Vertebral Osteomyelitis: Etiology, Pathogenesis, Routes of Spread Symptoms and Diagnosis

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40.1 Introduction

With 2–7% of all osteomyelitis, spondylodiscitis is rare, but is the third most common form of osteomyelitis after the femur and tibia [1]. The disease occurs more frequently in the sixth decade of life. Basically, a distinction is made between unspecific, also pyogenic and specific infections. While unspecific spondylodiscitis is a problem of developed industrialized countries, tuberculous spondylodiscitis, the most important specific form, is more prevalent in developing and emerging countries. However, due to increasing globalization, these statements are no longer completely true. Both nonspecific and specific spondylodiscitis have seen an increase in the number of diagnoses over the last few decades. The causes of these changes are not only the demographic development but also the medical advances in diagnostics. While incidence in the past has been reported as 1:250.000, studies and registry data currently show an increase of up to 5:100.000 with an increase in old age [2–4]. Despite improved diagnostics, the average time between the onset of first symptoms and diagnosis is between 2 and 6 months [5]. The delay of initial treatment by more than 60 days leads to a poorer clinical course [6].

The pediatric spondylodiscitis is also a rare entity with an incidence of 1:250.000, often as an unspecific kind caused by Kingella kingae and Staphylococcus aureus and a high rate of specific infections mainly in Africa and South Asia [7].

Since the main problem consists of securing the diagnosis and the specific detection of the germs in clinical routine, this chapter will mainly describe the etiology, pathologenesis and diagnosis.

The case presented shows a typical course of disease and a standardized diagnostic algorithm.

40.2 Case Description

A 56-year-old patient, with lumbar back pain, radiating into the right hip was presented. Five month back, he was suffering from a pharyngeal mucous membrane inflammation (aphthae) which was treated with local cortisone application.

Furthermore the following secondary diagnoses were observed: obesity BMI 40.2, NIDDM, nicotine abuse, chronic obstructive pulmonary disease and osteoarthritis of the right hip. At the time of admission he had the following blood investigations: Leucocytes 13/nl, CRP 13.7 mg/dl (norm <0.5) (Figs. 40.1 and 40.2).

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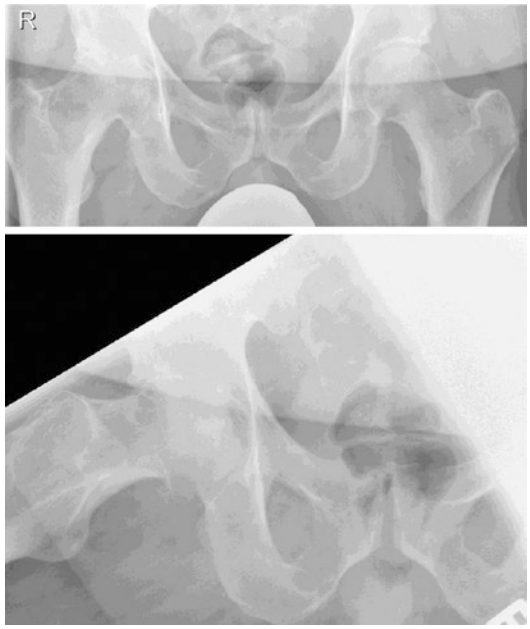

Fig. 40.1 x-ray pelvic ap and Lauenstein view right at the first time of admission

The MRI scans (T1 and T2-weightening) didn't show any signs of inflammation at the whole spine, but a central spinal stenosis. Due to a severe Osteoarthritis of the right hip and the clinical limitations of movement of the hip joint, the indication for a total hip replacement was performed. Due to the increased infectious parameters, normalization should be awaited.

4 month later, the patient was seen by the department of infectious diseases with joint and back pain, weight loss and reduced general condition. Until this time, no antibiotic therapy was performed.

Radiological diagnostics algorithm was performed (Figs. 40.3, 40.4, 40.5 and 40.6):

In conclusion the x-ray, mri and ct-scan showed clear signs of a unspecific spondylodiscitis L2/3 with a small inflammatory reaction for the psoas muscle on the right side. Blood investigations: Leucocytes 12.5/nl, CRP 14.1 mg/dl (norm <0.5). Subfebrile temperatures to moderate fever of 38.4 °C.

Further investigations were implemented. Therefore, blood cultures were taken on three different times. After three sterile results, an x-ray guided fine-needle biopsy was performed (Fig. 40.7).

The result of the sampling from the disc compartments were also sterile. The histological result showed floride and older inflammatory reactions with no evidence of specific infection.

Initiation of an empirical antibiotic therapy with Fosfomycin 2g 1-0-1 and Imipenem 0.5g 1-1-1 intravenous, after 10 days oralization to Levofloxacin 500 mg 1-0-1 and Clindamycin 300 mg 1-1-1-1 for the following 6 weeks (Figs. 40.8 and 40.9).

Six month after diagnosis a normalization of the laboratory parameters of infection and a significant reduction of lumbar back pain (VAS 2), without any medication was investigated. Only an inguinal pain on the right side was seen. Therefore the patient could return to work 9 month after starting of symptoms. Due to the low pain, currently a hip replacement isn't planned.

The illustrated case shows a structured algorithm of the diagnosis with a nonspecific anamnesis and nonspecific symptoms, the performance of a radiological diagnosis and measures to lead a germ detection by blood culture and biopsy.

40.3 Case Discussion

40.3.1 Etiology

Spondylodiscitis is caused by bacteria as the cause of specific, pyogenic infection and by mycobacteria, brucelles, and fungi as the cause of specific infections, and in very rare cases by parasites.

References show a certain constancy in the description of the pathogens, however, variations in selected patient groups with specific risk factors can be observed. The most common pathogen of pyogenic spondylodiscitis is Staphylococcus aureus with 20–80% of cases, followed by Gram-negative bacteria (leader E. coli) with 4–30% and streptococci/enterococci with 5–30% (leader Streptococcus epidermidis) [8–10].

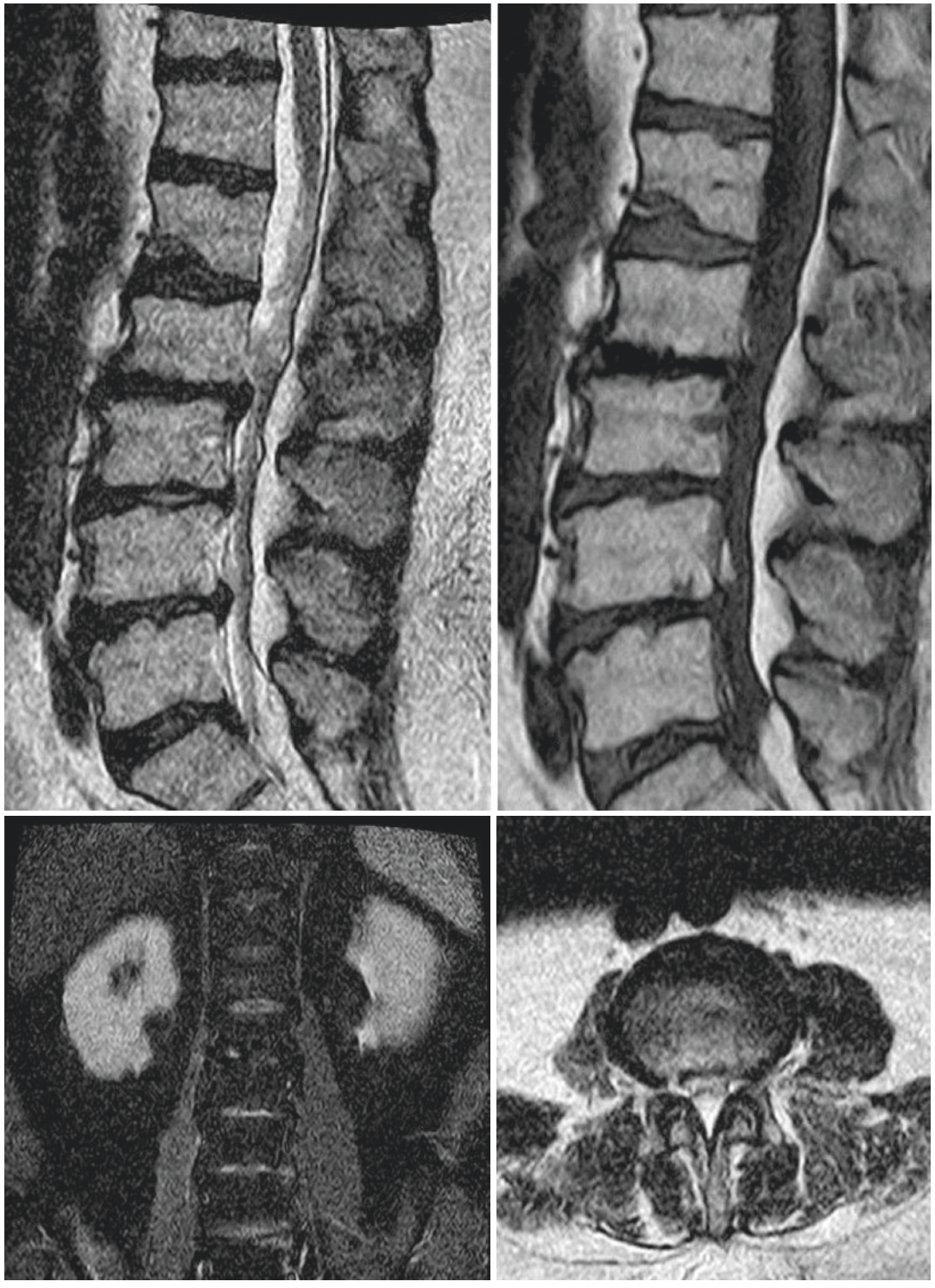

Fig. 40.2 Magnetic resonance imaging lumbar spine at the same time

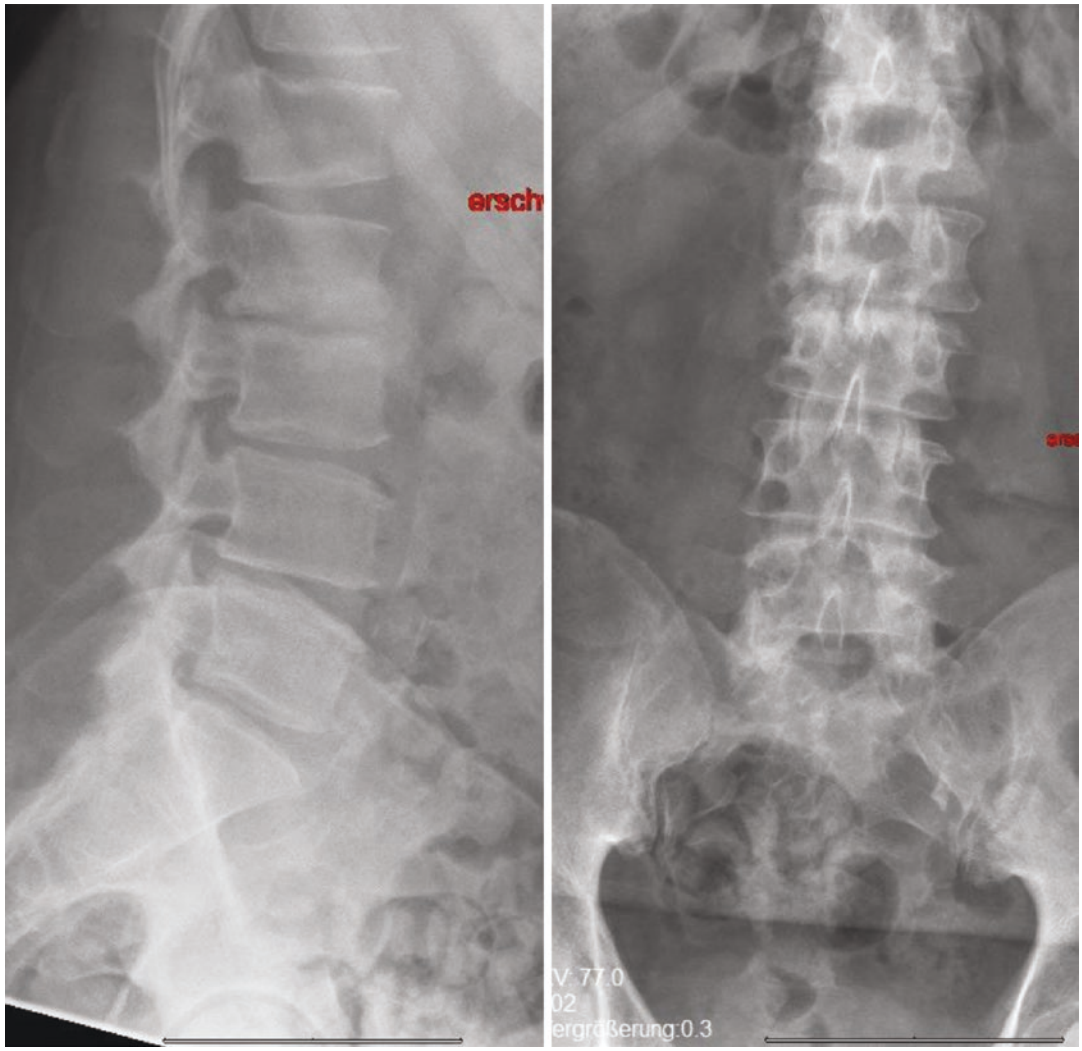

Fig. 40.3 x-ray ap and lateral view

Gram-negative pathogens such as E.coli, Proteus spp. and Pseudomonas spp. are identified as the cause of infection in immunodeficient patients [10]. Streptococci and enterococci are often associated with endocarditis and diabetes mellitus. Spondylodiscitis caused by bacteria with a primarily low virulence, such as Staphylococcus epidermidis and Streptococci, is clinically characterized by a slow progression. In clinical practice, a general increase of infections with germs that are more difficult to treat due to resistances, such as methicilin-resistant coagulase-negative staphylococci, streptococci, enterococci and gram-negative pathogens, is observed [11].

The specific spondylodiscitis is caused by the mycobacterium tuberculosis, with a noticeable increase in the rather rare infections by atypical mycobacteria (MOTT) [4]. Risk factors include poverty with malnutrition, inadequate hygiene and inadequate medical care [12].

40.3.2 Pathogenesis and Routes of Spread Symptoms

The endogenous spread of infection occurs mostly by a hematogenous scattering and only in rare cases by a continuitatem or lymphogenous way. The primary infection sites, which are often

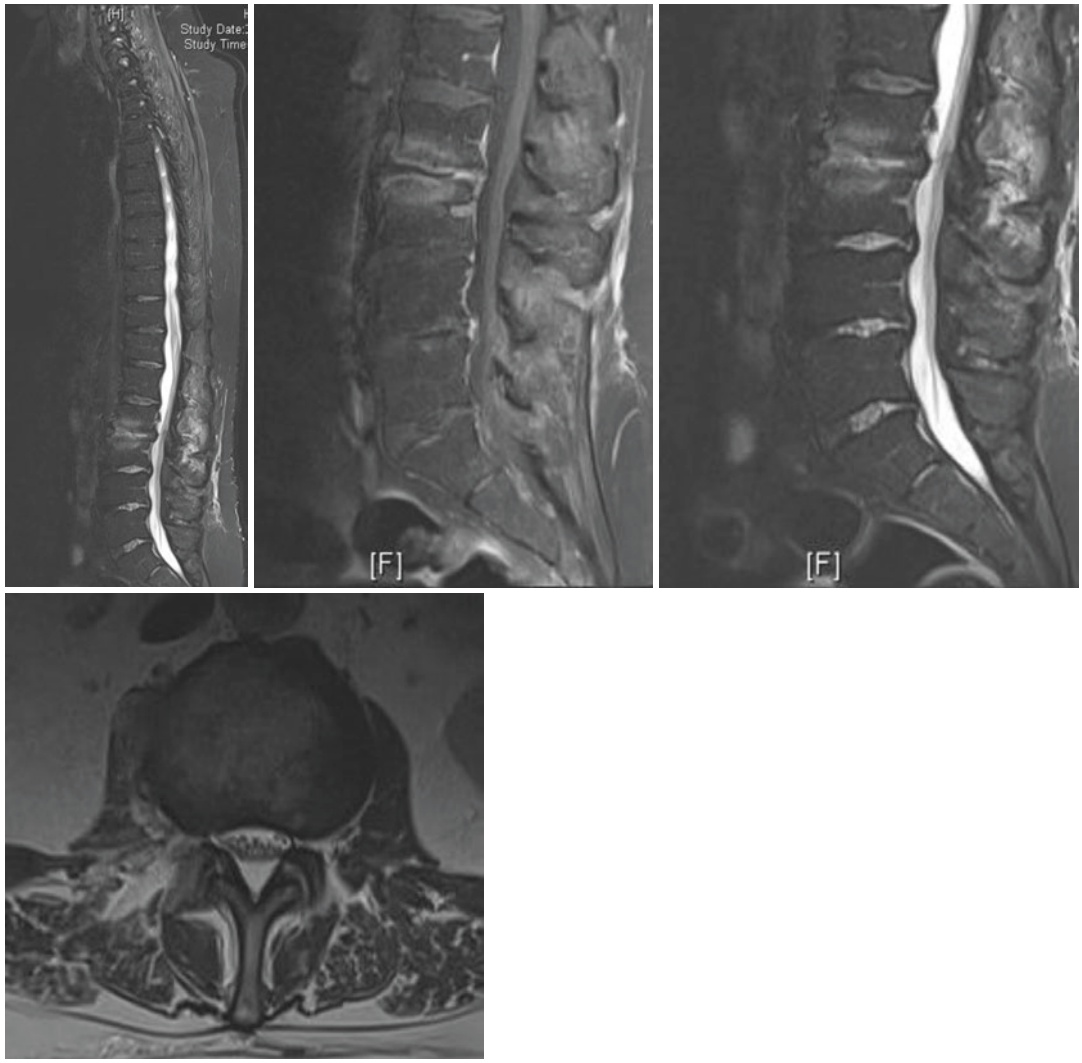

Fig. 40.4 Magnetic resonance imaging (T1, T2 and STIR) with contrast medium lumbar spine

no longer detectable at the time of diagnosis, are in the area of the pelvis, teeth or skin lacerations in the lower extremities. Anatomical particularities of the blood supply in the vertebral column may aid the hematogenous spread of infection. On the one hand, germination is aided by an arterial inoculation, which results from a rich arterial blood supply to the region of the anterior longitudinal ligament and/or infarction of the end arteries or silencing sinusoids by the bacterial embolus. On the other hand, venous scattering, caused by a valveless venous plexus connected to the organ veins of urogenital and gastrointestinal tract, increased blood flow and a long venous staging time, as well as reverse flow of intraabdominal pressure, promote colonization of the lumbar and thoracolumbar spine.

In adulthood, after hematogenous seeding, the infection begins as spondylitis and secondary, may spread to the intervertebral disc area. Studies show that many pathogens of nonspecific spondylodiscitis express collagen receptors and thus promote bone adhesion [13]. Subsequent to pathogen involvement of the terminal arterioles and development of local bone edema, local inflammatory reactions, microembolisms, and ischaemia associated with bone infarcts and necrosis can develop.

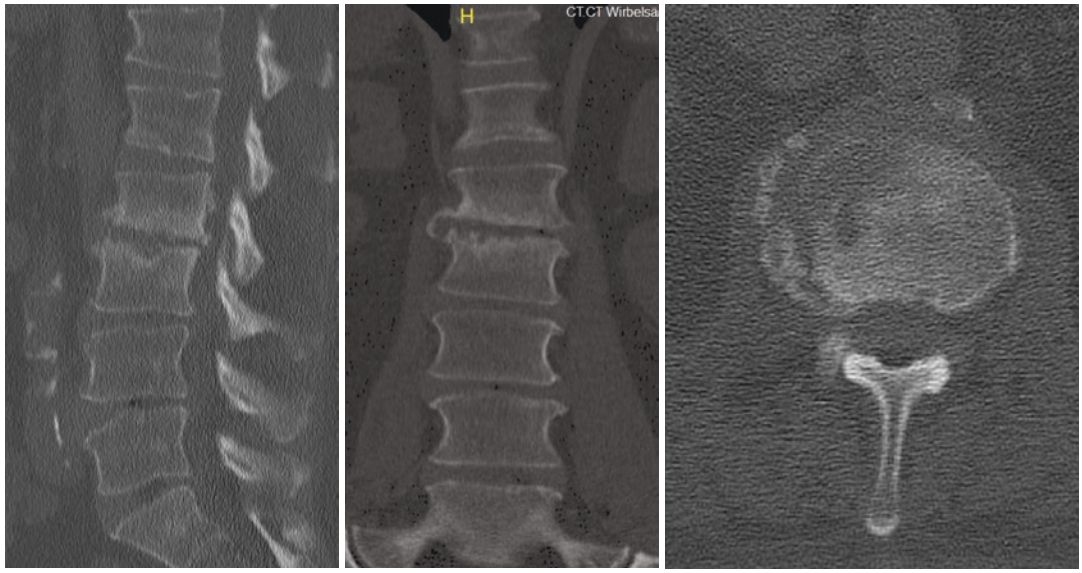

Fig. 40.5 Computer tomography of the lumbar spine

The spread of mycobacteria occurs essentially hematogenous through the arteries, with the typical picture of anterior vertebral body involvement. Spreading through the veins is also possible, via Batson's plexus with central and dorsal vertebral body involvement [12]. Finally, the granulomas characteristic for the specific spondylodiscitis may develop. Furthermore, tuberculous spondylitis typically occurs with so called "cold abscesses" which are typically huge in sice and descend along the psoas muscle to the inguinal region.

In childhood, the remaining vascularization of the intervertebral discs results in a typical kind of discitis, with the possibility to progress to the full picture of spondylodiscitis.

40.3.3 Diagnosis

The disease start's with local back pain accompanied by non-specific general symtoms, such as fever, night sweat and weight loss. Positive upsetting pain, "knocking pain" and heeldrop pain are possible. Restrictive posture, the prevention of loads of the anterior column and instability signs are further typical indicators. Just as unspecific as the clinical symptoms are the laboratory values (Leucocytes, CRP and blood sedimentation). Studies show a low sensitivity and specifity (Leucocytes 42–55%/97%, CRP 84%/71%, blood sedimentation 75–90%, 43%) [14]. In presence of an epidural abscess high leucocytes values are often noticed [10].

A crucial role in the successful treatment of spondylodiscitis is the early diagnosis and detection of the causative germ.

The early diagnosis of vertebral osteomyelitis and concomitant discitis is difficult, which may lead to a delayed diagnosis. Standard tools consist of primary imaging in patients with unclear back pain in conventional x-ray radiography in two planes with a sensitivity of 82% and specificity of 57% [15]. Because of the onset of infection in the metaphysis of the vertebral bodies, these first changes are not noticed in conventional radiological diagnostics. Signs of destruction of the corresponding endplates, especially in the ventral area, can be signs of the beginning disease. However, differentiation from erosive osteochondrosis is difficult. The destruction of spongeous bone occuring later in the course, the upper and lower endplate erosions and height reductions of the disc space are further signs that may indicate a spondylodiscitis. As the disease pro-

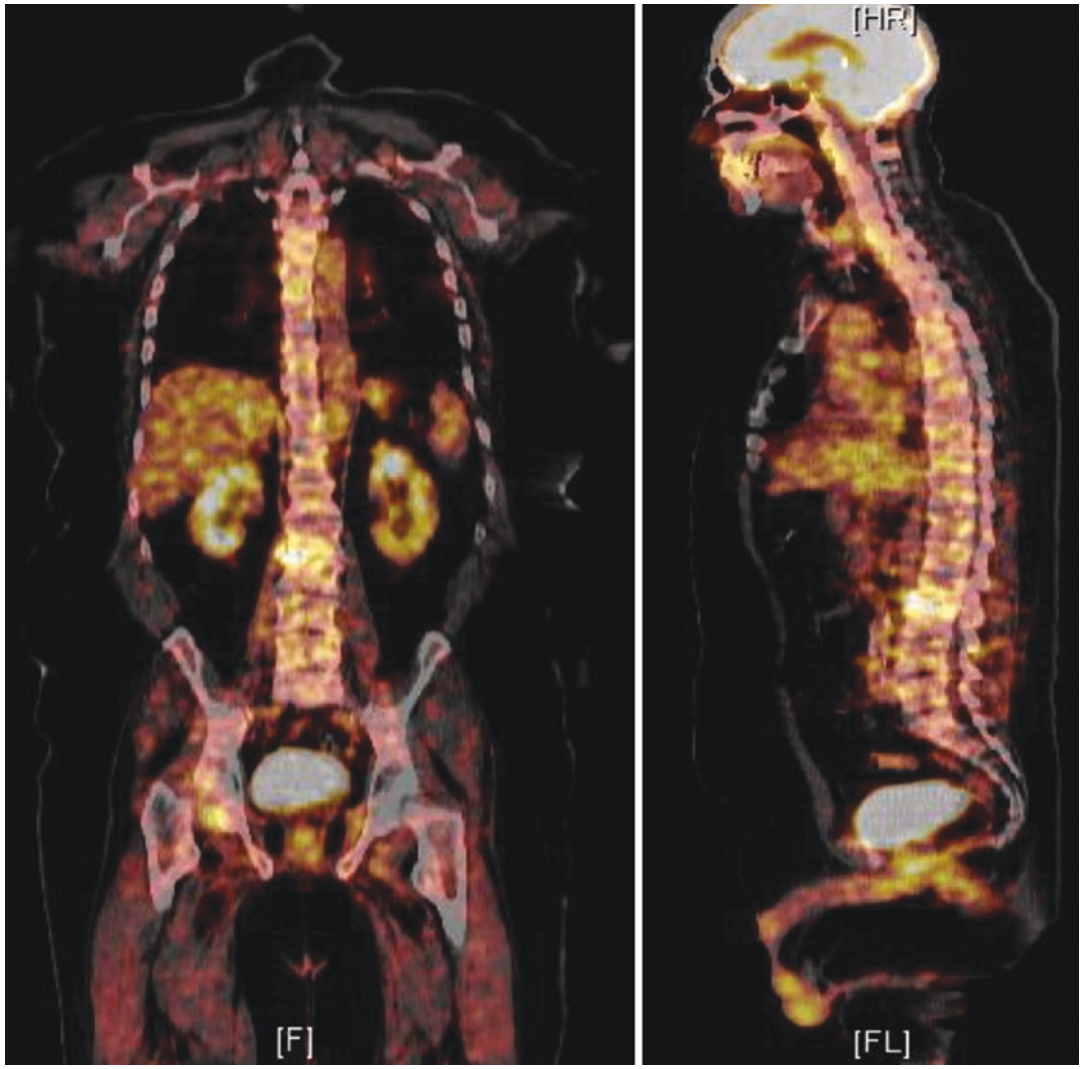

Fig. 40.6 Positron emission tomography (PET) for exclusion of further sources of infection

gresses, there is an increase in osteodestructive processes with loss of bone integrity and static malalignment of the sagittal profile. Finally, reparative processes lead to the presentation of sclerosis and bony overbridging.

Computertomography can show the bone destruction accurately and is often used as an alternative tool in cases of contraindications and in addition to MRI. The sensitivity of the examination can be increased to 83% by administering an additional contrast agent [16]. This contrast agent can also be used to differentiate between abscesses (marginal contrast agent admission) and inflammatory, pannus-like tissue (diffuse contrast agent admission). Computertomography can be helpful in differentiating between inflammatory and degenerative changes, since it shows subtile vacuum phenomena, which are mainly found in degenerative changes.

F-FDG-PET study is an alternative, especially in cases of contraindications for contrast-enhanced examinations. In evaluating the course of therapy, it is clearly superior to magnetic resonance imaging [17]. Since the scintigraphy is clearly inferior in its specificity of magnetic

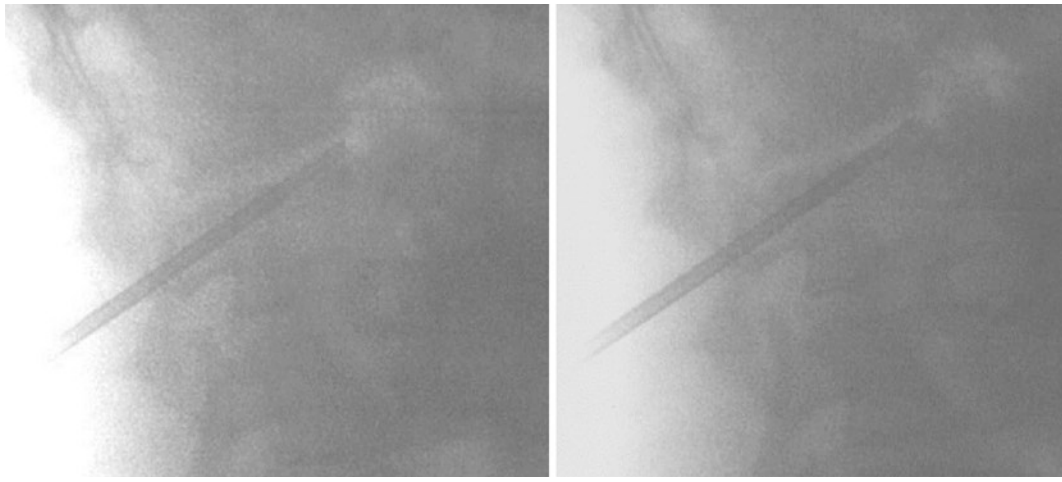

Fig. 40.7 Biopsy disc L2/3 and upper endplate L3, intraoperative x-ray documentation 2 weeks later

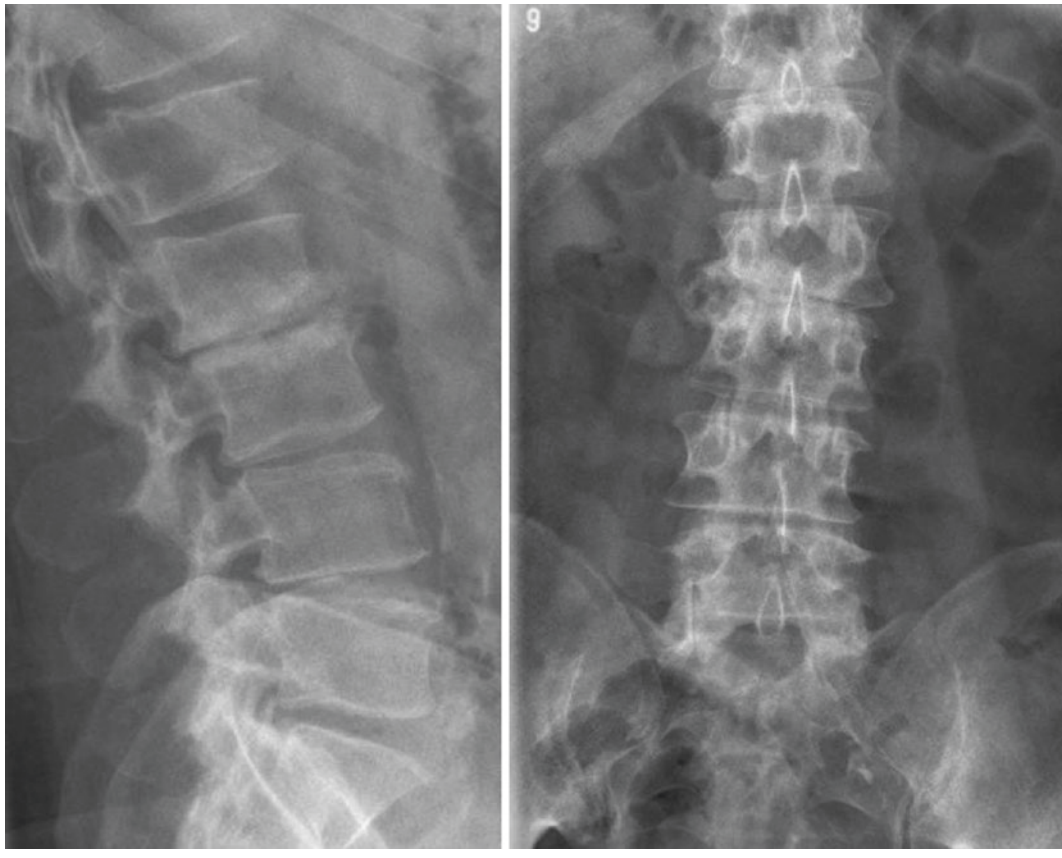

Fig. 40.8 x-ray ap and lateral view 4 month after diagnosis

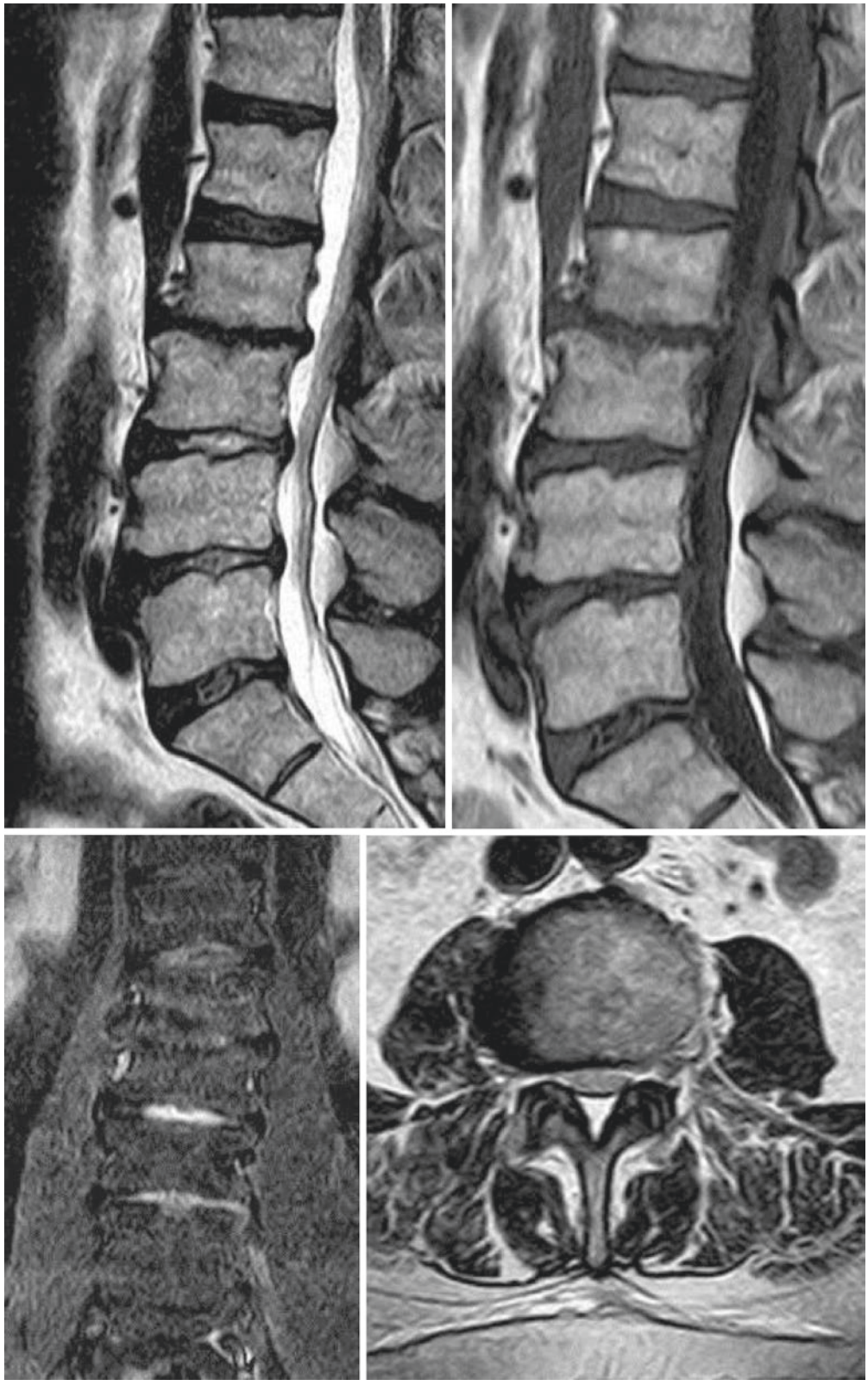

Fig. 40.9 Magnetic resonance imaging (T1; T2) with contrast medium lumbar spine. 5 months after diagnosis

resonance imaging, its main function lies in detecting multifocal infection spread.

With a sensitivity of 96% and a specificity of 92%, magnetic resonance imaging is the imaging method of choice for primary diagnosis [18]. In addition to the axial and sagittal T1 and T2 weighted sequences, a fluid-sensitive, fat-suppressing STIR sequence should be prepared. Axial and sagittal views allow the assessment of epidural abscesses, vertebral body and disc infections and provide an additional overview of the perivertebral tissue as well as the psoas muscles. In the T1-weighted sequence there is a signal reduction (hypointensity) for the affected vertebral body and the inflamed soft tissue, and a signal increase (hyperintensity) for the T2-weighted sequence. In the early phase of the disease, there is a blurring with a loss of demarcation of the endplates, which in the further course receive significant erosion. A disadvantage of magnetic resonance imaging is the poor correlation with the clinical course. A repeated MRI is probably unnecessary if clinical and laboratory outcomes are satisfactory. The persistence of bone/disc MRI findings alone does not represent therapeutic failure [19]. In this respect, the use of magnetic resonance imaging as a short-term follow-up should be viewed critically. The criteria for a healing tendency is a signal enhancement of the bone marrow in the native T1 weighting [20]. The MRI can be helpful to differentiate between inflammatory degenerative processes of osteochondrosis and a diagnosis of spondylodiscitis in clinical practice. Delineation is often possible when there is no signal enhancement of the disc in T2 weighting as well as the absence of extensive perivertebral inflammatory zones in degenerative diseases. The presence of gas inclusions in the intervertebral disc space, in the sense of a vacuum phenomenon, points to a degenerative process [21].

The detection of the causative agent plays a crucial role in the successful treatment of spondylodiscitis. Although this assumption is well established, it is not based on any evidence-based data. A retrospective study showed more positive treatment outcomes in empirically treated patients compared to patients receiving targeted therapy based on pathogen detection. The difference in the two groups of patients was, however, not significant and is limited by the assumption that negative disease pathogenicity was associated with a lower severity of the disease [22]. Several techniques are available as detection methods. Pathogen detection in cultures should be attempted primarily by preparing blood cultures. The detection through this examination method has a success rate of 40–89%. This rate is lower if antibiotic therapy has been initiated and it is higher in cases of a hematogenous pathogenesis of the infection [23–26]. An increase in the rate of positive detection can be achieved by taking of at least three blood cultures [27]. Should the results of the blood cultures be negative, even when radiological and clinical symptoms persist and the suspicion of spondylodiscitis remains, secondary pathogen detection should be done by sampling directly from the main focus of infection. Percutaneous biopsies can be performed fluoroscopically, under computerized tomography, or with magnetic resonance imaging. Studies show a superiority of computertomography-assisted biopsies with better targeting accuracy and a lower rate of complications [28]. Detection of bacteria is successful in percutaneous biopsies between 14% and 76% [26, 29, 30]. In this context, it should be remembered that local anesthetics have an antibacterial effect and may adversely affect the detection rate [31].

The French Société de Pathologie Infectieuse de Langue Francaise (SPILF), recommends percutaneous biopsies in cases of three negative blood cultures: two biopsies should be taken from the upper endplate area, two from the lower endplate area and two from the center of the disc space [32]. An increase in the yield of positive pathogens was achieved by puncture with saline injection [33]. The intraoperative sampling of inflammatory areas has the advantage of a large and safe material yield. The fact that antibiotic therapy has a negative influence on the detection rate in blood cultures has been proven [34]. However, the effect of antibiotic therapy on biopsy results is less clear. While some studies did not see any significant influence of concomitant antibiotic therapy [29, 35], others showed a significantly lower rate of detection, especially if antibiotic therapy had been administered for more than 4 days [36, 37]. In addition to the possibility

of a molecular pathogen detection, the histopathological examination complements the diagnosis and provides additional information with respect to necrotic-infectious changes in cases of negative pathogen detection.

Compared to non-specific spondylodiscitis, the clinical findings in specific cases are often bland, fever is rather rare. Typical in imaging is a massive bone destruction. Decisive for the diagnosis of a specific infection is the direct detection of Myobacteria tuberculosis via biopsy.

40.4 Conclusions and Take Home Message

For a successful treatment of vertebral osteomyelitis, a knowledge of the anamnestic and clinical symptoms as well as a rapid initiation of a sufficient diagnosis are necessary. Magnetic resonance imaging is the first choice for detecting an infectious disease in the spinal column. Alternatives are available with computertomography and nuclear medicine examinations. In cases with hemodynamically and clinically stable patients without neurological deficits, primary pathogen detection should be conducted. This can be done by the preparation of several blood cultures and in the absence of pathogen detection, by a percutaneous biopsy.

Diagnostic algorithm:

1. Anamnesis and clinical examination
2. Laboratory diagnostics and microbiological diagnostics (3 blood cultures, PCR)
3. Radiological diagnostics (MRI, CT, PET)
4. Biopsy

Pearls

- Anamnestic and clinical symptoms of spondylodiscitis are often very unspecific and lead to a delayed diagnosis. **Consider this disease !!!!**
- Magnetic resonance imaging is the diagnostic gold standard
- Microbiological diagnostics by blood cultures or by percutaneous biopsy are strongly recommended

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