

Primary solitary amyloidoma of the lumbar spine

Amiloidoma solitário primário da coluna lombar

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Abstract

Primary solitary amyloidoma of the spine is an extremely rare form of localized deposits of amyloid on bone tissue and has a predilection for the thoracic region. It arises within the bone marrow of the vertebral body, causing pain and neurologic symptoms due to bone destruction with fracture and collapse, visible on imagiologic studies as osteolytic lesions usually associated with adjacent soft tissue masses. The duration of symptomatology can be of several years before diagnosis, although clinical deterioration may be rapid and severe, with acute neurologic compression, radiculopathy, myelopathy and paraplegia, leading to the necessity of emergency surgery. The prognosis after total excision and spinal stabilization is generally excellent, as patients with solitary amyloidoma have no known risk of development of multiple myeloma or systemic amyloidosis. The authors report the case of a patient with solitary amyloidoma of the lumbar spine who unfortunately had a dismal outcome, due to acute nosocomial pneumonia and sepsis by *Acinetobacter baumannii* and extended-spectrum β -lactamase *Escherichia coli* occurring after open spinal biopsy.

Key words: primary amyloidoma, lumbar spine, amyloidosis.

Resumo

*O amiloidoma solitário primário da coluna vertebral é uma forma extremamente rara de amiloidose localizada do esqueleto ósseo, predominando os casos de envolvimento da coluna dorsal. O processo inicia-se ao nível da medula óssea do corpo vertebral, causando dor e sintomas neurológicos, resultantes de destruição óssea, fractura e colapso vertebral, visível nos exames imagiológicos como lesões líticas, frequentemente com extensão às partes moles adjacentes. A duração dos sintomas antes do diagnóstico é muitas vezes longa, mas a deterioração pode ser rápida e grave, por compressão neurológica aguda, radiculopatia, mielopatia e paraplegia, determinando por vezes a necessidade de cirurgia de emergência para aliviar a compressão neurológica. O prognóstico após a excisão total da lesão e estabilização operatória da coluna é em geral excelente, uma vez que o amiloidoma localizado não tem risco evolutivo de mieloma múltiplo ou de amiloidose sistémica. Os autores descrevem o caso de um doente com amiloidoma solitário da coluna lombar, que infelizmente faleceu pouco tempo após biópsia cirúrgica da lesão do corpo vertebral, devido a pneumonia aguda nosocomial e sepsis por *Acinetobacter baumannii* e *Escherichia coli* produtora de β -lactamase.*

Palavras chave: amiloidoma primário, coluna lombar, amiloidose.

Introduction

Amyloidosis is a group of disorders due to the deposition of insoluble fibrillary protein, nearly always in the extravascular space of organs and tissues. There are multiple clinical and biochemical distinct forms of amyloid that are classified according to the biochemical nature of the fibril-forming protein. The biochemical type of deposit may influence the geographic pattern of amyloid deposition.¹

The two most common forms of amyloidosis are AA amyloid, which is primarily associated with the secondary amyloidosis of such chronic diseases as chronic osteomyelitis, rheumatoid arthritis and Hodgkin's disease, and AL amyloid which is associated with primary amyloidosis, multiple myeloma and macroglobulinemia.² Subjects under chronic dialysis due to chronic renal failure are at great risk

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for amyloid bone tumors due to the deposit of β_2 -microglobulin in the skeleton, which usually causes large destructive lesions leading to fractures.³ The etiology and pathogenesis of amyloidosis is unclear, however, amyloid deposits cause tissue destruction by progressive intercellular accumulation and pressure atrophy of adjacent cells.¹

Isolated primary amyloidoma is a nodular mass of amyloid with no evidence of systemic amyloidosis or myeloproliferative disease, and that can occur in the bone, skin and soft tissues, larynx, lymph nodes, urinary bladder, eye, tongue, along the gastrointestinal tract, brain, peripheral nerves, heart, salivary glands, thyroid.⁴ A likely pathogenic hypothesis is that amyloidoma could be the manifestation of the local production of immunoglobulin associated with formation of amyloid substance at the level of a "burnt-out" immunocytoma tumor.⁵

Primary amyloidoma of the spine is very rare and has a predilection for the thoracic region. The tumor-like appearance and behavior of these lesions make it difficult to diagnose on imaging studies. It is important to know that diagnosis requires a high index of suspicion and, ultimately adequate tissue biopsy for histopathologic diagnostic studies. After correct diagnosis by histopathology, surgical treatment obtains excellent results.⁶ Very rarely it is possible to find a monoclonal gammopathy of light chain K on the urine immunoelectrophoresis without myeloma and no monoclonal immunoglobulin chain in the blood.⁷ Primary idiopathic amyloidoma of the spine originates from local production of light chain immunoglobulins.⁸ It causes functional compromise, pain, and deformity that is responsive to neurological decompression and spinal fusion.

To our knowledge the most recent publications on spinal amyloidoma report the occurrence of only twenty one cases of primary amyloidoma of the spine,⁹ only one being a case of primary lumbar vertebral body amyloidoma¹⁰. The authors present such a case, diagnosed by open bone biopsy. Unfortunately the patient died after a second open bone biopsy due to nosocomial pneumonia with sepsis due to *Acinetobacter baumannii* and extended-spectrum β -lactamase *Escherichia coli*.

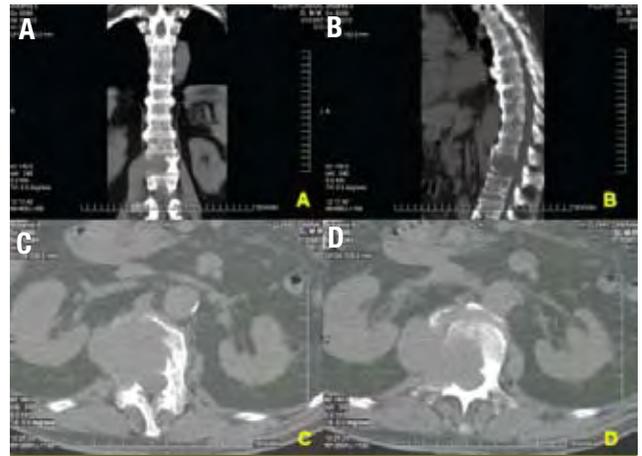
Case Report

On January 16 2007, a 76-year-old white man was admitted to our Unit complaining of four months of

permanent lumbar pain of increasing intensity, without irradiation, but with worsening on standing and leading the patient to stay in bed most of the time. The pain was associated with nocturnal sudoresis and weight loss of seven kg (83 to 76 kg), but the patient denied fever anytime. He referred on questioning to have slight paresthesia on the anteroexternal area of the right thigh. Therapy with parenteral analgesics, muscle relaxants and vitamin B12 were without effect. He denied any other symptoms. Smoking habits of 174 pack-years were stopped 20 years ago and there were no consumption of alcoholic beverages and of unpasteurized milk. He had no personnel and no family antecedents of tuberculosis and malignancy. He had a history of hypertension and gout, polyarticular osteoarthritis, and referred benign ulcers of the stomach and duodenum successfully treated 10 years ago. On a spinal CT scan dated November 30 2006 performed outside our Hospital, it was detected a lytic lesion of the body and right pedicle of the first lumbar vertebra (L1) extending to the anterolateral epidural space and right foramen and slightly compressing the thecal sac and the right L1 root. At physical examination the patient had a good general health state appearance, he had no fever, blood pressure was 290/91 mmHg and heart rate 106 bpm. No signs of anemia were present. He had intense pain at lumbar region during mobilization and also during digital pressure at the level of the upper lumbar spinal area. Right lateral decubitus was more painful than supinus position. Thoracic and abdominal semiology were normal and he had no peripheral edemas. Rectal touch detected an apparently benign prostatic hypertrophy. Neurologic examination revealed normal fundoscopic eye examination and no abnormalities of sensibility tests, osteotendinous reflexes and muscular strength and tonus. Babinsky sign and Lasègue manoeuvre were both negative.

Blood LAB tests revealed: Hb 13.7 g/dL; leukocytes $5.200/\text{mm}^3$ (78.4% N, 13.4% L, 7.8% M, 0.3% E); platelets $29.6 \times 10^9/\text{L}$; PCR 13.5 mg/dL (N < 1.00); ESR 79 mm (1st hour); electrophoresis without monoclonal peak but with slightly low gammaglobulin 0.5 g/dL (N 0.7-1.7), normal IgG and IgM and low IgA 46.70 mg/dL (N 88-410), normal immunoelectrophoresis, β_2 -microglobulin 4.40 mg/L (N < 2.00) All other blood tests were normal, including I.N.R., APTT, fibrinogen, glucose, urea, creatinine, calcium, phosphorus, ionogram, AST and ALT, cholesterol and

triglycerides, iron, transferrin, ferritin and folic acid, free T₄ and TSH. VDRL and serology of HBV, HCV and HIV were negative. Several tumor markers had normal values (CEA, PSA, CA 19.9, CA 125, α -FP). Twenty four hours proteinuria was 770.5 mg (N 42-225) and urine immunoelectrophoresis revealed a small monoclonal peak of light-chain K of 22.79 g/L. Three serial hemocultures for *Brucella spp* were negative as well as Huddleson reaction. Aseptic urine culture was positive for infection with *Enterococcus faecalis* sensible to ampicillin, nitrofurantoin and norfloxacin. Tuberculin Mantoux test was negative. Electrocardiogram, transthoracic B-mode echocardiography and thoracic X-ray were normal, as well as radiography of skull, pelvis and extremities. Thyroid ultrasonography revealed a multinodular colloidal goiter. Upper digestive endoscopy diagnosed chronic atrophic antral gastritis with positive *H. pylori* biopsy and colonoscopy showed only uncomplicated left diverticulosis. Thoracic and abdominal CT scans didn't show evidence of neoplasia. Endorectal ultrasonography was negative for prostatic neoplasia. Myelogram revealed normal appearance of all blood series with 2% of plasmocytes without abnormal aspects, and normal cellular immunophenotype of medullar blood. CT scans of cervical, thoracic and lumbar spine did not show any other bone lesion, only confirming the already known L1 lytic lesion affecting around two-thirds of the vertebral body involving the right pedicle, transverse process, and intracanal extension with tissue density in the anterior epidural space, compressing the antero-lateral aspect of the thecal sac, with extension to the L1-L2 right vertebral foramen. It also obliterated the right para-vertebral fat plane, involving the homolateral psoas muscle (Figs. 1 A, B, C, D). A first open biopsy of L1 vertebral body showed accentuated hypocellularity, with rare foreign body giant cells and scattered infiltration of small lymphocytes and plasmocytes, dispersed among abundant flocculent material that suggested to be amyloid (Figs. 2 A, B), but that was not confirmed in Congo red staining. Immunocytochemistry study of the biopsy was also negative. Stains for fungi, bacteria and acid-fast bacilli were negative. Congo red stain of subcutaneous abdominal fat was negative too. In the meantime the patient was treated with amlodipine, pantoprazole, norfloxacin and with dexametason and tramadol for the intense lumbar pain. It was decided to do more extensive open bone biopsy of



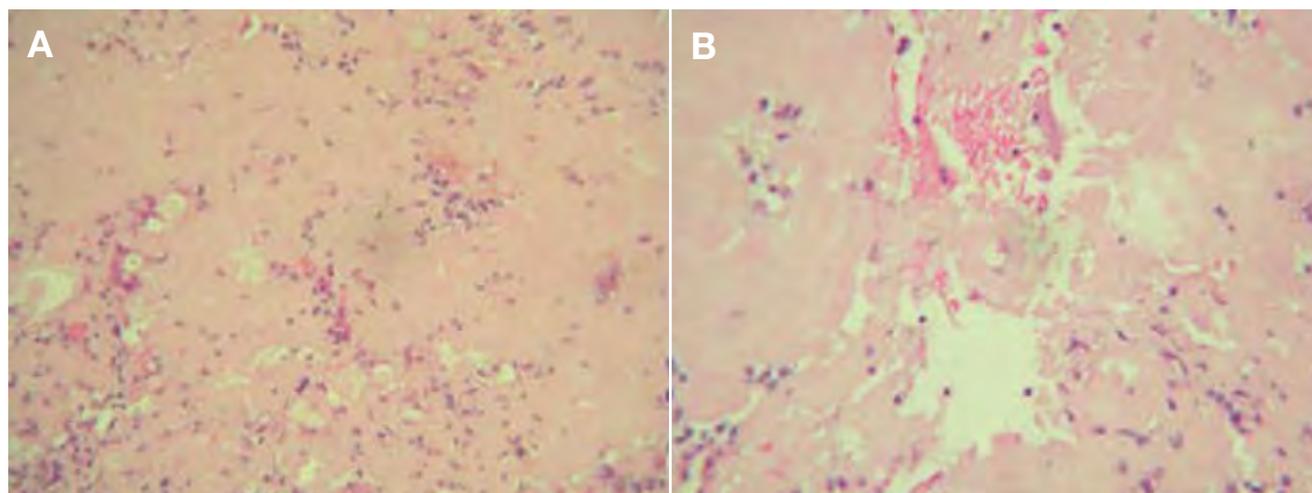
CT Scan of the spine: A - Coronal reformatted view: lytic lesion of the L1 vertebral body, with extension of the neoplastic process to the right psoas muscle; B - Sagittal reformatted view: lytic lesion of the L1 vertebral body with extension to anterior epidural space; C/D - Axial views: lytic lesion of L1 vertebral body and right inferior articular process, with extension of the process to the spinal canal and paravertebral space, and involvement of the right psoas muscle.

FIG. 1

L1 under general anesthesia, together with posterior spinal fusion of D11 to L3 vertebrae. The Congo red staining on that time diagnosed the flocculent material as amyloid substance by its characteristic apple-green birefringence on polarized light microscopy (Fig. 3 A). Immunohistochemistry of bone biopsy demonstrated the presence of monoclonal light-chain K (Fig. 3 B). Unfortunately soon after surgery in the Orthopaedic Unit the patient contracted severe nosocomial sepsis due to pneumonia and bacteraemia by *Acinetobacter baumannii* only sensible to gentamicin and extended-spectrum β -lactamase *Escherichia coli* sensible to gentamicin, meropenem and piperacillin/tazobactam, that was impossible to control. Despite therapy with tazobactam and gentamicin, the patient dying on the 7th day postoperative. Necropsy was not authorized by the family of the patient.

Discussion

Amyloidosis is so named because of its colour after staining with iodine and sulfuric acid. Light microscopy amyloid deposits stains eosinophilic to cyanophilic on Papanicolaou stain and deep blue with focal metachromasia on May-Grunwald-Giemsa stain. It appears as an irregular amorphous homogenous flocc-



Biopsy of vertebral body of L1: A - HE 5x10: amorphous hyaline eosinophilic tissue sprinkled with sparse vascular structures, lymphocytes and plasmacytes; B - HE 10x10: abundant hypocellular amorphous hyaline tissue with a vessel with inspissated wall due to amyloid deposition;

FIG. 2

culent hyaline extracellular substance, occasionally accompanied by a few plasma cells and foreign body giant cells, in absence of granulation tissue. Examination under polarized light after Congo red staining shows a characteristic apple-green birefringence of amyloid material, which makes possible its differentiation from other hyaline deposits, such as collagen. Immunocytochemical demonstration of monoclonal light chains in plasma cells and electron microscopy is specific. On electron microscopic examination, amyloid deposits are composed of rigid 7.5-10-nm non-branching fibrils, arranged in crossed β -pleated sheets, which are responsible for the characteristic polarized birefringence.¹¹

Primary localized amyloid deposits in bone are unusual and any bone may be involved. Skeletal amyloid deposits often have an associated soft tissue mass that may contain variable amounts of calcification. The lesions grow slowly and can produce significant local destruction of bone and soft tissue.¹²

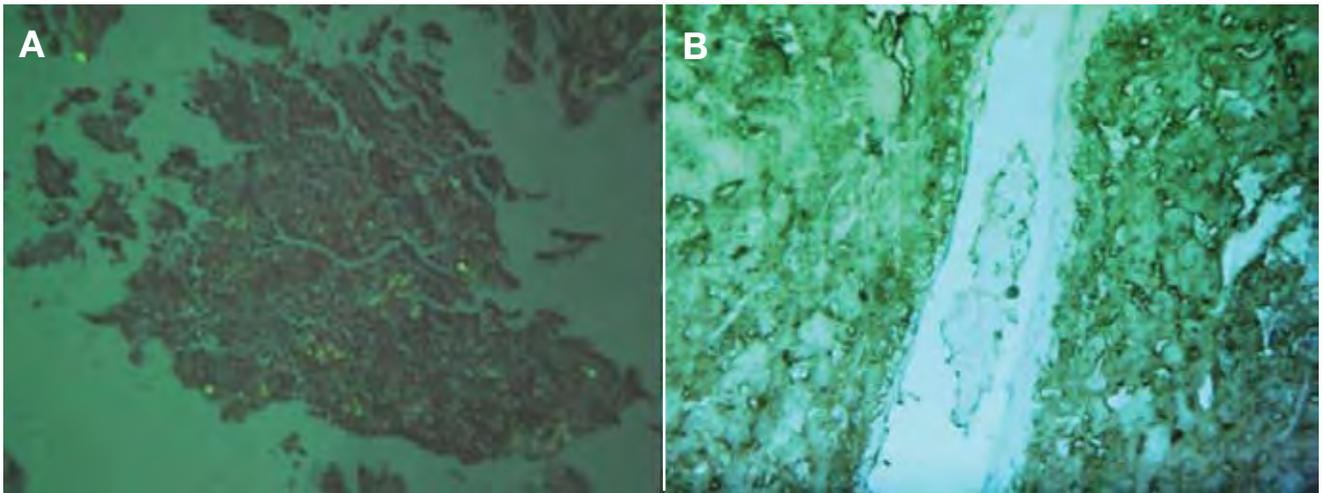
Spinal amyloidosis can occur due to two different situations. First the generalized amyloidosis in which the spine is involved in a patient presenting a predisposing disease causing AL or AA amyloidosis, and secondly the localized amyloid deposit – primary amyloidoma, which is much more rare.¹³

Primary amyloidoma of the spine usually arises from within the bone marrow of the vertebral body

without involving the disc space.^{14,15,16} Most of the cases were described in the thoracic region and rarely in the cervical spine.^{9,17,18,19} To our knowledge only one case of isolated primary amyloidoma of lumbar vertebral body was published until now.¹⁰ The case referred by Chang²⁰ report to a case of involvement of both thoracic and lumbar spine by amyloidoma, and we don't know about the posterior evolution of that case. Other reported cases of symptomatology referred to lumbar spine were amyloidomas not involving the vertebra, but due to localization on the epidural space²¹ or on the lumbosacral root and plexus.²²

The patients with amyloidoma of the vertebra become symptomatic with pain and neurologic deficits involving a single level.²³ The duration of the symptoms may be extremely long (up to 6 years) but clinical deterioration may be rapid and severe, with acute neurologic cord compression leading to acute radiculopathy and myelopathy with paraplegia. In these cases emergency surgery is mandatory for prompt decompression and stabilization of the spine.^{24,25}

Focal deposition of amyloid at the level of a vertebra usually causes bone destruction. Common radiological findings of spinal amyloidosis lesions are vertebral body fractures and collapse, osteopenia, osteonecrosis and lytic lesions. Radiologically, the differential diagnosis of an osteolytic lesion of a vertebra



A - Congo red stain 10x10: apple-green birefringence on polarized light microscopy, compatible with amyloid substance.
 B - Immunohistochemistry of bone biopsy. Immunoperoxidase250: showing the presence of monoclonal light-chain K in bone tissue and in the wall of a bone vessel.

FIG. 3

with an adjacent soft tissue mass and gadolinium-enhancement on MRI is diverse and includes metastasis of tumors, multiple myeloma, primary bone tumors, and inflammatory processes.²⁶

Despite its rarity and nonspecific radiological findings, primary spinal amyloidoma should be included in the differential diagnosis of an osteolytic and calcified mass of the spine.²⁶ Areas of calcification and paraspinal extension may be seen. The calcification seen within the soft tissue is due to the binding of large amount of divalent sodium and calcium bound proteins to the anionic amyloid fibrils. On CT scan the lesion is seen as a wide area of central lucency with a rim of cortical bone, the so called “bulby appearance”, contrast-enhancing following contrast administration. Reported MRI features of amyloidoma include a heterogenous mass with areas of low-to-intermediate signal on T1-weighted images, intermediate-to-high signal on T2-weighted images, and variable enhancement on contrast-enhanced T1-weighted images.¹⁴ A densely calcified mass is an unusual appearance of primary bone amyloidoma because the lesions are generally lytic. Avid uptake of bone radiotracers is common, due to the fact that amyloid deposits form ectopic ossification and calcification.¹⁶

Preoperative diagnosis of isolated primary amyloid tumor of bone can be rewarding because the prognosis is excellent. There are no clinical or roentgenographic

criteria that can establish the diagnosis. Spinal amyloidoma can be diagnosed preoperatively by open biopsy or by fine-needle aspiration.¹¹ But even with “optimal” biopsy material of open biopsy, it is usually impossible to assess the neoplastic nature of the plasma cells without the use of immunochemistry or gene-rearrangement studies to prove their clonality.

There is no benefit with melphalan and prednisolone therapy. Since the lesions are relatively acellular the role of radiotherapy is questionable and surgery is the sole mode of treatment.

After surgery most of the patients had improved neurological function if they had not irreversible neurological lesions. Emergent one-stage surgery combining radical excision of amyloidoma encasing the spinal cord with spinal stabilization is the procedure of choice in most cases, and can cure patients, even those with severe acute myelopathy, because primary amyloidoma of the vertebra occurs at only a single segment.²⁴ Recurrence after total excision has not been reported to date, so there is no need to adjunctive therapy. Patients with solitary amyloidoma have no known risk of development of multiple myeloma and do not have an increased mortality risk, contrasting with many patients with solitary plasmocytoma of the bone.⁸ However, as Pambucian²⁷ advises it is a good practice to follow-up these patients, because there is the possibility that some patients, even not

intentionally, could be incompletely evaluated, and they present later on with myeloma or generalized amyloidosis.

As some patients need urgent decompression and stabilization surgery, sometimes it will be necessary to complete the studies for diagnostic exclusion of myeloma or systemic amyloidosis only after the surgical intervention.

Our patient had unfortunately a dismal outcome. Due to technical reasons resulting in negative result of the first Congo red staining, the patient was submitted to a second open bone biopsy, after which the patient contracted serious nosocomial pneumonia with sepsis and death despite emergent treatment in Intensive Care Unit. The final diagnosis was obtained only after the death of the patient. Notwithstanding the authors think very useful to publish this case, due to the rarity of the situation and the great interest to offer the possibility to other medical doctors to be more useful to eventual future patients, as this is an eminently curable disease. ■

References

- Husby G. Amyloidosis. *Semin Arthritis Rheum* 1992; 22: 67-82.
- Resnick D. Plasma cell dyscrasias and dysglobulinemias. In: Resnick D, Niwimayama G. ed. *Diagnosis of Bone and Joint Disorders* 2nd ed. Philadelphia: Saunders 1998; 2387-2396.
- Onishi S, Andress DL, Maloney NA, Coburn JW, Sherrard DJ. Beta 2-microglobulin deposition in bone in chronic renal failure. *Kidney Int* 1991; 39: 990-995.
- Bauer WH, Kuzma JF. Solitary "tumors" of atypical amyloid (paramyloid). *Am J Clin Pathol* 1949; 19: 1047-1112.
- Glenner G. Amyloid deposits and amyloidosis: the β_2 -microglobulin type. *N Engl J Med* 1980; 302: 1333-1343.
- Leeson MC, Rehtine GR, Makley JT, Carter JR. Primary amyloidoma of the spine: a case report and review of the literature. *Spine* 1985; 10: 303-306.
- Brunin X G, Nubourgh Y, Cornut P, Fumiere E, Vanderkelen B, Delcour C. Amyloidome solitaire idiopathique du sacrum. Un diagnostic différentiel important. *J Radiol* 2001; 82: 495-497 (French).
- Dee CH, Missirian RJ, Chernoff IJ. Primary amyloidoma of the thoracic spine: a case report and review of the literature. *Spine* 1988; 23: 457-500.
- Iplikcioglu AC, Bek S, Gokduman CA, Cosar M, Sav A. Primary solitary cervical amyloidosis. Case report and review of the literature. *Spine* 2007; 32: E45-E47.
- Miossec P, Lormeau B, Valensi P, Arthuis F, Amouroux J, Attali JR. Bone amyloidoma in a diabetic patient with morbid obesity. *Diabetes and Metabolism (Paris)* 1999; 25: 261-263.
- Manucha V, Arora VK, Singh , Bhatia A. Aspirative cytology diagnosis of a primary amyloid tumor of thoracic vertebra: a case report. *Diagnostic Cytopathology* 2003; 29: 160-162.
- Hwang SS, Park YH, Kim JY, Jung SL, Ahn MI, Park CH et al. Primary amyloidoma of the cervical spine. *Am J Neuroradiol* 2000; 21: 601-603.
- Mulleman D, Flipo RM, Assaker R, Maurage CA, Chastanet P, Duclombier et al. Primary amyloidoma of the axis and acute spinal compression: a case report. *Eur Spine J* 2004; 13: 244-248.
- Mathew JM, Rajshekhar V. Primary amyloidoma of the thoracic spine. *Brit J Neurosurg* 1998; 12: 448-451.
- Suri VS, Tatke M, Kumar S, Gupta V. Amyloidoma of the thoracic spine. Case report. *J Neurosurg* 2001; 94 (2): 299-301.
- Cloft HJ, Quint DJ, Markert JM, Ianettoni MD, Papadopoulos SM. Primary osseous amyloidoma causing spinal cord compression. *Am J Neuroradiol* 1995; 16: 1152-1155.
- Dickman CA, Sonntag VK, Johnson P, Mexina M. Amyloidoma of the cervical spine: a case report. *Neurosurg* 1988; 21: 419-422.
- Porchet F, Sonntag VK, Vrodos N. Cervical amyloidoma of C2: case report and review of the literature. *Spine* 1988; 23: 133-138.
- Prasad BK, Andrews K, Dutton J, Reid H. Localized amyloid deposit causing paraplegia. *Brit Med J* 1981; 283: 1087.
- Chang YS, Ku MC, Lee TS. Primary amyloidoma of the spine. *Zhonghua Yi Xue Za Zhi (Taipei)* 1993; 51: 85-90 (in Chinese).
- Haridas A, Basu S, King A, Pollock J. Primary amyloidoma of the lumbar spine causing neurologic compromise: case report and literature review. www.neurosurgery-online.com
- Ladha SS, Dyck PJ, Spinner RJ, Perez DG, Zeldenrust SR, Amraami KK et al. Isolated amyloidosis presenting with lumbosacral radiculoplexopathy: description of two cases and pathogenic review. *J Periph Nerv System* 2006; 11: 346-352.
- Unal A, Sutlap PN, K_y_k M. Primary amyloidoma of thoracic spine: a case report and review of the literature. *Clin Neurol Neurosurg* 2003; 105: 167-169.
- Mizuno J, Nakagawa H, Tsuji Y, Yamada T. Primary amyloidoma of the thoracic spine presenting with acute paraplegia. *Surg Neurol* 2001; 55: 378-382.
- Villarejo F, Diaz CP, Perla c, Sanz J, Escalona J, Goyenechea F. Spinal cord compression by amyloid deposits. *Spine* 1994; 19: 1178-1181.
- Aydin MV, Sen O, Bolat F, Tufan K, Kizilvilic O, Altinors N. Primary amyloidoma of the thoracic spine. *J Spinal Disord Tech* 2006; 19: 145-147.
- Pambuchian SE, Horyd D, Cawte T, Huvos AG. Amyloidoma of bone, a plasma cell/plasmacytoid neoplasm – report of three cases and review of the literature. *Am J Surg Pathol* 1997; 21: 179-186.