



# Lvement in Systemic Mastocytosis: Multiple Osteoporotic Vertebral Fractures. Case Report and Review

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## Abstract

**Background Context:** Mastocytosis comprises a wide range of disorders characterized by an excessive proliferation and accumulation of mast cells in the tissue.

**Purpose:** To describe a rare case of aggressive systemic mastocytosis in the lumbar spine in a young patient.

**Study Design:** Case report.

**Methods:** We present the case of a 42-year old male patient, who presented episodes of general redness of 6 months of evolution, associated with diarrhea and lower back pain of one year of evolution. The physical examination reveals hyperpigmented macules on both lower limbs. We performed a biopsy with the results of aggressive systemic mastocytosis. We carried out a bilateral transpedicular vertebroplasty with a biphasic reabsorbable ceramic bone replacement in L4 and L5.

**Conclusions:** In view of the age of the patient and his recovery potential we have replaced the classic vertebroplasty of methyl-methacrylate with a biphasic reabsorbable ceramic bone piece with very satisfactory results.

**Keywords:** Aggressive systemic mastocytosis; Lumbar; Vertebroplasty; Methyl-methacrylate; Biphasic reabsorbable ceramic bone

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Received Date: 03 Mar 2018

Accepted Date: 07 Jun 2018

Published Date: 14 Jun 2018

### Citation:

Pescador D, Parrilla CM, Lorenzo JA, Fernández T, Montesdeoca A, Blanco J. Lvement in Systemic Mastocytosis: Multiple Osteoporotic Vertebral Fractures. Case Report and Review. *Ann Spine Res.* 2018; 1(1): 1004.

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## Introduction

Mastocytosis comprises a wide range of disorders characterized by an excessive proliferation and accumulation of mast cells in the tissue. In 1869, Nettle ship described urticaria pigmentosa and, in 1887, Unna described an increased amount of mast cells in that same pathology. In 1949, Ellis described a systemic disorder associated with mast cell hyperplasia infiltrating the skin, bone marrow, liver, spleen, digestive tract and lymph nodes [1,3]. Most of the affected patients are adults, although this condition may appear at any age, with a slight predominance in men.

The clinical symptoms are variable and take place as a consequence of the mast cell infiltration in the organs and tissues, as well as of the release of biochemical mediators. Mast cells contain cytoplasmic granules with powerful biochemical mediators, such as histamine, neutral proteases (including trypsin and chymase), heparin and several cytokines and arachidonic acid derivatives, such as prostaglandin D and leukotrienes. It is particularly important to suspect a systemic mastocytosis in patients with unexplainable vascular instability, anaphylactic shock of unknown origin, idiopathic reddened skin and face, diarrhea, cephalalgia and other symptoms that may be related with a secretion of mediators [2].

Systemic mastocytosis is characterized by an infiltration in the organs without altering their functions (among them, bone marrow in 100% of the cases). Bone lesions, which can affect the entire axial skeleton, may either appear as areas with osteoporosis secondary to malabsorption or as areas with osteosclerosis due to mast cell infiltration. They present a high degree of clinical variability, ranging from asymptomatic forms that go unnoticed quite frequently to aggressive forms of presentation that lead to multiple spinal fractures [3].

## Case Presentation

We present the case of a 42-year old male patient with a personal record of adverse reaction to iodized contrast, who presented episodes of general redness of 6 months of evolution, associated



**Figure 1:** A) MRI of the dorso-lumbar. Multiple vertebral compression fractures from L2 to L5 with loss of height over 50%; B) CT lumbar scan. Vertebral wedging in the 4 last lumbar vertebrae.



**Figure 2:** CT lumbar scan A) Sagittal. B) Axial. The imaging study revealed an adequate restructuring of the vertebral fractures.

with diarrhea.

The patient also reported repeated lower back pain of one year of evolution, which had increased in intensity in the last two months. The pain irradiated towards the anterior part of both thighs and it increases when walking and sitting. No dysesthesias, paresthesias or difficulty walking were found. The patient lost 5 kg in the last 3 months. He did not report traumatism. The physical examination reveals hyperpigmented macules on both lower limbs. Darier’s sign was negative. No peripheral adenopathies were observed on palpation. Moderate pain in the lumbar area of the column on palpation. The patient did not lose strength, muscle tone or sensitivity. Rotations were normal. Oswestry Disability Index (ODI) was 92% and Visual Analogue Scale (VAS) was 9.

The following complementary tests were carried out:

- Medical analysis: Complete blood count, biochemical analysis, calcaemia, phosphataemia, iron levels, vitamin B12, folic acid, quantitative determination of serum immunoglobulins and serum-free light chains, tumoral markers, TSH, T4L, intact PTH, FSH, LH, prolactin, cortisonemia, catecholamines and serum histamine, which were normal. Total serum tryptase: 34.4 mcg/ml (normal values 0-13.5). In the 24-hour urine test: hypercalciuria: 559 (normal values 50-260) and histamine: 67.2 (normal 0-61).
- Simple bone scan: General osteopenia and compression fractures in the lumbar vertebrae (L2, L3, L4 and L5). Multiple lytic lesions in the vault, pelvis and both femurs.
- MRI of the dorso-lumbar area: Slight loss of height in the lower dorsal vertebral bodies, with presence of Schmorl’s nodes in D6 and D11. Multiple vertebral compression fractures from L2 to L5 with loss of height over 50% (Figure 1A).
- CT scan of neck, thorax, abdomen and pelvis: Vertebral wedging in the 4 last lumbar vertebrae, with central collapse in the upper and lower discs of those vertebrae (Figure 1B).
- Bone scintigraphy: Compression fractures in the lumbar vertebrae (L3-L4-L5), with no other distant lesions.
- Bone densitometry: T-score in lumbar column (L2-L4): -3.3. Z-score in the neck of the femur: 0.0. Severe osteoporosis.

In view of these results, the initial differential diagnosis includes anaphylaxis, angioedema, carcinoid syndrome, pheochromocytoma, metastasis of a vasoactive intestinal peptide tumor, Zollinger-

Ellison syndrome, myelofibrosis, angioblastic lymphoma, chronic eosinophilic leukemia...

We performed a biopsy by needle puncture and aspiration of the bone marrow and the dermal lesions with the following results:

- Normocellular bone marrow with 2% of pathologic mast cells. Mast cells represent 0.03% of all cells, and 95% expresses an aberrant phenotype (CD117+/CD25+/CD2+), positive for the D816V mutation (A7176T) of the c-KIT. We found multiple areas with mast cells (>15) and lymphocytes.
- The dermal biopsy revealed the presence of mast cells in the perivascular and interstitial areas.

These findings reveal the fact that several major and minor criteria are met, as well as some C-type findings, such as vertebral fractures and osteoporosis, leading to a diagnosis of Aggressive Systemic Mastocytosis [4]. We carried out a bilateral transpedicular vertebroplasty with a biphasic reabsorbable ceramic bone replacement made of hydroxyapatite (40%) and calcium phosphate (60%) in L4 and L5. With regard to the treatment of severe osteoporosis, we prescribed zoledronic acid 5 mg i.v., teriparatide 20 mcg sbc/24h and tablets of calcium and vitamin D/24h. In order to prevent the symptoms of mastocytosis we prescribed ranitidine 300mg/24h and dexchlorpheniramine maleate 6mg/24h.

After two year, the patient showed a decrease in pain (VAS=2), with complete lumbar mobility and a slight disability for daily activities (ODI=52%).

The imaging study revealed an adequate restructuring of the vertebral fractures (Figure 2), and the densitometry showed an increase in bone mass (T -2.41).

## Discussion

We present a rare case of pathological vertebral fractures caused by secondary osteoporosis in a young male patient, in which a proper differential diagnosis and an adequate therapeutic approach are of paramount importance [5]. There are several causes for secondary osteoporosis, mainly endocrinopathies, gastrointestinal disorders, connective tissue diseases secondary to medication and hematological diseases such as mastocytosis [5,6].

Mastocytosis is a hemopathy characterized by an excessive infiltration of mast cells that may be either cutaneous or systemic. The incidence of this disorder is unknown, but it appears in 1.25% of all patients diagnosed with osteoporosis [7-9].

The symptoms are caused by the released biochemical mediators and the infiltration in the tissue and the organs. The most common clinical symptoms are syncope, hypotension, diarrhea, abdominal pain, gastrointestinal ulcer, bone pain, cephalalgia and flushing. The diagnosis is based on a series of criteria defined by the WHO, and it requires immunophenotypical, cytometric and genetic analysis after a biopsy of the bone marrow [7-9].

33% of the patients with systemic mastocytosis present bone involvement in the form of osteoporosis, and 16% present vertebral fractures. A radiological study and a densitometric analysis must be performed in all patients [10,11]. It is estimated that 70% of the cases present radiological bone alterations that are caused by mast cell infiltrates in the bone marrow [6].

The medical treatment of mastocytosis mainly focuses on preventing the triggers for the degranulation of the biochemical mediators that lead to the symptoms. These symptoms can be controlled with antihistamines and antileukotrienes. The reduction of cell proliferation is achieved via tyrosine kinase inhibitors [7,9].

In cases of severe osteoporosis, the treatment with bisphosphonates and/or PTH seems to be effective in order to improve the bone mineral density of the vertebral column [12]. In this case, we performed a vertebroplasty in order to lessen the pain of the patient and to prevent the worsening of the fractures [5,6].

In view of the age of the patient and his recovery potential we have replaced the classic vertebroplasty of methyl-methacrylate with a biphasic reabsorbable ceramic bone piece with very satisfactory results.

## References

1. Golkar L, Bernhard JD. Mastocytosis. *Lancet*. 1997;349(9062):1379-85.
2. Valent P, Sperr WR, Schwartz LB, Horny HP. Diagnosis and classification of mast cell proliferative disorders: Delineation from immunologic diseases and non-mast cell hematopoietic neoplasms. *J Allergy Clin Immunol*. 2004;114(1):3-11.
3. Valent P, Horny HP, Escribano L, Longley BJ, Li CY, Schwartz LB, et al. Diagnostic criteria and classification of mastocytosis: a consensus proposal. *Leuk Res*. 2001;25(7):603-25.
4. Pardanani A. Systemic mastocytosis in adults: 2012 update on diagnosis, risk stratification, and management. *Am J Hematol*. 2012;87(4):401-11.
5. Krüger A, Hamann C, Brendel C, Ramaswamy A, Schnabel M, Neubauer A, et al. Multimodal therapy for vertebral involvement of systemic mastocytosis. *Spine (Phila Pa 1976)*. 2009;34(17):E626-8.
6. Manara M, Varenna M, Cantoni S, Parafioriti A, Gallazzi MB, Sinigaglia L. Osteoporosis with vertebral fractures in young males, due to bone marrow mastocytosis: a report of two cases. *Clin Exp Rheumatol*. 2010;28(1):97-100.
7. Arock M, Valent P. Pathogenesis, classification and treatment of mastocytosis: state of the art in 2010 and future perspectives. *Expert Rev Hematol*. 2010;3(4):497-516.
8. Horny HP, Sotlar K, Valent P. Differential diagnoses of systemic mastocytosis in routinely processed bone marrow biopsy specimens: a review. *Pathobiology*. 2010;77(4):169-80.
9. Bains SN, Hsieh FH. Current approaches to the diagnosis and treatment of systemic mastocytosis. *Ann Allergy Asthma Immunol*. 2010;104(1):1-10.
10. Rossini M, Zanotti R, Bonadonna P, Artuso A, Caruso B, Schena D, et al. Bone mineral density, bone turnover markers and fractures in patients with indolent systemic mastocytosis. *Bone*. 2011;49(4):880-5.
11. Van der Veer E, van der Goot W, de Monchy JG, Kluin-Nelemans HC, van Doormaal JJ. High prevalence of fractures and osteoporosis in patients with indolent systemic mastocytosis. *Allergy*. 2012;67(3):431-8.
12. Barete S, Assous N, de Gennes C, Grandpeix C, Feger F, Palmerini F, et al. Systemic mastocytosis and bone involvement in a cohort of 75 patients. *Ann Rheum Dis*. 2010;69(10):1838-41.