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Clinical features, diagnostic and therapeutic approaches to haematogenous vertebral osteomyelitis

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Abstract. – This article review the clinical features and the diagnostic approach to haematogenous vertebral osteomyelitis in order to optimise treatment strategies and follow-up assessment. Haematogenous spread is considered to be the most important route: the lumbar spine is the most common site of involvement for pyogenic infection and the thoracic spine for tuberculosis infection. The risk factors for developing haematogenous vertebral osteomyelitis are different among old people, adults and children: the literature reports that the incidence seems to be increasing in older patients. The source of infection in the elderly has been related to the use of intravenous access devices and the asymptomatic urinary infections. In young patients the increase has been correlated with the growing number of intravenous drug abusers, with endocarditis and with immigrants from areas where tuberculosis is still endemic. The onset of symptoms is typically insidious with neck or back pain often underestimated by the patient. Fever is present in 10-45% of patients. Spinal infections may cause severe neurological compromise in few cases, but mild neurological deficit, limited to one or two nerve roots, was detected in 28-35% of patients. The diagnosis of haematogenous vertebral osteomyelitis may be very difficult, as the symptoms can be sometimes not specific, vague or almost absent. The usual delay in diagnosis has been reported to be two to four months, despite the use of imaging techniques: in the early diagnosis of vertebral ostemyelitis is important the role of bone scintigraphy. The general principles for the management of spine infections are non operative, consisting of external immobilization and intravenous antibiotics, followed by oral antibiotics. Indications for surgery should be given in case of absence of clinical improvement after 2-3 weeks of intravenous antibiotics, persistent back pain and systemic effects of chronic infection and with presence or progression of neurological deficit in elderly or in cervical infection. Chronic ostemyelitis may require surgery in case of a development of biomechanical instability and/or a vertebral collapse with progressive deformity.

Key words:
Vertebral osteomyelitis, Spondylodiscitis, Pyogenic osteomyelitis, Skeletal tuberculosis.

Introduction

Haematogenous vertebral osteomyelitis (HVO) is a relatively rare disorder which accounts for 2-4% of all cases of infectious bone disease[1]. In recent years, the incidence of spinal infections has seemed to increase according to the growing number of intravenous drug users in young people and in the elderly with the use of intravenous access devices, genitourinary surgery and manipulation. Males are more frequently affected than females with an average age of onset in the fifth and sixth decade. The onset of symptoms is typically insidious with neck or back pain often underestimated by the patient. The early diagnosis is also difficult due to the non-specific nature of laboratory and radiographic findings. The frequent observation of back pain also makes the diagnosis a challenge in most cases. Several studies in the literature report an average delay in the diagnosis of haematogenous vertebral osteomyelitis from 2 to 6 months after the beginning of the symptoms[2,3,4]. In this article we review the clinical features and the diagnostic approach to haematogenous vertebral osteomyelitis in order to optimise treatment strategies and follow-up assessment.

Etiopathogenesis

Spinal infections may affect the vertebral body, the intervertebral disc, the neural arch or the posterior elements but most commonly they involve the anterior and middle columns[1]. The infection can involve and cross cortical bone and longitudinal ligaments, leading to soft tissue abscesses. Epidural abscesses may arise adjacent to the area of osteomyelitis or, less commonly, occur *de novo*.

Haematogenous spread by means of the arterial system is considered to be the most important route, because the vertebral body is richly supplied by an arterial network, especially in the anterior subchondral region near the anterior longitudinal ligament[5]. Disc space infections that occurs in adults are usually associated with prior surgical disruption of the disc, while the most common site of *de novo* infection in children is within the disc. Indeed, histological analyses have confirmed that an endarteriolar supply to the disc is present until childhood but is then slowly obliterated in the first three decades of life. Thus, adult intervertebral disc is usually not primarily involved, since it is avascular[1].

As a result of haematogenous spread, multiple foci of infection can occur. A complex valveless venous drainage, known as Batson's paravertebral venous plexus, may also act as a potential route of infection, particularly for spread from the pelvic organs especially in instances of sepsis originating in the urinary bladder, bowel and female pelvic organs[5].

The lumbar spine is the most common site of involvement for pyogenic infection followed by the thoracic, cervical and sacral regions[1,5-7]. The thoracic spine is the most commonly affected site in tuberculosis infection[8], which may be explained by the frequent involvement of mediastinal lymphnodes and pleura in pulmonary tuberculosis, from where microorganism can reach the vertebral bone through the limphatic route[8].

Matsui et al.[9] noted that the degree of destruction may depend on the patients's biological reaction relating to their physical condition or age. Buchelt et al.[10], instead, suggested that it was influenced by the species of pathogen, reporting that more than two segments were involved in 23% of patients with tuberculous and 9% of patients with pyogenic infection. Others studies have reported multiple level involvement in pyogenic infection in 5 to 18% of patients[7,11-13].

The commonest cause of osteomyelitis is *Staphilococcus Aureus*. In adults enteric Gram negative organism are second cause, while H. Influenzae is more frequent in young infants[14] and Group B Streptococci in neonates[15]. In a retrospective analysis[16] in a population of 72 patients, the organism more frequently isolated were *Staphilococcus Aureus* and *Epidermidis*, *Brucella Melitensis*, *E. Coli*, *Mycobacterium Tuberculosis*. *Streptococcus pneumoniae*, *S. agalactiae*, *S. viridans*, *S. faecalis*, *Proteus mirabilis*, *Pseudomonas Aeruginosa*, *Candida Glabrata* were uncommon. *Hidatidosis*, *actinomicosis*, *aspergillosis* and fungal infections rarely cause osteomyelitis, while only one case of *Haemophilus paraphrophilus*[15] and *Pastourella dogmatis*[17] vertebral osteomyelitis have been reported. *Serratia marcenscens* and *Pseudomonas Aeruginosa* can be responsible of osteomyelitis in intravenous drug abusers[18].

The risk factors for developing HVO are different among old people, adults and children[18]. The literature reports that the incidence of HVO seems to be increasing in older patients. This may be related to the greater longevity of the general population as well as to the more intensive treatment of serious illnesses and the use of chemotherapy to treat cancer and immunological disorders. Carrage[7] reviewed 111 patients: sixty-one (55%) were sixty years old or more and forty-four patients (40%) had an impaired immune system. In a multicenter study, which included 219 adult patients, Colmenero et al.[19] reported similar figures concerning age and associated disease.

The source of infection in the elderly has been related to the use of intravenous access devices, with resultant nosocomial bacteraemia[20]. Others source were respiratory or oral infection, skin ulceration, genitourinary surgery, placement of indwelling bladder catheters or ureteral stents, or both. Typically, HVO caused by Gram-negative pathogens (mainly *Escherichia coli* and *Proteus Mirabilis*) derive from the urinary tract and it should be considered when elderly patients complain of back pain. In fact, asymptomatic urinary infections are very common in old people[21] due to urinary incontinence,

use of catheters, comorbid illness such as diabetes or neoplasms, vaginal bacterial colonization in postmenopausal period[16]. Renal insufficiency, chronic hepatic disease, alcoholism, recent surgery, haemodialisis are other recognised risk factor in the elderly. Recent studies demonstrated a relationship between surgical procedure, ageing and immune dysfunction. In fact, monocyte phenotype and function can be altered as well as the bactericidal activity of neutrophils following on surgical stress. A reduction of T-cell responsiveness and NK cell function is associated with ageing[16].

In young patients the increased incidence of HVO has been correlated with the growing number of intravenous drug abusers and with endocarditis[11,22,23]. Sometimes endocarditis may be complicated by septic arthritis and vertebral osteomyelitis. An early diagnosis is generally difficult because those patients are usually treated for fever, bone pain and stiffness, even underestimating or masking the endocarditis[24].

The recent increase in the incidence of tuberculosis may be related to a growing number of immunocompromised patients, which may be caused by the growing number of immigrants from areas where tuberculosis is still endemic[25].

Physical Findings

Back pain and paravertebral muscle spasm are the most common clinical findings[7,12,19,23,26] in HVO. Some authors report the presence of fever in 10-45% of patients, even in pyogenic osteomyelitis[7,11,19,25]. This fact frequently allow clinicians to suspect the possibility of infection. The absence of fever was significantly more frequent in spinal tuberculosis, with a greater presence of spinal deformity. The latter is in close relation with the considerable destructive character of caseating granuloma and is an important diagnostic clue[8,19]. Others reported a slight but persistent fever in spinal infections in 65% to 90% of the cases[13,27].

Mild neurological deficit, limited to one or two nerve roots, was detected in 28-35% of patients[7,11,13,19,27]. Rarely spinal infections may cause severe deficits such as complete or incomplete paraplegia[5,7]. Neurological deficit (in particular, paralysis) are frequently associated with epidural abscesses. Hadjipavlou et al[6] reported 33 cases of epidural abscesses as a complication of spondylodiscitis in study of 101 cases of pyogenic spinal infection. Out of this group of patients 15 had paraparesis or paraplegia. In a retrospective analysis of 29 cases of spinal tuberculosis, Nussbaum et al.[25] noted that 22 patients (76%) presented with neurological deficit: 11 cases had intraspinal granulomatous tissue causing neurological dysfunction in the absence of bony destruction, 2 cases had intramedullary tuberculomas, 9 had marked bone collapse with neurological injury. The possibility of serious neurological complication was higher in the thoracic and cervical spine as opposed to the lumbar spine. Therefore, when cephalic levels are involved, more caution should be exercised in assessing possible epidural abscess formation and preventing its neurological sequelae[6,28]. The greater diagnostic delay and the frequent existence of spinal deformity partially explain why neurological deficits were significantly more frequent in tuberculosis osteomyelitis[19,25,26].

Kyphosis is a rare complication and occurs more commonly in tuberculous spondylitis. A positive straight leg raising test, sinus tract formation and subcutaneous abscesses are present only in a few percent of the patients[29]. Colmenero et al[19] noted paravertebral masses in 49.7% of cases, epidural abscesses in 36.5% and psoas abscesses in 10.9%. Paravertebral and epidural masses were present respectively in 78% and 68% of tuberculosis infection with a statistically significant difference with respect to pyogenic and brucellar osteomyelitis.

The diagnosis of HVO may be very difficult, as the symptoms can be sometimes not specific, vague or almost absent. The onset of symptoms is insidious and often underestimated by the patient. Therefore, misdiagnosis or delayed diagnosis are very frequent.

The usual delay in diagnosis has been reported to be two to four months, despite the use of CT and scintigraphic bone scanning[30,31]. Carragee[7,32] presented a study with MRI scan: diagnosis of infection was obtained in a median time of less than 3 weeks after the onset of spinal symptoms. It is likely

that the use of MRI has made possible to diagnosis this disease in the early stages[27,33-35]. Buchelt et al[10] reported that the mean interval between onset of symptom and diagnosis was significantly longer for patients with tuberculosis. This fact can be explained by the slower progression of tuberculosis and should be evaluated as an anamnestic factor in differential diagnosis. Active or previously diagnosed extraspinal tuberculosis was showed in 33% to 52% of the cases[10,19,25]. The diagnostic delay in pyogenic infections was significantly shorter, which may reflect the higher clinical expression of this group of patients. Delay in diagnosis may result in vertebral destruction or perforation of the spinal canal[36].

Misdiagnosis are more common in 60-70 years old patients and the most frequent localization of osteomyelitis seems the lumbar spine. Spinal infections are often confused with metastatic carcinoma, spinal stenosis, herniated nucleus pulposus and back strain. In several analysis, misdiagnosis are significantly associated with the age of the patients, absence of fever and positive straight raising test[37].

Diagnostic approaches

Laboratory tests

The value of laboratory tests in HVO is still unclear. The leukocyte count is typically not elevated in spinal infection. According to reports in the literature, leukocyte counts range from 13% to 60%. Levels of ESR are more commonly elevated, ranging from 73% to 100%[6,11,19,23,26,27,31]. However, when leucocytosis, neutrophilia and high values of ESR and CRP are present, they strongly suggest a pyogenic infection[19]. In the presence of an epidural abscess these tests are more sensitive. As reported by previous studies[11,12,19,23,26], blood culture was the most useful routine test, providing microbiological diagnosis in 30% to 50% of cases[12,19]. During a fever spike, a higher percentage of cultures will be positive than during chronic phases of infection. If the cause of septicemia is known or the blood cultures are positive, patients are less likely to be referred for an additional invasive procedure. However, there is a chance that a secondary organism may be missed if biopsy is not performed[12]. Aetiological diagnosis of vertebral osteomyelitis is frequently difficult when blood cultures are negative. In these cases, spinal specimens were obtained in 30% to 70% of the patients by closed percutaneous or open surgical biopsy[19,26].

Differential diagnosis of the etiology between tuberculous and pyogenic infection may be difficult. A negative Mantoux test indicates non-specific etiology. A positive Mantoux test is not patognomonic for the diagnosis and bacteriologic or histological tests should be performed[7]. Belzunegui et al[16] suggest that even the isolation of *Mycobacterium tuberculosis* in other tissue, or fluid sample or histological evidence of caseating granuloma may be enough for the diagnosis of HVO. Nussbaum et al[25] reported 21% of cases with tuberculous spondylitis who had no previous or concurrent diagnosis of extraspinal tuberculosis, no family history of tuberculosis and a negative tuberculin skin test. The yield of routine bacteriological and serological tests (positive seroagglutination at titres 1/60) was very high in brucellosis infection[19].

Imaging Techniques

Infection of the spine must be differentiated from degenerative disease, non-infectious inflammatory lesions and spinal neoplasm. The infection can affect the vertebrae, the intervertebral disc, the paraspinal soft tissue, the epidural space, the meninges, and/or the spinal cord. Imaging plays an important role in the overall evaluation of these lesions and the ideal technique is expected to provide information that will help characterize and delineate the disease process, guide biopsy and/or drainage procedures, suggest the method of treatment (medical vs surgical) and assess the response to therapy[37].

Plain Radiography (Figure 1). Radiographs of the spine show no signs of spondylodiscitis in the early stages of the disorders and only subtle changes, including endplate demineralisation and/or irregularity, may be noted[38,39]. The earliest radiographic sign in pyogenic infection appears in the third week of the disease: it is a slight narrowing of the intervertebral space and a loss of definition in the superior endplate. This is followed by progressive disc space narrowing, gradual development of osteolysis with irregularity of

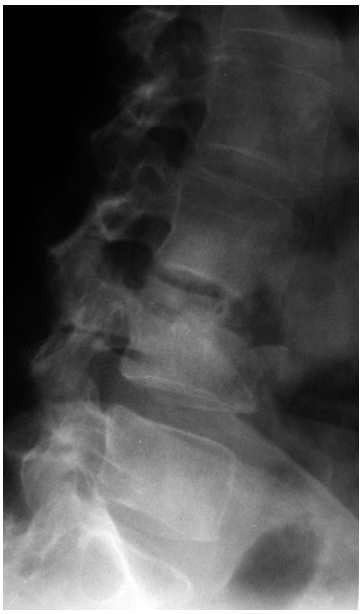

Figure 1. F.D., male, 51 years of age, spondylodiscitis at L3-L4 due to Staphilococcus aureus, latero-lateral x-ray.

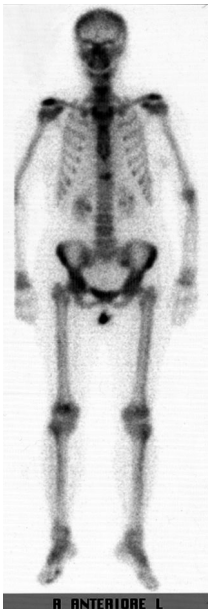

Figure 2. B.A., male, 28 years of age, tubercular spondylodiscitis at L3- L4. Tecnetium-99 total-body bone scintigraphy.

the vertebral body margins and further destruction of the subchondral plate. In the fourth week, signs of vertebral destruction may be seen in some cases and after six weeks, they are always evident.

In the differential diagnosis of infection from cancer, the appearance of a destructive vertebral bone lesion associated with a well-preserved disc space with sharp endplates favours a diagnosis of neoplastic infiltration, whereas the destructive bone lesion associated with a poorly defined vertebral bony endplate with or without loss of disc height suggests infection with a better prognosis. Disc space narrowing can be due to coincidental degenerative disc disease independent of any infectious process[5].

Bone scintigraphy (Figure 2)**.** The role of scintigraphy in the early diagnosis of vertebral ostemyelitis is important. First of all, bone scintigraphy is widely available, it is easily performed, safe to use and rapidly completed.

Tc-99m-MDP (methylene diphosphonate) with SPECT (single photon emission computed tomography) shows a sensitivity of 90% in the early detection of osteomyelitis[5,12,22,35,40,41]. Normal Tc-99m-MDP bone images of the vertebra exclude osteomyelitis with a high degree of certainty[42]. Further sites of infection not clinically suspected can also detected by an increased uptake in other part of the skeleton. An initial whole-body scan is crucial to the diagnosis when symptoms are difficult to localise and/or the patient is old, confused and febrile[5,43]. Unfortunately, the study is not specific[35,40,42,44]. Specificity depends on the underlying condition of the bone. In adults with normal radiographs and no reason for increased bone turnover, the specificity of the scan is higher. When bone remodelling is increased by fractures, tumors, activated ostheoarthritis, non-infectious inflammatory lesions or pseudoarthrosis, the specificity of the bone scan is reduced[5]. False-negative results of bone scans have been observed in elderly patients, presumably because of the regional ischemia secondary to arteriosclerotic disease. This suggests that a negative result of a bone scan may not reliably exclude infection, especially in older persons[40].

Recently the use of immunoscintigraphy with 99 Tc-labelled antigranulocyte antibodies Fab' fragments in the management of neonates and infants with fever of unknown origin has been reported and this procedure has shown high sensitivity and specificity in the diagnosis of osteomyelitis and soft tissue infections[45].

Ga-67 Citrate Imaging. Several studies confirmed the utility of Ga-67 imaging to identify vertebral osteomyelitis[41,42,46]. Ga-67 imaging is often used as a complement to bone scintigraphy to enhance the specificity of the study and detect extraosseous sites of infection[40,43,46]. Ga-67 citrate SPECT is able to identify unsuspected causes of endocarditis, paravertebral abscess, subaxillary soft tissue abscess and other additional sites of infection. Unlike 99 Tc-SPECT imaging or planar Ga-67 citrate imaging, Ga-67 citrate SPECT can estimate the severity of infection[42].

Despite the excellent results achieved, the dual-tracer technique has its disadvantages. The procedure requires two different tracers and multiple prolonged imaging sessions on different days. There is also an increased cost and inconvenience to patients, many of whom are elderly or debilitated, or both.

Ga-67 imaging may be a better tool in the follow-up of the response to treatement since is less sensitive to bone remodelling and gives a more accurate degree of the infectious process activity. 99 Tc-scintigraphy remains active until complete healing takes place, and may remain active after infection has become quiescent due to its sensitivity to bone remodelling and repair[5]. For this reason, it remains positive for a long time compared with Ga-67 scan, which will become positive only when the infection is in a active phase[47].

Computed Tomography. CT scans yield positive findings in the early stages, because the involved disc shows small hypodense areas. CT also shows the disc flattening and the vertebral endplate destruction, which are not visible on conventional radiographs in the early stage[13]. The extent of the inflammatory process is defined. Paravertebral abscesses with psoas involvement are easily identified after contrast administration. Intraspinal extension of the process with an epidural abscesses is better defined by MRI (Figure 3)[13].

The CT scan may also be used more directly in diagnosis by assisting with needle aspiration of a suspected lesion (Figure 4)[1]. In particular even when the diagnosis of infectious discitis is established by means of diagnostic imaging, a specific microbiologic diagnosis is highly desirable for definitive medical treatment with the antibiotics to which the pathogens are sensitive. In any event, without the identification of a specific pathogen, the choice of antibiotic therapy would remain empiric. This technique may be used in the thoracic and lumbar spine, but is generally too dangerous to attempt in the cervical spine because of the surrounding structures[1]. Chew et al[48] reported that CT-guided needle aspiration is an accurate method for identifying bacterial or granulomatous infection of the disc space, but all false negative results originate from cases of fungal infection. Previously reported series of imaging-guided needle biopsy in spontaneous infection have been variable in their yield of microbiologically identified pathogens. Chew et al[48] reported a 91% yield (39 out of 43 patients with infection), Perronne et al[26] reported a 74% yield (29 out of 39), Carragee[7] reported a 61% yield (27 out of 44). Three explanations have been given when negative cultures were obtained: concurrence of antibiotic administration before biopsy, small-bore biopsy needle precluding a satisfactory retrieval of tissue samples, and the natural healing of intervertebral disc infection as postulated by Fraser[49]. According to Fraser's theory[49,50], vascular granulation tissue from the vertebral subchondral plate invades and resorbs the infected disc space, enabling the infected re-

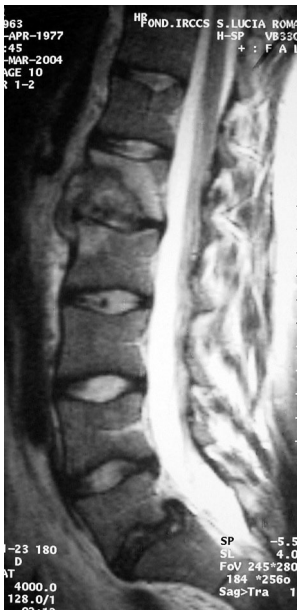

Figure 3. B.A., male, 28 years of age, tubercular spondylodiscitis at L3-L4. Magnetic resonance.

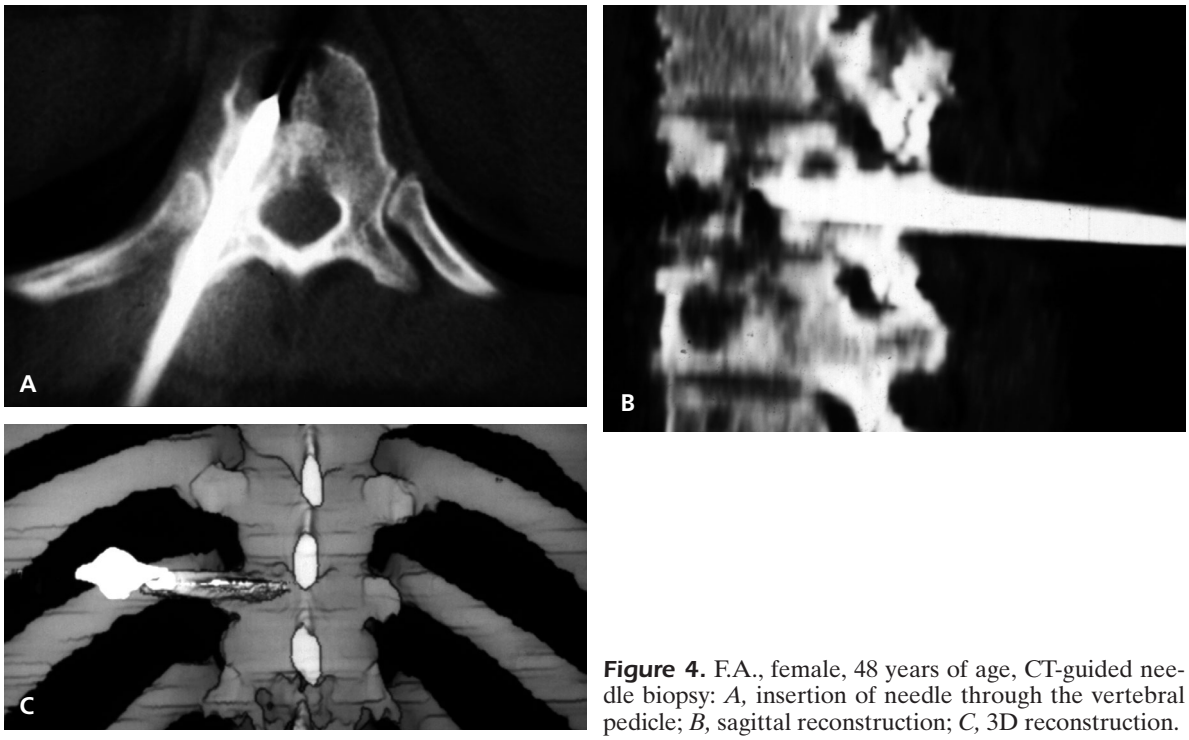

Figure 4. F.A., female, 48 years of age, CT-guided needle biopsy: *A,* insertion of needle through the vertebral pedicle; *B,* sagittal reconstruction; *C,* 3D reconstruction.

gion to heal spontaneously after approximately 6 weeks, thus leading to negative cultures. This also explains why spondylodiscitis can have a self-limited course in uncompromised hosts. The inability to identify a pathogen does not necessarily indicate that no infection is or was present or that such patients would not benefit from empirically chosen antibiotic therapy.

MR Imaging (Figures 3 to 5)**.** With an accuracy rate of 90%, Magnetic resonance Imaging (MRI) is the preferred diagnostic imaging method for spinal osteomyelitis. MRI permits early diagnosis of infection and provides direct visualization of the spinal cord, subarachnoid space, extradural soft tissue and spinal column, without intrathecal contrast[35,40]. This technique may not be suitable for patients with movement disorders, orthopedic hardware, pacemakers and certain prosthetic heart valves. MRI cannot always distinguish osteomyelitis from severe degenerative arthritis[40,43]. The earliest sign of an infectious process on MRI is altered marrow signal within the vertebra, caused by accumulation of oedema in the vertebral body. The inflammatory tissue and the ischemic areas, which replace the bone marrow, lead to a long relaxation time. MRIs are obtained with T1-weighted image and T2-weighted image spin-echo pulse sequences. Plain or contrast-

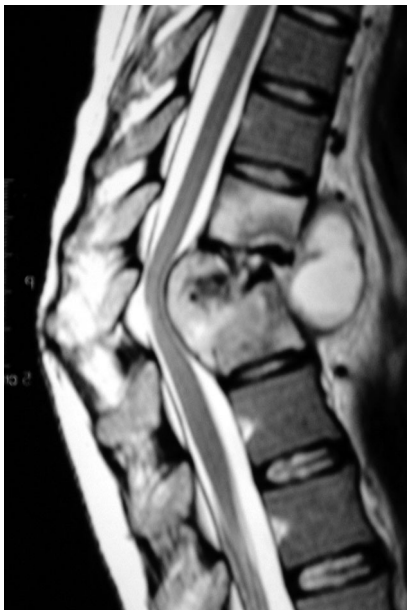

Figure 5. M.A.F., female, 29 years of age; the magnetic resonance shows a tubercular abscess at T10-T11 with spinal cord compression.

enhanced sagittal (for bony structures) and transverse (for paravertebral abscesses) studies are performed. Infection is considered if: (A) the T1-weighted sequence shows decreased signal intensity of the vertebral marrow and intervertebral disc space, together with an inability to discern a margin between the disc and the adjacent vertebral marrow; (B) the T2-weighted sequence shows increased signal intensity of the vertebral marrow adjacent to the involved disc and an increase in signal intensity from the disc itself; (C) the intravenous Gd-DTPA shows a homogeneous contrast enhancement of the disc and the vertebral bodies are visible. MRI almost invariably demonstrates paravertebral soft tissue swelling. This can extend posteriorly into the epidural space, and postero-laterally into the intervertebral foramina. Epidural abscesses are defined clearly on sagittal planes as hyperintense extradural lesions in T2-weighted images. The epidural abscess and the dural sac are usually separated by a hypointense stria, which probably corresponds to the leptomeninges[13]. Abnormal soft tissue within the epidural space is due to an epidural inflammatory mass of granulation tissue or an epidural abscess. Precise definition of the epidural mass is possible only with the administration of intravenous Gd-DTPA. A homogeneous enhancement corresponds to inflammatory tissue without purulent collection; a peripheral enhancement with a central hypointense area corresponds with a true abscess with fluid purulent contenent[13]. Intravenous Gd-DTPA can highlight abnormalities within the cord. Infectious myelitis is uncommon. It is usually associated with neurological deficit without extradural compression and is enhanced following intravenous Gd-DPTA.

Tuberculous spondylitis is characterized by some peculiar findings, including a normal signal of the intervertebral disc space, the presence of a paraspinal soft-tissue mass, the involvement of many vertebral bodies and localization in the posterior vertebral bodies and arches. The size of the paraspinal mass is usually larger in tuberculosis than in other pyogenic infections[13,35]. MRI is useful for the differential diagnosis between tuberculous infection and other forms of spondylodiscitis in the chronic stage: the first case shows a slightly high signal on T1-weighted images in the late stage, whereas the second shows low-signal intensity[13]. Other differential diagnoses were obtained with different spinal pathologies, including postoperative changes, spinal degenerative disease, vertebral metastases. In metastatic spine localizations, the intervertebral discs are not involved and the affected vertebral bodies do not show contrast enhancement[13].

Therapeutic approaches

Antibiotic therapy

The therapy in osteomyelitis is significantly addressed to eradicate established bone infection and to prevent the progression. Those specific aims are obtained by administration at of appropriate antimicrobial drugs and, if necessary, by surgical approach.

Since the medical treatment must be initiated before identifying the responsible organism and its in vitro sensitivity, the therapy must be chosen on the basis of the most common causes of the infection. Therefore Betalactam antibiotics represent the first choice because they are safe, able to penetrate to the site of infection and active against the most common pathogens causing osteomyelitis. The broad spectrum treatment may be changed to a specific antimicrobial therapy based on bone cultures[51].

The optimal duration of therapy for pyogenic spinal infections has been debated in the literature, with several studies recommending 6 to 8 weeks of intravenous therapy and others recommending only 4 weeks[7,11]. This is the main reason for the long hospital stay. However in account of the cost, the inconvenience of maintaining an intravenous line and danger of nosocomial infection, other routes can be evaluated. Anyway, parenteral drugs, for at least a week, are often necessaries before using only oral therapy. However there are some studies showing that a parental treatment of less than 4 weeks duration is associated with a 25% relapse rate[28,52]. For this reason, Hadjipavlou et al[6] proposed 6 weeks of intravenous antibiotics followed by 6 weeks of oral medication to provide an extra margin of safety. Antituberculous chemotherapy, consisting of at least two medications, should be administered for a period of at least 12 months. The addition of a third agent for the initial 2 to 6 months is also advised[25].

ESR levels should be taken into account in the first critical month, when the decision to undergo to a surgical treatment is usually made. Carragee et al[53] suggest that as a general trend, a decreasing ESR during the first month of non-surgical treatment is a good prognostic sign. However a rapid response of less than 50% of the ESR is rarely associated with treatment failure and successful of conservative treatment is seen in 40% of cases with persistently elevated or rising ESR. Evaluation of the clinical indicators, including a reduction in back pain and constitutional recovery, risk factors, age, immunosuppression and stability of neurological status against the ESR results may be helpful in order to assess the efficacy of the medical treatment.

When osteomyelitis become recurrent, surgical approaches can be more important than antibiotic management and it may be necessary to use local aggressive therapy or to remove infected bone.

Some reports have suggest also that elimination of risk factors, supplementation with calcium, bisphosphonates, and/or vitamin D, and the treatment with testosterone and/or estrogen may promote bone repair[51].

Surgical treatment

The general principles for the management of spine infections are non operative, consisting of external immobilization and intravenous antibiotics, followed by oral antibiotics[6].

However, despite the effectiveness of medications, some patients require surgery.

Indications to operative debridement should be given in case of absence of clinical improvement after 2-3 weeks of intravenous antibiotics, with presence of persistent back pain and systemic effects of chronic infection such as malnutrition and cathexis.

Presence or progression of neurological compromise may result from abscess or vertebral collapse, with highest risk if the age increased and in cervical infection[28]. An abscess formation is an indication for surgery also because antibiotics are generally ineffective and a drainage is necessary (Figure 6)[55]. As the infection becomes chronic, despite adequate medical treatment, other two complications may require surgery: a development of biomechanical instability and related chronic pain and/or a vertebral collapse with progressive deformity[56].

In surgical management the infected tissue should be thoroughly debrided and the infected area receive adequate blood flow to allow for tissue healing. Spinal stabilization should be maintained with bone fusion or restored if compromised by either preoperative infectious process or by iatrogenically induced instability following decompression.

Because the infection involves disc space and subjacent vertebral body, an anterior approach is warranted[56]; moreover it allows placement of a structural bone graft to reconstitute lost height as well as anterior load sharing[57] (Figure 7). A posterior decompression fail a direct access to the affected area (anterior spinal elements). Further posterior bone and ligamentous structures, essential in maintaining biomechanical, are usually uninvolved and removes this structures contributes for progressive deformity. Adding a posterior stabilization is indicate to better achieves spinal stability and to correct the kyphotic deformity[57]. Stabilization of the spine using posterior pedicle screw has the advantage of restoration of spinal alignment without any communication with the infection site, which usually is anterior[56,58]. Several studies[54,57] demonstrate the efficacy of autologous bone grafts to achieve a solid fusion. Traditional autologous bone grafts include iliac crest, rib or fibula. Further structural allograft has used in the reconstruction of the anterior spinal column with high fusion rates and a with a advantage of avoided the morbidity associated with a second operative site[59].

Early surgical decompression results in rapid improvement of neurological deficit, decrease in kyphotic deformities and stabilization with bony fusion. Same-day simultaneous anterior and posterior approaches with arthrodesis and internal fixation can be successfully used in the treatment of spinal infection (Figure 7). The presence of active infection does not preclude the use of internal fixation[56,57].

Follow-up strategies

After 70 days of therapy, MR imaging, TC scans and bone scintigraphy must be repeted.

If Bone Scintigraphy is still positive for infection, another two months of immobiliza-

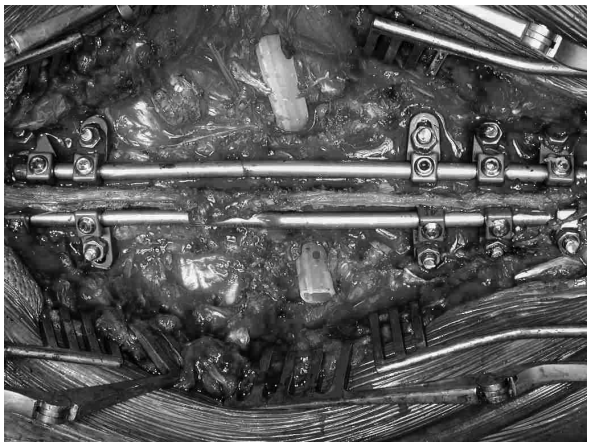

Figure 6. M.A.F. female, 29 years of age; tubercular spondylodiscitis at T10-T11; the tubercular abscess has been sucked dry by applying a circumferential drainage, the thoracic spine being acceded via posterior approach.

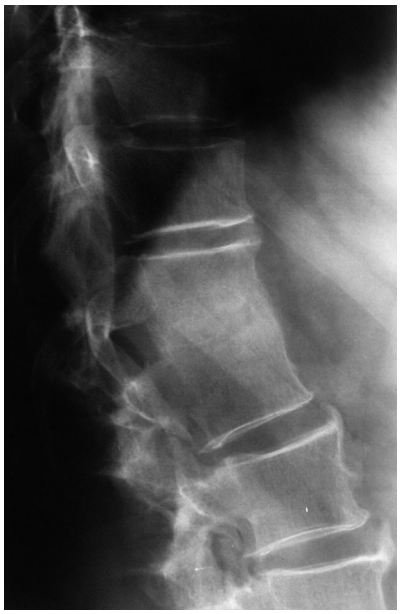

Figure 8. C.L., male, 53 years of age, spondylodiscitis a L1-L2. The latero-lateral x-ray shows a full vertebral fusion following conservative treatment, a sign that the infection has healed.

tion and antibiotics are required. Laboratory test and bone scan will be repeated until they are negative.

If bone scintigraphy is negative for infection, SPECT Ga-67 scan is performed to confirm the recovery and if SPECT Ga-67 is negative, the patient has recovered, oral antibiotics are discontinued and mobilization with orthesis is permitted. Clinical findings and plain radiography are checked after 3 and 12 months (Figure 8). If Ga-67 scan is positive, another two months of immobilization and antibiotics are required. Laboratory test and Ga-67 scan will be repeated until they are negative.

With clinical and imaging worsening or after 4 months of conservative treatment without recovery, surgical approach should be considered.

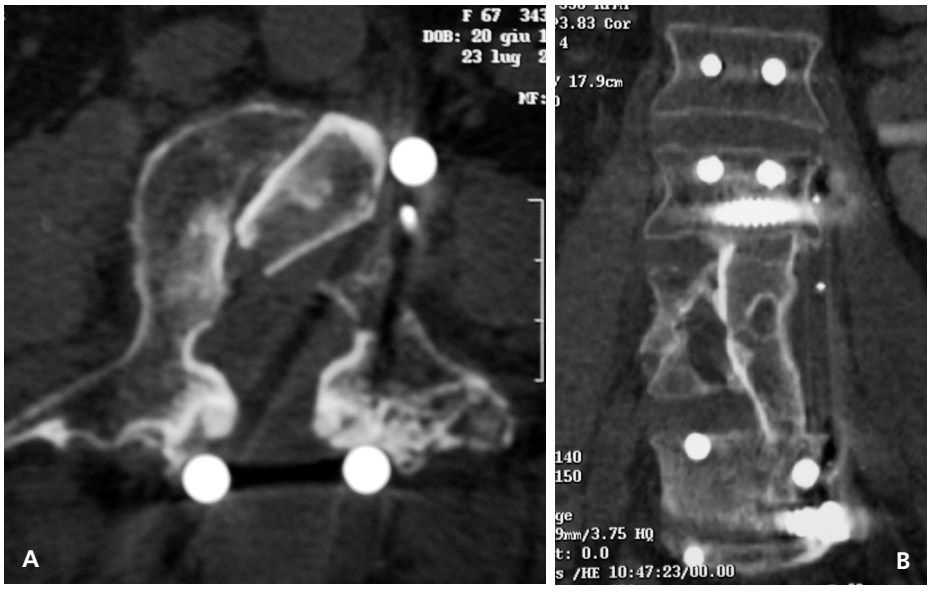

Figure 7. B.A., female, 68 years of age, spondylodiscitis at L3-L4; CT scan for decompression and posterior stabilization, arthrodesis with allograft and plate. *A,* transverse; *B,* frontal reconstruction.

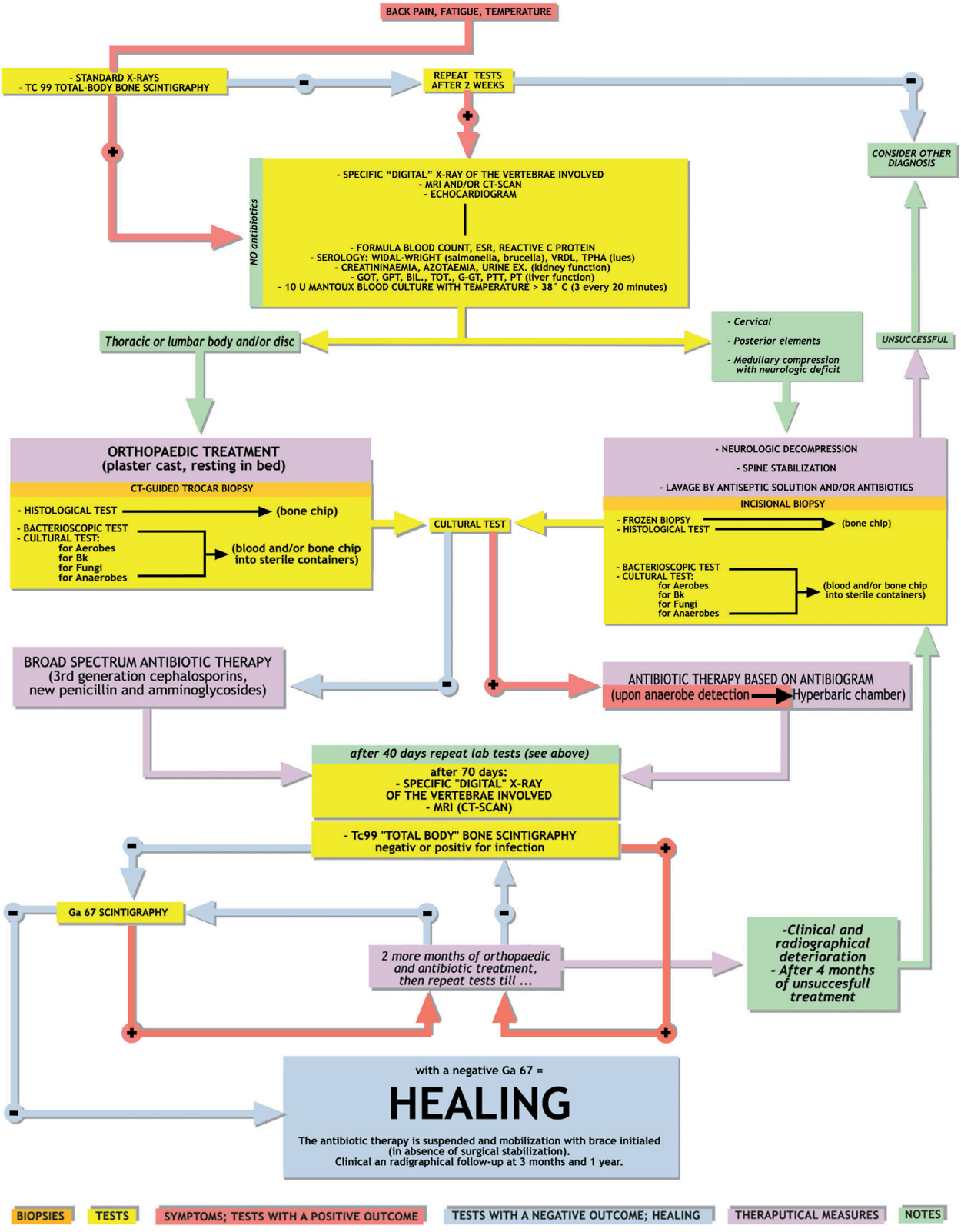

Figure 9. Algorithm for diagnosis and treatment of vertebral osteomyelitis.

The validity of MR imaging in following the therapeutic response remains to be defined because the clinical findings may not correlate with the MRI findings[32,34]. Despite the clinical improvement of patients, MRI may improve, worsen, or stay the same within the first weeks after institution of therapy. Caution should be used in interpreting the follow-up MR-images in assessing therapeutic response. For this reason, there is no justification for routine use of MRI to follow a patient's response to antibiotic therapy. The development of new radiculopathy or cauda equina syndrome should remain an indication for repeat MRI, to exclude the development of an abscess or other space-occupying lesion.

In conclusion, most of the studies in the literature identified haematogenous vertebral osteomyelitis as a challenge for the physician: symptoms are not specific and sub-acute or chronic presentation is most common. In general, a delay in diagnosis is a rule rather than the exception. This is an easily missed infectious process, particularly in old people, in whom degenerative radiographic changes and condition resulting in back pain, such as osteoporotic fractures or spinal metastases, are common and signs of sepsis may not manifest. However, persisting localized back pain and tenderness with elevated ESR should prompt the physician to also consider haematogenous vertebral osteomyelitis, although fever and leukocytosis may often not be present.

Once a haematogenous vertebral osteomyelitis is suspected, a long series of imaging and laboratory tests, and if necessary surgical procedure, must be started. The purpose of the study is to formulate a systematic, comprehensive and simple approach to the management of this disease following the diagnostic algorithm suggested (Figure 9).

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