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Review

Vertebral involvement in Paget's disease: Morphological classification of CT and MR appearances



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ARTICLE INFO

Article history:

Accepted 30 July 2014

Available online 22 September 2014

Keywords:

Spine

Paget's disease

Magnetic resonance imaging

Computed tomography

ABSTRACT

Vertebral Paget's disease produces a large panel of radiologic appearances sometimes atypical and pseudotumoral. Classical classifications of bone alterations based on pathophysiological hypotheses do not always match the imaging findings. This article will review the computed tomography (CT) and magnetic resonance imaging (MRI) features of Paget's disease of the spine with special emphasis on morphological findings that differentiate Paget's disease from tumors. Combined CT and MRI analyses usually provide the diagnosis of Paget's disease.

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1. Introduction

Paget's disease (PD) or osteitis deformans is a common, chronic, benign disease characterized by excessive and abnormal bone texture remodeling that causes changes in bone shape and alterations in bone marrow. The cause of PD remains unclear [1–6]. The spine is among the sites most often affected with PD. Although the radiological findings are often suggestive, they cover a broad range that includes misleading pseudotumoral presentations. In-depth knowledge of the typical changes in bone texture, vertebral body shape, and bone marrow is therefore crucial to ensure the correct diagnosis.

We therefore tried to subcategorize the different presentations of uncomplicated vertebral PD as demonstrated by computed tomography (CT) and magnetic resonance imaging (MRI) on the base of diffuse and focal morphological abnormalities.

2. Epidemiology of Paget's disease (PD)

PD was first described in 1877 by Sir James Paget in 5 patients [7,8]. PD is a common disease whose prevalence increases with age

from about 1% in adult Caucasians aged 40 to 50 years to 10–11% after 80 years of age [9–12]. In Asia and Africa, in contrast, PD is very uncommon. Recent studies have suggested a decrease over time, in the prevalence of PD with less severe disease but older age at presentation [13–15].

The spine is the second most common site of involvement with PD (29% to 57% of cases), after the pelvis (30 to 75%) [11,16,17]. PD is polyostotic in 66% of patients [18], and, among patients with polyostotic PD, 35% to 50% have vertebral involvement [19]. The most commonly involved spinal segment is the lumbar spine (58% of cases), most notably L4 and L5 [20], followed by the thoracic spine (30%), whereas the sacrum and cervical spine are less often affected (14% of cases) [2,21].

PD is often an asymptomatic condition that is diagnosed fortuitously, although some patients experience symptoms or complications [22]. At the time of diagnosis, PD usually has a polyostotic distribution.

3. Pathophysiology of Paget's disease (PD)

The bone changes that characterize PD reflect disturbances in bone remodeling [23–25]. Several pathophysiological hypotheses have been put forward to explain the radiological findings. PD is generally viewed as a dystrophic disease in which osteoblastic and osteoclastic overactivity leads to accelerated and abnormal bone turnover, with three phases [26,27]:

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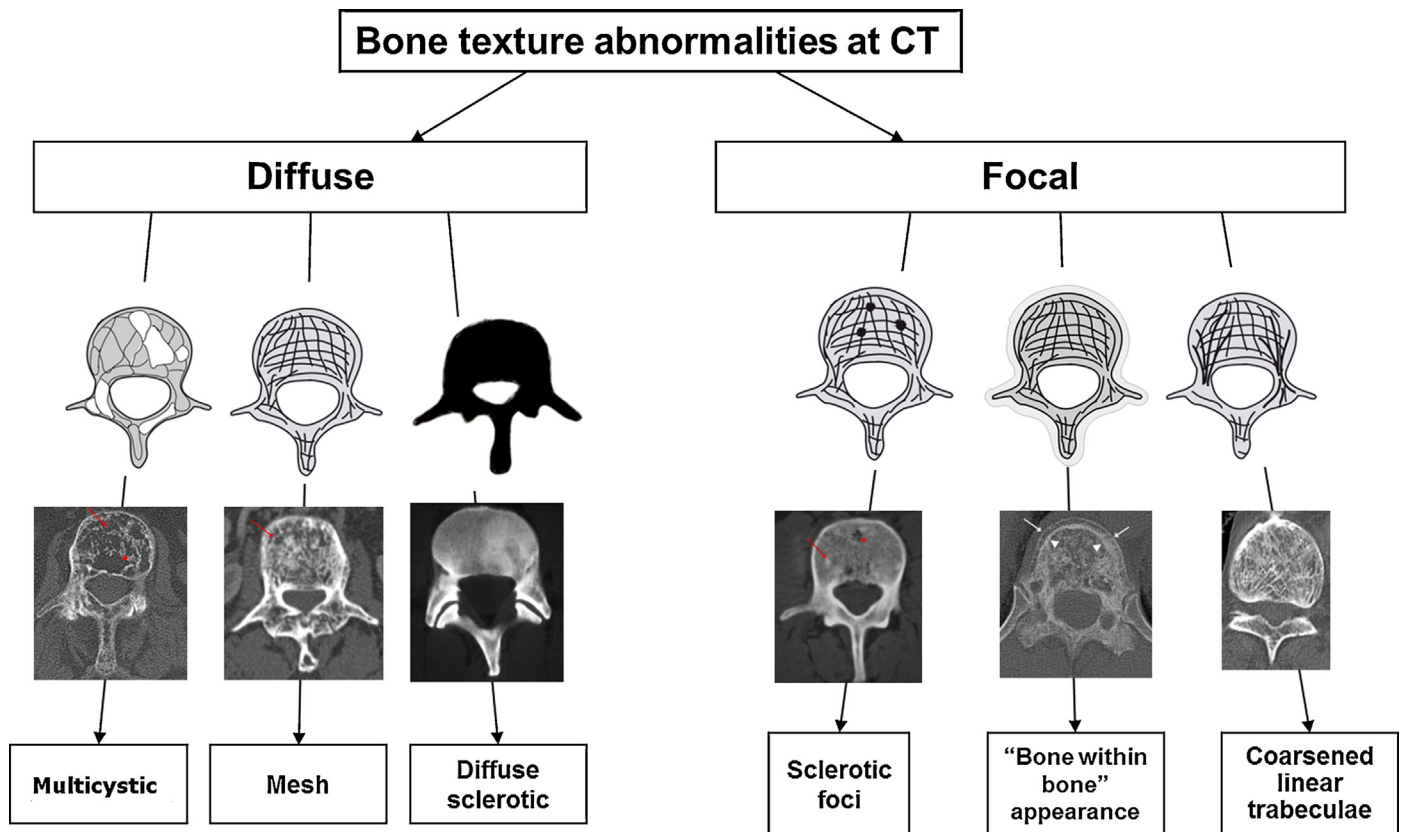


Fig. 1. Pagetic bone texture abnormalities visualized by CT.

- a phase of predominant osteoclastic activity seen as bone loss on radiographs;
- a mixed phase combining osteoclastic and osteoblastic activities with a mosaic appearance of coarse, thick sclerotic bone trabeculae;
- a phase of predominant osteoblastic activity producing thickened disorganized bone with a coarse architecture and fibrous or fatty bone marrow.

However, these three phases occur along a continuum and may co-exist in the same patient at different sites or within the same site. However, this three-stage classification was devised before CT and MRI were available and it is uncertain if it could be applied to the spine. Occurrence of new sites of bone involvement, many years after the disease onset is uncommon but possible [28,29] and may be even rarer in patients under bisphosphonate therapy [30]. In addition to bone remodeling abnormalities, changes in bone size and shape occur.

Lander et al. developed a pathophysiological classification based on the osteoblastic and osteoclastic activities at the periosteal and endosteal bone surfaces, to explain that both bone expansion and bone contraction may be observed in PD [23]. However, in our experience, classifications of bone alterations based on pathophysiological hypotheses do not always match the imaging findings. Therefore, in the present article, a simple morphological imaging classification of the main CT and MRI findings of vertebral PD were preferred.

4. Radiological findings in vertebral Paget's disease (PD)

The radiological alterations seen in vertebral PD fall into three main categories according to whether they affect the bone texture, bone marrow, or vertebral shape. In typical cases, the diagnosis of

PD is based on radiographs, which show bone sclerosis, thickening and hypertrophy of bone trabeculae, and an increase in the antero-posterior and lateral dimensions of the vertebral body. CT and MRI are performed in case of atypical presentation to rule out alternative diagnoses, such as vertebral hemangioma, vertebral metastatic disease, lymphoma, and in case of complication, such as spinal stenosis or suspicion of malignant transformation.

4.1. Bone texture abnormalities (remodeling): CT patterns

Diffuse and focal changes should be distinguished but often occur in combination. In addition, the morphological appearance may be different in the vertebral body and neural arch. Bone texture abnormalities consist of bone sclerosis and bone trabeculae alterations, which are best visualized on CT images (Fig. 1 Supplementary data, Fig. S1) [24].

4.1.1. Diffuse bone texture abnormalities: three main patterns

Three patterns of diffuse bone texture abnormalities can be distinguished at CT [18]:

- the multicystic pattern (Fig. 2a and b) is the most common. Thin sclerotic or normal remaining bone trabeculae delineate cystic spaces that range in size from small (1–5 mm) to large (>5 mm). Posteriorly, the lucency may involve the entire neural arch, producing a hollow bone appearance with replacement of the cancellous bone by soft tissue densities, contrasting with preservation or sclerosis of the cortical bone. The multicystic pattern is often visible both in the vertebral body and neural arch;
- the mesh pattern (Fig. 3) is characterized by scarce and thick intersecting bone trabeculae. The resulting mesh appearance of the cancellous bone may be either loose or dense, depending on the distance between bone trabeculae;

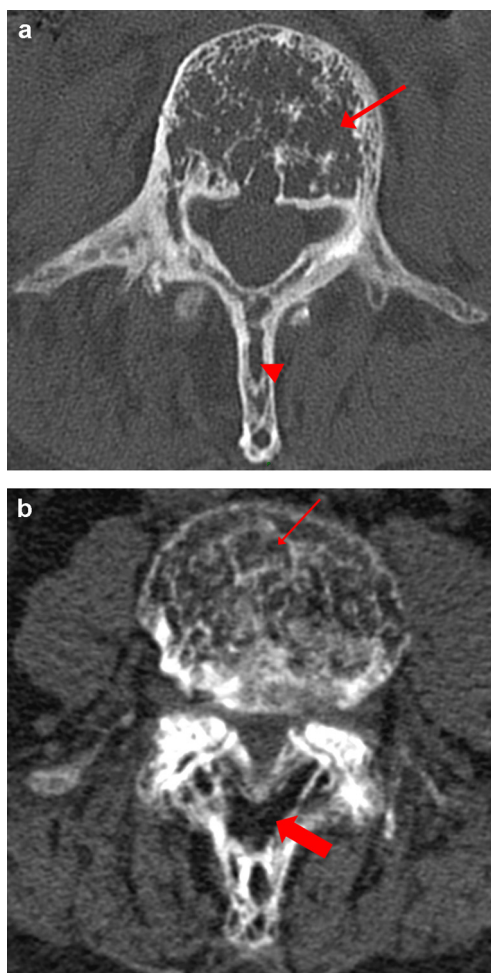


Fig. 2. Diffuse bone texture abnormalities by CT: multicystic pattern. Diagram and examples in three different patients. a: axial CT image: large lytic spaces within the vertebral body (arrow) and neural arch (arrowhead). Nearly all the sclerotic margins in the vertebral body have been erased: vacuolar pattern; b: axial CT image: small lytic spaces within the vertebral body (arrow). Pagetic involvement of the neural arch with a very large lytic lesion (large arrow).

- the diffuse sclerotic pattern (ivory vertebra) (Supplementary data, Fig. S2) is characterized by a diffuse and homogeneous increase in bone density of the vertebral body, whose size and contours remain normal. A similar appearance can be seen in conditions other than PD, such as metastatic disease and lymphoma [31,32].

However, extension of the sclerotic pattern to the entire vertebra, from the vertebral body to the spinous process, is a consistent finding that strongly suggests PD.

4.1.2. Focal bone texture abnormalities: three patterns

Three types of focal abnormalities are commonly encountered: sclerotic foci, horizontal coarse trabeculae, and bone-within-bone appearance:

- sclerotic foci (Supplementary data, Fig. S3) may be solitary or multiple and appear as foci of compact bone with thorny edges. They may suggest sclerotic metastatic disease or malignant transformation complicating PD. However, most patients also have typical diffuse changes, which facilitates the diagnosis of PD;
- bone-within-bone appearance (Supplementary data, Fig. S4a and b) is produced by bone apposition at the periosteal surface of the vertebral body, over the original cortex producing a “double con-

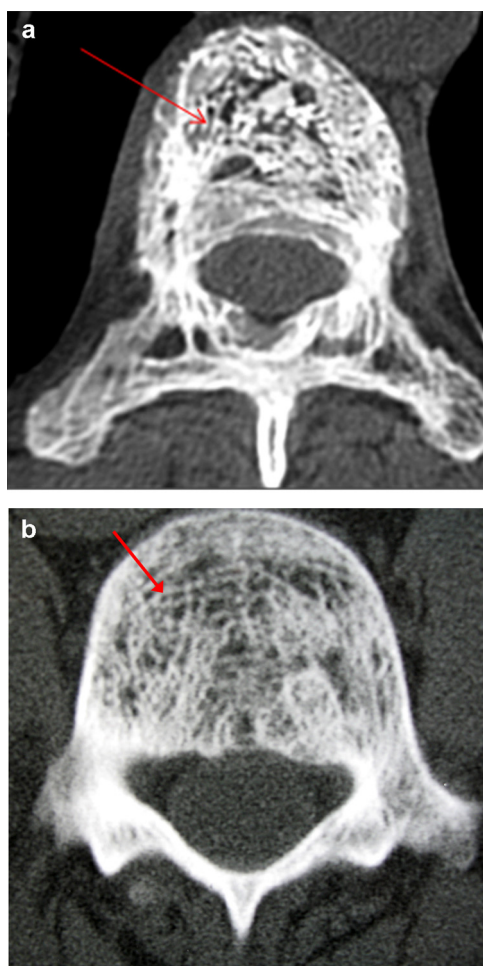


Fig. 3. Diffuse bone texture abnormalities by CT: mesh pattern. Diagram and examples in three different patients with thickened intersected bone trabeculae (arrows). Axial CT image: mixed dense and loose mesh. Axial CT image: dense mesh.

tour” appearance of the vertebral body [23], which seems highly characteristic of PD, especially when associated with diffuse bone texture abnormalities;

- focal thickening of horizontal trabeculae converging toward the pedicles (Fig. 4) may be seen in the vertebral body and/or neural arch. The horizontal, coarse trabeculae are almost parallel to each other, with no intersections, in contrast to the mesh pattern. They correspond to coarsened bone trabeculae located below the sclerotic vertebral endplates. This CT finding is an early stage of the classical picture-frame sign seen within the vertebral body on radiographs.

4.2. Bone marrow abnormalities: MRI patterns

Cancellous and cortical bone are more difficult to evaluate at MRI compared to the CT-scan but should receive careful attention since CT-scan and MRI do not carry the same information. CT-scan allows fine evaluation of bone texture, which is very useful to differentiate PD from other conditions, such as vertebral hemangioma and to some extent, metastatic disease and lymphoma. On the contrary, MRI images the bone marrow and is indispensable to rule out causes of bone marrow replacement, such as metastatic disease and lymphoma. Several diffuse or focal MR patterns of bone marrow abnormalities may be encountered alone or in combination (Fig. 5a and b).

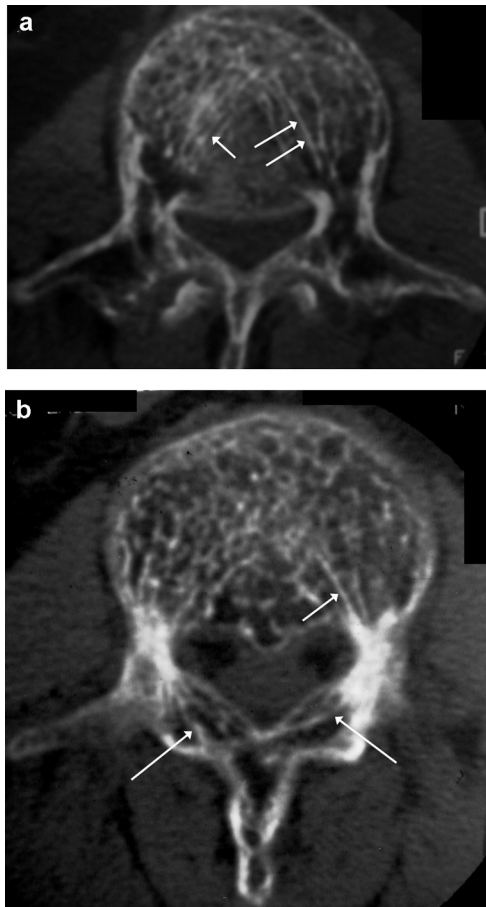


Fig. 4. Focal bone texture abnormalities by CT: horizontal coarsened trabeculae pattern. Diagram and examples in two different patients. a, b: axial CT image through L2: focal thickening of horizontal trabeculae (arrows) oriented almost parallel to one another, within the vertebral body (a, b) and neural arch (b) and converging toward the pedicles.

4.2.1. Diffuse bone marrow abnormalities: four MR patterns

- Normal bone marrow [Supplementary data, Fig. S5a, b and c](#)): at the earliest stages of PD, the bone marrow is preserved or only minimally involved, whereas the trabecular bone is affected [33]. PD may therefore be missed at MRI, as the signal intensity of the vertebral bone marrow may be normal. At this stage, only subtle changes in structure and texture, such as anteroposterior vertebral expansion and minimal cortical thickening, may be visible by MRI. Concomitant evaluation of the radiographic, CT, and MRI findings in the entire vertebra, from the vertebral body to the spinous process, is useful in difficult cases;
- bone marrow edema ([Supplementary data, Fig. S6](#)): at the intermediate stage, the bone marrow in pagetic bone generates high signal intensity on T2-weighted images and low signal intensity with post-gadolinium enhancement on T1-weighted images. These findings indicate non-specific bone marrow edema and occur in 30% of cases of vertebral PD [34]. However, tumoral replacement can produce similar images. MR changes suggesting bone marrow edema rather than bone marrow replacement include:
 - mild and homogenous low SI on T1-WI,
 - mild and homogeneous high SI on T2-WI,
 - mild diffuse and homogeneous enhancement on gadolinium enhanced T1-WI,
 - preservation of bone texture and contours on all MR sequences;
- sclerotic pattern ([Supplementary data, Fig. S7a, b and c](#)): the entire vertebral body exhibits low signal intensity on both T1- and

T2-weighted images, as a result of increased trabecular thickness, sclerosis, and bone marrow fibrosis. Vertebral shape abnormalities and involvement of the entire vertebra support a diagnosis of PD in difficult cases (see above);

- fat pattern ([Supplementary data, Fig. S8](#)): the entire vertebral body generates high signal intensity on T1- and T2-weighted images and low signal intensity on fat-saturated T2-weighted images. At a late stage, confluent areas of normal yellow-bone marrow signal predominate, indicating residual or repopulated fatty marrow. This pattern is also seen in radiation-induced changes, but clinical setting associated bone texture and shape changes and coexistence of typical pagetic lesions at other skeletal sites usually ensure the diagnosis of PD.

4.2.2. Focal bone marrow abnormalities: three MR patterns

Focal abnormalities may be visible by MRI in addition to diffuse changes and may assist in the diagnosis of PD:

- fatty foci ([Supplementary data, Fig. S9a and b](#)): fatty foci generating high signal intensity on T1-weighted images may be seen within the vertebral body or spinous process. They usually correspond to fat-containing vacuoles on CT images ([Supplementary data, Fig. S10b](#)). The presence of fatty foci within the bone marrow is sometimes very useful to rule out a malignancy [35];
- low signal intensity foci ([Supplementary data, Fig. S10a and b](#)): foci of low signal intensity on both T1- and T2-weighted images correspond to sclerotic foci at CT. They often occur in combination with fatty foci;
- picture-frame appearance of the vertebral body or spinous process: a thin high signal peripheral rim on T2-weighted images only also supports a diagnosis of PD ([Supplementary data, Fig. S11a and b](#)).

4.3. Vertebral shape abnormalities

Vertebral shape abnormalities are due to the remodeling effect of the PD process. They are best evaluated by CT.

Enlargement of the vertebral body is the most common shape abnormality, being present in 63% of patients in earlier work [11]. Both the anteroposterior and the lateral vertebral body dimensions may be increased ([Supplementary data, Fig. S12a](#)). Vertebral body dimensions are normally intermediate between those of the suprajacent and infrajacent vertebrae. The anterior and posterior heights of the vertebral body are not increased, since there is no periosteum/endosteum interface at the endplates [36]. In contrast, biconcave deformity of the vertebral endplates due to diffuse bone softening is common in advanced PD ([Supplementary data, Fig. S12b](#)).

Loss of the normal concavity of the anterior vertebral body cortex is a very suggestive other characteristic and early sign of PD ([Supplementary data, Fig. S13](#)).

4.4. Extension within the vertebra

A highly suggestive finding on radiographs, CT, MRI and radionuclide bone scans is involvement in the entire vertebra, from the vertebral body to the spinous process. Vertebral tumors, including malignancies, may involve both the vertebral body and part of the neural arch but, in the vast majority of cases, spare the spinous process. In a previous CT study of patients with vertebral PD, the entire vertebra including the vertebral body and the process was involved in 82% of cases [24]. Isolated involvement of the vertebral body, in contrast, occurred in only 12% of cases [24]. Thus, when non-specific vertebral body changes are found, the visualization of concomitant spinous process involvement at imaging strongly suggests PD.

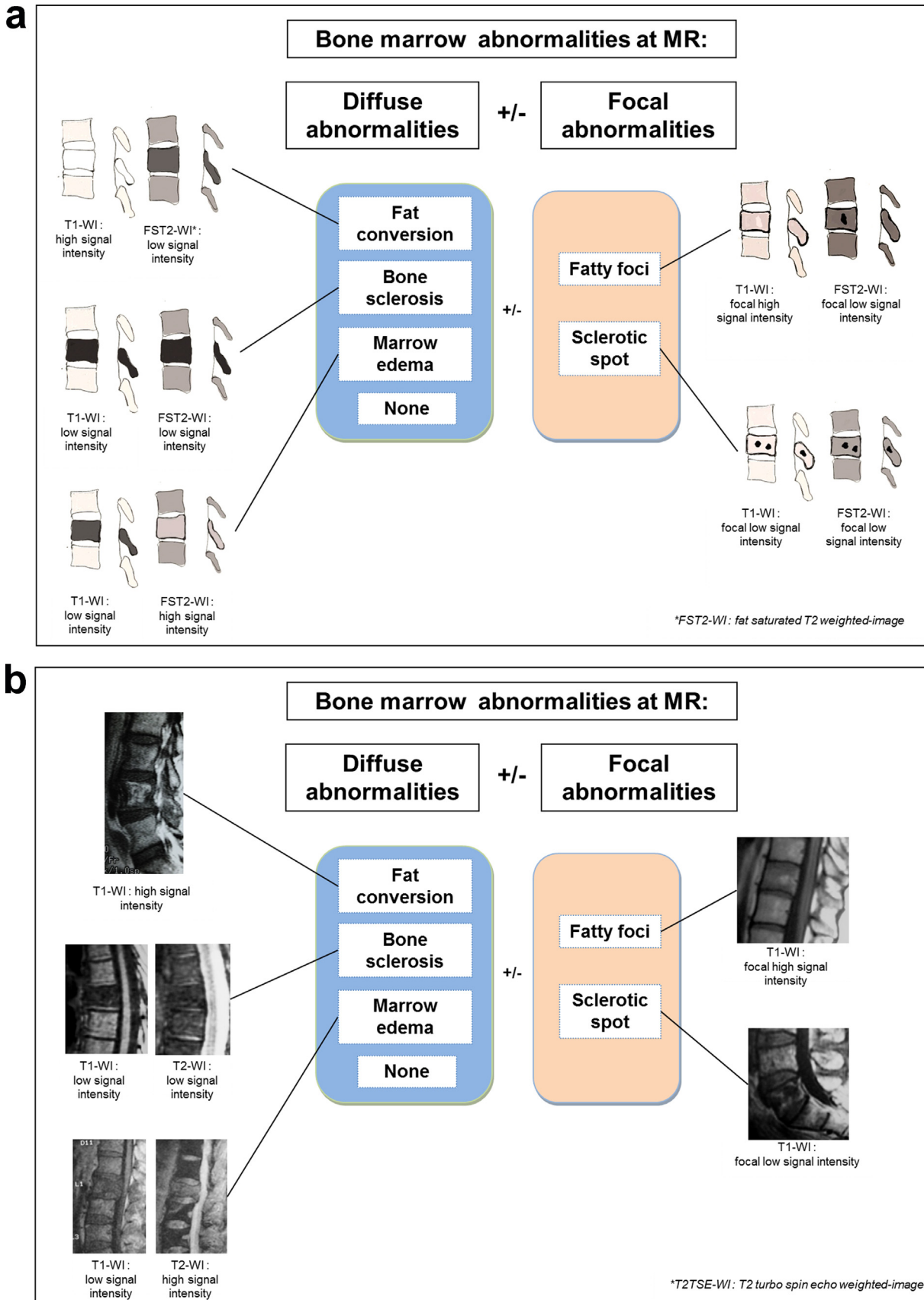


Fig. 5. Patterns of pagetic bone marrow abnormalities by MR. a: diagrams; b: examples.

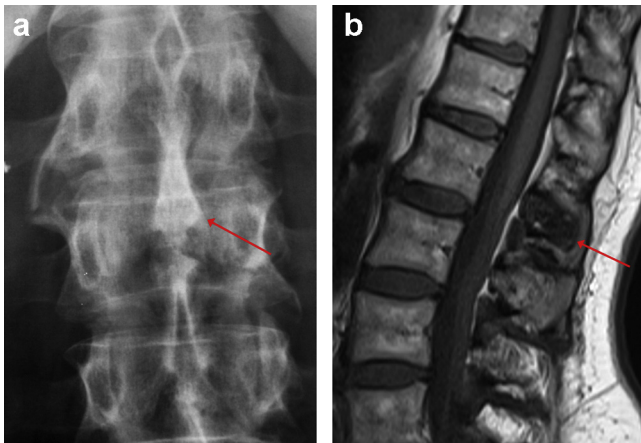


Fig. 6. Extension within the vertebra: isolated involvement of a spinous process. Radiograph and MR correlation in a 55-year-old man with Paget's disease of L1. a: radiograph: enlargement and sclerosis of the L1 spinous process (arrow); b: sagittal MR image, T1-weighted sequence: diffuse low-intensity signal from the spinous process (arrow) and normal signal from the vertebral body.

Isolated involvement of the spinous process has been reported in 6% of cases of vertebral PD (Fig. 6a and b) [11]. However, the proportion of cases with subtle pagetic changes detected in other parts of the vertebra increases when CT or MRI is used instead of radiographs alone.

5. Differential diagnosis

5.1. Vertebral hemangioma

Among benign lesions, vertebral hemangioma is the most challenging condition to differentiate from PD, as coarsened trabeculae are present in both conditions. Typically, vertebral hemangiomas exhibit a predominance of vertical coarsened trabeculae producing a characteristic vertically striated appearance, whereas in vertebral PD the coarsened trabeculae under the endplates have a predominantly horizontal orientation (Supplementary data, Fig. S14a) [37]. In addition, vertebral body size is normal in quiescent vertebral hemangioma, and the neural arch is usually spared (Supplementary data, Fig. S14c). Aggressive hemangiomas, however, usually present with neural arch involvement and an epidural soft tissue mass [38]. The mid-height of the vertebral body may be enlarged, with convex anterior and posterior cortices, but the anteroposterior dimension of the vertebral endplates is not increased, in contrast to PD (Supplementary data, Fig. S14b) [38].

5.2. Other differential diagnoses

Vertebral sclerosis due to PD must be differentiated from several other conditions, especially vertebral metastasis and lymphoma. The above-described CT and MRI features assist in this task.

In conclusion, vertebral PD usually produces suggestive radiological changes. However, the broad range of possible radiological presentations includes several pseudotumoral patterns, most notably ivory vertebra. Careful attention to a number of features that strongly suggest PD can help to rule out a malignancy. The combination of CT and MRI findings that most strongly suggests PD is as follows:

- diffuse multicystic or mesh patterns of bone structure;
- vertebral enlargement;
- involvement of the entire vertebra from the vertebral body to the spinous process;
- fatty or normal bone marrow content.

After a detailed evaluation of all the features described in this review, a bone biopsy to rule out a malignancy is required in only a very small percentage of cases.

Contributors

All authors approved the entirety of the submitted material and contributed actively to the study.

Disclosure of interest

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

Appendix A. Supplementary data

Supplementary data (Figs. S1–S14) associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jbspin.2014.07.009>.

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