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CERVICAL SPINE CORD COMPRESSION BY EOSINOPHILIC GRANULOMA

CASE REPORT

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ABSTRACT – Eosinophilic granuloma is a term reserved for the most often and benign form of disorder known as Langerhans cells histiocytosis. It is a disease of children and adolescents that very rarely affects adults, representing the localized form of a pathological proliferation of histiocytes in bones, like skull and long bones. Vertebral involvement is uncommon, approximately 8% of the cases, being the cervical localization the least affected. Moreover, the involvement of the spinal cord and roots remains a rare occurrence. Only five cases characterized by signs of cervical spinal cord compression have been reported. We report the sixth case in a 42-year-old-man who evolved with resolution of symptoms, and has remained asymptomatic after treatment. The clinical, radiological and histological features and, also, the value, in selected cases, of surgical treatment followed by low-dose radiation therapy is discussed. A review of the pertinent literature is also presented.

KEY WORDS: cervical eosinophilic granuloma, cervical spinal cord compression, Langerhans cells histiocytosis.

Compressão medular cervical por granuloma eosinofílico: relato de caso

RESUMO – Granuloma eosinofílico é um termo reservado para a forma mais frequente e benigna da enfermidade conhecida como histiocitose das células de Langerhans. É uma doença de crianças e adolescentes, muito raramente afetando adultos, representando a forma localizada de uma proliferação patológica de histiócitos em ossos, crânio e ossos longos. O acometimento vertebral é incomum, aproximadamente 8% dos casos, sendo a localização cervical a menos descrita. Além disso, o acometimento da medula espinhal e das raízes é de rara ocorrência. Na literatura foram relatados apenas cinco casos caracterizados por sinais de compressão medular cervical. Relatamos o sexto caso, de um homem de 42 anos de idade que evoluiu com regressão dos sintomas após tratamento, tendo permanecido assintomático. As características clínicas, radiológicas, histopatológica e o valor, em casos selecionados, do tratamento cirúrgico seguido de radioterapia em baixas doses são discutidos. Revisão da literatura pertinente também é apresentada.

PALAVRAS-CHAVE: granuloma eosinofílico cervical, compressão medular cervical, histiocitose das células de Langerhans.

The term eosinophilic granuloma was introduced in 1940 by Jaffe and Lichtenstein[1] in order to describe an isolated bone tumour, and also to nominate the most benign form of histiocytosis X or, more recently[2], Langerhans cells histiocytosis, which is a generic term that includes two uncommon diseases: Hand-Schuller-Christian and Letterer-Siwe diseases. Such pathological entities have in common a histopathological characteristic pattern of histiocytary nature (Langerhans cells) associated with eosinophils[1-10].

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Although it represents less than 1% of all primitive bone tumour[7,11], it also corresponds to arround 75% of all the histiocytosis X that primarily attack adolescents and young adults with 80% of the cases occurring before the age of 10 years[8,9,11-13]. The osteolytic lesion can occur in any skeleton's bone, with the vertebral body accounting for aproximately 80% of the cases. Of this 54% are located in the thoracic region, 35% in the lumbar, and 11% in the cervical segment[12,13]. In adults the localization in the cervical region, associated to symptoms of spinal cord compression or myelorradiculopathy, is still rarer[9,12]. A review of the recent literature referable to these condition, related to the cervical localization disease, there were compiled only five cases with characteristics signs of spinal cord compression[3,4,8,12,13]. We are reporting an additional case of eosinophilic granuloma, the sixth to add to the literature, issuing a displacement of the spinal cervical cord and compression of the roots, whose diagnosis was established after the complete investigation and also by the lesion histopathology. We underline the rarity of the case, the excellent response to the submitted treatment, and the disease's good prognosis in agreement with the results from the reviewed literature.

CASE REPORT

NRAF, 42-years-old-man, white, born in Rio de Janeiro, 12 days interned (june 17th to 29th, 1990), showed at the moment of admission intense right cervicobrachialgy, adopting an antialgic posture of head and neck to the left, along with weakness in the proximal upper limb and numbness in great toe. On this occasion he reported that the cervical pain had started six months ago, with moderate intensity, that increased during playing football or a car trip. He added that 30 days before the internation, he had a drop from a height equivalent of his own over his left upper limb with evolution to local and cervical pain, but showing progressive recovery in a short term. At that time, plain cervical spine X-ray films showed only a slight scoliosis. Since then there were periods of increasing pain, despite being in resting and after treatment with analgesics and nonsteroidal anti-inflammatory drugs presenting no satisfactory responses. Noting progressive strength loss in the right arm, he looked for an orthopedist that asked him for a cervical CT myelography and also prescribed a neurological evaluation.

On the examination the patient showed facies of pain followed by antialgic posture of neck to the left and intense muscle spasm, which hindered the flexing movement of neck and cephalic segment lateralization to the right side; right upper limb paresis, with proximal predominance, involving deltoid, supraspinatus, infraspinatus and biceps, along with weakeness of the right fingers' extension and flexion muscles; hyporeflexia in right biceps and brachioradialis, but with reflexes hyperactives in lower limbs and normal bilateral plantar stimulation responses; right great toe paresthesia. No sphincter dysfunction.

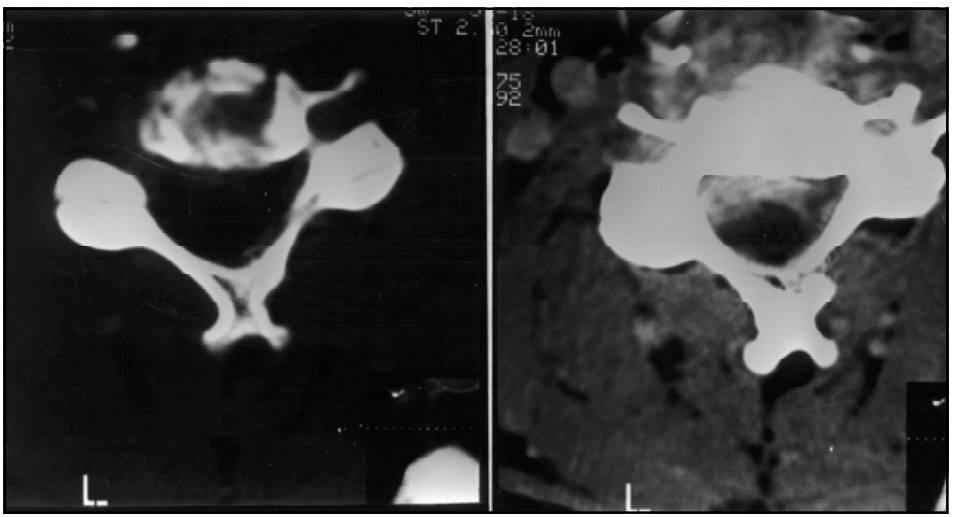

Fig 1. Preoperative venous contrast administration cervical CT scan. A (left) - Showing destruction of the C4 vertebral body. B (right) - Demonstrating the extention of the mass into the vertebral canal at C5 level.

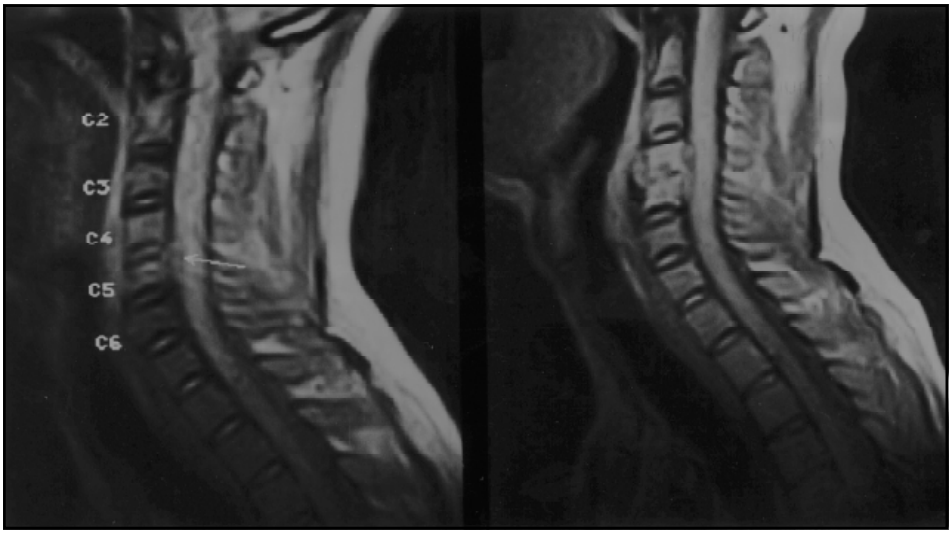

Fig 2. Cervical T2-weighted MRI scans. A (left): Preoperative – demonstrating C4 and C5 vertebral bodies lesions; extradural mass determining compression of the spinal cord, as well as, invading the retropharyngeal space. B (right): Postoperative and postradiotherapy – showing the extradural mass decreased in relation to the previous image and, also, a increased signal involves C4 and C5 bodies suggesting spondylitis.

Routine laboratory tests, like protein immunoelectrophoresis and Bence-Jones protein urine tests were under the standard specifications of normality. X-ray study of the skull and the spinal cord did not exhibit any lytic lesions. Computed tomographic myelography made before the internation, showed that the spinal canal was blocked up almost completely, leaving only a minimum passage at the C6 level of the contrast, due to extradural lesion. A computed tomographic (CT) scan of the cervical spine revealed a lytic lesion of the of 3th, 4th and 5th vertebral bodies with canal obliteration due to extradural mass at the C4-C5 level (Fig 1). Magnetic resonance imaging (MRI) of the cervical spine confirmed the lesion of the 3 th, 4 th and 5th vertebral bodies and the extramedullary, extradural mass at the C4-C5 level determining spinal cord compression and also invading retropharyngeal space (Fig 2A).

The patient was submited to surgical decompression through an anterior approach to the cervical spine with partial exeresis of soft tissue mass and discectomy in C4 level. The histopathological examination of the material showed a typical infiltrate composed of lymphocytes, plasmocytes, histiocytes and eosinophils associated to discrete vascular tissue beside a reticular element confirming eosinophilic granuloma (Fig 3). Eight days after the surgery, radiotherapy was started with low doses (1200 rads) associated with 40mg/day of prednisone and it was noted an evolution marked by a complete regression of the neurological impairment. Postoperative cervical MRI scan showed alteration of the 4th and 5th vertebral bodies signal (T2-weighted), a pattern in agreement with spondylitis encompassing C4 and C5 bodies and also the intervertebral disc, as well as a significant reduction of the lesions in comparison to previous study (Fig 2B). In eight years follow-up, no relapsing was observed and the patient stayed asymptomatic.

DISCUSSION

In 1953, Lichtenstein grouped three diseases under the denomination “histiocytosis X ”: Hand-Schuller-Christian (HSC), Letterer-Siwe (LS) diseases and eosinophilic granuloma (EG), referring to the basic subjacent proliferation of histiocytes (Langerhans’cells) in all three conditions and to the unknown ethiology[2,13-16]. On this occasion, they were already known as variations in extents, involvement stage and localization of the same basic disease of the reticuloendothelial system, with sharp differences both in prognosis and therapy[2,6,10,14].

Although Hand (1893), Schuller (1926) and Christian (1920) had been recognized as an eponym to that disease, there are evidences that Thomas Smith had related the first case 28 years prior to Hand’s report in a 4-years-old-child. The clinical characteristics of the HSC disease observed in infants

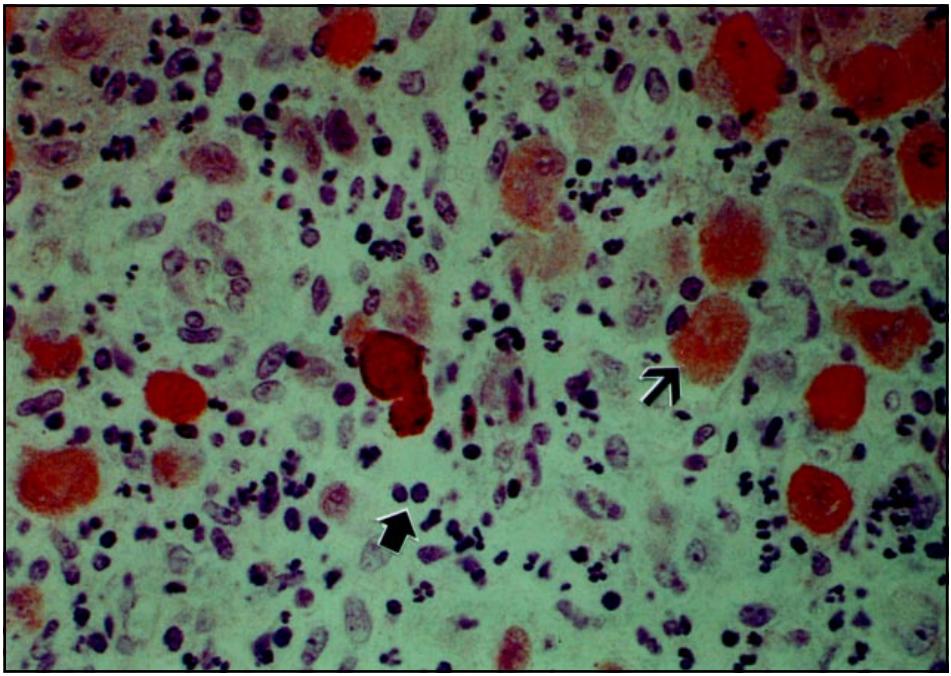

Fig 3. Histopathological study. Prepared antibody protein anti S-100 disclosed infiltrate composed of Langerhans' cells (fine arrow) and eosinophils (broad arrow), characteristic pattern of the eosinophilic granuloma.

and young children includes calvarial or other bones defects, exophthalmos and diabetes insipidus with granulomas affecting bones, hypothalamus, pleura, lung, pericardium, liver, spleen and skin[2,14].

The expression " LS disease " was coined by Abt and Denenholz in 1936, after a description of the cases of Letterer and Siwe respectively in 1924 and 1933[14]. It is a disseminated and fulminant disorder of infancy, clinically characterized by hemorrhagic diathesis, eosinophilia, hepatosplenomegaly as well as histiocytic infiltration of lymphonodes and skin[2,14].

The term "eosinophilic granuloma" was coined by Lichtenstein and Jaffe in 1940 when they reported two cases of solitary lytic bone lesions consisting microscopically of clusters of phagocytic cells and significative collections of eosinophils[1,13,14]. There is considerable disagreement about the nature of the histiocytoses. The term histiocyte refers to a macrophage derived from circulating monocytes of myeloid origin. The histiocytic disorders were generally considered to be closely related conditions varying in the level of maturity and differentiation of the proliferative cells (Langerhans' histiocytes). These disorders range from those of a neoplastic nature to those of reactive proliferations to unknown stimuli[16].

EG is the more frequent and benign form of histiocytosis X (75%), more commonly observed in children and young adults, being the male/female ratio approximately 2:1. In the majority of the cases it consists of a solitary osteolytic lesion with a growth behavior similar to a tumour affecting skull, pelvis, ribs, long bones or spine. The multifocal lesion affecting the skeleton is also described, but less frequently; only approximately 10% of the patients with solitary bone lesion develops multifocal involvement of extra-skeletal sites such as liver, spleen, lymphonodes, skin, oral cavity and lungs as also occurs in HSC and LS diseases[1,8,13,14].

Inside the skeletal spectrum, the solitary vertebral involvement accounts for something like 10% of the cases, more than a half (54%) consisting of thoracic localization followed by lumbar localization (35%)[17,18]. In only 11% of the cases, the cervical spine is affected[10,13].

The cervical lesion commonly appears as a lytic lesion involving the vertebral body with preserved disc spaces[10], nevertheless, atypic cases involve erosion or destruction of pedicles and posterior elements[5,13]. Although the vertebral affection was frequently reported, the involvement of the spinal cord and of the roots is rarely discussed in the literature. Such neurological complications can be due to the vertebral collapse or instability or, also, to the extradural spread of the mass[6,10,11,19,20].

The more common clinical manifestation is local pain and stiffness[11], but the patient could be entirely asymptomatic, developing the symptoms after slight trauma which eventually could imply in a pathologic fracture[10]. In addition, radiculopathy, motor and/or sensitive deficit are observed in the presence of spinal root and cord compression.

Radiographically, the EG lesions range from varying degrees of involvement of the vertebral body and may result in a completely flattened of the vertebra plana, the classical aspect of "coin-on-edge"[10,13], but in the beginnings the lesions could be absent[22]. The cervical lesions usually are lytic, in the core of the vertebral body, while the thoracic and lumbar ones have more tendency towards collapse[8]. Generally the lytic lesion do not generates sclerotic edge, the disc space is not involved and eventually there is a slight paravertebral periosteal reaction[10,13].

The CT scan is useful to detect the vertebral lesion extention, while the MRI is more sensitive to detect medullary and paraspinal soft tissue involvement by vertebral EG[2,11,13].

The management of the patients suffering vertebral EG has been extremely variable and controversial. Some authors sustain that typical lesions do not require biopsy and can be safely followed up by serial radiographs; however other authors justify biopsy for histopathological diagnosis to patients who present solitary vertebral lesion without other skeletal or visceral lesions[10].

Immunological studies have demonstrated that the Langerhans' cells express CD1 (T6) and CD4 (T4) membrane surface antigens and also contain high concentration of S-100 protein in the cytoplasm[2]. In the histopathological diagnosis, whose material can be collected by open or percutaneous biopsy, are used antibodies to protein S-100 or PNA ("peanut –agglutinin") as a specific histiocytic marker revealing the typical lymphohistiocytic and scattered eosinophils infiltrate[2,6,8,10,22].

The differential diagnosis must include the neural tumours (neurofibroma or schwannoma), the Paget's disease, primary benign bone tumours (osteoblastoma, osteoid osteoma), primary malignant bone tumours (Ewing's sarcoma), immunoproliferative diseases (plasmocytoma), leukaemic or lymphoma infiltrations, metastatic diseases and infections (osteomyelitis and tuberculosis)[6,8,10,11,13,23]. The association of thoracic spine EG with HIV infection was described in a recent report. Although underlining the rarety of the concomitance in the literature reviewed, the authors point out to their consideration in serumpositive patients with bone lesions due to the fact that the Langerhans'cells be one of the more important HIV reservoirs in the human organism[24].

Up to now there is no agreement about the best treatment for the vertebral EG since cures have been reported even without any treatment due to the high regenerative and growth potential of the sane tissue[13]. The conservative treatments such as bedrest or external cervical immobilization and corticosteroids are the therapy of choice in patients without progressive neurological impairment, considering the self-limiting nature of the solitary lesion and the high bone regenerative potential in younger patients[9,10,25].

The surgery is recommended in cases of progressive neurological impairment and in the spinal instability. The surgical procedure can be limited to a percutaneous biopsy or a simple curettage of the lesion by open biopsy up to a wide spinal cord decompression which could be made through two ways: by an anterior approach to the cervical spine, including total or subtotal corpectomy with intersomatic fusion or, by a laminectomy and fusion through a posterior approach, depending of the involved elements[9,10,11,13].

The treatment with low-dose radiotherapy (450-1,800 rads) plays a controversial role because the solitary EG is a benign lesion. In the past, it was routinely recommended[23], but nowadays some authors consider it unnecessary[9], being advocated only in the multiple lesions, after biopsy[10,11].

Chemotherapy, principally based upon the intravenous administration of vinblastine and 6-mercaptopurine, is only justified in cases of multiple lesions and whenever the surgery and the radiotherapy have failed[9,10].

In conclusion, based on the literature and following the present case analysis, we suggest that the EG should be considered in the differential diagnosis of the cervical vertebral lesions, even though the radiologic findings do not evidentiate characteristics erosions, what means that the study must be complemented by CT and/or MRI scans; the decompression and surgical stabilization of the cervical spine are both essential in treating patients with neurological impairment. The postoperative radiotherapy, mainly in multiple lesions, aids in a good prognosis, preventing relapse or spread of the lesion. Although considered as the most benign and self-limiting form of histiocytosis X, the malignity potential of the EG is related to the lesion's localization and spread, confirming its relationship with the two other more severe kinds of this reticuloendothelial system disease.

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