



Systemic Amyloidosis with Predominant Spine Involvement: A Case Report

Silvia Terzi², Teresa Calabrò^{1*}, Giovanni Barbanti Brodano², Alessandro Gasbarrini², Stefano Boriani²

¹Department of Orthopedics, University of Bologna, Istituto Ortopedico Rizzoli, Bologna, Italy

²Department of Oncologic Spine Surgery, University of Bologna, Istituto Ortopedico Rizzoli, Bologna, Italy

Abstract

Purpose: Primary systemic amyloidosis with main bone involvement is a rare disease. Clinical symptoms and radiographic findings are usually nonspecific and may be confused with primary bone tumor, metastatic disease, metabolic disorders or infections. The occurrence of an amyloidoma in the spine is rare.

Methods: We describe the case of a 57-year old man presenting with a pathological fracture of T7 in presence of a large, soft tissue mass narrowing the spinal canal, responsible for a worsening paraplegia. Diagnosis of systemic amyloidosis was made after surgical treatment. Pathological examination showed an amorphous eosinophilic material, positive staining with Congo red, birefringence under polarized light relating to amyloid, with the presence of rare plasma cells.

Results: After surgical procedure patient's symptoms improved but with incomplete neurological recovery. PET-CT scan revealed multiple bone locations without, at the beginning, extra-skeletal involvement. The patient underwent oncological and surgical treatment with progression of the disease and visceral involvement. He died two years after the diagnosis.

Conclusions: Bone involvement during systemic amyloidosis is rare and often underestimated, it had predominantly visceral involvement (kidney, heart, liver, gastrointestinal tract, lung) and unfavorable clinical course if not treated. Appropriate histopathologic studies are an essential step to define diagnosis and treatment of these patients. Treatment consists of chemotherapy, steroids, autologous blood stem cell transplantation and biologic anti-inflammatory drugs. Spine localization can bring to nerves compression or pathological fracture and, in these cases, surgical treatment has a role to improve patient's quality of life.

Keywords: AL amyloidosis; Systemic amyloidosis; Decompression; Spine surgery

Introduction

Amyloidosis results from accumulation of inappropriately folded proteins, called amyloid. The latter can be histologically diagnosed using Congo red stain combined with polarized light on microscopy. Amyloidosis can be systemic or organ-specific, idiopathic or secondary to other chronic diseases. Skeletal involvement, concerning in particular the spine, is often reported in the literature both as solitary amyloidoma, usually with a good prognosis, both as part of a systemic form with visceral involvement, often with an unfavorable prognosis. We describe the clinical case of a patient with systemic amyloidosis with spinal onset.

Case report

In November 2011 a 57-year old man, with a 3 months history of back pain, was admitted at the Emergency Department because of difficulty maintaining upright position. He was admitted in our Department for an incomplete paraplegia with hypertonus, exhaustible bilateral clonus and acute urinary retention. The CT scan and MRI showed a pathological fracture of T7 with the presence of a large soft tissue mass narrowing the spinal canal for more than 50% of its diameter (Figure 1 A-B). Anamnesis was negative for cancer and only revealed a history of HBV-related steatosis. Laboratory tests showed elevation of Ca 19-9 (263.4), Ca 125 (96.1), alkaline phosphatase (199) and γGT (325); at that time there was no serum monoclonal component. After arteriography and selective embolization (with pathological finding of a modest circle), he underwent urgently to tumor debulking, decompression and stabilization from T5 to T9 (Figure 2 A-B). The decision to proceed with decompression in the absence of histological

diagnosis was taken because of the rapid neurological deterioration. The involvement of the whole vertebral body and both the two pedicles didn't allow an "en bloc" resection, even if required by the oncological criteria based on Enneking proposals and WBB staging system [1,2]. After the procedure patient's symptoms improved but with incomplete neurological recovery; low back pain persisted. PET-CT scan revealed multiple bone locations without extraskelatal involvement. In L5, in particular, a large soft tissue compressed the dural sac; that was confirmed by MRI (Figure 3). Because of this compression, one month after the first surgery laminectomy was performed, followed by curettage and vertebroplasty of L5. During both surgical procedures a lot of grayish-white and crumbly tissue was collected. Pathological examination showed an amorphous eosinophilic material, positive staining with Congo red, birefringence under polarized light relating to amyloid, with the presence of rare plasma cells.

In February 2012 treatment with Bortemomid and Dexamethasone (three cycles) was initiated, without relevant response, and later Cyclophosphamide was associated. The therapy was discontinued

***Corresponding author:** Teresa Calabrò, Istituto Ortopedico Rizzoli, Clinica Ortopedica, Via G.C. Pupilli 1Bologna, 40124, Italy; Fax: +390516366948; Tel: +393381845257; E-mail: teresa.calabro@studio.unibo.it

Received November 29, 2015; **Accepted** December 05, 2015; **Published** December 14, 2015

Citation: Terzi S, Calabrò T, Brodano GB, Gasbarrini A, Boriani S (2015) Systemic Amyloidosis with Predominant Spine Involvement: A Case Report. Orthop Muscular Syst 5: 202. doi:10.4172/2161-0533.1000202

Copyright: © 2015 Terzi S, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

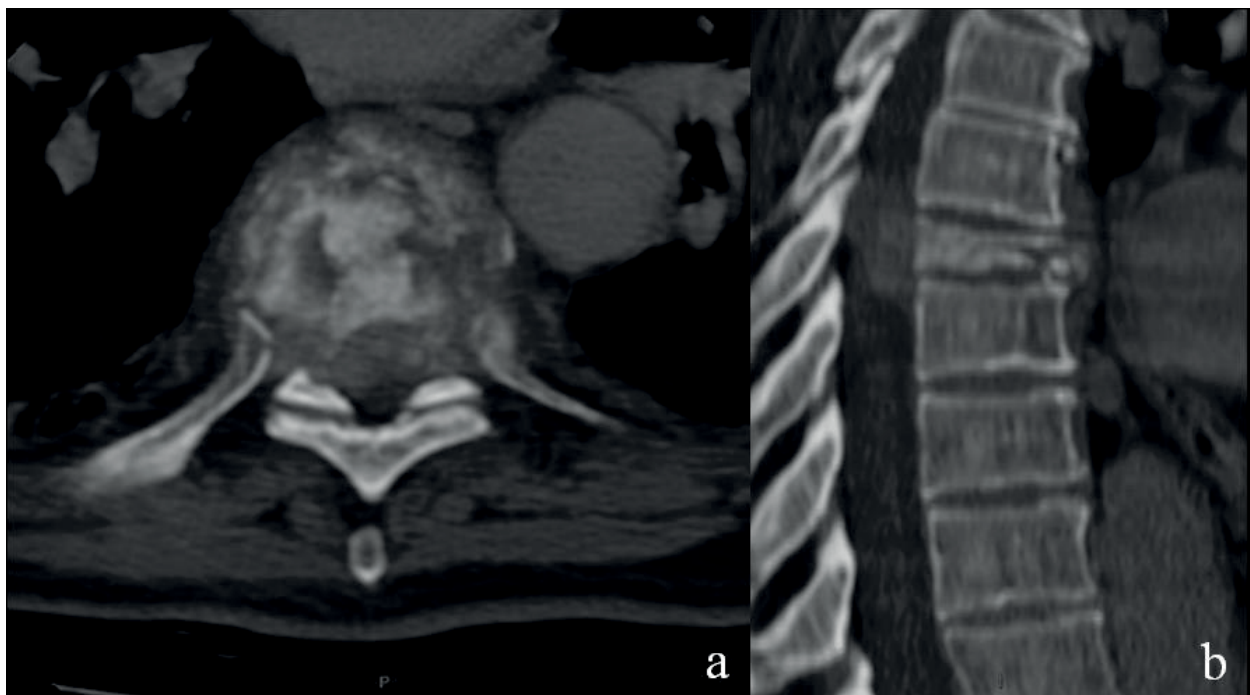


Figure 1: Axial (A) and sagittal (B) computer tomography images showed a pathological fracture of T7 with a large soft tissue mass narrowing the spinal canal.

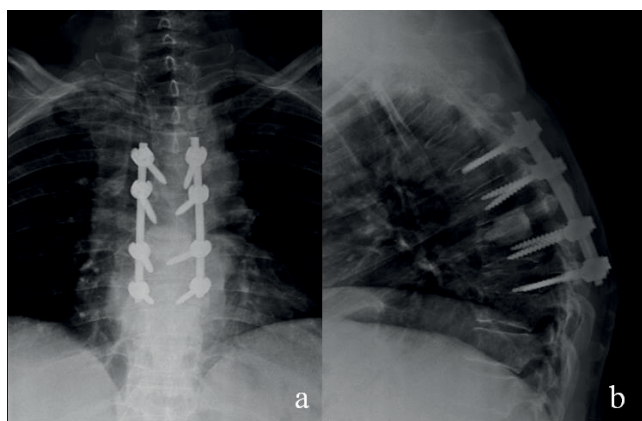


Figure 2: Anteroposterior (A) and lateral (B) X-ray images taken 6 months post procedure.

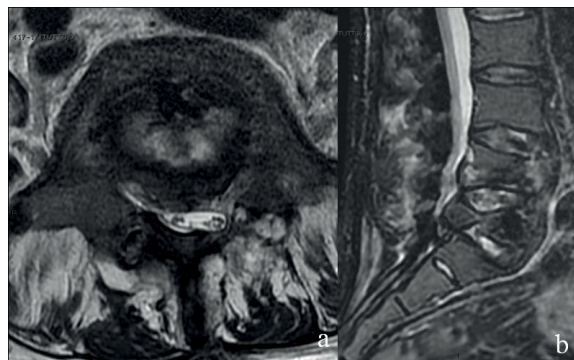


Figure 3: Axial (A) and sagittal (B) magnetic resonance images reveals a large soft tissue compressing the dural sac at L5.

in September for worsening of the Sciatica pain with loss of walking ability and the patient was sent to our Department again. MRI showed local recurrence in L4 and L5 with plenty of new tissue in the anterior and posterior position (Figure 4). After embolization, the patient underwent decompression by laminectomy and foraminotomy, followed by vertebral reconstruction by vertebroplasty. The material taken was examined and it resulted to be amyloid protein without cellular component. Blood tests showed an increase of cancer markers (Ca 19-9, Ca 125). It was identified a serum monoclonal component IgG κ with alteration of the relationship κ/λ . No signs of cardiac and renal involvement were detected, but a persistent hepatomegaly was found with subverted echo-structure. The diagnosis was AL Amyloidosis (IgG κ) with bone and probably liver involvement. It was decided to continue treatment with Bortezomid, Cyclophosphamide

and Dexamethasone. The patient presented an immediate response of laboratory test results, but he was forced to stop the treatment for two months due to an intercurrent respiratory infection. In the meanwhile, liver infiltration expanded, supporting the diagnosis of systemic visceral amyloidosis. The patient was referred to us again in July 2013, after the resumption of treatment: he complained worsening symptoms, profound fatigue, low chest pain; the neurological objectivity was unchanged. CT scan showed a T11 fracture, probably due to bone weakness. In agreement with oncologists, we recommended a support brace and continuation of drug therapy. The patient died after 3 months because of complications related to the disease and the chemotherapy treatment.

Discussion

We describe the case of a patient with amyloidosis with acute

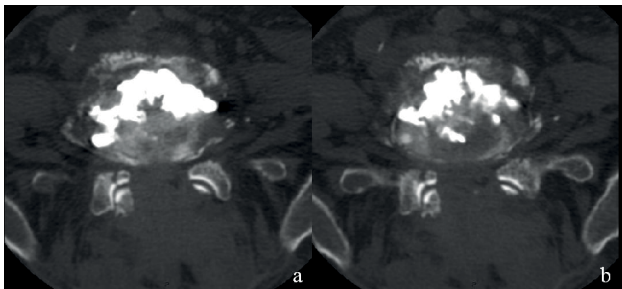


Figure 4: MRI showed local recurrence in L4 and L5 with plenty of new tissue in the posterior (A) and anterior (B) position.

spinal onset, characterized by pathological fracture and spinal cord compression, initially without apparent visceral involvement. The extracellular amyloid deposit occurs frequently secondary to many chronic diseases (rheumatoid arthritis, ankylosing spondylitis, sickle cell disease, Hodgkin's disease, Alzheimer's disease, intravenous drugs abuse, dialysis), configuring the framework of secondary amyloidosis, with variable clinical impact [3-9].

The primitive or idiopathic amyloidosis arises from immunosecretory disorders [10,11], including multiple myeloma with its variants and diseases characterized by deposit of monoclonal Ig. All these pathologies are characterized by the presence of a clone of plasma cells, or plasmacytoid cells, secreting complete Ig or light/heavy chains of Ig, which are phagocytized and fragmented by macrophages and accumulate in the extracellular environment as an insoluble and non-degradable substance (amyloid); these diseases are classified according to the characteristics of the precursor protein [12]. The form that most frequently involves the skeleton is the AL amyloidosis (light chain amyloidosis), that only in 20% of cases is associated with multiple myeloma, although the bone involvement is less frequent in isolated AL Amyloidosis [11,13]. Osteoarticular manifestations are more often arthropathy, polyarthritides (rheumatoid like bilateral symmetric), carpal tunnel syndrome, less often bone involvement, with preferential localization in the spine [6]. The signs and symptoms of AL Amyloidosis with spinal localization are completely non-specific and tumor-like: bony destruction and compression of neural structures [13,14].

The literature describes several cases of amyloidosis with bone localization: however, these are isolated and solitary forms ("amyloidoma"), which have an excellent prognosis once removed, and represent a disease entity in itself [14-17].

The AL amyloidosis is instead typically systemic, with predominant visceral involvement (kidney, heart, liver, gastrointestinal tract, lung) and unfavorable clinical course if not treated. It presents a monoclonal component in serum or urine in 80-90% of cases [6] and the age of onset ranges between 50-60 years old. Treatment consists of chemotherapy, steroids, autologous blood stem cell transplantation and biologic anti-inflammatory drugs as Bortezomib [10]; it is borrowed from the treatment of multiple myeloma, but with higher incidence of complications [12]. AL amyloidosis rarely presents with predominant bone disease, simulating a multiple myeloma [18]; however, in all cases reported, visceral involvement always coexists.

Our patient presented a typical picture of systemic amyloidosis only in the full-blown stage of the disease. At the beginning, in fact, he showed multiple bony vertebral localization with neither systemic

involvement nor monoclonal component in serum or urine. Moreover, the detection of some abnormal laboratory findings (high level of CA19-9 and Ca125) could lead one to think of a disease secondary to occult malignancy. In the cases reported by Schonland [18] systemic amyloidosis has a prevalent bone involvement, simulating multiple myeloma, but visceral localization and monoclonal component are present from the beginning.

After few months, clinical findings and laboratory tests became consistent with typical of AL amyloidosis, but with very fast disease progression and poor response to treatment. Decompression and stabilization surgeries improved patient's quality of life, allowing him to keep walking autonomy until the end and good pain control.

References

1. Boriani S, Fisher CG (2015) Evaluation and Decision Making in: Vialle LR, Gokaslan ZL, Fisher GC, Boriani S (2015) *AOSpine Master Series 2*: 1-14.
2. Boriani S, Weinstein JN, Biagini R (1997) Primary bone tumors of the spine. Terminology and surgical staging. *Spine* 22: 1036-1044.
3. Amir AR, Sheikh SS (2006) Hodgkin's lymphoma with concurrent systemic amyloidosis, presenting as acute renal failure, following lymphomatoid papulosis. *J Nephrol* 19: 361-365.
4. Corlin DB, Heegaard NH (2012) β (2)-microglobulin amyloidosis. *Subcell Biochem* 65: 517-540.
5. Guerrero-Muñoz MJ, Castillo-Carranza DL, Krishnamurthy S, Paulucci-Holthausen AA, Sengupta U, et al. (2014) Amyloid- β oligomers as a template for secondary amyloidosis in Alzheimer's disease. *Neurobiol Dis* 71: 14-23.
6. Hadj Sadek B, Radoui A, Al Hamany Z, Benamar L, Bayahia R, et al. (2011) Renal amyloidosis: uncommon complication of sickle cell disease. *Med Trop (Mars)* 71: 185-186.
7. Manner I, Sagedal S, Røger M, Os I (2009) Renal amyloidosis in intravenous heroin addicts with nephrotic syndrome and renal failure. *Clin Nephrol* 72: 224-228.
8. Mercieca C, Van der Horst-Bruinsma IE, Borg AA (2014) Pulmonary, renal and neurological comorbidities in patients with ankylosing spondylitis; implication for clinical practice. *Curr Rheumatol Rep* 16: 434.
9. Nakamura T (2011) Amyloid (2011) A amyloidosis secondary to rheumatoid arthritis: pathophysiology and treatments. *Clin Exp Rheumatol* 29: 850-857.
10. Gatt ME, Palladini G (2013) Light chain amyloidosis 2012: a new era. *Br J Haematol* 160: 582-598.
11. Shaheen SP, Talwalkar SS, Medeiros LJ (2008) Multiple myeloma and immunosecretory disorders: an update. *Adv Anat Pathol* 15: 196-210.
12. Pinney JH, Hawkins PN (2012) Amyloidosis. *Ann Clin Biochem* 49: 229-241.
13. M'bappé P, Gateau G (2012) Osteo-articular manifestations of amyloidosis. *Best Pract Res Clin Rheumatol* 26: 459-475.
14. Dickman CA, Sonntag VK, Johnson P, Medina M (1988) Amyloidoma of the cervical spine: a case report. *Neurosurgery* 22: 419-422.
15. Mizuno J, Nakagawa H, Tsuji Y, Yamada T (2001) Primary amyloidoma of the thoracic spine presenting with acute paraplegia. *Surg Neurol* 55: 378-382.
16. Mullins KJ, Meyers SP, Kazee AM, Powers JM, Maurer PK (1997) Primary solitary amyloidosis of the spine: a case report and review of the literature. *Surg Neurol* 48: 405-408.
17. Werner BC, Shen FH, Shimer AL (2013) Primary cervical amyloidoma: a case report and review of the literature. *Spine J* 13: 1-7.
18. Schonland SO, Hansmann J, Mechttersheimer G, Goldschmidt H, Ho AD, et al. (2008) Bone involvement in patients with systemic AL amyloidosis mimics lytic myeloma bone disease. *Haematologica* 93: 955-956.