Systemic mastocytosis involving bone: a diagnostic challenge for the radiologist.

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Learning objectives

To expose and review the mastocytosis' radiological patterns.

Revise the differential diagnose of bone marrow involvement with similar imaging characteristics.

Background

Systemic mastocytosis is a haematogenous disease characterized by the abnormal spread and aggregation of mast cells in one or many locations, being the cutaneous form the most prevalent. Involvement of the axial skeleton in seen in the 70% of cases in the systemic form representing a major diagnostic criteria.

Clinically, it usually remains asymptomatic, with roughly localized pain in 20% of the cases. Even so, this subgroup is supposed to have a more aggressive course. Its unspecific onset presentation, in conjunction with its low frequency, estimated in 1/30,000, force to take into account this entity in the differential diagnosis of a wide range of diseases.

The complex pathogenesis of the disease is still unknown although histamine secretion seems to stimulate the fibroblastic activity with osteoid formation. Simultaneously, heparin and prostaglandin secretion could promote osseous reabsorption. [1] Bone can be affected by a direct path with abnormal cell accumulation and by indirect secondary hormone-related effects.

Findings and procedure details

CT SCAN

CT scan is the gold standard, for its sensibility in detecting focal and diffuse disease as well as secondary complications or as to guide the biopsy. Imaging presentation includes lytic and blastic lesions representing the concurrent decreased and increased bone mass, respectively. Even though no specific radiological pattern can be emphasized, osteopenia and osteoporosis predominate, followed by osteosclerotic and mixed forms [6]. Radiologists must suspect this pathology when multiple blastic lesions (with no oncologic previous history) or atypical osteoporotic forms arise [2]. In our group, the most common presentation was osteosclerosis with suspected metastatic disease as the first
option Fig. 13. Just one case presented as an idiopathic male osteoporosis complicated with vertebral fractures Fig. 13. Moreover, characterization of the lesions (presence, location, extent and type) is important as, when treatment is established, lesions can undergo dynamic changes turning from focal lesions to diffuse lesions and reversing its density Fig. 3 on page 5 [4].

NUCLEAR MEDICINE STUDIES

Complementary, MRI is used to evaluate the medullar involvement, correlating the histopathological findings with cellular infiltration. Hypo-intensity signal in T1-weighted images is identified while T2-weighted and STIR images are more unspecific, displaying hiper-, iso- and hipointensity, signal, depending on the fibroblastic activity. Sclerotic lesions show low intensity on both T1 and T2-weighted images Fig. 4 on page 7. Contrast administration is not imperative, but if it is administered, marrow enhancement traduce mast cell infiltration [5]. MRI can also contribute in assess complications Fig. 5 on page 7 and on the follow-up studies, increased signal in T1 images and decreased in T2 images, can be interpreted as response to treatment. Diffuse-weighted imaging can help distinguishing mastocytosis bone lesions from normal hematopoietic tissue in young patients, demonstrating restricted diffusion [5].

Other nuclear techniques don't seem to contribute portentously nowadays even though the role of PET is still unclear [7]. The FGD uptake presents a physiologic distribution with eventual uptake in lytic lesions. Nuclear technique imaging are frequently inconclusive. Fig. 13

HISTOLOGIC STUDIES

The anatomic-pathologic study, with an immune-histochemical analysis, will eventually lead to a final diagnosis [1]. In the microscopic view of a histologic sample of affected bone marrow, an important proliferation of irregular bone trabecula is visualized and a significant homogeneous cell population can be identified with the hematoxylin-eosin and Giemsa stains Fig. 7 on page 8. CD117 expression confirms the presence of mastocytes Fig. 8 on page 9. In our group, despite many analytic and imaging studies were performed, definite diagnose was not achieved until bone marrow biopsies were obtained and further analyzed Fig. 9 on page 10 [3].

DIFFERENTIAL DIAGNOSE
The differential diagnose in lytic forms must consider osteoporosis, sickle cell anemia, hyperparathyroidism, plasma cell myeloma and thalassemia. On the other hand, in sclerotic forms, metastatic lesions (mainly from breast, Fig. 10 on page 10, and prostate cancer, Fig. 11 on page 11), tuberous sclerosis, idiopathic myelofibrosis and Paget's disease must be evaluated [12].

Images for this section:

Fig. 1: A 48-year-old women with no relevant medical history and multiple poorly defined sclerotic lesions in the thoracic and lumbar vertebral bodies and sacrum bone (red arrows), discovered as an incidental finding. The first possible diagnose was metastatic disease from an unknown primary tumor but posteriorly biopsy revealed the systemic mastocytosis diagnose.

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**Fig. 2:** 42-year-old women with multiple sclerotic disease affecting predominantly the axial bones with biopsy-proven systemic mastocytosis. Axial CT image in osseous window showing increased bone density in three sclerotic lesions with well-defined margins in L2 (red arrows). Axial volume rendering image showing the corresponding nodular mast cell infiltration in the vertebral body (red arrows).

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<th>Región</th>
<th>Área (cm²)</th>
<th>CMO (g)</th>
<th>DMO (g/cm²)</th>
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Fig. 3: Male patient of 44 years-old and multiple spontaneous vertebral fractures. Densitometry images in the left femoral bone showing a T-score of 2.5 and a Z-score of 2.3, indicative of osteopenia.

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Fig. 4: Axial plane T1-weighted and STIR images showing low signal intensity in comparison with the adjacent muscular tissue in the right pubis (red circle). In the inferior CT axial image, the correspondent sclerotic lesion can be identified (red circle).

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Fig. 5: Same patients as Fig.3. Sagittal plane in T1-weighted images showing multiple cervical, thoracic and lumbar fractures affecting either plates or the superior plate. No nerve damage secondary to compression was visualized.

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Fig. 6: Same patient as Fig.1. Anterior and posterior delayed technetium-99 whole body scintigraphy images showing homogeneous tracer distribution without asymmetry or areas of pathologic uptaking. Corresponding CT coronal images show diffuse undefined sclerotic vertebral lesions.

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Fig. 7: Histopathological findings of systemic mastocitosis. Sample of affected bone marrow with an important proliferation of irregular bone trabecula can be identified (red arrows) as well as a significant centrally located homogeneous cell population (red dashed line). Same sample with hematoxylin-eosin and Giemsa stains.

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Fig. 8: Immunohistochemistry for CD117. Expression of this marker confirms the presence of mastocytes with a strong cytoplasmatic and membrane staining pattern.
Fig. 9: Same patient as Fig.1. Right iliac bone CT-guided biopsy with 8G needle in the patient in prone position with a transgluteal access.

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Fig. 10: CT sagittal images corresponding to 44(right) and 83(left) year-old women with diagnosed breast cancer. Right image shows a diffuse marrow sclerosis of the cervical spine, corresponding with metastatic disease (Notice complete collapse of C6 and inversion of the anatomical lordosis). Left image shows sclerosis well-delimited focus in the spine processes also corresponding to metastatic disease. Both imaging findings could match with mast cell infiltration in another clinical context.
**Fig. 11:** Sagittal T1-weighted images corresponding to 80(right) and 74(left) year-old men with diagnosed prostate cancer. Right images shows diffuse low signal intensity in the lumbar spine (Notice L1-L2 partial collapses). Left image shows countless focal lesions with low signal intensity affecting the lumbar vertebral bodies (Notice collapse of the superior plate of L4). Both imaging findings are equivalent with metastatic disease but could match with mast cell infiltration in another clinical context.

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Conclusion

Bone involvement in systemic mastocytosis must be included in the differential diagnosis of atypical osteopenia and diffuse osteosclerotic lesions.

The inexistent clinical correlation, make its filiation even more difficult. Bone involvement is a prognostic factor as it entails an aggressive course of the disease.

Radiologists must be aware and be able to identify the imaging features in order to accomplish a prompt and accurate diagnose in the appropriate clinical context.

From a radiological point of view, in many cases it is impossible to distinguish mastocytosis bone involvement from metastatic disease and, consequently, biopsy is mandatory.

Personal information

References

