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Case Report

Bone Presentation of a Systemic Mastocytosis: Clinical, Imaging and Histopathology

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Abstract

We present a 28-year-old male patient with a history of health who 4 months before going to the center began to present pain in the upper dorsal spine that radiated to the right scapula after physical exertion, improving little with the usual treatments, which is why he went to the doctor, who indicated X-rays, presenting multiples sclerotic lesions in pelvis, both humerus and proximal femurs. Given the diagnostic possibility of systemic bone mastocytosis, decides to admit it for study. Because it is an infrequent and difficult to treat tumor, it is an important to take advantage of the scientific-technical means that we have at our disposal that help us reach a diagnosis of certainty.

Keywords: Mastocytosis; Hematology; Diagnosis

Introduction

Mastocytosis is a rare clinic event (prevalence 1/10,000), characterized by the abnormal proliferation of mast cells, often painless and non-neoplasm. This disease can occur at any age, being more frequent in adulthood and can affect both sexes but especially males. The etiology is unknown and they are very heterogeneous in their form of presentation, evolution and prognosis.

Mastocytosis can be divided into two categories: located in the skin and systemic that affects several organs such as the gastrointestinal tract, liver, lymph nodes and bone marrow. Clinical findings are determined in part by histamine secretion by mast cell and produced the clinic event: focal urticaria, redness, episodes of shock, diarrhea and vomiting. In the most severe cases, weight loss, weakness, poor general condition and peptic ulcers are observed. Among the hematological alterations are observed: leukopenia, thrombocytopenia and eosinophilia. The prognosis is variable, depending on the degree of systemic involvement. The bone marrow represents the most frequently chosen extracutaneous biopsy site to establish the diagnosis of systemic mastocytosis.

Case Report

This is a 28-year-old male patient with a history of health who comes to our centre with a history that 4 months ago after a physical effort begins with intense pain at the level of the upper

dorsal spine with irradiation to the right scapula that did not yield with the usual treatments (analgesics, anti-inflammatory and physical therapy). It is decided to a radiological study and before the appearance of sclerotic bone lesions disseminated by the pelvis and both proximal humerus it is decided to admit them for study.

Clinical exam

- **Inspection:** Several decrease of the adipose panicle. Patient attitude in discrete__dorsal cyphoescoliosis, difficulty maintaining the position. No tumor, no flushing, and no other inflammatory symptoms.
- **Palpation:** Intense pain under pressure of the spine processes of dorsal 3, 4, 5, 6, as well as on the inner edge of the right scapula, firm, non-painful axillaries and inguinal a lymphatic nodes. The abdomen palpation present the left lobe of the liver exceed the midline by 2 cm.
- **Joint mobility:** Limited movements of the trunk due to pain, rest of the joints preserved mobility.
- **Reflections:** Present.
- **Sensitivity:** Preserved.
- **Vascular pulses:** Present and synchronic. Do not varicose veins or microvarices.

Laboratory test

- Hemoglobin: 13.4 g/L.
- Hematocrit: 0.38.
- Leucogram: $4.2x10^9$/L.
- Platelet count: 150 x 10^9/L.
- Eritrosedimentatión: 16 mmol/h
- Protein C reactive: Negative.
- Calcium: 2,65 mmol/L.
- Phosphorus: 1,5 mmol/L.
- Alkaline phosphatase: 4950 U/L.
- Uric acid: 460,5 mmol/L
- Creatinine: 480.3 mmol/L
- TGP: 24 U/L.
- TGO: 8 U/L. U/L.
- GGT: 114,7 U/L.
- PSA: o.17 mg/L
- Serology: Non-reactive
- HIV: Negative

Imagin study

Digital bone survey

In vertebral bodies, pelvis, proximal and distal of both humerus and proximal femurs, multiple lesion, predominantly sclerotic and mixed lesions of various sizes and appearance, showing some well defined and homogeneous especially in the proximal portions of the long bones, while in the pelvis and vertebral bodies they are diffuse in D 12, L1 and L3.

Figure 1: Spine and pelvis view: Anteroposterior pelvis (AP) and lumbar spine AP. There is a loss of the definition of the posteroinferior cortical of D4 with irregularity of its lower wall in relation to pathological fracture at that level. Osteoporosis of the segments studied.

Chest x-rays

Diffuse and disseminated nodular reticulum pattern in both pulmonary, at lung right predominance associated with heterogeneous paracardiac radiopacity. Discreet right hiliar thickening.

Abdominal ultrasound

Liver of homogeneous ecostructure, the left lobe lowers the midline by 2 cm. Rest of the organs of superior hemiabdomen of normal appearance and size.

Osseous scintigraphy

(Technetium 99 MDP): Intense accumulation in shoulders, sternum, wings of the iliac bones, upper third of both femurs, skull, ribs and vertebral body of D3 and D4.

Chest tomography

Observe osteolytic and osteoblastic lesions disseminated in the pulmonary parenchyma of various diameters.

Fracture by crushing D4 whose posterior wall penetrates into the spinal canal compressing the medulla and narrowing the holes of conjunction to left predominance, the osteolytic lesions at this level have extended towards the transverse processes and posterior arches.

Disseminated and interstitial pattern in both pulmonary fields to hiliar predominance.

Figure 2: Thorax cross section tomography.

Figure 3: Chest reconstruction.

Observe the right lung there is an hyperdense image of nodular appearance whose contours are irregular. The interlobal fissure is thickened. Towards the anteroexternal portion of the left pulmonary base there are other lesions with similar characteristics. Presence of mediastinal adenopaties.

Abdomen tomography

From the lower half of D12 to the sacrum including the pelvis and hips there are extensive mixed lesions, some well delimited. The vertebral body of L3 is totally sclerotic.

Hepatomegaly, periaortic and peripancreatic linfo nodes.

Figure 4: Abdomen transversal slide.

Clinic and imaging diagnosis

- Hodgkin lymphoma
- Mastocytosis systemic associated with leukemia or other hematologic disease.
- Mastocytes leukemia.

Histology diagnosis

Bone Mastocytosis. (B21-079).

Discussion

Mastocytosis constitutes a rare group of diseases (prevalence 1/10,000), characterized by the abnormal proliferation of mast cells, often painless and non-neoplasm. Mastocytosis can occur at any age, being more frequent in adulthood and can affect both sexes but especially males. The etiology is unknown and they are very heterogeneous in their form of presentation [1], evolution and prognosis.

Systemic mastocytosis (SD), a clonal proliferation of mast cells, is defined by the World Health Organization (WHO) as the infiltration of these cells into at least one extracutaneous organ, in the presence or absence of signs of skin involvement [2]. MS is a very heterogeneous disease, including indolent forms with a normal life expectancy [2,3]. Virulent forms such as aggressive MS (MSA), mast cell sarcoma, and mast cell leukemia are also described [2,3]. MS associated with haematological clonal proliferation of a different mastocyte lineage (MS-NHNM) constitutes 20% to 30% of cases [2,3].

The evolution of patients with this association depends fundamentally on the prognosis of concurrent hematological neoplasm.

Bone involvement in systemic mastocytosis

In a recent study in which 213 cases published between 1977 and 1997 in the universal literature have been reviewed, the predominance of diffuse forms (90% of cases) is revealed. The radiological pattern that appears mentioned in a greater number of subjects is osteoporotic (49.5%), followed by osteosclerotic (33%) [4].

Circumscribed lesions appear equally in prepubertal and postpubertal, while 90% of diffuse lesions occur after puberty and half of them in those over 50 years of age. Circumscribed areas present as small, well-delimited osteoblastic and osteolytic areas. Localized condensation images take the form of spots or islets similar to metastatic nodules in the metaphyses of long bones; forming linear condensations in the iliac wing; triangular or rounded in one or more vertebrae; dense islets in the skull; thickening in the cortical of the long bones. Osteolytic images, less frequent, are located mainly in the skull and in the long bones.

Circumscribed lesions do not progress and may disappear spontaneously. They are usually not associated with systemic disease and no cases have been reported that progressed to the diffuse form. The diffuse ones are distributed throughout the skeleton and do not present a net demarcation with respect to the surrounding bone. They present as osteoporosis and osteosclerosis. Injuries settle more in the spine and ribs. Diffuse lesions may remain static for years or progress slowly or quickly. Patients often acquire the malignant form of the disease [5-7].

In the indolent form of systemic mastocytosis, the most frequent bone involvement is osteoporosis, mainly vertebral [8,9], and osteosclerotic lesions may appear simultaneously in the pelvis, long bones, etc., with osteolytic lesions being rare. In aggressive systemic mastocytosis, osteosclerotic lesions are more frequent, being osteoporosis very rare.

The diagnosis and classification of mastocytosisis based on the identification of mast cells by morphology, immunophenotype or genetics, using the criteria of the World Health Organization 2008, which divides tumors into the following categories:

- Cutaneous mastocytosis (limited to the skin),
- Extraccutaneous mastocytoma (unifocal mast cell tumor with non-destructive characteristics),
- Mastocyte cell sarcoma (unifocal mast cell tumor with destructive characteristics and poorly differentiated),
- Systemic mastocytosis that invariably affects the bone marrow, manifests with skin lesions and is more frequent in adults [10,11].

The clinical manifestation of mastocytosis is heterogeneous, from a disease limited to the skin, as in the case of cutaneous mastocytosis 12 to more aggressive manifestations with extracutaneous damage that can occur with dysfunction or multi-organ insufficiency and decrease life expectancy. Generalmente affects adult patients [13,14].

Mastocytosis can affect the skin (cutaneous mastocytosis); the stomach, intestine, liver, spleen, lymph nodes and bone marrow (systemic mastocytosis) producing some dysfunction in the organs. Systemic mastocytosis has another form: aggressive systemic mastocytosis that evolves rapidly and is related to organ damage.

Other forms of systemic mastocytosis are mast cell leukemia and mast cell sarcoma. The most frequent symptoms that may appear are focal urticaria, redness, episodes of shock, diarrhea and vomiting. In the most severe cases, weight loss, weakness, poor general condition, hepatosplenomegaly, adenopathies, and peptic ulcers are observed. Among the hematological alterations are observed; anemia, leukopenia, thrombocytopenia and eosinophilia. The bone marrow represents the most frequently chosen extracutaneous biopsy point to establish the diagnosis [15].

Terapeutic

At present there is no curative treatment of systemic mastocytosis and pharmacological treatment shows no increase in survival. The current treatment recommended by the World Health Organization against systemic mastocytosis is mainly palliative and aimed at symptoms caused by mast cell degranulation, such as pruritus, urticaria, angioedema, erythema, nausea, vomiting, abdominal pain, diarrhea, anaphylaxis, skin diseases (for example, urticaria pigmentosa) or organ dysfunction due to mast cell infiltration.

Terapeutic options range from observation-only, measures to avoid symptoms related to the release of mast cell mediators, support measures (transfusions or osteoporosis treatment) to cytoreductive treatment, aimed at reducing neoplastic cells, which is reserved for patients with aggressive conditions or severely affected by adverse effects. Neuropsychiatric symptoms, such as headache, loss of concentration, memory loss, fatigue or depressive symptoms, are seen in approximately 33% of adults with mastocytosis [16,17]. Treatment includes second-generation antihistamines, leukotriene antagonist, antidepressants, and psychological support.

Bone and soft tissue pain is common in mastocytosis [18] and is related to the synthesis of prostaglandins; however, the mechanisms are poorly understood. Treatment should include nonsteroidal anti-inflammatory drugs, second-generation antihistamines, leukotriene antagonists, in addition to exercise and physiotherapy [19]. Bisphosphonates relieve pain in patients treated for osteoporosis [20]. Interferon alfa (IFN- α) is the first-line cytoreductive therapy [21] in patients with symptomatic systemic mastocytosis. Since its first report in 1992 it has been administered (IFN-α) in small doses with significant reports of symptom relief.

Cytoreductive treatment: It is necessary. Danorrubicin, doxorubicin and vincristine have shown usefulness.

In the latest research, Imatinib is the only KIT-targeted drug that has received approval from the U.S. Food and Drug Administration for the treatment of aggressive systemic mastocytosis [22]. Second-generation drugs, such as dasatinib and nilotinib, have shown little clinical efficacy.

Conclusions

Systemic mastocytosis is a rare disease of varied symptomatology related to the release of mast cell mediators and tissue infiltration of organs. For its correct diagnosis, clinical, cytometric and pathological criteria are necessary (aggregates of mast cells of 15 or more mast cells in bone marrow or other organs), and therefore bone marrow biopsy is considered indispensable.

Participation of the Authors

Dr. Vilma Rondón García radiologist of the case who gave the first diagnostic impression, interpreted the images and wrote the reports, Dr. Alicia Tamayo Figueroa and Dr. Ragnar Calzado Calderón doctors of assistance, surgeons of the case and editors of the first manuscript, Dr. Eddy Sánchez Noda, pathologist in charge of the pathology diagnosis, Lic. Juan Carlos Álvarez Rodríguez, reviewer of the bibliography and the final document, Physiotherapist in charge of rehabilitation.

Conflict of Interest

The authors declare that there are no conflicts of interest in this work.

Bibliography

1. Muro MD., *et al*. "Mastocytosis and clinical expression. A follow-up study of three cases". *Spain Allergology and Clinic Immunology Journal* 9 (1994): 277-281.

2. Horny HP., *et al*. "Mastocytosis (Mast cell disease)". In: Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, Vardiman JW, eds. World Health Organization (WHO). Classification of Tumours. Pathology and Genetics. Tumours of Haematopoietic and Lymphoid Tissues, IARC Press: Lyon, France 2 (2008): 54-63.

3. Lim KH., *et al*. "Systemic mastocytosis in 342 consecutive adults: survival studies and prognostic factors". *Blood* 113 (2009): 5727-5736.

4. Sánchez Montero MB., *et al*. "Bone Mastocytosis, diagnosis". *Internal Medicine* 17 (2000): 267-273.

5. Uzcátegui L and Rodríguez Santana. "Bone metabolism unusual diseases in adolescents". Sclerosis disease. In REEMO, 8 (1999): 74-79.

6. "Bone disease radiologic diagnosis: Panam Ed". Mexico (1984): 325-334.

7. "Non frecuent osteoporosis causes". II Virtual Patology Hispanoamerican Congress (1998).

8. Schoanaers P., *et al*. "Systemic mastocytosis, an unusual cause of osteoporosis". *Clinical Rheumatology* 6 (1987): 458-462.

9. Grardel B and Hardouin P. "Mastocytosis and bone manifestations. Results of the survey of the bone and phosphorus-calcium metabolism. Section of the French Society of Rheumatology". *Revue du rhumatisme et des maladies ostéo-articulaires* 9 (1992): 57-63.

10. Horny HP., *et al*. "WHO Classification of tumors of hematopoietic and lymphoid tissues". Lyon: IARC, (2008): 54-63.

11. Metcalfe DD. "Mast cells and mastocytosis". *Blood* 112 (2008): 946-956.

12. Caplan RM. "The natural course of urticaria pigmentosa. Analysis and follow up of 112 cases". *Archives of Dermatology* 87 (1963): 146-157.

13. Uzzaman A., *et al*. "Pediatric-onset mastocytosis: a long term clinical follow up and correlation with bone marrow histopathology". *Pediatrics Blood Cancer* 53 (2009): 629-634.

14. Lim KH., *et al*. "Systemic mastocytosis in 342 consecutive adults: survival studies and prognostic factors". *Blood* 113 (2009): 5727-5736.

15. Donald Resnick MD. "Bone and articulations in Image 2da Ed". Marban books, SL (1998): 640-648.

16. Moura DS., *et al*. "Evidence for cognitive impairment in mastocytosis: prevalence, featuresand correlations to depression". *PloS One* 7 (2012): 39468.

17. Moura DS., *et al*. "Depression in patients with mastocytosis: prevalence, features and effects of mast therapy". *PloS One* 6 (2011): 26375.

18. Johnstone PA., *et al*. "Radiotherapy of refractary bone pain due to systemic mast cell disease". *American Journal of Clinical Oncology* 17 (1995): 328-330.

19. Horan RF., *et al*. "Cromolyn sodium in the management of systemic mastocytosis". *JACI* 85 (1990): 852-855.

20. Lim AY., *et al*. "Systemic mastocytosis: a rare cause of osteoporosis and its response to biphosphonate treatment". *Annals of the Rheumatic Diseases* 64 (2005): 965-966.

21. Valent P., *et al*. "Diagnostic criteria and classification of mastocytosis: a consensus proposal". *Leukemia Research* 25 (2001): 603-625.

22. Alvarez-Twose I., *et al*. "Complete response after imatinib mesylate therapy in a patient with well-differentiated systemic mastocytosis". *Journal of Clinical Oncology* 30 (2012): 126-129.