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Differential diagnosis of rheumatic diseases using conventional radiography

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The approach to the differential diagnosis of rheumatic diseases using conventional radiography is systematic and module-oriented, which, with respect to future developments, forms the basis for computer-assisted diagnosis (CAD). The indications follow consensus-based referral criteria and attempts should be made to raise the evidence level of the recommendations. Investigation techniques have been improved in the last few years with the use of digital radiography. New imaging technologies may be available in the future that will achieve at least the same quality of images, while exposing patients to a significantly lower radiation dose. The interpretation of radiographical signs could be enhanced through a correlation with other imaging modalities. Computer-assisted techniques with image processing tools for automated measurements, lesion detection and in the form of expert systems are under development. With conventional radiography embedded in CAD systems, promising options will be available to enhance the differential diagnosis of rheumatic diseases.

Key words: arthritis; radiography; diagnosis; differential; joint diseases; imaging.

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Technical developments in conventional film-screen radiography and empirically driven recommendations for film reading have formed the basis of image interpretation for more than two decades since the 1970s. Even subtle bone changes could be detected by using dedicated exposition techniques and these were regarded as important indicators for differentiating the various manifestations of rheumatic diseases.[1] With the implementation of digital radiography, significant improvements in the optical density and dynamic range of the images could be achieved, thus leading to a more complex access for analysing inflammatory changes in the joints and the bones. This, together with a closer collaboration between clinicians in subdisciplines of internal medicine, radiology, orthopaedic surgery etc, has meant that new concepts for the differential diagnosis of rheumatic diseases could be developed.[2]

Differential diagnosis may be regarded as a distinct process within a module-orientated approach to diagnostic reasoning that is based on mathematical proof.[3,4] Differential indications for choosing the proper imaging modality should be made by using evidence-based referral criteria. Investigation techniques have to be performed by following standards that are embedded in quality management programmes. In image interpretation, new concepts about the anatomical spread of rheumatic disease should be considered and the differentiation of the disease entities to be short-listed should reflect modern treatment options. The final diagnosis to be established at the end of this four-step reasoning process forms the beginning of the next cycle of diagnostics during the patient's follow-up.[5] A computer-assisted approach for improving each of these sequentially performed diagnostic modules seems to be a possibility for the future.

This chapter will focus on those aspects of differential diagnosis that are relevant to early and commonly occurring forms rather than to advanced stages of disease manifestation, because they seem to be more important in clinical practice.

INDICATIONS FOR IMAGING

Referral criteria have been developed for all of the major imaging procedures following the recommendations of the European Union (EU).[6] Imaging strategies suggested under the index term 'arthropathies' have been established in a brochure produced by the European Commission, as well as in similar publications in some member states of the EU.[7,8] In this way, conventional radiography is still defined as definitely 'indicated' with an evidence strength of 'C' on a scale with three increments (A–C), for imaging an affected joint or the hands and feet, despite the major advances in ultrasound (US) and magnetic resonance imaging (MRI). X-ray exposures of multiple joints have been assigned as 'indicated only in specific circumstances' and should be performed in selected cases of patients with uncertainties in classifying the type of rheumatic diseases present (Figures 1 and 2). For the radiological documentation of multiple joints, detailed recommendations exist for the major disease entities (Table 1). Radiation protection issues have been regarded as a major problem when exposing films for imaging multiple joints, especially in younger patients and in patients receiving a great number of follow-up studies. The potential harm due to radiation should, however, be weighed against the potential benefits of initiating a proper treatment. Considering the modern options in drug therapy, the risks are considered to be much lower than those of the potential adverse effects due to inadequate therapy.

Conventional radiograms are, despite a relatively small number of relevant scientific publications during the last decade, still of major importance in the differential diagnosis of

rheumatic diseases.[9] Demand is increasing for the detection of early changes of arthritis when there are only subtle abnormalities of the bones and the soft tissues.[10,11] By taking into account the imaging benchmarks of early arthritis, the precision of documentation, the display of multiple joints and aspects of health economics, conventional radiography is regarded as being generally superior to other imaging modalities.

Figure 1. Rheumatoid arthritis with (A) soft tissue swelling that obliterates the fat stripes between the joints, but with only tiny erosive changes (arrows) in the hands. (B) Lesions on the foot are more impressive, with deep erosions being visible especially at the second metatarsal head, thus strongly supporting the diagnosis.

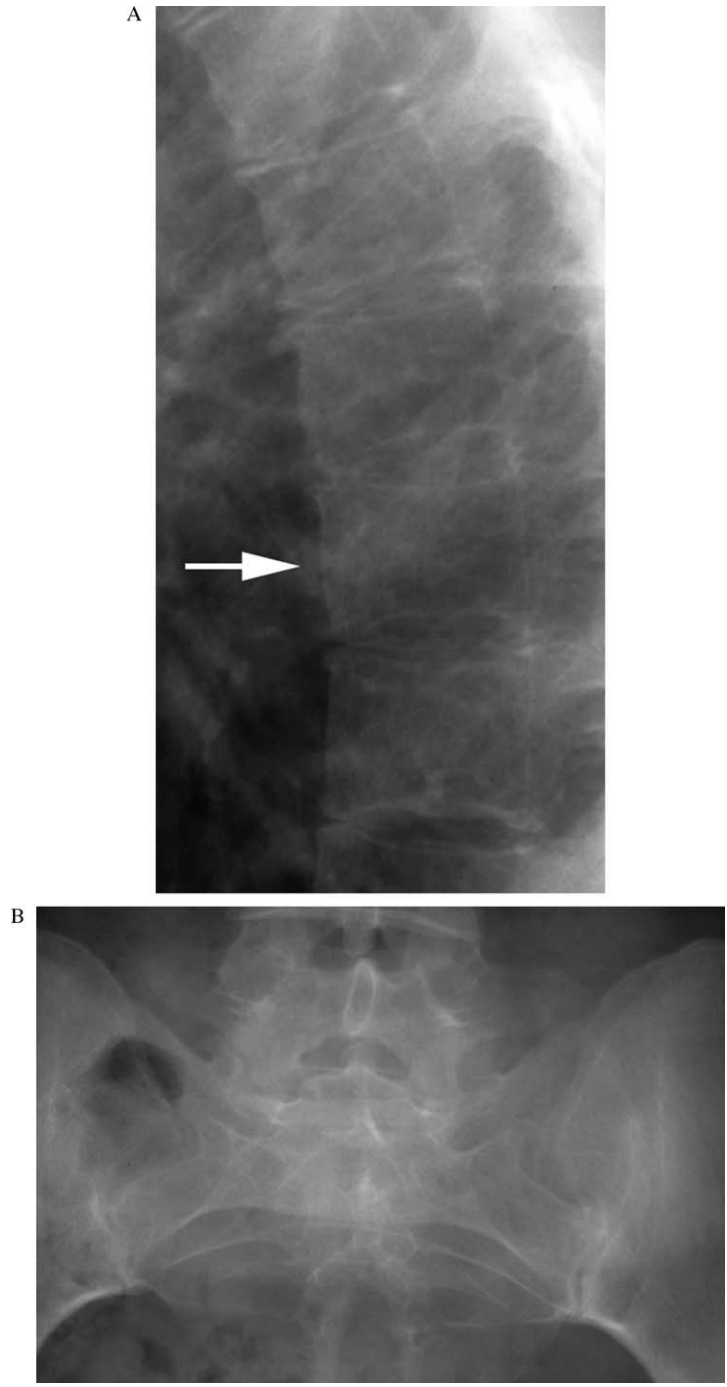

Figure 2. Radiologically mild form of Bechterew's disease with (A) typical anterior spondylitis of the thoracic vertebrae (arrow), whereas (B) the sacroiliac joints appear normal.

Table 1. Imaging strategies for baseline documentation of multiple joints in systemic rheumatic diseases.

	Both hands and both feet	Lumbar spine and sacroiliac joints	Other	Other symptomatic joints
Rheumatoid arthritis	+		Cervical spine with flexion views	+
Ankylosing spondylitis		+[a]		+
Psoriatic arthropathy	+	+		+
Reiter's disease			Ankle	+
Collagen vascular diseases	+	+		+
Calcium pyrophosphate deposition disease (CPDD)			Knee, hands, hips	+
Gout			Feet	+

Source: modified from Freyschmidt.[47]

[a] Image documentation should include the thoracolumbar junction.

INVESTIGATION

Film-based versus digital radiography

Image quality standards have been established with the aim of documenting both the bony abnormalities and the soft tissues involved in the inflammatory process (Figure 3).[12]

Figure 3. Soft tissue swelling around the ulnar styloid is an important indication of extensor carpi ulnaris tendovaginitis (arrow).

Because of the significantly lower spatial resolution of digital radiograms compared to film-based images, concerns have been raised regarding the use of digital equipment for both the initial and the differential diagnosis in rheumatology. It could be shown, however, that even with the early digital systems, based on the principle of phosphor storage, a maximum resolution of 5 line pairs per millimetre (which is only about 50% of the resolution gained with an average film used in musculoskeletal radiology) was sufficient to detect erosions and other joint abnormalities.[13,14] With newer phosphor storage systems a higher spatial resolution can be achieved.

Flat-panel radiography is another digital imaging technology and it provides improved contrast detectability and a potential for exposure reduction compared to storage-phosphor radiography. The best performance is achieved under conditions that are comparable to those used for radiography of the trunk, while the worst performance occurs under conditions that simulate radiography of the extremities.[15]

Despite limitations in spatial resolution, the major advantages of digital radiography are its wider dynamic range with better contrast resolution and its post-processing options for brightness optimisation. These two attributes account for significant improvements in documenting not only abnormalities of the bony surfaces within the joints, but also of the synovial structures and other soft tissues (Figure 4).

With post-processing the overall image quality can be further improved, however, the results of a reader experienced in detecting signs that are prone to a subjective impression, such as abnormal soft tissue densities, osteoporosis, or the disappearance of the subchrondal bone, may be hampered (Figure 5). A detailed knowledge of the potential limitations of digital radiography, its imaging characteristics and its potential artefacts is regarded as an indispensable prerequisite for performing proper film reading.[16]

Exposition techniques

A variety of dedicated X-ray views have been recommended for differential diagnostic purposes in order to display specific types of erosions, bony outgrowths, or other signs. Some of them, such as the oblique, insight or Ferguson views of the sacroiliac joints or the Noergaard views of the hands, have been abandoned. With respect to the high diagnostic potential of computed tomography (CT), US and MRI the majority of these techniques may only be applied in order to answer specific diagnostic questions (Figure 6).[17]

IMAGE INTERPRETATION

Radiological anatomy

Following an established concept, marginal erosions develop primarily in the ‘bare areas’ in the periphery of joints with little or no coverage of the bone by hyaline cartilage. This understanding of the regional distribution of inflammatory disease could be expanded by observations using US and MRI and may support a better differentiation of the rheumatic diseases. As well as the thickness of cartilage, there seem to be influences from the degree of vascularisation, from the thickness of the synovium, from the extent of inflammation within the bone and from the anatomical orientation of the ligaments.

Figure 4. Digital radiogram taken using a phosphor storage system. (A) Small and large erosions are well displayed as in (B) the swollen soft tissue around the ulnar styloid (arrows).

The thickness of the cartilage has not only been used to explain the typical location of erosions in the metacarpophalangeal and metatarsophalangeal joints, but also for explaining the preponderance of sacroiliac joint inflammation on the iliac portion (Figure 6C).[18,19] A similar situation exists at the subachilles bursa, which is not bordered at the calcaneus by periosteum but is in the direct vicinity of the cortical bone.

Figure 5. Juxta-articular demineralisation, or rheumatic ostitis, predominantly around the wrist and the metacarpophalangeal joints in a patient with rheumatoid arthritis.

The influence of vascularisation has been used in order to understand why some areas have a higher degree of destruction. One of these is the site of insertion of the highly vascularised radioscapholunate or Testut's ligament on the distal surface of the radius, where typical deep erosions or cysts, the Mannerfelt crypts (Fig 7), may be observed.[1]

The thickness of the synovium has been suggested to play a role in those parts of a joint with anatomically preformed plicae or marginal folds, where a local reservoir of effusion may lead to a higher concentration of destructive fluid components. A part of

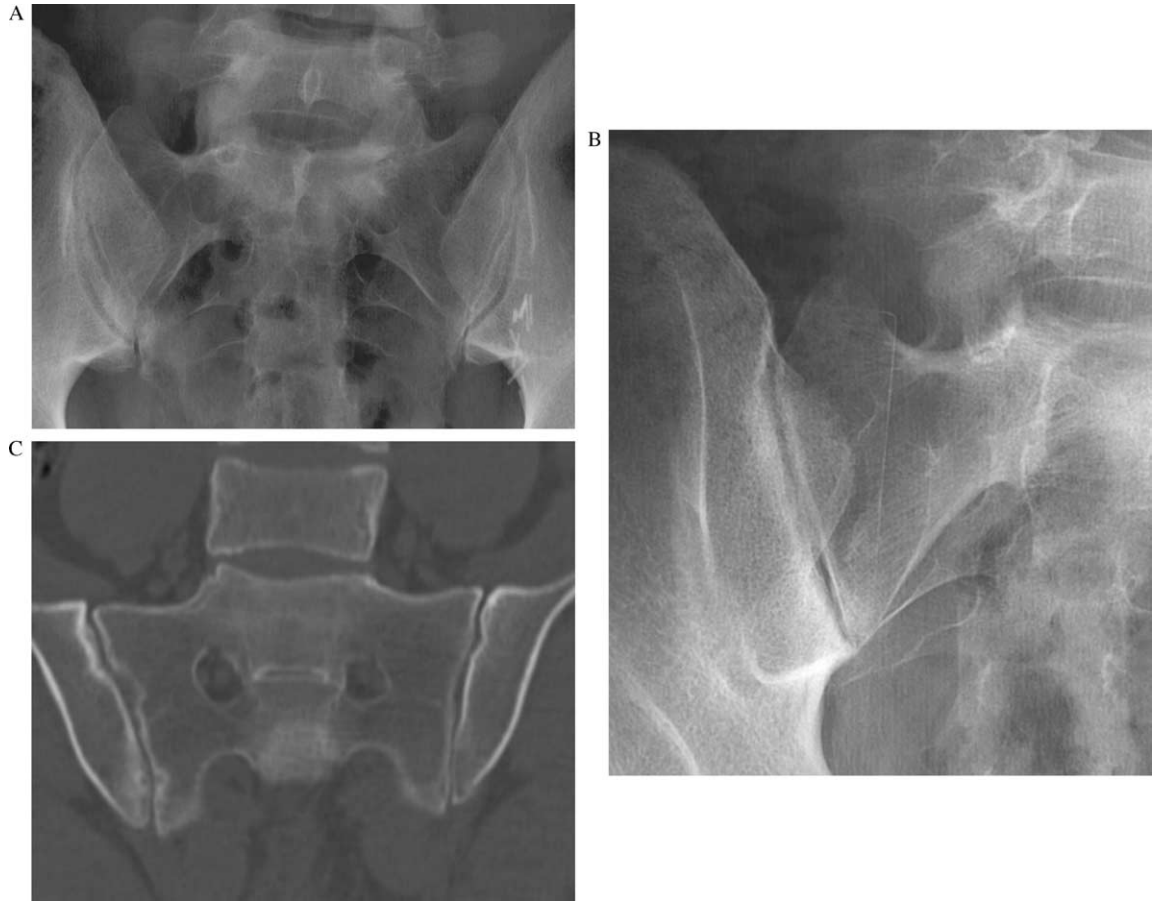

Figure 6. Ankylosing spondylitis with normal findings in the right sacroiliac joint in (A) antero-posterior view and (B) oblique view, but with multiple erosions and subchondral sclerosis seen in (C) computed tomography image.

Figure 7. Deep cystic lesion in distal radius at insertion of Testut's ligament, the so-called Mannerfelt's cyst.

this concept is the typical involvement of large juxta-articular bursae and tendon sheaths. Classic examples are the ankle tendon sheaths (Figure 8), the Baker's cyst in the popliteal fossa, the iliopsoas bursa of the hip, or the subacromial-subdeltoid bursa of the shoulder.[20,21]

In seronegative forms of arthritis, in particular, the inflammatory process is often located in the juxta-articular bone, with standard forms of distribution of the typical bone marrow oedema. 'Rheumatoid ostitis' is a new term used to describe these osteopaenic or osteosclerotic abnormalities in bones due to non-infectious inflammation (Figure 9).

In the metacarpophalangeal joints, the anatomical orientation of ligaments has been considered to be important in that the position of the radial collateral ligaments had an effect on erosion formation that was independent of synovitis.[22]

Signs of arthritis

Imaging findings of inflammation, of degeneration or of other forms of joint and bone disease are generally not specific. The differential analysis should be performed by grouping the signs and weighting the degree of severity of each sign against the others to define characteristic constellations for certain rheumatic diseases. Such groupings may

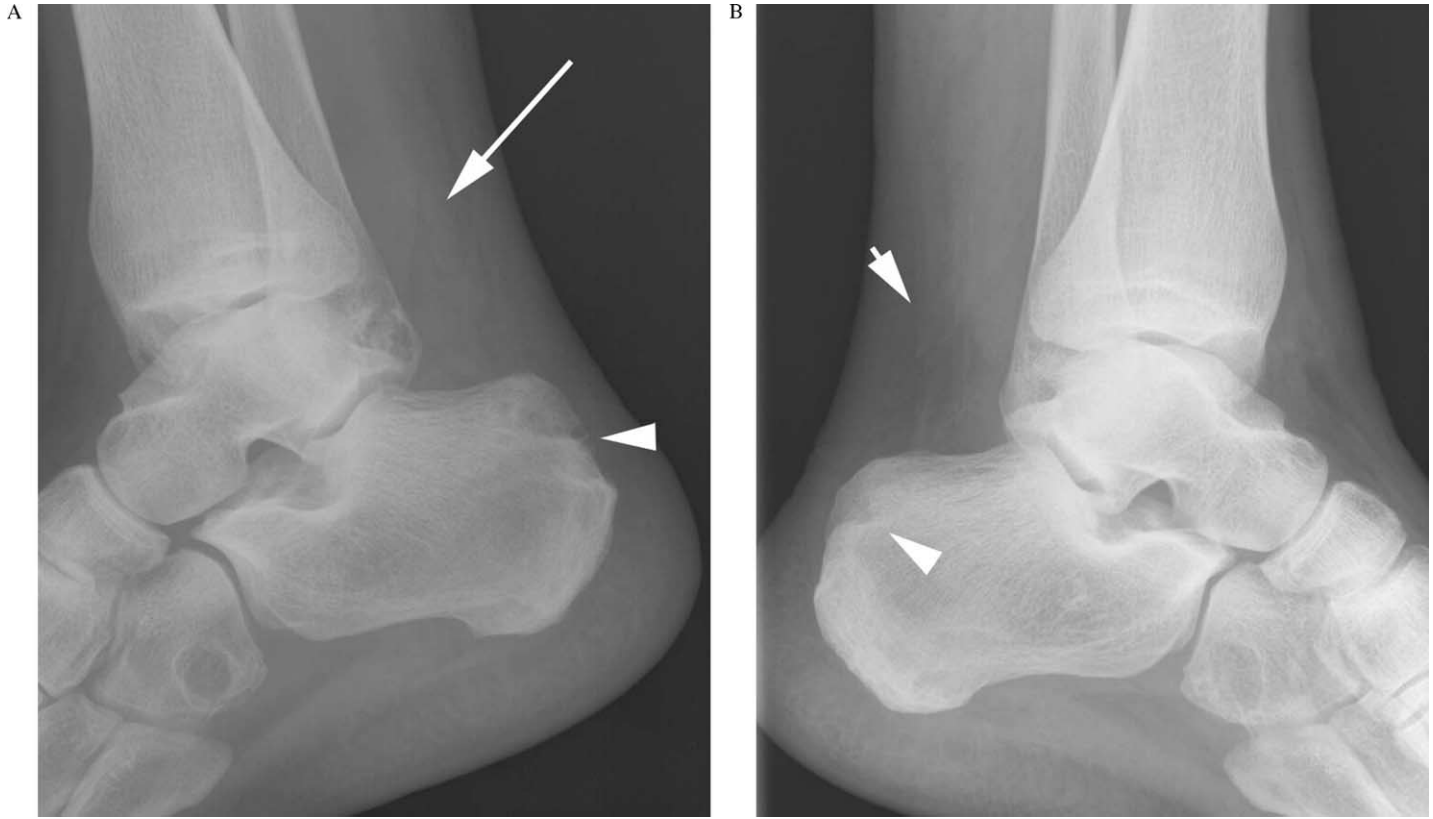

Figure 8. Soft tissue density of (A) Kager's triangle, which represents the pre-Achilles fat pad (arrow) and which is (B) normally hyperlucent (short arrow) compared to the Achilles tendon and muscles. (C) On a corresponding magnetic resonance image the cause of the density is displayed in the form of extensive tendovaginitis with undulating borders (arrows); the peroneal tendon is hyperintense indicating partial rupture (arrowhead). The cockscomb-like posterior aspect of the calcaneus in (A) and (B) is due to rheumatic Achillobursitis (arrowheads).

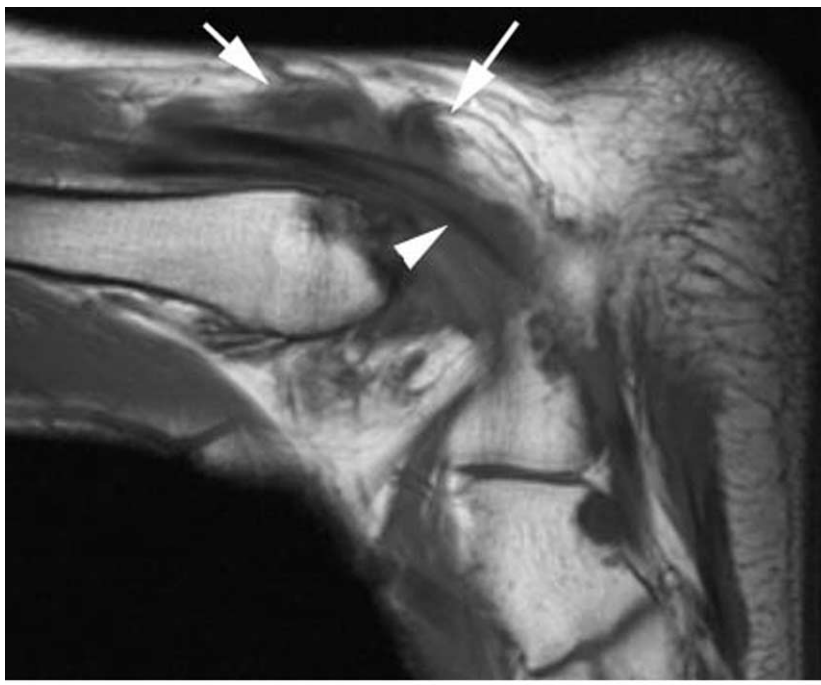

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Figure 8. (*continued*)

Figure 9. Psoriatic arthropathy of the third finger with extensive sclerosis of the metacarpal bone and joint lesions in the form of extensive soft tissue swelling and marginal erosions. Further bony sclerosis with periosteal appositions is visible on the distal radius.

follow the anatomical distribution of the disease by using such parameters as malalignment as well as abnormalities of the soft tissues, the joint space and the bones.

The forms of malalignment that are associated with rheumatic diseases are, in most cases, due to insufficiency or rupture of ligaments. Typical forms may occur at the wrist in the form of ulnar translocation of the lunate bone (Figure 10) or at the shoulder as a result of shortening of the acromiohumeral interval, which is indicative of a rupture of the rotator cuff. At the cervical spine an increased atlantoaxial distance is an important sign of instability, with or without the stepladder phenomenon of the caudal vertebral

Figure 10. Typical ulnar translocation of the lunate, which normally should not project more than half of its length over the ulnar border of the distal radius. Extensive joint space narrowing and subchondral sclerosis indicate osteoarthritis secondary to rheumatoid arthritis.

segments (Figure 11). In the foot, typical forms of malalignment are a talar subluxation or other complex deformities due to the destruction of the spring ligament and synovitis of the subtalar space.[23,24] Following our own experience and other preliminary reports, digital measurements are more accurate than those taken from conventional films.

Swelling, increased density, or calcification of the soft tissues are important parameters for documenting the regional distribution of disease, especially in cases without bone destruction.[25] The displacement of fat layers between joints or beneath tendon sheaths (Figure 1), increased density in cases of tophaceous gout (Figure 12), or calcifications in crystal deposits or in scleroderma are characteristic findings.

Joint space narrowing is an important benchmark that indicates thinning of the hyaline cartilage. New digital techniques have been developed to measure the width between opposing subchondral bone layers with high precision.[26–28]

Bony abnormalities occur in the form of erosions, demineralisation, focal outgrowths or sclerosis. Erosions and their preliminary stage, the pre-erosions, are

Figure 11. Increased antlantoaxial distance (arrow) in (A) anteflexion view of cervical spine compared to (B) the retroflexion view.

Figure 12. Extensive form of chronic tophaceous gout with dense soft tissue swelling and califications of (A) the hands and (B) the elbows.

important hallmarks for both the differentiation and the quantification of diseases. The term 'regional osteoporosis' has been used for many years with the ARA-criteria system for diagnosing rheumatoid arthritis (RA) and also for describing the decreased density that is due to bone marrow oedema syndrome.[29] With 'juxta-articular demineralisation' or 'rheumatic ostitis,' the complex mechanisms of decalcification of the bone in non-infectious inflammation seem to be described more properly.[2] Generalised demineralisation of bone associated with rheumatic diseases is of complex aetiology and may mainly result from the effects of steroid therapy, immobility and of systemic mediators of inflammation.[30,31] The production of certain cytokines (including transforming growth factor beta (TGFβ) in the subchondral bone has been attributed to the new bone formation in seronegative spondylarthropathies.[18,32,33]

Focal bony outgrowths may be of degenerative, i.e. such as osteophytes, or of inflammatory origin. The latter manifest as periosteal irregularities (protuberances) in peripheral joints, as enthesitis at tendon insertions, or as syndesmophytes at vertebral bodies.[1]

Figure 13. Mutilating arthropathy of the hip with deep cystic lesions due to rheumatoid arthritis.

Figure 14. Typical deformities in end-stage rheumatoid arthritis. Cortical thinning of metacarpal and other bones indicate severe osteoporosis.

Articular bones may be extensively destroyed in advanced stages of disease (Figures 13 and 14), sometimes allowing the establishment of a differential diagnosis of such a mutilating arthritis only by exclusion (Table 2).

DIFFERENTIAL DIAGNOSIS

As a result of modern treatment options the radiographical appearances of rheumatic diseases are continuously changing. Today, typical findings such as a swan-neck or buttonière deformities of the fingers are only rarely observed.

Table 2. Differential diagnosis of mutilating arthritis.

Severe forms of RA, PsA, or MCTD
Charcot or pseudocharcot joint
Multicentric reticulohistiocytosis
Joint infection
Rapidly-destructive osteoarthritis
Vascular joint tumour
Haemophilic arthropathy

RA, rheumatoid arthritis; PsA, psoriatic arthritis; MCTD, mixed connective tissue disease. Source: modified from Kainberger.[48]

Rheumatoid arthritis

The key radiographical findings of manifest disease include marginal erosions in the hand and finger joints (Figure 1), a typical soft tissue swelling at the ulnar styloid process due to tendovaginitis of the adjacent ulnar flexor tendon and an ulnar translocation of the lunate. Similar forms of erosive joint disease occur in the feet, predominantly in the second to fifth metatarsophalangeal joints (Figure 15), in the interphalangeal joints of the big toes and at the posterior aspect of the calcaneus due to subachilles bursitis (Figure 8). Cervical spine involvement with atlantoaxial subluxation is important

Figure 15. Rheumatoid arthritis with typically located erosions (arrows) in the fifth metatarsophalangeal joint and the interphalangeal joint of the big toe.

because of the potential associated spinal cord compression. Other joints commonly involved are the knees, the shoulders and the hips.

Early RA generally manifests with soft-tissue swelling, slight joint space narrowing and often flat erosions.[10,34] Indicators of disease activity are the degree of soft tissue swelling (Figure 1A) and the sharpness of erosion borders.[1] The later stages manifest with significant and diffuse joint space narrowing, small soft tissues due to muscle atrophy and extensive subchondral sclerosis. If osteophytes are present, such a constellation should be differentiated from degenerative joint disease due to other causes (Figure 10).

In the differential diagnosis from other disease entities, the location, size and form of erosions is important and the findings should not be mistaken for inflammatory polyarthritis, psoriatic arthropathy, crystal-deposit diseases or other rare joint inflammations of the hands.[35–37]

Seronegative spondylarthropathies

The typical appearance of these diseases includes an early inflammation of the osseous tissue and of tendon insertions together with inflamed joints. In contrast to RA, these diseases are slowly progressive with signs of damage and of repair being observed simultaneously. Therefore, the concomitant appearance of small erosions, broad subchondral sclerosis and ankylosis within the sacroiliac joints is characteristic for

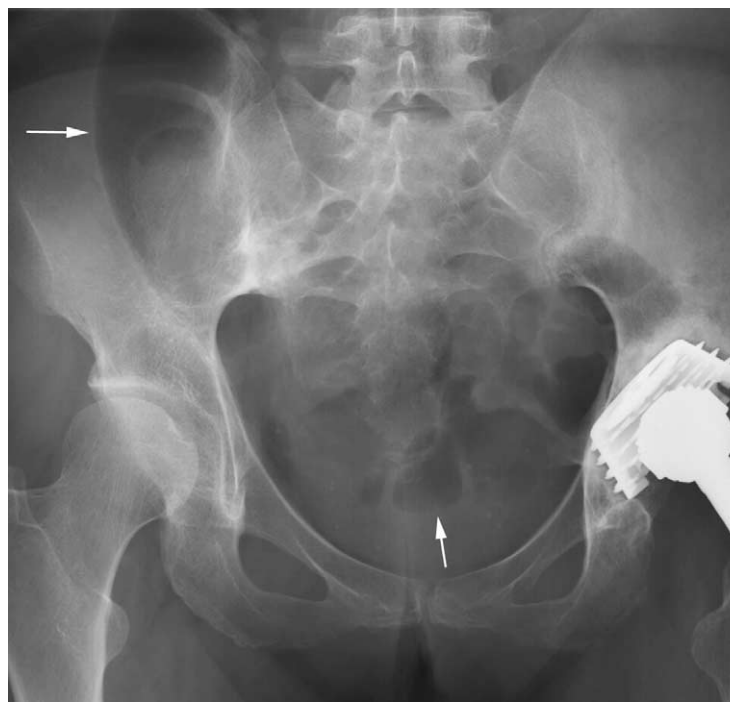

Figure 16. Asymmetric sacroiliitis associated with Crohn's disease with distended bowel loops and intestinal air-fluid levels (arrows).

ankylosing spondylitis, enteropathic arthropathies (Figure 16), psoriatic arthropathy, Reiter's disease and others.

Ankylosing spondylitis manifests with sacroiliitis and inflammatory changes of the spine. The latter occur as tiny erosions at the ligament insertions of the vertebral bodies, in the facets and other vertebral joints, as subchondral sclerosis and as ankylosis (Figure 17). Peripheral manifestations are typical at the hip, shoulder (Figure 18), knee and ankle joints with associated erosions or bony proliferations at tendon insertions.

Psoriatic arthropathy is visible in the spine and the sacroiliac joints in a similar form as that seen in Bechterew's disease, sometimes with more unilateral joint inflammation or typically with parasyndesmophytes in the vertebral bodies (Figure 19). Peripheral manifestations of this disease are often associated with extensive soft tissue swelling (sausage digits) and tiny marginal joint erosions (rate bite erosions) that are surrounded by sclerotic bone or by small or larger focal periosteal irregularities (Figures 20 and 21).

Reiter's disease and other forms of reactive arthritis are accompanied by the typical radiographical features of seronegative spondylarthropathies. Characteristically, an asymmetric arthritis of the knee or the ankle becomes evident. Lesions in this form may be associated with HIV-linked articular disease.

Other rare forms of seronegative arthritis include the spondylarthritis hyperostotica pustule-psoriatica (SAPHO) syndrome, with skeletal lesions predominantly in the sternocostoclavicular joints, the spine and the sacroiliac joints, Behcet's disease with predominantly unilateral sacroiliitis and joint inflammation at various sites. They all present radiographically in the above described form.

Monarticular or oligoarticular presentations of a polyarticular disease may be a diagnostic challenge.[38] Such an appearance is typical for psoriatic arthritis and for Reiter's disease and has been reported in 5–20% of RA cases.[39] If in some patients with

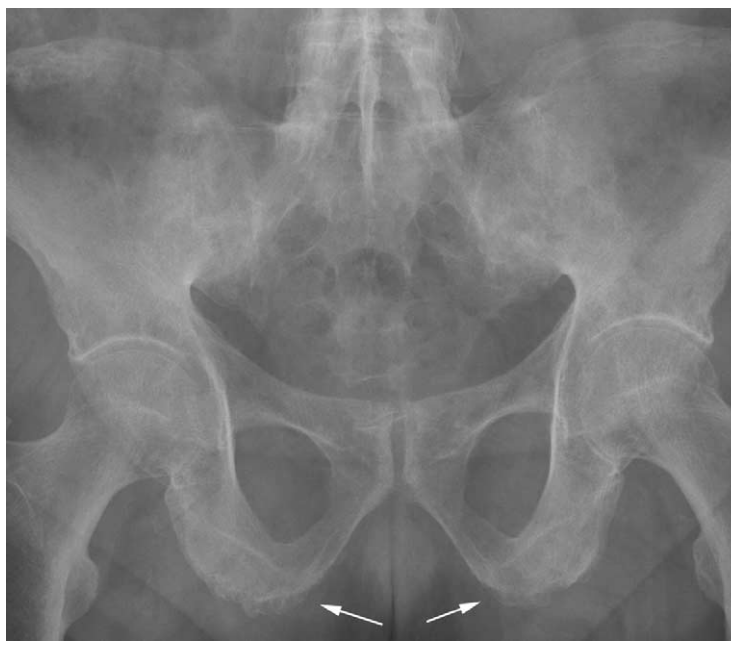

Figure 17. Ankylosing spondylitis with sacroiliitis and enthesitis on the pubic bones (arrows).

Figure 18. Extensive destruction of the humeroglenoid joint with secondary osteoarthritis due to Bechterew's disease.

psoriatic arthritis the associated typical skin and nail lesions are not found, this constellation has been called 'psoriatic arthropathy sine psoriase' and the diagnosis may strongly rely on the subtle radiographic abnormalities.[1]

In the late stages of seronegative spondylarthropathies the inflammation leads to a complete ankylosis of the affected joints and vertebral segments, which may be associated with extensive destruction at certain anatomical sites. In Bechterew's disease, fractures of the spine may result from episodes of acute inflammation with deep erosions around a vertebral disk or from increased biomechanical stress with insufficiency fractures of the bamboo spine. In psoriatic arthritis, the marginal erosions may extend to the inner part of the joint (surface erosion) or to the capsular insertion (enthesitic erosion) with extensive mutilation ('pencil-in-cup' or 'cup-and-saucer' appearances).

Inflammatory systemic connective tissue disorders

These conditions include systemic lupus erythematosus (SLE), scleroderma, dermatomyositis and polymyositis, vaculitis and overlap syndromes (Sharp syndrome, mixed

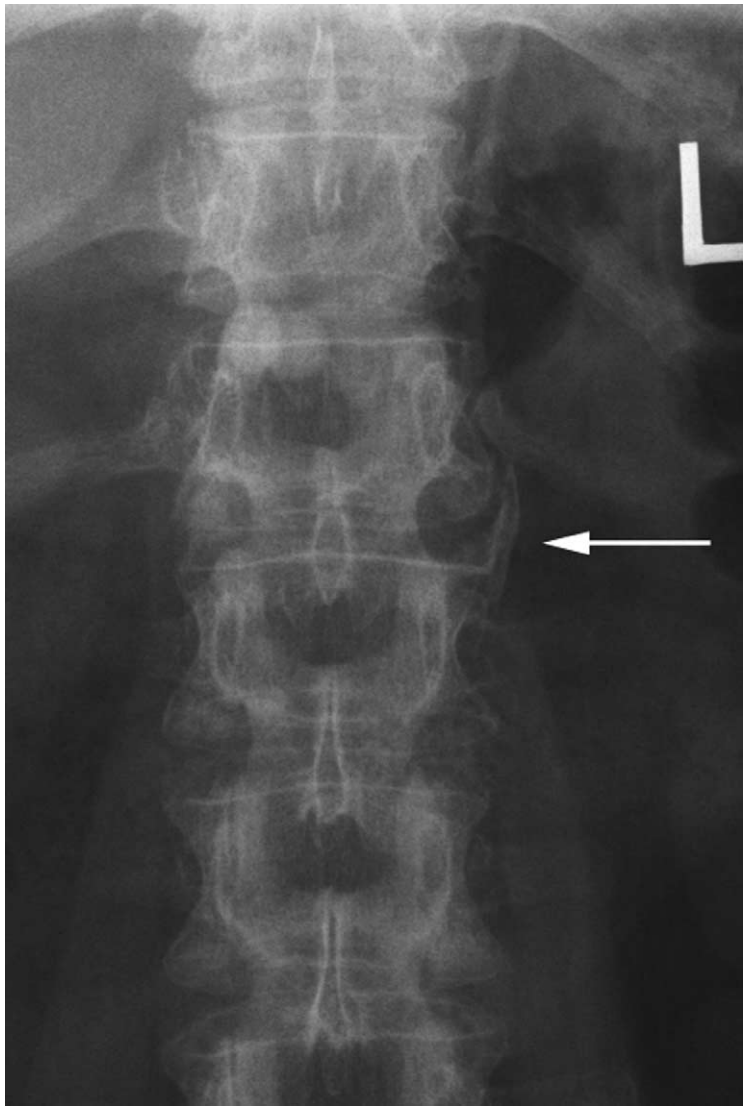

Figure 19. Parasyndesmophyte (arrow) which, in contrast to syndesmophytes, originates from the border of the vertebral body.

connective tissue disease). In many cases soft-tissue swelling and juxta-articular demineralisation are present (Figure 3) and destruction is a rare finding. In scleroderma, acro-osteolysis is a typical finding, sometimes associated with interstitial calcinosis.

Crystal-induced arthropathies

Gout (Figure 12), calcium pyrophosphate deposition disease (CPDD) and hydroxyapatite (peri)arthropathy are commonly encountered under this term.

Figure 20. Discrete manifestations of psoriatic arthropathy in the form of (A) rat-bite erosions and (B) periosteal apposition (arrows).

Figure 21. Periosteal phalangeal tuft reactions in psoriatic arthropathy, here seen as the so-called 'psoriatic morning stars.'

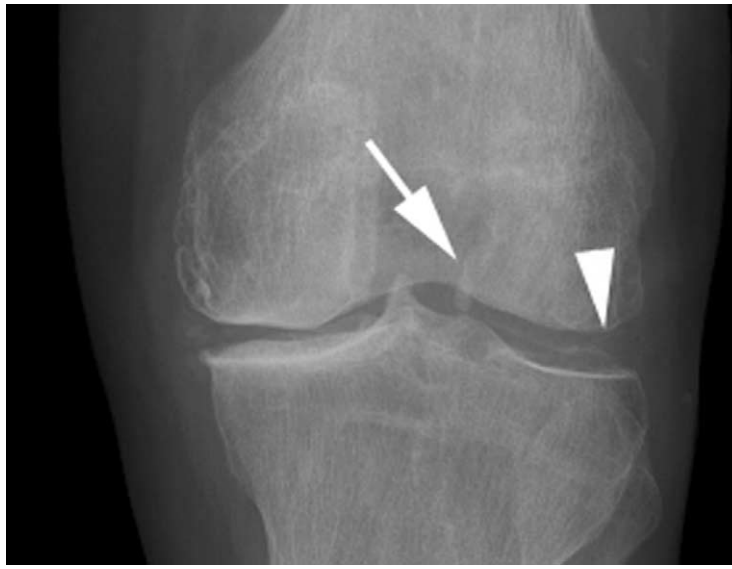

Figure 22. Calcium pyrophosphate deposition disease (CPDD) with calcifications of both menisci, the superficial layer of hyaline cartilage (arrowhead) and ossification of the fibrous joint capsule (arrow).

Typical radiographical manifestations are soft tissue swelling, sometimes deep articular or juxta-articular cysts or erosions, deformities of the juxta-articular bones and calcifications. The latter occur in typical forms in CPDD (Figure 22) in tissues with a large amount of collagen fibres (i.e. in fibrocartilage of the disci and menisci, in the superficial layers of hyaline cartilage and in the fibrous component of the joint capsules). In hydroxyapatite disease, calcifications occur in the large periarticular tendons (calcifying tendonitis). In the early stages, characteristic calcifications may not be visible and oedematous soft tissue swelling may be the main radiographic finding, thus suggesting the correct diagnosis by exclusion.

The differential diagnosis includes osteoarthritis, RA in its cystic form and monarthritic lesions associated with deep cysts or erosions. These latter include osteoarthritis, intraosseous ganglion, septic arthritis, synovial (osteo)chondromatosis, pigmented villonodular synovitis, gout, amyloidosis and particle disease (due to polyethylene, silicone, or metallic fragments left after joint arthroplasty).[37]

CONCLUSIONS AND FUTURE DEVELOPMENTS

The approach to determining a differential diagnosis using conventional radiography is systematic and module-oriented with the potential for the application of computer-assisted diagnosis (CAD). The indications follow consensus-based referral criteria and attempts are being made to develop a digital prompts-and-reminder system.[40] Attempts should also be made to raise the evidence level of the recommendations. The investigation techniques have been improved with the use of digital radiography in the last few years. Imaging technologies with new detector systems are being constructed and may be available in the future whereby the same quality of images can be achieved but with exposure to a significantly lower radiation dose.[41]

The interpretation of radiographical signs could be enhanced through correlation with other imaging modalities. Computer-assisted techniques using image processing tools for automated measurements, for lesion detection and in the form of expert systems are under development.[26,42–46] With conventional radiography embedded in CAD systems, promising options will be available to enhance the differential diagnosis of rheumatic diseases.

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