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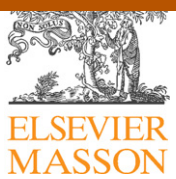

CONTINUING EDUCATION PROGRAM: FOCUS...

Imaging orthopedic implant infections

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Abstract The diagnosis of infections associated with orthopedic implants is based on a combination of clinical signs, laboratory findings and imaging studies. There is no gold standard imaging technique: conventional radiography is indispensable, although 50% of the time the radiograph is normal. Computed tomography (CT), magnetic resonance imaging (MRI) and ultrasonography are valuable to detect soft tissue abnormalities. Bone scintigraphy (BS) rules out active infection. For infections involving the peripheral skeleton, labeled white blood cell (WBC) scintigraphy coupled with colloid scintigraphy is the reference technique, whereas a gallium scan is always necessary for imaging the spine or pelvis. To confirm or rule out infection, needle aspiration with analysis of aspirated fluid is the cornerstone of the diagnostic algorithm.

Orthopedic surgical hardware is increasingly used for fracture reduction, arthrodesis and most of all for arthroplasty. Thanks to perioperative antibiotic prophylaxis, improved surgical technique and laminar airflow operating theaters, infection rates for prosthetic implants have dropped considerably in recent years. However, as the use of orthopedic implants continues to rise, the number of infections remains substantial. These periprosthetic infections are a frequent cause of implant failure, estimated at approximately 5% [1], with a fairly low infection rate in the case of closed fractures (generally less than 1 to 2%) but as high as 30% for open fracture reduction. Periprosthetic infection is the leading cause of revision total knee arthroplasty (TKA) and the third most common cause for total hip arthroplasty (THA) [2]; the incidence of these periprosthetic infections has been estimated at 1 to 3% [3]. The infection rate after revision surgery is considerably higher than for the primary arthroplasty. These infections have a major impact on the psychological morbidity of patients, impairing joint function and quality of life, and sometimes requiring arthrodesis, permanent removal of the prosthesis, or even amputation.

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The management of a failed prosthesis differs significantly according to whether it is aseptic or septic. In the first case, single-stage revision is generally performed, replacing the prosthesis in a single step with a focus on restoring function. In the case of infection, it is first necessary to eradicate the pathogen, and then to restore function. Thus, the first stage may consist in removing the prosthesis, debriding the joint, implanting antibiotic-coated spacers and administering systemic antibiotics, and it is only afterwards that revision arthroplasty can be performed. A periprosthetic infection that goes unrecognized will lead to failure of a revision arthroplasty for loosening. Imaging plays a minor role in acute infections (occurring less than 2 weeks postoperatively), but it is much more useful in chronic infections. In the latter case, since clinically overt infection and systemic manifestations are rare, the clinical presentation can easily be subtle or even absent, and mechanical impairment takes the forefront: delayed consolidation of an osteosynthesis or a painful arthroplasty. The presence of certain risk factors like diabetes, obesity, or corticosteroid or immunosuppressive therapy should alert the physician to minor symptoms such as chronic drainage, erythema around the incision, etc. [4]. Despite the increasing number of clinical, laboratory and imaging techniques available, the diagnosis of orthopedic implant infections (in particular periprosthetic) can be very difficult and there is no gold standard, although a line of converging evidence can lead the physician to suspect or confirm infection [5].

Pathogenesis and definition of orthopedic implant infections

Implant-associated infections are caused by microorganisms which grow in biofilms and adhere to the implant surface in a highly hydrated extracellular matrix. The microorganisms within biofilms form complex, highly organized communities. Metabolically inactive, they are up to 1000 times more resistant to antibiotics than systemic bacteria. Such infections can occur by direct contamination during surgery (intraoperative infections), bacteremia secondary to a remote site of infection (hematogenous infections) or else by contact with an adjacent site of infection or an open wound (contiguous infection). Infections are classified as early if they occur within 3 months of arthroplasty (within 2 weeks for osteosynthesis), and are usually the result of direct exogenous contamination by a highly virulent microorganism. Subacute infections occur 3 to 24 months postoperatively (2 to 10 weeks for osteosynthesis) and are caused by low-virulence pathogens contaminating the implant during surgery. Late infections occur more than 2 years after surgery (more than 10 weeks for osteosynthesis) and usually result from blood-borne dissemination. These infections are very hard to differentiate from mechanical loosening because they progress insidiously and produce very similar symptoms.

Imaging

Abnormalities of both bone and soft tissues detected on imaging studies can be suggestive of implant-associated infections [6,7]. On periprosthetic bone structures, multiple and often discreet signs have to be recognized. A small, very dense bone fragment isolated from the other trabeculae, corresponding to a sequestrum (fragment harboring a pathogen), is very highly suggestive of active infection, but this is a rare event (< 8%); rapid changes in bone structure on serial scans, such as a lucent line around the prosthesis widening by more than 2 mm per year, is highly suspect; multifocal zones of osteolysis with blurred edges at the prosthesis margins, especially when located outside areas subjected to mechanical stress, or else an extensive, poorly circumscribed or solid, thin periosteal reaction, not adherent to the cortex, are also signs of infection (Figs. 1—3); bipolar loosening rules out a septic process; the presence of gas around the prosthesis suggests an anaerobic organism. Analysis of soft tissue is crucial because an abnormality here may be the only clue (sensitivity 100%, specificity 87%). A number of modalities are at the physician's disposal: arthrography, ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI). In particular, one looks for sinus tracts and collections, which have a positive predictive value of 100%, inflammatory edema (only visible on MRI or ultrasound) or joint distention. The absence of effusion around a prosthetic joint has a negative predictive value of 100%. Fluid-filled bursae have lower predictive value because they may be secondary to multiple mechanical conflicts, involving the tendons in particular.

Radiography

Serial plain radiographs have a sensitivity of 14% and a specificity of 70% in detecting implant-associated infections [8]. Depending on the location of the implant, bone structures (the spine in particular) may be very difficult to analyze

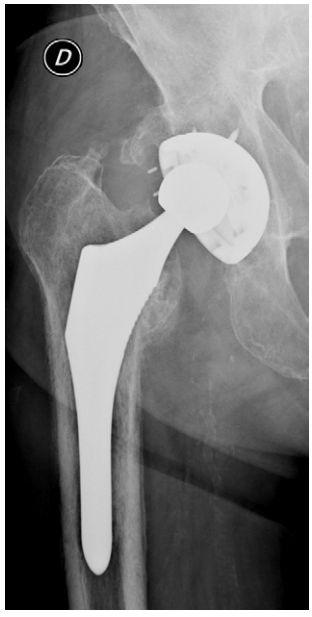


Figure 1. Radiograph of right hip in a 75-year-old woman with a painful total hip prosthesis: thickened, blurred femoral cortical remodeling with periosteal appositions. Infection was confirmed by needle aspiration.

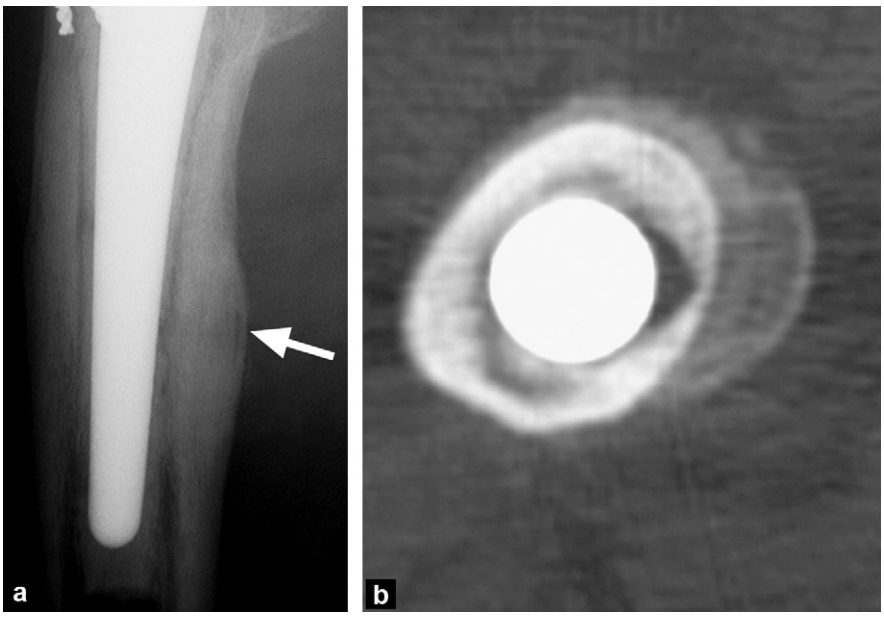


Figure 2. Radiograph (a) and axial computed tomography (CT) scan (b) of a prosthetic stem of the femoral shaft: periosteal apposition. Infection was confirmed at surgery.

and the use of additional imaging techniques is essential. Despite this lack of sensitivity and specificity, radiography should be part of the initial work-up even though it only permits a crude analysis of soft tissues and there is no typical radiographic appearance. Finally, 50% of radiographs remain normal despite the presence of infection. In a retrospective review of septic hip prostheses, Tigges et al. reported that 20% of radiographs showed bone findings consistent with infection, 20% had signs of mechanical loosening and 10% had nonspecific findings [9]. Despite these limitations, radiography serves as a reference to monitor the progression of bone abnormalities.

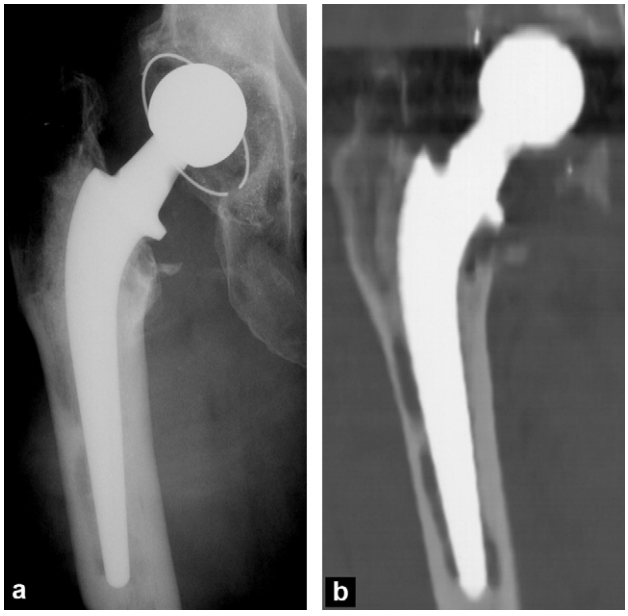


Figure 3. Radiograph of right hip (a) and coronal computed tomography (CT) scan (b) reconstructed with bone algorithm in a 67-year-old man with painful total hip prosthesis: multifocal osteolysis outside weight-bearing area. Infection was confirmed by needle aspiration.

Computed tomography (CT)

Improvements in imaging methods that reduce metal artifacts due to beam hardening have now made it possible to analyze periprosthetic bone structures as well as soft tissues [10,11]. Depending on the implant, the severity of artifacts will vary, ranging from moderate for titanium hardware, more important for inox, and most problematic for cobalt-chrome hardware. Whenever possible, the axis of the implant should be aligned so that the beam traverses the smallest cross-sectional area of the implant. Acquisition parameters such as use of a high voltage (125 and 140 kV) and high amperage, narrow collimation and thin sections can help reduce artifacts [12]. Image reconstruction can also help reduce artifacts by generating thick sections combining several acquired thin sections, and by using low kernel values (standard reconstruction algorithm) and an extended CT scale (possible up to 40,000 HU on some scanners) [13—15]. Bone findings to be looked for are identical to those that can be seen by conventional radiography, although CT is obviously more detailed, especially at certain anatomical sites difficult to analyze on conventional films, such as the cervicothoracic junction, for example. CT can depict sequestra, difficult to detect on plain radiographs due to bone remodeling and sclerosis, or periosteal appositions (Fig. 4).

Analysis of soft tissues is crucial and intravenous iodinated contrast material can aid in diagnosis by enhancing the contours of a fluid collection or inflammatory synovium [16] (Figs. 5 and 6). An abscess close to the surgical hardware appears as an infiltrated, thick-walled collection that is contrast-enhanced; the differential diagnosis is hematoma if surgery was recent. Arthritis on the implant, when a

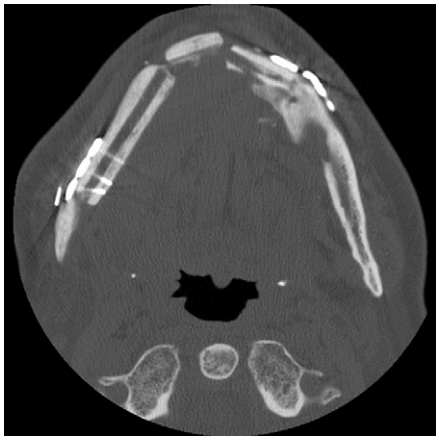


Figure 4. Computed tomography (CT) scan of the lower jaw 3 months post-osteotomy: small, very dense bone fragment isolated from the other trabeculae, corresponding to a sequestrum (fragment harboring a microbe) and very highly suggestive of active infection, confirmed during surgical revision.

septic prosthesis is suspected, associates effusion and capsular thickening enhanced by contrast injection. A sinus tract along the surgical incision may sometimes be difficult to differentiate from fibrosis, making it necessary to look for infiltration of adjacent fat or fluid or gas along the fistula. In a study of 22 infected total hip prostheses, Cyteval et al. found that periostitis was 100% specific for infection but had only 16% sensitivity. Soft tissue findings were accurate for detecting infection with 100% sensitivity and 87% specificity. Fluid collections in soft tissues had a 100% positive predictive value and the absence of joint distention had a 96% negative predictive value [11].

Ultrasonography

Ultrasonography can certainly be useful for analyzing soft tissues if the lesions are accessible, as is often the case for the limbs, but it is less contributory for imaging the hip or spine, where depth and bone structures limit the acoustic window [17—19]. In addition to fluid collections, joint distention and fluid-filled bursae, which are also demonstrated on CT, soft tissue thickening and hyperemia on Doppler sonograms may suggest the presence of infection.

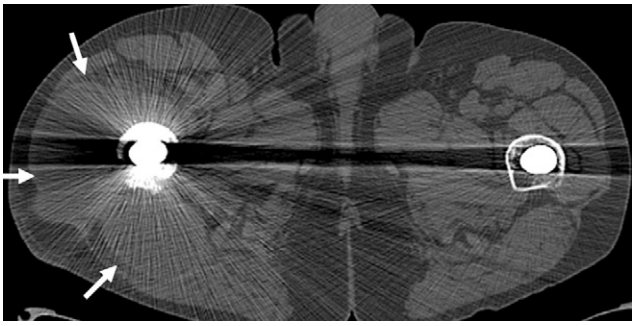


Figure 6. Computed tomography (CT) scan of right hip in a 76-year-old man with painful total hip arthroplasty. Large collection in perifemoral soft tissue. Infection was confirmed by needle aspiration.

Magnetic resonance imaging (MRI)

Artifacts from metallic implants are well known in MRI and have certainly limited the use of this technique. They correspond to the special case of magnetic susceptibility artifacts which occur as the result of very localized magnetic field gradients occurring near the interfaces of substances with different magnetic susceptibilities (different ability to magnetize). This causes dephasing of spins, which increases with the strength of the magnetic field. This produces local distortion in the magnetic field resulting in three effects: a varying degree of image distortion, and a local signal intensity void with a surrounding area of high signal intensity. These artifacts can be considerably reduced by simple modifications of acquisition parameters [15,20]:

- artifacts are less severe when the axis of the implant is aligned in the main magnetic field B0 (for example, by positioning a wrist screw in the axis of the magnetic field);
- the frequency or phase encoding direction can be changed so that the artifact projects as little as possible into the area under study; the strength of the frequency encoding gradient can also be increased (by widening the bandwidth);
- it is possible to decrease the echo time, although this can change the weighing of the sequence;
- the use of smaller voxels, by reducing section thickness and by modifying the matrix and FOV (field of view), reduces the artifact but also results in a smaller signal-to-noise ratio;

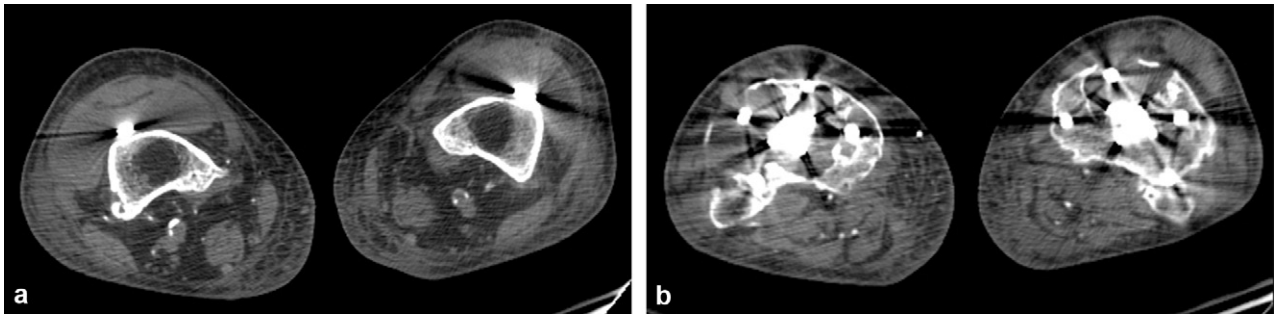
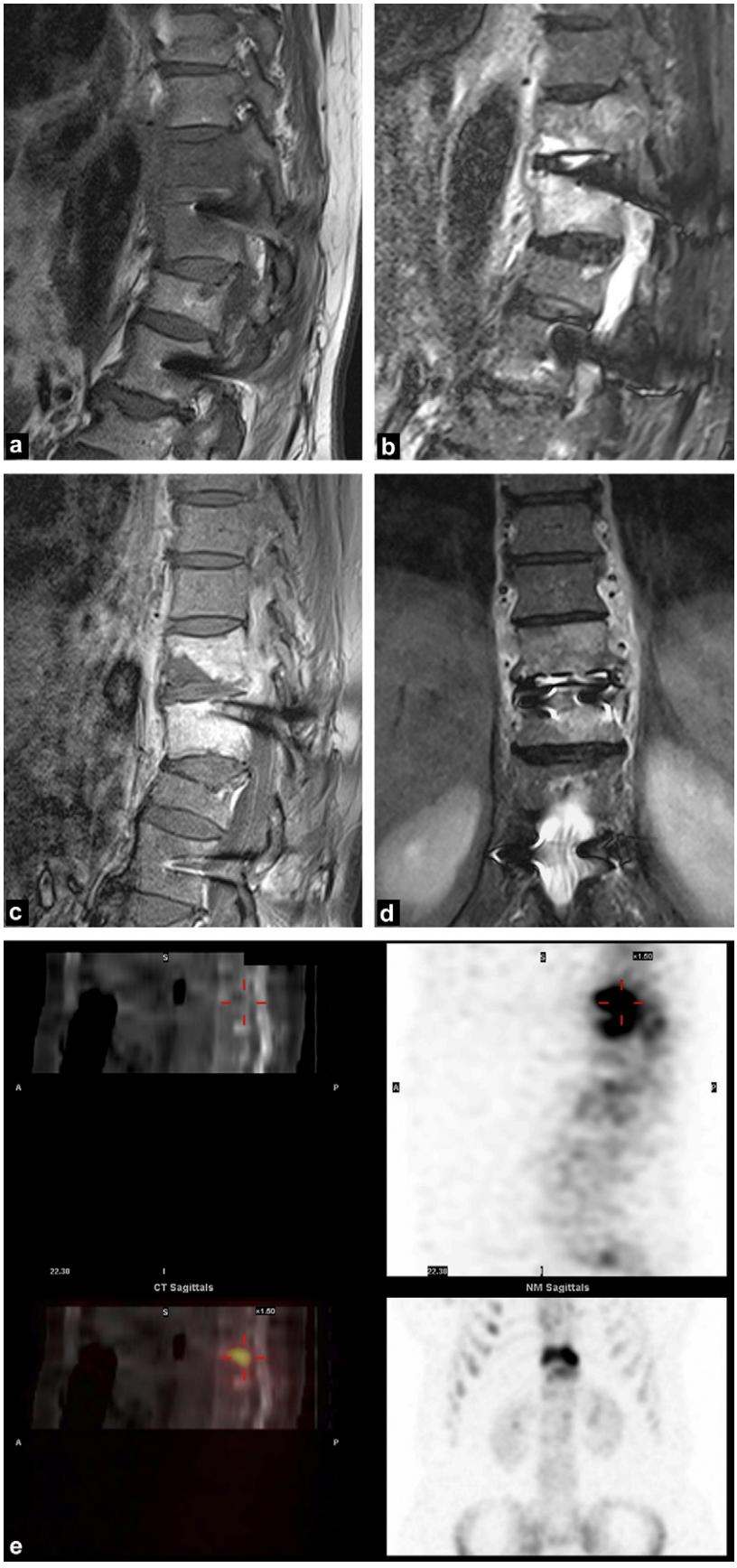


Figure 5. Computed tomography (CT) scan of both knees in a patient with rheumatoid arthritis and two total knee prostheses which had caused pain for several months. No clinical signs of infection: a: abundant bilateral joint distention; b: extensive periprosthetic osteolysis. Infection was confirmed by needle aspiration.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- fast spin echo rather than gradient echo sequences should be used, because this artifact is due to dephasing, itself due to heterogeneity in the magnetic field. Spin echo sequences are therefore much less sensitive, thanks to their 180° rephasing pulse; during these fast spin echo sequences it is also preferable to use higher echo train lengths in a short time;
- to suppress the hypersignal due to fat, fat saturation (Fat Sat) should not be used, since it is sensitive to heterogeneities in the magnetic field; Short Time Inversion—Recovery (STIR) sequences should be preferred;
- 3D sequences avoid distortions in section thickness compared to 2D sequences because the second phase encoding is in the direction of section thickness;
- finally, specific new sequences can be used (Iterative Decomposition of water and fat with Echo Asymmetry and Least-square estimation [IDEAL] sequence).

Intravenous gadolinium often improves the detection of soft tissue abnormalities [20—23]. In particular, it is useful for depicting inflammatory edema of soft tissue or bone, which is hyperintense on T2-weighted images, enhanced by gadolinium, or else bone or soft tissue collections, with contour enhancement and a dark purulent central zone, or else sinus tracts which produce a very marked T2-weighted hypersignal enhanced by gadolinium (Fig. 7).

Joint distention or fluid-filled bursae, hyperintense on T2-weighted images, do not enhance with gadolinium. Bone sequestra remain hypointense in all sequences.

Opacifications: fistulography or arthrography

Arthrography or fistulography were widely used in the 1980s and provided much information on the existence of communications between small cutaneous channels and bone, periprosthetic effusions and peri-articular communicating cavities [24,25]. These methods have since become rare (or unnecessary) now that newer methods like CT, MRI and ultrasound can achieve good visualization of these lesions. However, they are sometimes performed in conjunction with diagnostic needle aspiration (Fig. 8).

Nuclear medicine

Nuclear medicine provides a number of techniques that complement conventional imaging methods and serve as a useful aid to physicians. The choice of technique depends mainly on location. Since the development of hybrid cameras allowing coupled monophoton emission tomography (MPET)/CT, diagnostic performance and image quality have greatly improved.

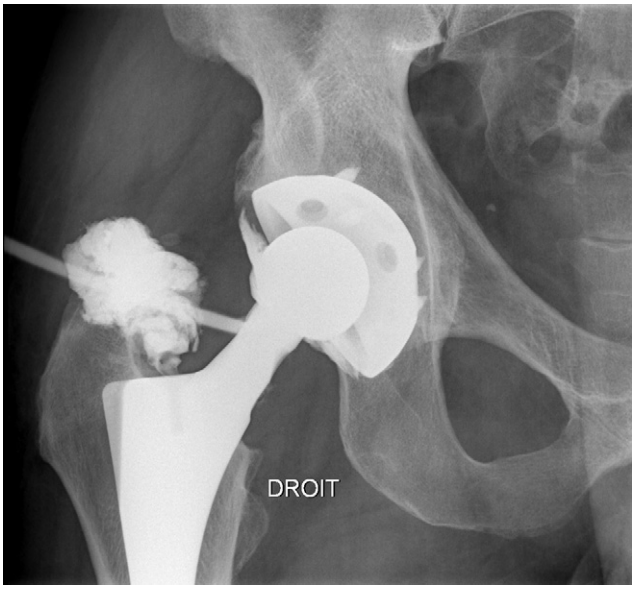

Figure 8. Arthrogram of right hip in a 67-year-old man: paraarticular collection communicating with the prosthesis. Infection was confirmed on the specimen taken before opacification.

Bone scintigraphy

^{99m}Tc-labeled diphosphonate bone scintigraphy (BS) is the primary modality in nuclear medicine when bone infection is suspected. This is an easy, noninvasive procedure which, in this indication, requires three acquisition times (angioscintigraphy, tissue scintigraphy and late phase). It enables the detection of bone remodeling at the contour of a prosthesis or in contact with osteosynthesis material. Uptake of the radionuclide tracer occurs in proportion to local vasodilatation during the blood flow phase, extravascular diffusion of the tracer during the blood pool phase and bone turnover during the late phase. A combination of hyperemia, increased tissue diffusion and increased tracer uptake during the late phase predicts infection with excellent sensitivity (90 to 100%) within 24 to 48 hours of onset [26] (Fig. 7). On the other hand, specificity is poor (only about 35%), which does not allow differentiation between infection and mechanical loosening of a hip or knee prosthesis, for example. There have been many attempts to improve the performance of BS, in particular by studying the distribution of uptake around the prosthesis. Williamson et al. considered that diffuse uptake around the contour of a total hip prosthesis (femoral and cotyloid components) indicated infection whereas on the contrary, focal activity corresponded to loosening [27]. These findings were questioned by Williams et al., who noted that diffuse activity could be observed in both septic and aseptic loosening [28]. Furthermore, periprosthetic uptake during the first few months following surgery can be considered normal. This osteoblast activity can be observed up to 12 months after

Figure 7. Sagittal magnetic resonance imaging (MRI) sections: a: T1-weighted; b: STIR; c: T1-weighted after gadolinium enhancement and fat saturation; d: coronal STIR; e: bone scan in a 72-year-old woman who underwent arthrodesis for T12 vertebral fracture, presenting with dorsal pain and CRP = 120. Major signal abnormality in T10 and T11 vertebrae with discreet involvement of soft tissues and scintigraphic uptake. *Staphylococcus epidermidis* spondylodiscitis was confirmed by T10-T11 discal biopsy.

total hip replacement and up to 2 years after total knee replacement in completely asymptomatic patients [27]. BS is therefore used for its excellent negative predictive value to rule out active infection. On the other hand, an abnormal bone scan remote from surgery calls for the use of other functional imaging techniques, such as gallium-67 scanning or, even better, labeled white blood cell (WBC) scanning, to achieve better specificity.

Gallium-67 scintigraphy

Gallium-67 has been in use since the 1970s, initially for cancer diagnosis (lymphoma for example) and then for imaging of inflammation and infections. Its biodistribution follows that of ferric iron (Fe^{3+}). After intravenous injection it binds to transferrin and then undergoes extravasation at the site of inflammation as a result of increased capillary permeability and blood flow. Gallium-67 scans are interpreted in combination with bone scans, the first reflecting inflammation and the second, osteoblast activity. Images are acquired repeatedly for up to 48 hours. The two scans can be performed on the same day since the emitted gamma photons have different energies. The interpretation of gallium-67 scans is tricky. False negatives are due mainly to the use of antibiotics and conversely, false positives are present in case of major inflammatory osteoblast activity. Schematically, the scan is interpreted as positive for infection if gallium uptake is more extensive or exceeds that of the technetium bone scan. In contrast, if gallium uptake is strictly concordant and less than on the bone scan, or in the absence of gallium uptake, the diagnosis of infection is ruled out. Uptake which is concordant and of equal intensity on the two scans is inconclusive for diagnosing infection. This situation may be encountered in patients on antibiotic therapy [28]. In a fairly old study but which used needle aspiration as gold standard, Kraemer et al. found that sequential technetium-gallium scan had a low sensitivity of 38% and a specificity of 100% for predicting septic loosening of a total hip prosthesis [29].

Gallium-67 scan is preferably reserved for diagnosis and monitoring of spinal infections.

In vitro labeled leukocyte scintigraphy

This is the routine technique most specific for infection. Labeling of either all WBCs or selective labeling of polymorphonuclear neutrophils (which is preferable to avoid harming lymphocytes) has now been well codified. Cells are labeled with either ^{111}In-oxinate or ^{99m}Tc-HMPAO. The procedure is long (approximately 3 hours) and delicate so as not to damage the cells. It requires the patient to come for numerous visits to the nuclear medicine center with static ± coupled scanner (MPET/CT) image acquisitions at 20 minutes, 3 hours and 24 hours after injection. The tracer distributes throughout the reticuloendothelial system, i.e., hematopoietically active bone marrow, liver and spleen. In case of infection, accumulation of the labeled leukocytes (or polymorphonuclear neutrophils) is concordant with technetium uptake and increases over time. MPET/CT imaging more precisely localizes infected foci (soft tissue versus bone), which is not always possible with planar acquisitions alone. For suspected infections involving orthopedic prostheses or hardware, the scan must be performed and interpreted rigorously, often in combination (in addition to BS) with colloid scintigraphy which depicts hematopoietic marrow. This is because there are many reasons for variations in the distribution of hemapoietically active bone marrow, including fractures and implants in contact with bone. An interpretation coupled with ^{99m}Tc-colloid scintigraphy can differentiate a bone infection from a marrow localization in which marked accumulation of labeled leukocytes also occurs [30]. Love et al. confirmed that combined labeled leukocyte/^{99m}Tc-colloid scans predicted infection of hip and knee prostheses in 150 patients with 96% sensitivity, 87% specificity and 91% diagnostic accuracy [31]. Several hypotheses have been advanced to explain false negatives. The infection may be one that does not involve a neutrophil response (tuberculosis, mycotic or parasitic infections), or there may be an alteration of leukocyte functions. Also, in the case of subacute or chronic infections, monocytes and lymphocytes predominate over polynuclear neutrophils [32]. Treatment with antibiotics may also alter the sensitivity of labeled leukocyte scintigraphy, since there will be less leukocyte migration to the site of infection. Labeled WBC scanning is not used to diagnose infections of the axial skeleton due to their physiologic uptake by hematopoietic bone marrow. Usually, low accumulation is observed in case of infection or medullary fibrosis, without being able to differentiate between the two. The technique can nonetheless be useful in case of a suspicious collection in soft tissues in contact with the spine. In this axial location, combined technetium-gallium scanning is the most effective nuclear medicine modality. Love et al. reported a sensitivity and specificity of 91% and 77%, respectively, in spinal infections [33]. This technique may be a good alternative if MRI cannot be performed.

In vivo labeled leukocyte scintigraphy

LeukoScan® (^{99m}Tc-Sulesomab) is a murine monoclonal antibody Fab' fragment directed against the NCA90 antigen present on the polymorphonuclear cell surface. It was developed for its ease of use; however, it may induce the development of human anti-mouse antibodies (HAMA) which would preclude repeated use of this procedure. Sensitivity is globally comparable to in vitro labeled leukocyte scans but specificity is more variable [34].

^{18}F-FDG-PET/CT

^{18}F-FDG-PET is being developed in indications other than oncology, and particularly in the field of infection. It has several advantages over labeled leukocyte scintigraphy: cell labeling is not necessary, uptake is low in normal bone marrow, the procedure is rapid to perform, and it gives superior resolution. PET/CT scans should be interpreted on attenuation-uncorrected images so as to minimize reconstruction artifacts related to metallic hardware. The performance of ^{18}F-FDG-PET is nonetheless debatable, especially in terms of specificity. Zhuang et al. studied periprosthetic activity in total hip prostheses several years after surgery in asymptomatic patients. After a mean of 71.3 months, approximately 81% of patients had uptake at the femoral head and neck [35]. However, in a study of

127 painful hip prostheses, using clinical follow-up, peroperative tests and histopathology as the gold standard for diagnosing infection, the sensitivity, specificity, positive and negative predictive values for ^{18}F-FDG-PET were 85%, 93%, 80% and 95%, respectively [36]. ^{18}F-FDG-PET appeared to have slightly better diagnostic performance in septic hip prostheses than in septic knee prostheses. Van Acker et al. compared ^{18}F-FDG-PET with the reference nuclear medicine technique—^{99m}Tc-HMPAO-labeled WBC scintigraphy in combination with BS - in 21 patients with suspicion for infected total knee arthroplasty. The combination of the latter two techniques had superior performance over ^{18}F-FDG-PET (sensitivity 100%, specificity 93%, positive predictive value 83% versus sensitivity 100%, specificity 73%, positive predictive value 60%) [37]. Few studies have investigated the performance of ^{18}F-FDG-PET for detection of spinal infections. This technique was superior to gallium scanning in differentiating spondylodiscitis and degenerative abnormalities from infection [38]. In a study of spinal infections in patients with or without metallic implants, ^{18}F-FDG-PET had an excellent negative predictive value of 100% and 86% accuracy for both groups. On the other hand, specificity was 65% in the group with metallic implants versus 92% in the group without implants [39]. In the group without metallic implants, two false positives were observed within the 6 months following surgery, while in the group with implants, the 6 false positives were not confined to recently operated patients. New PET tracers are being evaluated in the field of infection. Gallium-68 has shown encouraging preliminary results. Nanni et al. recently published a study in 31 patients, with bone biopsy as the gold standard. The study cohort was fairly heterogeneous, including acute and chronic infections as well as different localizations (hip, tibia, humerus, pelvis, knee, intervertebral disc) and the presence or absence of hardware. They found a sensitivity of 100%, specificity of 76%, positive predictive value of 85% and negative predictive value of 100% [40].

Needle aspiration

Staphylococcus epidermidis is the most common causal pathogen of orthopedic implant infections. Rigorous aseptic technique is essential during needle aspiration to avoid false positives. Normally, an 18 or 20 gauge needle is used (aspiration is more difficult with smaller needles). Traditionally, aspiration was performed with the aim of culturing the aspirated fluid, which required several days to demonstrate the presence or absence of microbial growth, thus delaying appropriate patient management. Studies analyzing the value of joint aspiration report different levels of specificity and sensitivity, respectively ranging from 50 to 93% and 82 to 97% [41], and a non-negligible rate of false positives (3 to 16%) [42,43]. These large differences are due in part to the different prevalence of infection in the cohorts under study. Periprosthetic tissue biopsies have a false positive rate of 6% and a false negative rate of 10% [3]. These observations explain why many authors no longer consider this the gold standard [44—46].

More recently, many institutions have been performing WBC and differential polymorphonuclear neutrophil counts in aspirated joint fluid, alone or in combination with serologic tests, as a rapid and inexpensive way of assessing the likelihood of infection [47]. A synovial fluid cell count less than 1100 WBC/μL with less than 64% polymorphonuclear cells had a negative predictive value of 99.6% to rule out periprosthetic infection [48]. Another recent study showed that synovial fluid with more than 9000 WBC/μL and an elevated erythrocyte sedimentation rate or C-reactive protein level had a positive predictive value of 100% and 98% accuracy in determining the presence of periprosthetic infection [47]. These two studies illustrate the importance of these tests and stress the fact that a percentage of polymorphonuclear cells greater than 65% is a strong predictor of infection. Needle aspiration can be performed bedside or intraoperatively during revision arthroplasty, but many institutions stress the very high profitability of image-guided aspiration using either radiography, ultrasound [49] or CT [50], depending on the location of the collection and the experience of the radiologist. Regardless of the imaging technique used, image-guided aspiration has the twofold advantage of avoiding damage to adjacent structures (vascular for example) and making it easier to aspirate fluid from a small collection. Ideally, the aspirated fluid should be sent to the laboratory for cell counts and aerobic culture. Since the volume of aspirate is usually too small to send multiple samples, priority should be given to the cell count. Due to their cost, there is no consensus on sending the fluid (if there is enough) for additional anaerobic, fungal or BK culture. In many institutions these latter tests are only done after a second aspiration in patients for whom there is a strong suspicion of infection despite conventional cultures being negative.

A ''dry'' tap does not rule out the presence of infection: in a series of patients with painful THA, Ali et al. found that 23% had infected hip joints, with an approximately equal volume of fluid aspirated in septic and sterile joints [41]. In this study, dry taps were washed with nonbacteriostatic saline and the aspirated joint fluid sent for culture. This technique had 83% sensitivity, 93% specificity, 63% positive predictive value, 93% negative predictive value, and 83% accuracy compared with intraoperative tissue cultures. Many surgeons are nonetheless reluctant to use this technique, pointing to the risk of contaminating a sterile joint. It is crucial that systemic antibiotics not be started before joint aspiration (and diagnostic confirmation). Although their impact on the cell count is unknown, systemic antibiotics, bacteriostatic solutions and local anesthetics are well known to reduce the likelihood of detecting an organism in the aspirated fluid [51]. To avoid false negatives, antibiotics should be stopped at least 2 weeks before joint aspiration.

Conclusion

The diagnosis of orthopedic implant infections is currently based on a combination of clinical signs, laboratory findings and imaging studies. After detailed history-taking and a thorough physical examination, serologic testing of inflammatory markers (erythrocyte sedimentation rate and C-reactive protein) is crucial for ruling out the diagnosis of infection and should be part of the initial work-up. There is no gold standard imaging technique: conventional radiography is essential although in 50% of cases it is normal. CT, MRI

and ultrasound are reliable for soft tissues. With its excellent negative predictive value, BS can rule out an active infectious process. ^{18}F-FDG-PET appears to be a promising tool for spinal and pelvic infections, gradually supplanting gallium scanning. On the other hand, for infections of the peripheral skeleton, labeled WBC scans coupled with colloid scans remain the reference technique. Needle aspiration with joint fluid analysis (leukocyte count and percentage of polymorphonuclear cells) is ultimately the most reliable way to confirm or rule out infection.

TAKE-HOME MESSAGES

- Periprosthetic bone structural abnormalities suggestive of infection:
  - bone sequestrum;
  - rapid alteration of bone structure (especially outside areas subjected to stress);
  - lucent line around the implant widening by more than 2 mm per year;
  - multifocal zones of osteolysis with blurred edges at the implant margins;
  - extensive, poorly circumscribed or solid, thin periosteal reaction, not adherent to the cortex;
  - gas around the implant;
  - bipolar loosening of a prosthesis.
- Periprosthetic soft tissue abnormalities suggestive of infection:
  - sinus tracts;
  - collections;
  - edema of soft tissue (inflammation);
  - joint distention.
- Reduction of CT artifacts:
  - during acquisition: use of a high voltage (125 and 140 kv) and a high amperage, narrow collimation and thin sections;
  - during image reconstruction: use of thick sections combining thin acquisition sections, standard reconstruction algorithms and an extended CT scale.
- Reduction of MRI artifacts:
  - change the direction of phase coding and frequency;
  - decrease the TE;
  - use smaller voxels;
  - use fast spin echo sequences rather than gradient echo sequences; prefer STIR sequences to suppress hypersignal from fat.
- Nuclear medicine:
  - for infections of the peripheral skeleton: labeled WBC scintigraphy in combination with colloid scintigraphy;
  - for spinal and pelvic infections: gallium scintigraphy (18F-FDG-PET).
- Needle aspiration: analysis of cell content in aspiration fluid (WBC count and percentage of polymorphonuclear cells).

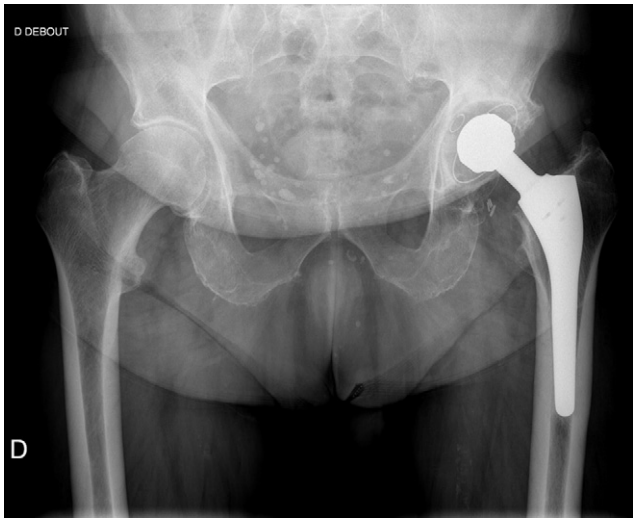

Figure 9. Frontal radiograph of the pelvis.

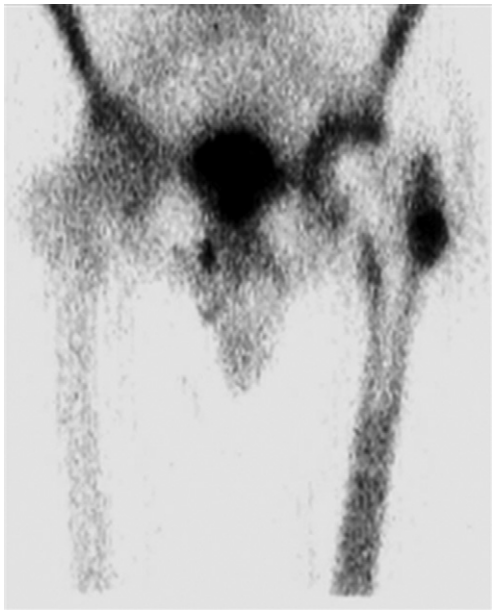

Figure 10. Scintigraphy.

Clinical case

A 68-year-old male who underwent left total hip arthroplasty 8 years earlier presenting with crural pain for the past few months. Apyretic. CRP = 55. Conventional radiography (Fig. 9) and technetium scintigraphy (Fig. 10) were performed.

Questions

1. Do you suspect mechanical or septic loosening or are the findings normal?
2. What would you do to confirm your diagnosis?

Answers

1. The conventional radiograph is normal, which does not rule out a diagnosis of loosening. The large area of focal

uptake on the great trochanter and the more diffuse uptake over the entire femur suggest loosening. Bone scanning may demonstrate increased activity for up to 18 months after THA but certainly not 8 years afterwards. Infection is suspected mainly because of the elevated CRP level.
2. You have to look for periprosthetic soft tissue abnormalities (effusion, collections) and, if possible, perform needle aspiration to get a leukocyte count and percentage of polymorphonuclear cells. In the absence of effusion or collections, labeled polymorphonuclear cell scintigraphy with increasing uptake between 3 hours and 21 hours, concordant with the bone scan, would confirm the diagnosis of septic loosening.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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