The potential consequences of undiagnosed vertebral osteomyelitis are devastating, so when referring to a differential diagnosis, laboratory and imaging tests are mandatory.

Thus, according to the studies of Butler et al and Frangen et al, the diagnosis should be supported by clinical, laboratory, and imaging findings (1, 11)

LABORATORY TESTS

Usual blood tests that help diagnose patients with suspected epidural abscess or vertebral osteomyelitis include: hemoleukogram, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP). These tests are not completely reliable indicators for the presence of the disease and must be correlated with: clinical suspicion, patient history and imaging study. Leukocytosis is variable and does not indicate the severity of the disease. Increased ESR is important in the early diagnosis of patients with osteomyelitis.

CRP has a sensitivity of 84-100% in the case of the presence of epidural abscess and is a necessary analysis for the initial diagnosis.

However, according to Curry and coworkers, ESR and CRP are more useful than the white blood cell count (WBC), because a normal WBC does not exclude the presence of a spinal infection. (3)

Also, the positivity of blood cultures indicates the presence of a generalized infection, the most often isolated germ in most cases being *Staphylococcus aureus*.

As some studies show, up to 59% of positive blood cultures identify the etiological microorganism

in patients with monomicrobial pyogenic spondylodiscitis (24)

IMAGING

Radiological evaluation of a patient with vertebral osteomyelitis reveals changes only after a few weeks. The first obvious changes after a few days are local edema and loss of the psoas shadow. In the next 7-10 days, the reduction of the vertebral space and the erosion of the adjacent vertebral plates ("mirror image") are observed. Sclerosis at this level generally appears on the radiological image at 10-21 days and it may take 3 to 6 weeks from the onset of the symptoms for bony destruction of the vertebrae to become evident according to Jevtic V's study (20) (Figure 1). This results in a delay of the diagnosis.

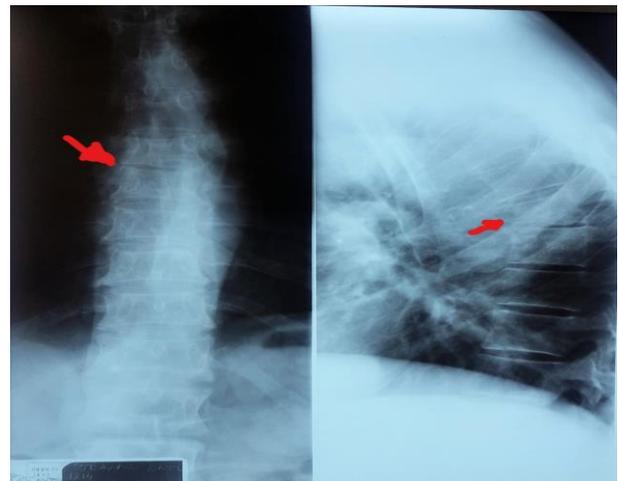


Figure 1. Preoperative thoracic spine radiograph: major narrowing of T7-T8 disc space (personal collection).

The gold standard for imaging diagnosis is MRI, which distinguishes hypointensity in T1, hyperintensity in T2 and capture of Gadolinium in the T1-weighted sequence. This investigation has a sensitivity of 96% and a specificity of 93% and is also used in the differential diagnosis of this pathology. (12, 13)

In case of an MRI contraindication, a CT scan is performed, which distinguishes bone abnormalities, abscess formation and the degree of bone damage. Another investigation that can be performed in the case of MRI contraindication is Tc99m Technetium Bone Scintigraphy, but it has a sensitivity of 90% and a much lower specificity than MRI. (17) (figures 2,3)

According to Hadjipavlou and coworkers, positive blood cultures and other paraclinical investigations

in association with clinical symptoms do not confirm the diagnosis of a spinal infection. The definitive diagnosis can be obtained by histopathological examination through a surgical or CT-guided biopsy. An exact diagnosis of this disease should be achieved in order to ensure a well-conducted management. (16, 17)



Figure 2. Thoracic MRI with intravenous contrast T2 sagittal plane: T7-T8 osteomyelitis with intraspinal abscess (personal collection).

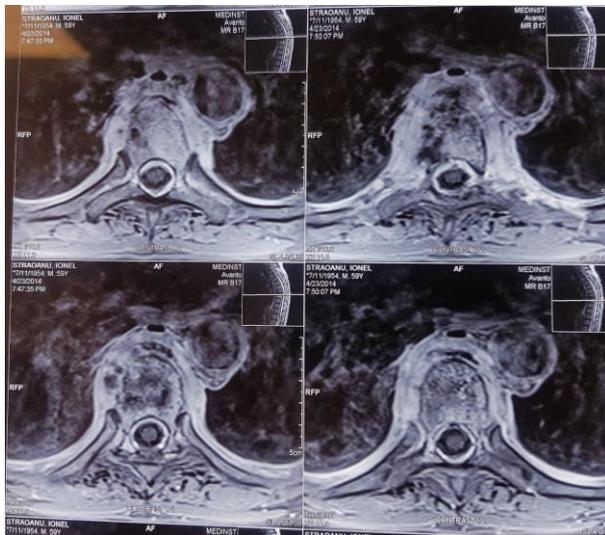


Figure 3. Thoracic MRI with intravenous contrast T2 transverse plane: T7-T8 osteomyelitis with intraspinal abscess (personal collection).

DIFFERENTIAL DIAGNOSIS

The main pathologies with which the differential diagnosis can be made are: vertebral tumors,

vertebral fracture and degenerative diseases of the spine (disc herniation, spinal canal stenosis, vertebral spondylolysis).

In a study conducted by Tyrell PN et al, it is demonstrated that a destructive bone lesion of the vertebrae associated with a preserved disc space with sharp endplates guides the diagnosis to a neoplastic infiltration, while a destructive bone lesion associated with an undefined vertebral body with loss of definition of the vertebral endplate with or without modification of disc height suggests an infection, which has a better prognosis than cancer. (35)

CONSERVATIVE AND MEDICAMENTOUS TREATMENT

Conservative treatment of vertebral osteomyelitis consists of prolonged bed rest and antibiotic therapy for 6 to 12 weeks.

During immobilization, the patient is placed in a corset or cervico-thoracic or thoraco-lumbar orthosis depending on the location of the lesion.

According to the studies of Fleege C et al and Skaf GS et al, the first line of treatment is a conservative approach. This choice is made especially for the patients with minor or no neurologic deficits and in case of severe associated comorbidities that limit surgery. Antibiotics with a large spectrum are used initially (Clindamycin + Ciprofloxacin or Cefotaxim + Flucloxacillin) in order to cover a wider area of potential pathogens. Afterwards, the antibiotic treatment is switched to an appropriate medication guided by the antibiogram. These last antibiotics are applied iv for 2-4 weeks or until the CRP is markedly dropped. In the final step of the treatment oral antibiotic is continued for a total of 6 to 12 weeks. This treatment is accompanied by prolonged bed rest and pain medication with or without orthosis for at least 6 weeks. (10, 33)

Medicamentous treatment is a symptomatic as well as an etiological treatment.

Symptomatic treatment addresses mainly pain, febrile syndrome and includes various types of analgesics and anti-inflammatory drugs.

The etiological treatment is addressed to the germ in question and is represented by third generation cephalosporins and / or Vancomycin for bacterial and tuberculostatic treatment in cases with Mycobacterium Tuberculosis (20).

Medicamentous treatment must also take into account the biological balance of each patient and in

this context, we refer to parenteral hydration with various osmolar solutions, parenteral nutrition in cases of severe sepsis, combating anemia in cases of severe sepsis through blood transfusions, hypoproteinemia and balancing the metabolic rate of the patient (17).

If conservative treatment fails and proper mobilization of the patients is not achieved surgery is then performed as many complications due to immobilization are critical to patients, especially to the elderly.

SURGICAL TREATMENT

Several studies suggest that the main indications for surgical treatment are represented by the following: severe lesional changes in vertebral endplates, formation of abscesses, biomechanical instability due to chronic osteomyelitis, appearance of neurological deficits, decompensated kyphosis, septic pseudarthrosis, pain that does not respond to pharmaceutical treatment, and non-responsive patients to conservative treatment. (4, 14, 30)

The surgical treatment has the following important objectives: evacuation of infection and debridement, decompression of the dural sac and spinal roots and vertebral fixation / fusion.

The main principle of the surgical treatment of this disease is radical and aggressive debridement of all unviable tissues and material according to a study conducted by Fayazi AH and coworkers. This study states that all necrotic and infected tissues are mandatory to be removed and all abscesses evacuated for a good management of the disease. (9)

The choice of surgical approach depends on the location of the lesion in the spine. Thus, the anterior cervical approach, the lateral cavitory approach and costotransversectomy for the thoracic spine, laminectomy, hemilaminectomy and foraminotomy for the lumbar spine are described.

Choosing between an anterior or posterior approach is debatable.

The studies of Emery SE, Fang D and Fukuoka M show that due to affection of the vertebral bodies and disc spaces the majority of surgeons incline to an anterior approach for direct access to the infection site and better reconstructive stabilization. (6, 7, 12)

Fayazi et al and Korovessis et al reveal that a posterior approach is used in order to drain the abscesses and for posterior stabilization of the spine

and that a combined approach needs to be chosen in relation to the surgical goals that are aimed to be achieved. (9, 22)

Several studies show that a combined approach results in a lower incidence of postoperative infection and revision surgery and a higher mortality rate with an isolated anterior approach for cervical spine lesions. The increased mortality rate of an anterior approach is also explained by a higher incidence of associated comorbidities of patients with cervical spine lesions. (4, 8, 13, 15, 23)

The vertebral fixation is performed using transpedicular screws and rods, but also the reconstruction techniques of the anterior column, with the help of fixed or expandable titanium cages. A relatively new method of treating this disease is represented by minimally invasive surgery.

Muckley T and coworkers demonstrated in their study that treating VO through video-assisted thoracoscopic surgery has advantages and disadvantages. The main advantages are debridement and surgical instrumentation of multiple levels can be achieved with minimal dissection of the surrounding soft tissues. The disadvantages of this technique are represented by a technically demanding procedure in which special instrumentation and experience of the surgeon are required. (25)

Hadjipavlou et al revealed in their study of 34 cases an immediate pain relief of 26 patients and stated that the most common long-term complications of the use of minimally invasive surgery are implant failure with axial pain and instability or severe kyphotic deformities. (16)

A controversial debate is between the use of single-stage surgery versus two-stage surgery.

Safran et al revealed in his study of 10 patients with osteodiscitis operated through single-stage surgery that it is a secure and efficient method of controlling the infection and reconstruction of the spine, shortening the hospitalization and mobilization time of the patient and also reducing hospitalization costs for the patient and the institute. The surgery is performed based on the experience of the surgeon and the overall condition of the patient, taking into consideration that medically unstable patients may not be able to withstand a second anesthesia, surgery or increased period of immobilization. (31)

Increased surgical debridement of a

compromised anterior column of the spine results in massive loss of bone tissue and increased axial instability, therefore it is mandatory to perform surgical reconstruction in order to prevent residual instability.

Bone grafting is required for the reconstruction of the anterior column either with autogenous bone graft or allograft. A study by Emery SE et al demonstrated that 19 patients operated for vertebral osteomyelitis through aggressive debridement and the use iliac bone grafting in the presence of an active infection had immediate pain relief and no septic complications 2 years after surgery. (6)

Many surgeons suggest that allografting can be used instead of autogenous grafting. Schuster et al conducted a study of 47 patients operated using allografts consecutive to surgical debridement, posterior instrumentation and iv antibiotics and demonstrated that it is a secure method of treating vertebral osteomyelitis. The main advantages of using allografts are lowering the operation time and morbidity associated with harvesting of the graft and the main disadvantages are the host's immune response and an increased risk of pathological transmission of diseases. (32)

Hodgson demonstrated in 1956 through his work on the treatment of Pott's paraplegia that anterior debridement and vertebral fusion with autogenous bone grafting rapidly correct axial alignment, however, long-term results show spinal instability with the collapse of the vertebral column, correction malalignment and formation of pseudarthrosis. (19) Therefore, the use of spinal instrumentation is mandatory in most cases associated with spinal instability. (Figures 4,5)

In their studies Hee et al. and Fayazi et al. reported that the use of a titanium mesh cage with posterior instrumentation for the reconstruction of the spine is an excellent method in improving the mobilization of the patient and a rapid fusion in patients that underwent surgery for active vertebral osteomyelitis. Therefore, they demonstrated that the patients had less postoperative complications, lower infection recurrence rates and improved spinal alignment and stability. The loss of kyphosis correction was noted due to collapse of the cage into the adjacent vertebrae, but overall the cases had a good prognosis because of the lower infection rates and early and pain free mobilization. (18, 9)

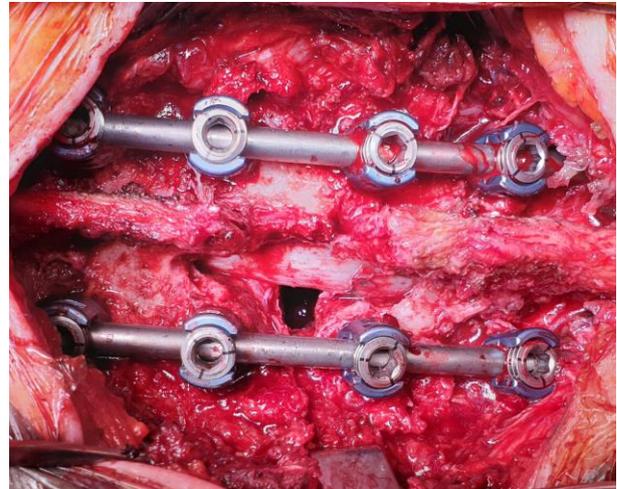


Figure 4. Intraoperative view showing spinal fixation using 8 transpedicular screws and rods after radical debridement (personal collection),

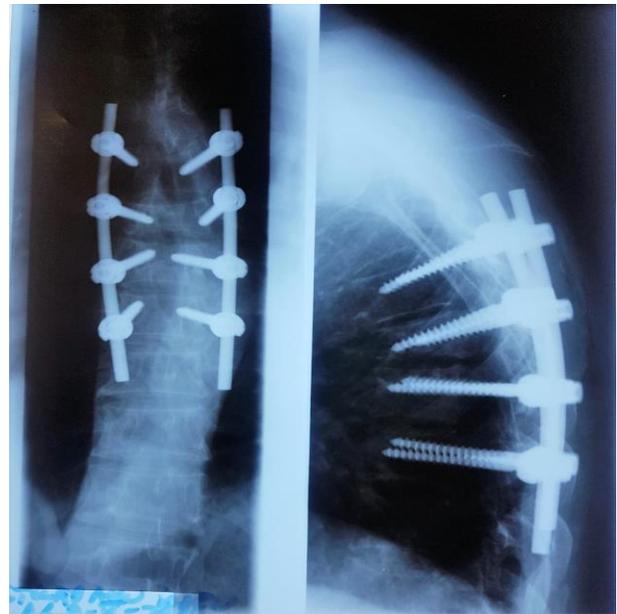


Figure 5. Postoperative radiographic control: stabilization with 8 transpedicular screws and 2 titanium rods (personal collection).

CONCLUSION

Most cases of vertebral osteomyelitis respond well to conservative treatment if diagnosed in an early stage. In cases that are unmanageable by conservative treatment, surgery is mandatory. Aggressive debridement of all necrotic tissues is needed along with surgical stabilization of the spine to ensure a good management of the disease. Vertebral fixation and fusion ensure immediate vertebral stability, which allows the patient to

mobilize quickly in the first days after surgery. This is beneficial for neurological recovery, starting physical therapy and preventing complications associated with prolonged bed rest. The patient can be discharged from the surgery department in the first week after the operation after wound healing and thread extraction, which allows rapid transfer to the infectious diseases department where prolonged and targeted antibiotic treatment will be continued. This reduces hospital stay and costs per patient. This paper will demonstrate that the combination of surgical treatment represented by decompression and fixation-fusion vertebral with targeted antibiotic treatment eliminates local recurrence and allows the patient to quickly return to a normal socio-professional life.

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