



REVIEW / *Musculoskeletal imaging*

Multimodality evaluation of musculoskeletal sarcoidosis: Imaging findings and literature review



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Abstract Whilst the detailed X-ray features of thoracic manifestations of sarcoidosis are now clearly defined and known by most radiologists, the same does not apply to osteoarticular and muscular features of the disease, which may however raise major diagnostic problems, either because they are the presenting features of the disease (7% of cases) or because they develop during its course. The bony lesions of sarcoid dactylitis (classical Perthes-Jüngling disease) are very characteristic and well known. Many other presentations of bone and bone marrow sarcoidosis may however raise major diagnostic difficulties, particularly uni- or multifocal osteolytic and sclerotic forms of the disease. The articular manifestations of sarcoidosis are difficult to distinguish from those of the other inflammatory and degenerative arthropathies. The muscular lesions in sarcoidosis are generally clinically silent and therefore often missed. MRI has shown them to be very common in active sarcoidosis. Acute forms carry a good prognosis whereas chronic lesions are a presenting feature of multi-organ sarcoidosis. Finally, clinicians should always think about the possibility of an iatrogenic origin for musculoskeletal abnormalities seen in sarcoidosis, particularly those related to corticosteroid therapy.

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General features of sarcoidosis and its ‘rheumatological’ manifestations

Sarcoidosis, major clinical features and features of progression

The skin lesions of sarcoidosis were described for the first time by Jonathon Hutchinson, surgeon and cellular pathologist in 1863, although he had linked these to the tophaceous gout from which the patient was suffering. Besnier, a dermatologist, described the symmetrical skin lesions of the extremities in 1889 whereas Boeck, also a dermatologist, reported ‘‘multiple benign skin sarcoidosis’’ and suspected that the disease was the systemic, a concept which was confirmed by Schaumann in 1926 who named it ‘‘lymphogranulomatosis benigna’’ to distinguish it from malignant lymphoma, the histological features of which may be similar whereas its clinical natural history is of course extremely different. The term sarcoidosis is therefore due to Boeck. The disease has long been known by the acronym Besnier-Boeck-Schaumann’s disease (BBS in common language).

The pathogenesis of sarcoidosis still involves many unknown features. The existence of familial cases suggests an inherited role through susceptibility to specific infectious or non-infectious environmental agents. The basic histological appearance is that of the sarcoid granuloma, made up of epithelioid cells and giant cells with no caseous necrosis (Fig. 1) [1].

Sarcoidosis classically presents in adults under 40 years old with a peak incidence at between 20 and 29 years old. The presenting features are usually relatively non-specific general signs of weight loss, asthenia, fever, deterioration in general health and evidence of mediastinal lymphadenopathy in suggestive sites, often associated with parenchymal disease. Note that 50% of patients suffering from thoracic sarcoidosis are asymptomatic.

The extra-thoracic features of sarcoidosis may be the presenting features of the disease and are seen in half of symptomatic patients. The characteristic skin lesions such as erythema nodosum and lupus pernio are seen in a quarter

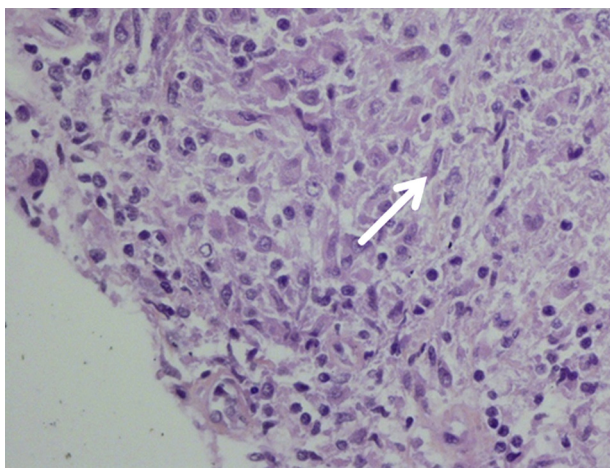


Figure 1. Histological section (MAG $\times 40$) of a bone biopsy. Granuloma with epithelioid cells and lymphocyte crown – Langerhans cell: extended dendritic cell (arrow).

of patients [2]. Ocular presenting features are common, as are hepatic, splenic, parotid central nervous system and urogenital disease.

The clinical progression of the disease is very variable: it has been suggested that subjects with black skin have more severe forms of the disease. Extension of lesions is correlated with the natural progression of the disease. Two thirds of patients achieved spontaneous remission whereas 10 to 30% progressed to chronic disease. An insidious onset with multiple extra-pulmonary sites carries a poor prognosis. Some sites seriously worsen the prognosis, particularly cardiac disease. Recurrences are believed to be more common in musculoskeletal disease.

The most classical treatment given is corticosteroid therapy, which may achieve a rapid response resulting in regression and stabilization. Relapses are seen in 16 to 74% of cases when the treatment is decreased or stopped. If treatment fails or in forms of the disease which are highly aggressive from the outset, immunosuppressant therapies such as methotrexate, azathioprine or cyclophosphamide are commonly used.

‘Rheumatological’ aspects of sarcoidosis; general features

Joint manifestations of sarcoidosis are the most common sites in the locomotor system, with a prevalence of 10 to 35% being reported depending on the series. These are often a presenting feature of the disease.

Bony sarcoidosis is rarer, although it is under-estimated as it is often asymptomatic. It develops later in the course of the disease and is only seen in advanced sarcoidosis. The reported prevalence in the literature is 1 to 15% and it is commoner in women and in people with black skin (African-Americans, West Indians, etc.). Phalangeal involvement is typical and the best known to radiologists (Perthes-Jüngling disease).

The muscular features of sarcoidosis are often asymptomatic and are almost always found on routine muscle biopsies [3,4]. There are three forms of these: chronic myopathy, nodular myopathy and acute myopathic disease.

Imaging for sarcoidosis and for its ‘rheumatological’ features

General features

If initial musculoskeletal sarcoidosis is suspected, the first diagnostic imaging approach is to investigate for other sites, particularly thoracic, which are present in over 90% of patients. If chest radiography is normal, a sub-millimeter section CT scan should be performed particularly if respiratory function tests confirm the presence of abnormalities. In practice the diagnosis is often made late in patients with isolated musculoskeletal sarcoidosis.

Isotopic imaging has an important role to play in the diagnosis of sarcoidosis in general and its musculoskeletal sites in particular (Table 1). Bone scintigraphy with ^{99m}Tc labelled bisphosphonates is a sensitive [5] but relatively non-specific method for detecting musculoskeletal sites, which has the advantage of being ‘‘whole body’’ investigation. The

Table 1 The use of different scintigraphy imaging techniques.

	Diagnosis of bone lesions	Diagnosis of sarcoidosis	Follow-up
Bone scintigraphy and SPECT-CT	+++ Sensitive	–	–
¹⁸ F-FDG PET-CT	+	+++ Combination of the Lambda signs (increased uptake from intra-thoracic lymph nodes) and Panda sign (symmetrical increased uptake of the lachrymal and parotid glands), highly specific	+++ Increased uptake correlating with disease activity

abnormalities precede those seen on standard radiographs (Fig. 2). PET-CT can detect hypermetabolism in lymphadenopathy and the lachrymal and parotid gland lesions of the sarcoidosis. It can also show acute muscle and nodular disease. The level of hypermetabolism reflects the activity of the lesions [6]. Gallium 67 scintigraphy shows uptake in muscle nodule lesions with a “leopard man” appearance [7]. These isotopic techniques, however, are non-specific and may show similar appearances in lymphoma.

In terms of imaging osteoarticular sites of sarcoidosis, it is important to emphasize the complementarity of CT and MRI for a detailed study of the components of the segments involved: cortical bone, trabecular bone, periosteal, soft tissue, etc. MRI is of course the best performing technique to investigate for soft tissue lesions in general and muscular involvement in particular.

Imaging the different musculoskeletal forms of sarcoidosis

Because of the considerable variability in clinical presentations, the different forms of musculoskeletal sarcoidosis need to be considered in their context.

Imaging articular disease in sarcoidosis

Sarcoid arthropathy, described in 1936 by Burmann and Mayer [8], is the commonest in women. It may take on several forms: Löfgren’s syndrome, acute joint disease, and chronic arthropathy. The lesions are symptomatic at the time of diagnosis in 14% of cases and become symptomatic during the course of the disease in 25 to 30% of cases [9,10].

Löfgren’s syndrome

Arthralgia, often a presenting feature, polyarticular and flitting, affecting the ankles, knees and also the proximal inter-phalangeal joints, wrists and elbows, is commonly associated with other classical features of Löfgren’s syndrome (fever, erythema nodosum, symmetrical non-compressive bilateral inter-bronchial hilar lymphadenopathy). These are due to an increase in inflammatory cytokines in the joint rather than to the presence of granulomas. The joint fluid is inflammatory in nature, with lymphocytes predominating. The radiological features are limited to slight epiphyseal demineralization associated with fusiform thickening of the neighboring soft tissues (Fig. 3). This picture may occasionally be combined with tenosynovitis.

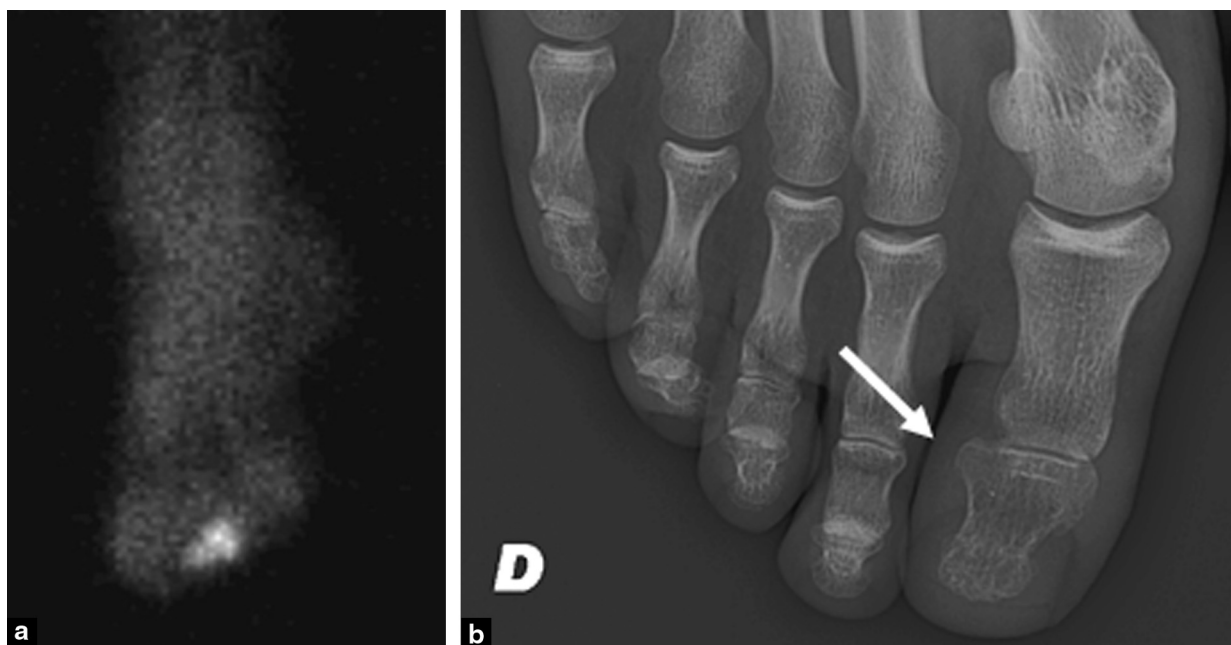


Figure 2. Patient presenting with a swelling of the first digit inter-phalangeal joint. Late phase bone scintigraphy (a): increased fixation centered on the extremity of the first digit. Standard radiograph (b): demineralization of the phalanx, thinning of the external border of the proximal cortex of the first pharynx indicating early dactylitis.



Figure 3. Löfgren's syndrome: standard radiograph of the right hand: fusiform thickening of the soft tissues next to the proximal inter-phalangeal joints of the 2nd, 3rd and 4th digits with no associated bony abnormality (arrow heads).

Löfgren's syndrome develops in the first six months of the disease and is usually seen in women between 30 and 40 years old. African-American men are only rarely affected.

Acute joint involvement in sarcoidosis

This may affect all of the joints but particularly the large and middle sized lower limb joints. Attacks of pain are typically brief and fitting, recurrent and occasionally symmetrical. They have a seasonable peak in spring. Less commonly, oligo- or monoarthritis is seen. These may be combined with periarticular dermal-hypodermal infiltration, myalgia, tenosynovitis and enthesopathies (Fig. 4). Unlike the above, synovial biopsies show sarcoid granulomas.

On imaging, often only soft tissue swelling epiphyseal demineralization and/or a fluid joint effusion are seen [11]. High-resolution ultrasound is useful to distinguish soft tissue infiltration from a joint effusion and to guide a diagnostic puncture [12].

In 90% of cases of acute joint involvement, chest imaging shows the presence of inter-bronchial lymphadenopathy, with or without interstitial disease. Symmetrical inflammatory arthritis of the ankles present for less than two months in a man under 40 years old combined with erythema nodosum is almost specific for sarcoidosis. In this presentation, particularly if symptoms began in spring, appropriate chest investigations are required [13].

Chronic arthropathies in sarcoidosis

The chronic forms of articular sarcoidosis are very rare (0.2% of joint manifestations of sarcoidosis) [12] and only develop after the disease has been present for six months. They represent granulomatous disease [11,14] and are usually seen in patients with black skin with advanced multi-organ sarcoidosis. They generally involve polyarthritis or less commonly oligoarthritis.

The ankles, knees and hands are preferentially affected in this order and the shoulders and wrists more rarely. Concomitant tenosynovitis is common. Lupus pernio is often seen although erythema nodosum is very rare. Bilateral hilar lymphadenopathy is present in 80 to 90% of cases [15] and rheumatoid serology is positive in 10 to 47% of cases making the differential diagnosis difficult. The joint fluid is inflamed, predominantly with lymphocytes and a synovial biopsy confirms the presence of non-caseous granulomatous lesions.

Standard bone radiography is often normal but may show epiphyseal demineralization combined with periarticular soft tissue infiltration. Some more destructive forms of the disease may be accompanied by narrowing of the joint line and demineralization of the subchondral bone plate. Tenosynovitis, particularly involving the extensor tendons of the fingers or more rarely the flexor tendons may co-exist. One case of secondary carpal tunnel syndrome has been reported. The diagnosis of tenosynovitis, tendinitis, bursitis or non-specific synovitis is made on MRI (Fig. 5).

A specific problem: sacro-iliac joint sarcoid disease

Sarcoid disease in the sacro-iliac joints is controversial. This also needs to be distinguished from infectious sacroiliitis (possibly promoted by corticosteroid therapy) or from inflammatory sacro-ileitis secondary to spondylarthropathy [16]. Only two cases of biopsy proven sacro-iliac sarcoidosis have been reported.

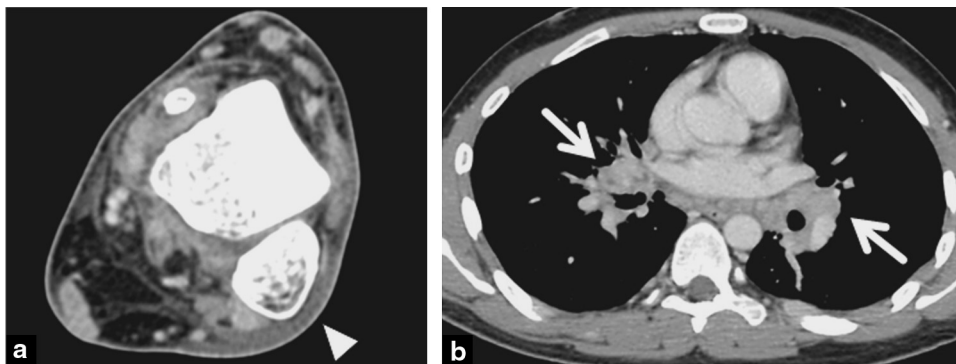


Figure 4. Young man with ankle arthralgia. Enhanced CT, axial view of the right ankle (a): infiltration of the periarticular soft tissues (arrowhead). Enhanced chest CT scan, mediastinal window (b): bilateral, non-compressive hilar enlarged lymph nodes (arrows) highly suggestive of pulmonary type II sarcoidosis.

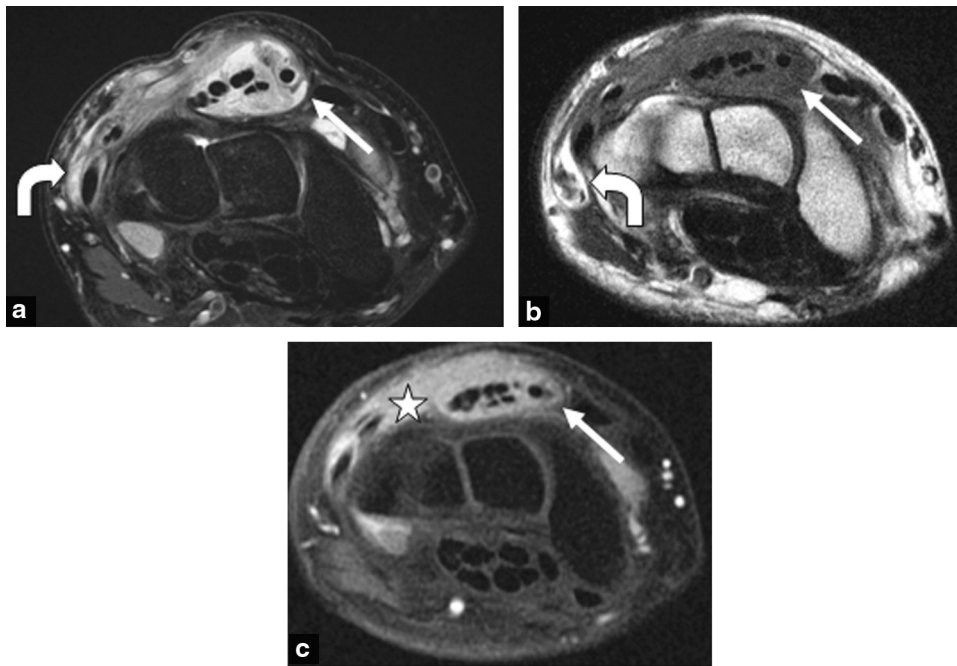


Figure 5. Chronic sarcoid arthropathy of the left wrist in a young man. Axial T2 weighted MRI image with fat saturation (a): thickening of the finger extensor tendon sheath (right arrows) and of the ulna extensor of the carpal bone (short arrows), hypointense on T1 weighted imaging (b) and enhancing with gadolinium (c), indicating tenosynovitis. Soft tissue infiltration (star).

Imaging the bone features of sarcoidosis

The bony lesions of the small bones of the hand and foot described in 1920 and then in 1926 by Jüngling, a student of Perthes, and known as “tuberculosa multiplex cystica” which are still a must for the radiological diagnosis by osteoarticular projection, must be distinguished from other less well known presentations of bone and bone marrow sarcoidosis which raised diagnostic difficulties: disseminated sclerotic or osteolytic skeletal axial or appendicular skeletal lesions.

Sarcoidosis lesions of the small bones of the hand or foot

These are seen in 5 to 7% of patients with sarcoidosis and are common in people with black skin and women between 30 and 50 years old. They occur in young patients with active multi-visceral sarcoidosis and are usually associated with chest disease and chronic skin lesions such as lupus pernio.

Small bone lesions represent 90% of the bony lesions in sarcoidosis and are found particularly in the distal and intermediary phalanges of the 2nd and 3rd digits. They are unit or bilateral and usually asymmetrical [12]. The soft tissues are infiltrated and thickened causing typical “sausage finger” or “radish” deformities and finger clubbing. Distal phalangeal involvement causes cyanosed discoloration of the skin and nail striations (Fig. 6). Pain is variably present: it is present if acro-osteolysis is present. The lesions are secondary to perivascular infiltration of Havers canals by granulomatous lesions and destroy the cortical bone producing a moth-eaten appearance. Nodules, which infiltrate canalicular, bone lysis some bony lines causing compensatory thickening of other trabecular structures. This results initially in diffuse demineralization and cortical thinning followed by the development of the

formation of “cysts”, which are variable in shape and are responsible for the classical “grid” appearance. If the nodules coalesce, areas of osteolysis develop. Localized involvement of cortical bone may be responsible for pathological fractures, which may lead to sequestration. Once lesions are quiescent on treatment, the inflammation and

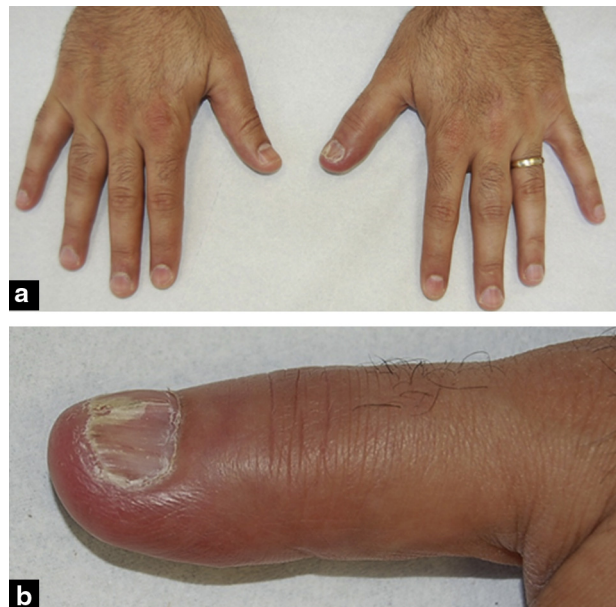


Figure 6. Sarcoid dactylitis. Fusiform thickening of the soft tissues next to the proximal inter-phalangeal joint of the 4th right digit and 3rd right left digit (a). Clubbing of the first left finger with chapped nail (b).

number of granulomas decrease, being replaced by fibrous tissue. The cystic lesions and deformities persist [17].

Initially radiographs are normal or show minor abnormalities: bone scintigraphy is then more sensitive and "high-resolution" CT is very valuable for a detailed analysis of changes. Later on, radiologists find lytic lesions of the intermediary and distal phalanges of the 2nd and 3rd fingers.

Three types of sarcoidosis bone lesions of the small hand bones are described:

- type I: bullous lesion, the rarest with appearances of large bone geodes which predispose to pathological fractures;
- type II: small pseudocystic lesions, which are the most common. Multiple well delineated, rounded and occasionally confluent polycyclic geodes develop and are preferentially located in the head of the phalanges. These may be associated with acro-osteolysis (Fig. 7);
- type III: "lace-like" or "bees nest" or "grid" reticulated appearance with thickened bone sheets and thin cortex (Fig. 8).

These types of disease may co-exist in the same bone or in several bones in the same person. Typically no periosteal reaction or joint involvement is seen on standard radiography. Progressive rash finger deformity is complicated by pathological fractures. This may be associated with acro-osteolysis secondary to confluent granulomas. Less commonly, acro-osteosclerosis made up of dense bone marrow nodules and endosteal thickening responsible for ivory phalanx usually in the distal phalanx is seen.

MRI is the most sensitive method for identifying sarcoid disease in the small bones of the hand. It may show occult lesions with inflammation of the bone marrow and adjacent soft tissues together with tenosynovitis [18]. MRI is useful to exclude differential diagnoses such as tophaceous gout: the tophi are mostly hypointense on T2 weighted images whereas sarcoid nodules are hyperintense [19].

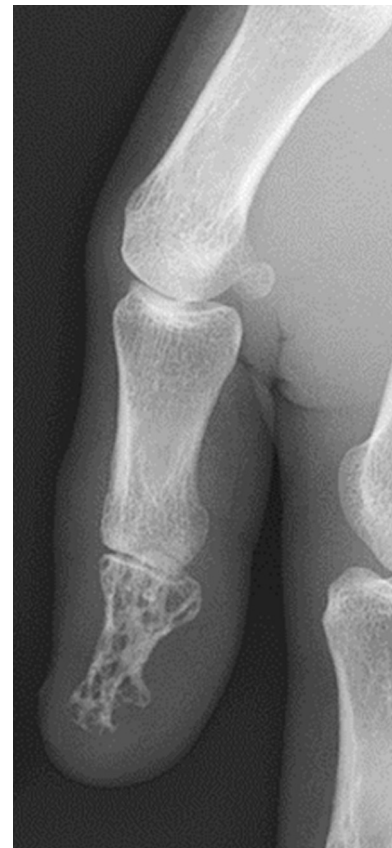


Figure 7. Sarcoid dactylitis. Radiograph of the 1st digit of the right hand: type 2 dactylitis with multiple pseudocystic lacunae within the bone which are clearly demarcated, confluent and polycyclic. Early acro-osteolysis.

Sarcoidosis sites in long bones

Sarcoid involvement of long bones is generally silent and is predominant in the proximal and distal thirds particularly of the forearm. The radiological changes are often

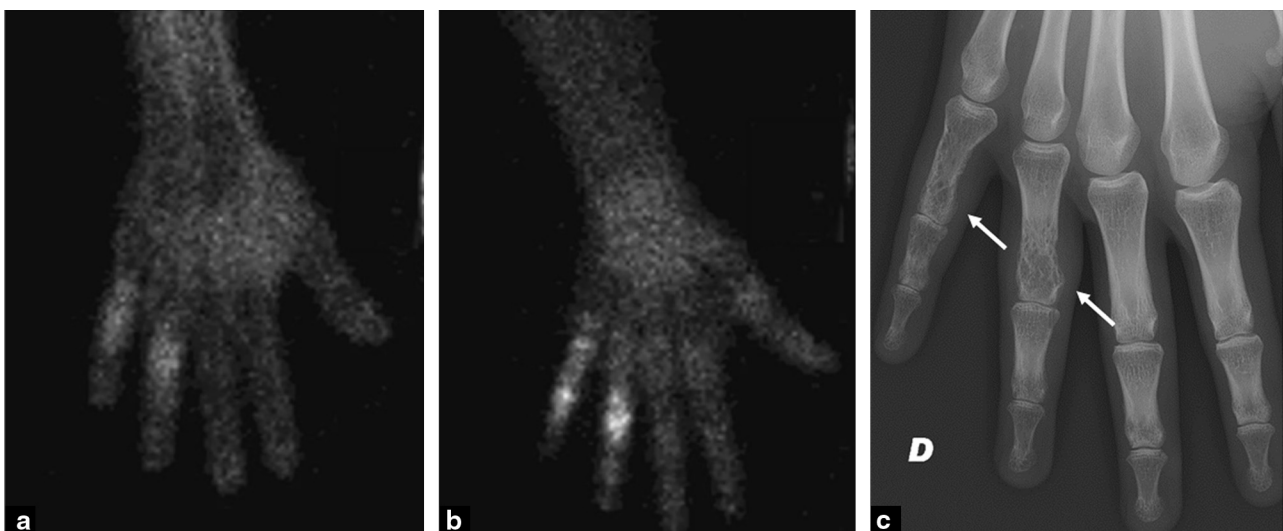


Figure 8. Type 3 dactylitis. Early phase (a) and late phase (b) bone scintigraphy of the right hand: increased uptake in the proximal inter-phalangeal joints of the 4th and 5th digits. Corresponding standard postero-arterial radiograph (c): lesions in the 1st, 2nd and 5th digits, 1st phalanx of the 4th digit with a "bees nest" appearance in the bony framework (arrows). The adjacent soft tissue should display fusiform thickening.

more specific showing demineralization or less commonly osteosclerosis. They may also, particularly when focal, mimic a tumour with considerable osteolysis and co-existent signs of local inflammation may be needed to assist with diagnoses such as tenosynovitis (Figs. 9 and 10). This may precede the other abnormalities [20]. One case of infiltrating osteolysis of the tibia mimicking an infectious lesion has been described [21]. A biopsy is then needed to make the diagnosis.

Sarcoid sites in the axial skeleton

Spinal sarcoidosis is common, often painful and under-diagnosed. It is seen particularly close to the thoracolumbar junction in young people with black skin [22].

This is rarely a presenting feature of the disease and causes mechanical pain and stiffness [9].

Radiologically, the typical findings are focal lytic lesions with a peripheral line of sclerosis affecting the vertebral bodies and pedicles and less commonly the posterior arches [23]. Multiple lesions may occur. On CT, the lesions may mimic a vertebral angioma with the appearance of a grid similar to what is seen in dactylitis. Local sclerotic lesions appearing as ivory vertebra may be present (Fig. 11). A pseudo-Pott's appearance has been described with a paravertebral spindle but preservation of the intervertebral disc.

Finally, diffuse involvement may occur with osteosclerosis of the whole axial skeleton predominantly the lumbar spinal segment and pelvic girdle.

The very wide variety of radiological expression of spinal sarcoid disease clearly raises major problems with differential diagnoses.

Osteolytic lesions are hypointense on T1 weighted imaging and hyperintense on T2 weighted imaging with variable enhancement after contrast injection [11]. MRI may provide additional information in grid like lytic focal lesions which are hypointense on T1 weighted imaging without fat saturation (Fig. 12). These findings are, of course, never specific and a biopsy is required if any doubt is present about infection or tumour (metastasis, plasmocytoma, NHL, etc.) [24]. Occasionally, a diagnosis of tuberculosis cannot be definitively excluded based on histological examination.

Pelvic sarcoidosis is rare but painful [9]. Sclerotic and lytic lesions occasionally combine with a sclerotic line have been described (Fig. 13).

Sarcoidosis sites in the cranial vault

Sarcoidosis of the cranial vault is rare and generally isolated [12]. Its incidence is widely under-estimated because of the minor nature of its associated symptoms, such as local inflammation or pain. Radiographs show osteolysis throughout the thickness of the cranial vault without peripheral sclerosis. The lesions are of variable size and sites and are generally extensive. They may be assessed on CT

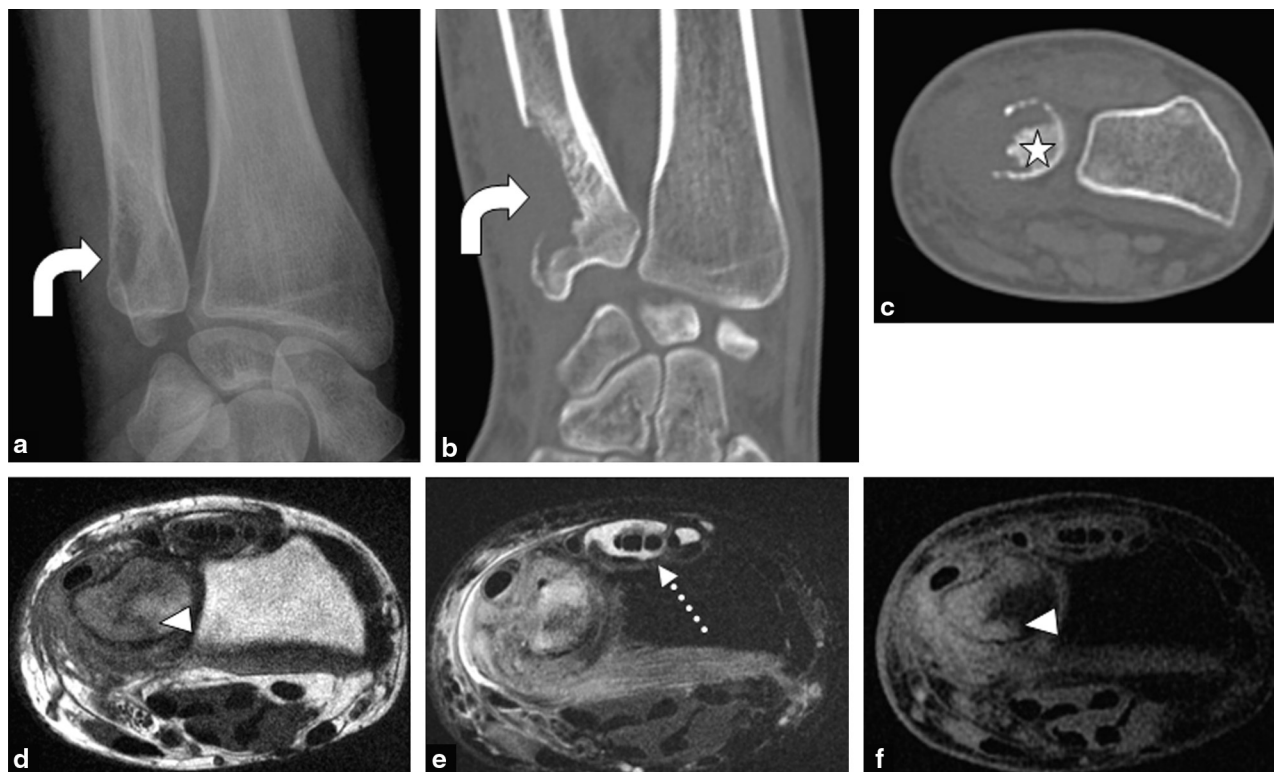


Figure 9. Long bone involvement mimicking tumour. Postero-anterior radiograph of the right wrist (a): large lytic lesion in the inferior end of the right tibia with no periosteal reaction (curved arrow). Frontal CT (b): lytic lesion associated with a grid appearance in the bone marrow (arrow) strongly suggestive of sarcoidosis. Axial CT (c): large interruption of the cortical bone (star). On MRI: "ghost" cortex (arrowheads) which are hypointense on T1 weighted imaging (d), less clearly visualized on T2 weighted imaging with fat saturation (e) and on enhanced T1 imaging (f). Extensive infiltration of the soft tissues. The combination of the bone lesion with the right extensor tenosynovitis (dotted arrow) suggests an inflammatory disease. The grid appearance points towards sarcoidosis.

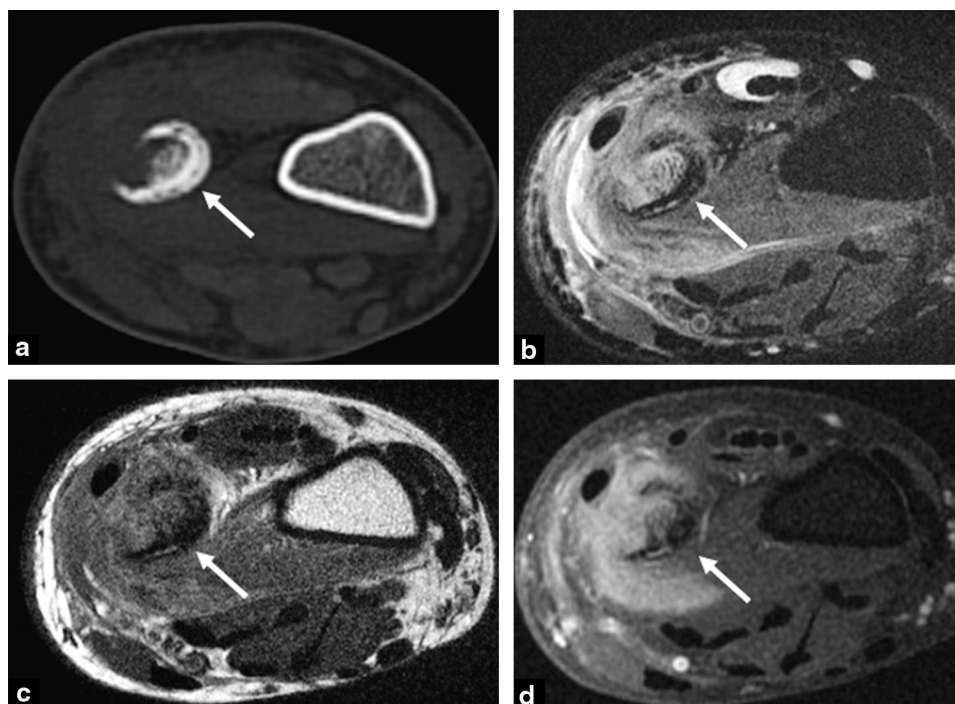


Figure 10. Same patient as in Fig. 9 with disease of the right ulna. Axial CT (a): periosteal reaction with splitting of the cortex (arrows). Same features on T2 weighted MRI imaging with fat saturation (b), T1 weighted imaging before (c) and after gadolinium enhancement (d).

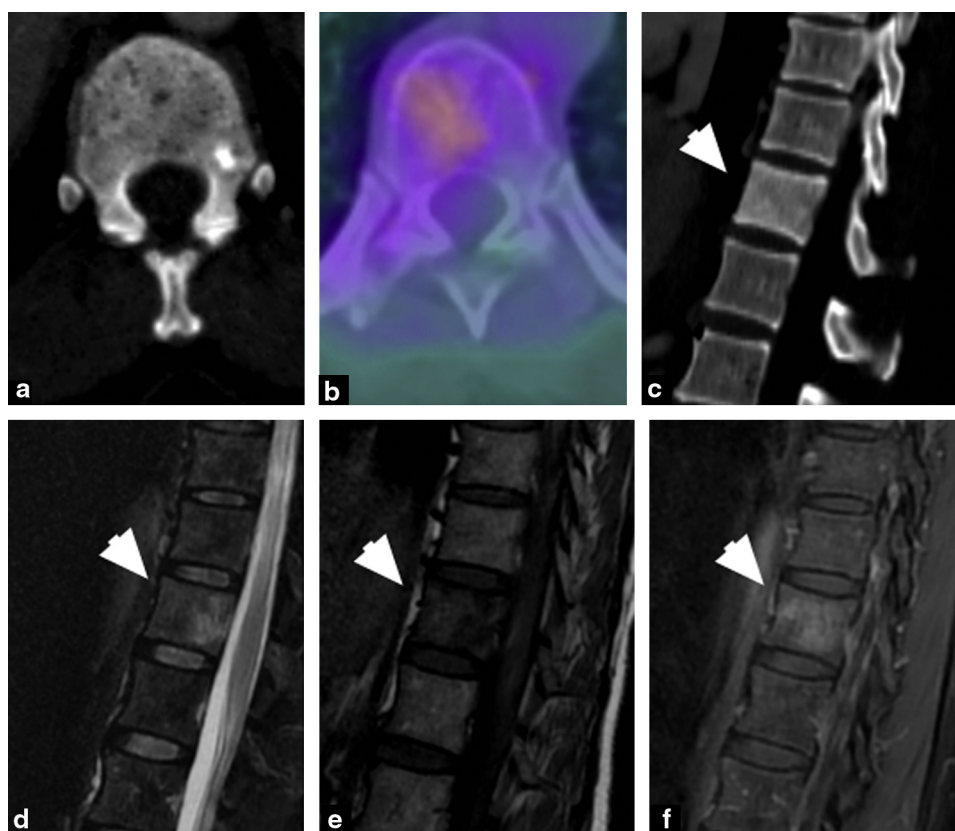


Figure 11. A rare case of sclerotic vertebral involvement in a 55-year-old woman followed up for multi-organ sarcoidosis. Axial (a) and sagittal (c) CT in the bone window: sclerotic ivory vertebra at the thoracolumbar junction. No deformity on ^{18}F -FDG PET-CT (b): increased uptake suggesting the activity of the lesion. MRI: classical sign of vertebral disease: hyperintensity on T2 weighted imaging (d), hypointense on T1 weighted imaging (e) enhancing after contrast injection (f).

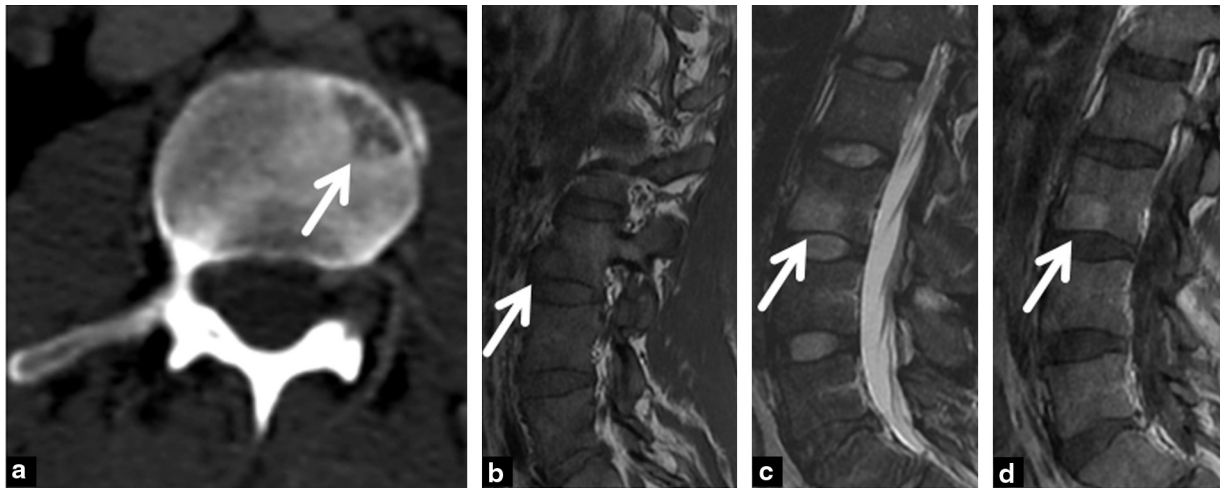


Figure 12. Vertebral lesion mimicking an angioma. Axial and bone window CT (a): grid like lesion in the anterior part of the body of the vertebra mimicking an angioma. MRI: hypointense lesion on T1 weighted imaging without fat saturation (b), unlike a possible angioma. T2 (c) and T1 weighted imaging after gadolinium enhancement (d) providing no additional information, as the lesion has the appearances as those of an angioma.

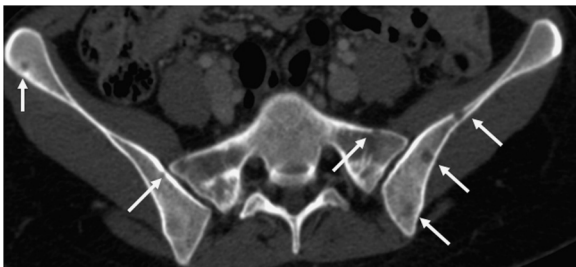


Figure 13. Pelvic disease in a 29-year-old woman. Bone window axial view of the pelvis. Multiple punched out lytic lesions some of which are responsible for rupture of the cortex.

whereas MRI provides additional information in the event of extension to soft tissues. Cases of partial or complete spontaneous regression or regression on treatment have been described [9]. The differential diagnoses to be considered are hemangioma, histiocytosis, metastases or a primary tumour (lymphoma, osteosarcoma or plasmocytoma, etc.).

Imaging muscular lesions in sarcoidosis

Muscular sarcoidosis was described for the first time in 1908 by Licharew [25]. Muscle involvement is very common although conversely is only symptomatic in 0.5 to 2.5% of patients [26]. Routine histological studies have shown muscle lesions in 50 to 80% of patients with sarcoidosis. In addition, gastrocnemius muscle biopsies are consistently positive in patients with hilar lymphadenopathy and symptoms compatible with sarcoidosis [12]. Symptomatic forms of the disease mostly affect people who are on average 65 years old and mostly affect women. Sarcoidosis is the leading cause of granulomatous myopathy, three varieties of which can be distinguished: chronic myopathy, acute myositis and nodular myositis.

Chronic sarcoidosis myopathy

This is the most common form (86%), is diffuse and occurs predominantly in the girdles. It may be the only

manifestation of the disease [1] and usually affects post-menopausal women [27]. It is responsible for bilateral, symmetrical, proximal muscle weakness which gradually worsens possibly with co-existent atrophy and myalgia. CT and MRI are usually normal although MRI occasionally shows muscle atrophy with fatty degeneration [11,26].

Acute sarcoidosis myositis

Acute sarcoid myositis (11% of muscle involvement) is reflected by deterioration in general health combined with symmetrical proximal myalgia affecting young patients (average age 37 years old). The myalgia may progress to muscle contractures with hypertrophy of the affected muscles. Muscle weakness is rare. MRI may be normal because of the small size of the lesions or may show a diffuse muscle intensity on T2 weighted imaging [28]. Secondary corticosteroid myopathy should be excluded.

Nodular form of sarcoid myositis

The nodular form of sarcoid myositis is a rare feature (3% of muscle involvement) characterized by multiple muscle nodules preferentially located in the lower limbs [11]. Occasional cases of a single nodule have been described [27]. Clinical examination reveals myalgia and less commonly a muscle deficit associated with signs of inflammation and ultrasound shows nodules with a hyperechogenic center and hypoechogenic periphery compared to the adjacent muscles (Fig. 14) [25]. The lesions are rarely seen on CT, but may enhance with contrast.

MRI is the investigation of choice and shows fusiform nodules extending along the direction of the muscle fibers usually at the muscle-tendon junction [10]. Their center is hyperintense on T1 and T2 weighted imaging because of the presence of dense connective tissue and low cellularity hyaline tissue. If the granulomas persist the connective tissue is entirely replaced by fibrous hyaline tissue. The peripheral inflamed crown of the granuloma is hypointense on T2 weighted imaging and on T1 and T1 weighted imaging after gadolinium enhancement. On axial views the nodule appears therefore as a "star" with a stellar hypointense center. On

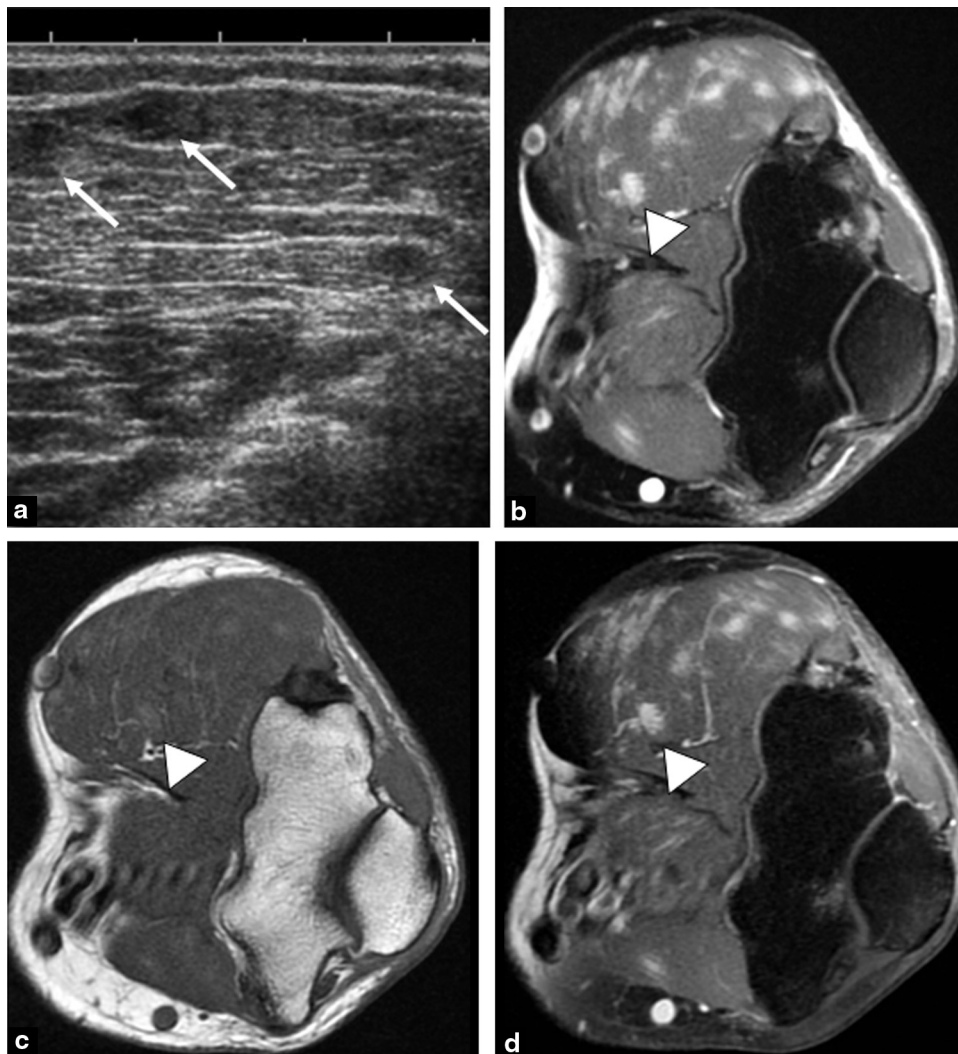


Figure 14. Female patient with nodular muscular sarcoidosis. Ultrasound (a): hypoechoic nodules (arrows) compared to the adjacent tissues, infiltrating the muscles. MRI: nodules (arrowheads) which are hyperintense on T2 weighted imaging with fat saturation (b), heterogeneous on T1 weighted imaging T1 (c) enhancing with contrast (d). T2 weighted MRI (b) with fat saturation and enhanced T1 image with fat saturation (d) mimicking “leopard man” appearances described in nuclear medicine (gallium scintigraphy).

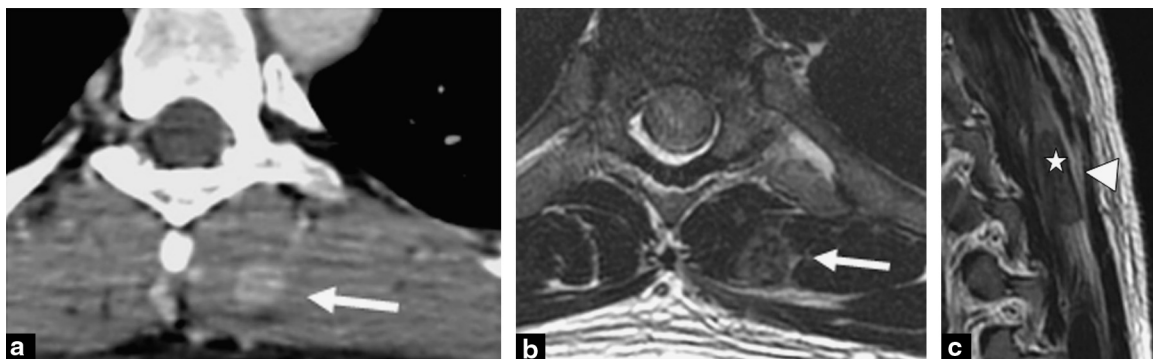


Figure 15. Typical nodular muscle lesion in a 28-year-old man. Axial CT image (a): nodule (arrow) which enhances. T2 weighted axial MRI view (b): nodule (arrow) with a central hypointensity and peripheral hyperintensity (black star sign). Sagittal view (c): three band sign with a hypointense nodule (star) bordered by two hyperintense bands (arrowhead) secondary to the inflammation.

coronal and sagittal views the nodule forms three bands with a central hypointense band and two hyperintense peripheral bands (Fig. 15) [25,28]. In the case of a single lesion the MRI appearance may mimic a giant cell tumour, soft tissue sarcoma or infection [29].

Other muscle lesions in sarcoidosis

The diaphragm and intercostal muscles may also be affected in sarcoidosis. Patients with musculoskeletal sarcoidosis have been shown to have deficient respiratory muscles.

Progressive features of musculoskeletal sites of sarcoidosis

Löfgren's syndrome carries an excellent prognosis with a 90% remission rate. Acute arthritis resolves spontaneously over 3 to 6 months although occasional recurrences may occur and some people occasionally develop chronic pulmonary sarcoidosis [15]. Chronic arthropathy is characterized by periods of exacerbation without repercussions on functional prognosis. Both nuclear medicine and conventional imaging returns to normal (Fig. 16). Occasional cases of joint destruction or deformities are described, including Jaccoud arthropathy.

Small bone lesions usually stabilize. These may extend to the neighboring bones and joints and be responsible for deformities [4]. On treatment the long bone lesions become fibrous or fatty in nature [19]. Initially lytic lesions may remain stable or their outlines may become cortical

(Fig. 17). Soft tissue invasion regresses as do the related signs of inflammation such as tenosynovitis. Pathological fractures may occur most commonly affecting the phalanges although fractures of the ulna, femur, metacarpal and costal bones have been described (Fig. 18). On treatment, vertebral lesions regress partially after follow-up for 10 years [4]. Isotopic imaging is useful for follow-up and to diagnose relapses or reactivation of the disease (Fig. 19). Neurological compression is rare but may occur as a result of cervical lesions [9].

Limited information is available about the long-term outcome of chronic myopathy on treatment. It is usually refractory to the various treatments and the disease progresses in successive flares and remissions. Acute myositis is sensitive to corticosteroid therapy [26]. Nodular myopathies recur frequently and one case of acute peripheral nerve compression by a granuloma has been described.

Indirect osteoarticular lesions of sarcoidosis

Granulomas containing activated macrophages causing uncontrolled over-production of 1,25 OH₂-D₃, causing osteoclast activation and bone resorption may occur which increases the risk of osteoporosis. Bone loss also occurs secondary to the high levels of parathyroid hormone present in the granulomas.

Corticosteroid may cause avascular epiphyseal necrosis, bone and bone marrow infarctions, osteoporosis and fractures and result in corticosteroid induced myopathy [11].

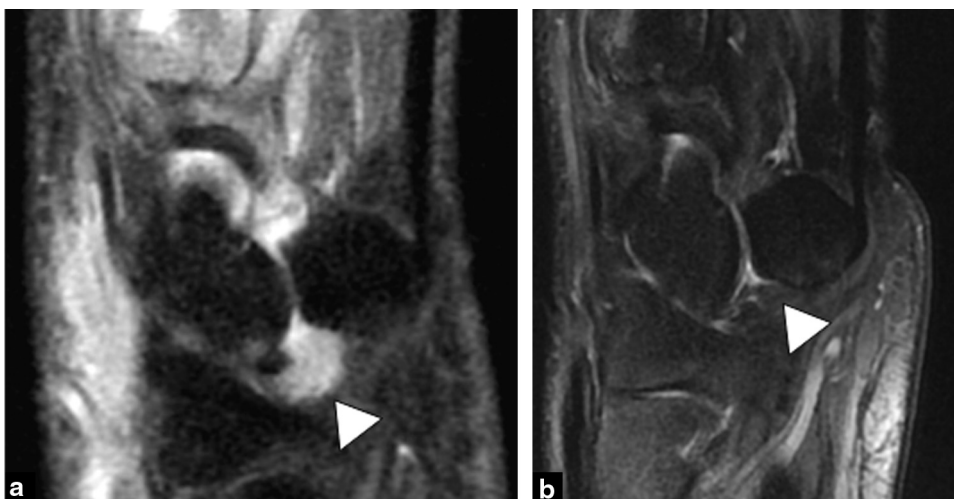


Figure 16. MRI changes in chronic sarcoid sinuovitis of the pisotriquetral joint. Sagittal T1 weighted view with gadolinium enhancement and fat saturation (a) showing an effusion in the pisotriquetral joint (arrowhead). One year after treatment (b): complete regression of the effusion on T2 weighted MRI with fat saturation with *restitutio ad integrum*.

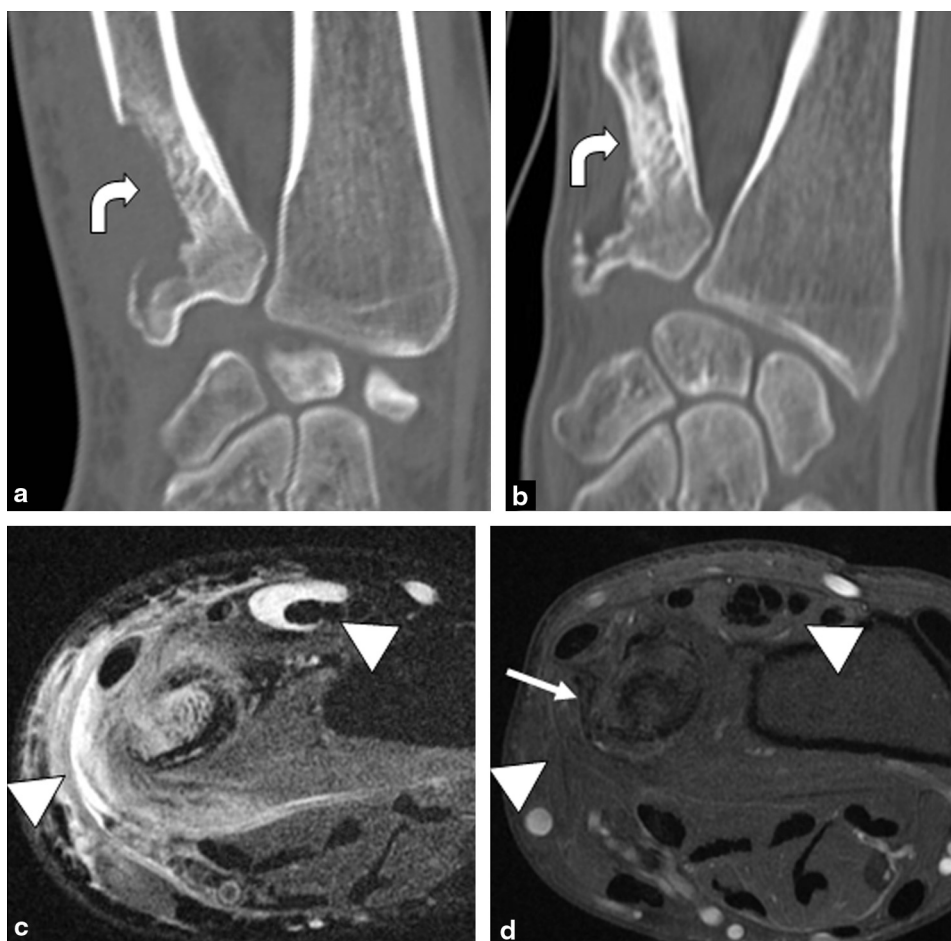


Figure 17. Follow-up of long bone disease after two years of treatment (same patient as in Figs. 9 and 10). Initial frontal CT image (a): large lytic lesion with rupture of cortical bone (curved arrow). After two years (b), partial corticalization of the margins of the lesion (curved arrow). Infiltration of the soft tissues and tenosynovitis of the finger extension tendons (arrowhead) seen on the initial MRI on T1 weighted imaging with gadolinium enhancement and fat saturation (c). Regression of the infiltration (arrowhead) and bone marrow edema on the repeat at two years (d). Neocortical bone (arrow) appearing as a thin hyperintense border.

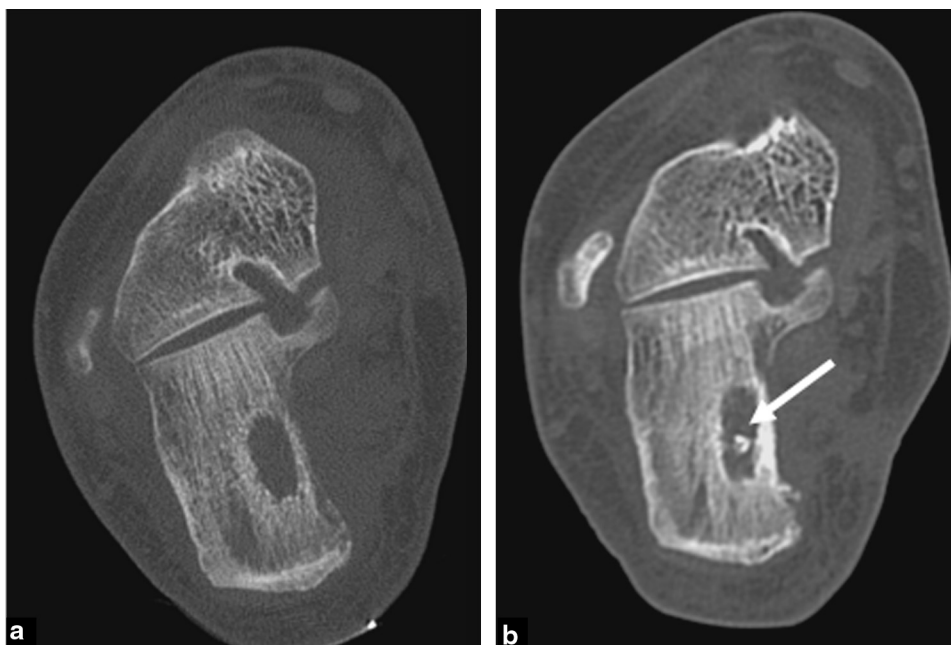


Figure 18. Changes in a right calcaneal lesion in a 48-year-old female patient after 3 years. Axial CT in the bone window (a) showing a rounded lytic lesion with slightly sclerotic borders. After three years on treatment (b): sclerosis of the margins of the lesions and development of a bony sequestrum (arrow) indicating a pathological fracture.

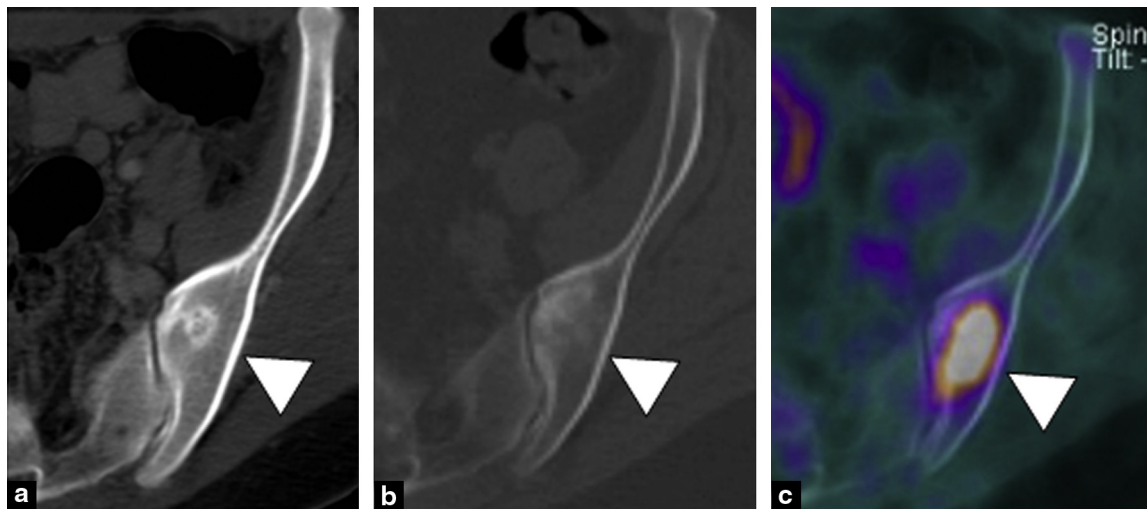


Figure 19. Follow-up of a left iliac wing lesion in a patient with sarcoidosis on treatment. Initial CT in the bone window: large mixed sclerotic and lytic lesion present in the left iliac wing, which is clearly demarcated (arrowhead). After 6 years: increase in size of the lesion which is poorly demarcated mimicking sclerotic iliac osteosis, myeloma or sacro-iliitis. Increased uptake on PET-CT suggestive of local reactivation of the disease.

Conclusion

High-resolution lung parenchymal CT has transformed the diagnosis of thoracic sarcoidosis because of the image quality of interstitial disease which usefully supplements the already well known examination for mediastinal lymphadenopathy by conventional chest radiology. The diagnosis of extra-thoracic sites of sarcoidosis is far more delicate as apart from the bone disease of the phalanges (classical Perthes-Jüngling disease) is far less well known. This explains the occasionally major delays in diagnosis despite multiple investigations.

The features of osteoarticular and muscular sarcoidosis, particularly when they are the presenting manifestations of the disease, are a good example of circumstances in which the radiologist may play a major role in the diagnosis.

The clinical and radiological features which should suggest sarcoidosis as the origin of the disease include:

- inflammatory joint involvement of both ankles in a young person;
- disseminated nodular heterogeneous osteosclerosis predominantly in the axial skeleton and pelvic girdle;
- multiple osteolytic lesions at different geographical sites with a type 1A outline in a young adult, too old an age for eosinophilic granuloma and too young for myeloma or metastases not without checking the blood calcium in order to avoid missing the brown tumours of primary hyperparathyroidism (von Recklinghausen fibrocystic osteitis);
- nodular sarcoid myositis is a rare entity but may be seen on ultrasound imaging or MRI.

In all of these circumstances, investigation for the characteristic thoracic lesions should be the first step to confirm the diagnosis although this cannot be made definitively in most cases without histological examination of biopsy samples.

Systems diseases such as sarcoidosis are one of the most passionate areas in imaging. In both conventional and

atypical presentations the insight of the radiologist may completely transform patient management. To do this, radiologists should advance their knowledge from the beginning of their training and throughout their occupational life, specifically by active participation in multidisciplinary team meetings which undoubtedly represent one of the major advances in medicine in the last two decades.

Disclosure of interest

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

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