Intramedullary Ependymoma: a literature revision following the diagnosis of a clinical case

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Abstract

Low back pain is a common complaint in daily clinical practice. The authors present a clinical case of a 33 year-old man, with a long history of low back pain, shown through supplementary assessment to be an intramedullary ependymoma at D9-L1. Ependymoma is a glial tumor and the most frequent intramedullary neoplasia in the adult patient. The authors present this case to highlight that spinal cord neoplasia, particularly the ependymoma, must be taken into account in the differential diagnosis when investigating patients with a complaint of back pain, especially if shown sensory or motor deficits.

Regarding this case, the authors made a short literature review on intramedullary ependymomas

Key words: intramedullary ependymoma, low back pain.

Introduction

Spinal cord intramedullary neoplasia account for 4-10% of all CNS neoplasia and 2-4% of glial tumors. The most frequent histologic variety is the ependymoma. These tumors have a wide age range, slow growth and can evolve with rare symptoms, what delays any diagnosis, being the most frequent manifestations a local pain in the spine, sensorial and motor deficits. The diagnosis is made based on imagiology, particularly through nuclear magnetic resonance, although a surgical approach should always be tried, helped when necessary by radiotherapy and in exceptional circumstances by chemotherapy. These lesions prognosis depends on its extent and whether the possibility of total removal exists.

Clinical case

A 33 year old man, married, Caucasian, born and residing in Coimbra, office clerk, with complaints of pain located on the lumbar and sacral region for the last 6 months, of a grinding kind, irradiating for the right lower limb, getting worst while walking and drinking alcohol and improving while resting. About 2 months after the pain onset, he mentioned a reduced muscular strength on the right lower limb, paresthesia on the right foot, leg and thigh and trouble walking. He denied fever, asthenia, anorexia, weight loss, as well as any other symptoms.

Without any history of relevant conditions, drinking low amounts of alcohol and without a suggestive epidemiology of any infectious disease or other.

In the family history, it should be highlighted his father death by non-Hodgkin lymphoma of low malignant grade.

On the physical exam there was an accentuated muscular atrophy on the right thigh, reduced muscular strength (grade IV in V), mainly while bending, reduced right patellar reflex, painful bilateral hypoesthesia at L1 sensitivity level and spastic paretic gait. The remaining physical exam showed no alteration.

We came up with several diagnosis hypothesis, namely an intervertebral disc condition, infectious pathology, possibly brucellosis or tuberculosis, and primary tumoral pathology or column or spinal cord metastasis.

This patient supplementary study has shown a normal hemogram, CRP 5 mg/dL, ESR 30 mm on the 1st hour, normal glycemia, ionogram, liver and kidney functions, proteins and urinalysis II showed no changes and the Rose-Bengal test was negative. Lumbosacral spine X-ray did not show any alterations and the electromyography has revealed a chronic

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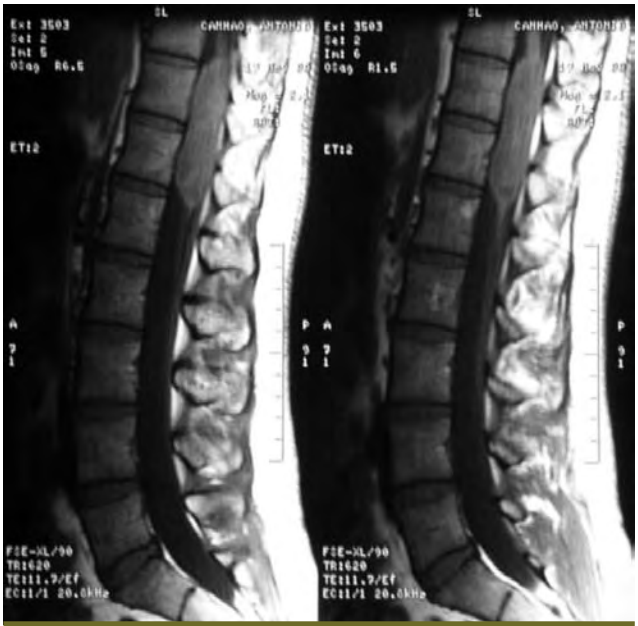
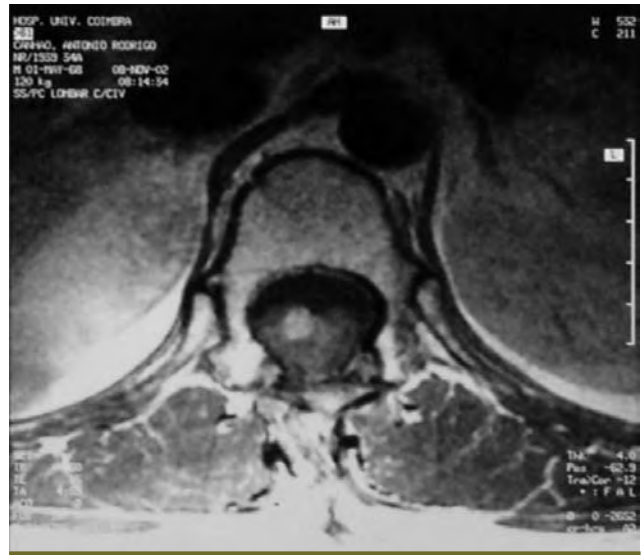


Spine MRI (intramedullary lesion D9-L1).

FIG. 1



Spine MRI (Paramedian lesion in D12).

FIG. 2

right L3-L4 radiculopathy. The spine MRI *(Fig. 1)* has shown a growing intramedullary injury, from the lower part of D9 body to the upper part of L1 body (7.3x2.2 cm – 2.8 x 0.8 inch), with a hypersignal in T2 and hyposignal in T1 and homogeneous aspect after gadolinium. ADA dosage was also requested and proven normal with a negative Mantoux test.

The patient was then subject to D9-L1 laminectomy removing part of the intramedullary tumor, having the histologic study revealed to be an ependymoma. After the surgery he underwent several radiotherapy sessions.

Clinically, he kept all radiculopathy complaints and the follow-up MRI has revealed a small anterior paramedian right formation facing D12 *(Fig. 2)*.

This result has suggested a lesion recurrence, leading to PET to be performed with a 16-Fluorodeoxyglucose (FDG), showing a marked reduction capturing FDG in the spine from D8 to L3 comparing to previous radiotherapy, without FDG enhanced or abnormal capturing foci, namely in D12. It was concluded then, not to be a recurrence. At present the patient has kept a non-progressive L3-L4 right radiculopathy which leads to spastic paretic gait.

This case shows that a long time can pass between the symptoms onset and these lesions diagnosis as sometimes patients do not pay much attention to pain located in the spine, as it is this patient example who only looked for medical care when he realized his muscular atrophy in his right thigh. Another current difficulty in this condition is the fact that the spine X-ray does not show, in most cases, any changes. So, before all the complaints kept with normal X-ray, the patient should undergo another kind of imagiology test, namely CAT scan or MRI. Another factor worth mentioning in this case is how difficult it is to try an excision of intramedullary tumors, because the attempt of total removal of intramedullary tumors, mainly the ependymoma with a very slow growth, may have much more serious sequella than its partial removal.

Discussion

Spinal cord intramedullary neoplasia account for 4-10% of CNS neoplasia and 2-4% of glial tumors[1]. Most spinal cord neoplasia are malignant and 90 to 95% are glioma, most of which are ependymomas or astrocytomas. Ependymomas are more frequent in adults (up to 60% of glial tumors[2]) and astrocytomas in children.[1]

These tumors have a wide age range, from the early months of life to after 80 years of age. The average is

39 years old, being most patients of the male gender (57%).[2-5]

Frequently there is a significant time gap from the symptoms onset to the ependymoma diagnosis, an average of 36.5 months[2], and most patients are oligosymptomatic. Initially they can present low back pain or cervicalgia, depending on the location (67%), sensorial deficits (52%), paresis (46%) or sphyncter dysfunction.[2-5] Sensorial symptoms are more associated to more central locations of the tumor in the spinal cord, while motor symptoms usually have underlying lesions of large dimensions.[1]

Intramedullary ependymomas usually have a slow growth and tend to compress more than invading the adjacent spinal cord.[2-5] They come from the ependymal cells in locations from the brain to the spinal cord[6] forming frail lesions, gray, well delimited leading to a spinal cord symmetric expansion and might be associated to syringomyelia and cysts.[7] 6 histologic types are known: cell (the most common), papillary, clear cells, tanycytic, myxopapillary and melanotic (the most rare). Cystic degeneration occurs in 50% of the cases being bleeding a common occurence.[7] Recently rare cases of an ependymoma variant, named as epithelioid were described.[8]

Intramedullary tumors can occur sporadically or in families and several gene mutations have been associated with these tumors.[9] It is thought that several genetic routes are involved in its formation and progression. [6] In some intramedullary ependymomas neurofibromatosis 2 (NF2) gene mutations, loss of heterozygosity on the chromosome 22 long arm and rearranged in 11q13 were found. In this last region it is located the gene MEN1, and the loss of such gene seems to be implicated when ependymomas evolve towards malignancy[6].

Most ependymomas are located exclusively in the cervical region (44%), 26% have a dorsal location, 23% attain simultaneously both regions the cervical and dorsal and only 6.5% are located on the lumbosacral region.[2-5] When in this region, they are more often located in the conus medullaris and in the cauda equina, but they can also arise in the sacrum in an extradural position, in the pre-sacral tissues and in the subcutaneous tissue over the sacrum, being usually the myxopapillary type and are associated with spina bifida.[10] Intradural tumors can spread into the CNS, while extradural ones are a reason for concern due to the likelihood of extraneural metastases.[11]

After the age of 50, ependymomas account for 83% of intramedullary tumors and most are located in the thorax (up to 55% of cases). Characteristically the symptoms are sensory (dysesthesia) and seldom are motor, usually with a wider time gap from the symptoms onset to the diagnosis.[12]

In terms of diagnosis, imagiology plays a crucial role. Conventional radiology can show: scoliosis (16%), widening of the vertebral canal (11%), vertebral bodies deformed and eroded pedicle.[4] Myelography, less and less used, can reveal a partial or total block of the contrast material flow and CAT scan with iodated contrast can show an expansive non-specified lesion.[4] MRI is the best imagiology method to diagnosing intramedullary tumors and in general, shows a formation with a T2 hypersignal that can be isointensive, or it might have an hyper- or hyposignal in T1.[13,14] After using gadolinium contrast, such tumors have an homogenous aspect, although sometimes it looks heterogenous with cystic images, in which case the differential diagnosis with astrocytoma and hemangioblastoma must be made.[14] When the tumor borders are well defined, the post-contrast aspect is homogeneous and the tumor is located centrally, it favors an ependymoma diagnosis instead of other intramedullary tumors.[15] Recently, also PET (*Positron Emission Tomography*) with 18F- fluorodeoxyglucose or 11C-methionine, was used to the diagnosis of intramedullary tumors showing usually hyperabsorption. However, PET does not show any additional usefulness compared to MRI at the diagnosis stage, but it can be important while evaluating the residual or recurrent disease.[16,17]

The early diagnosis, before the symptomatic progression, is critical for the adequate treatment of such patients.[18] Their treatment goal is the total removal of the post-surgical neurologic deficit. The optimum treatment for intramedullary tumors is controversial, as both surgery as conventional radiotherapy are associated with potential morbidity.[19] In most intramedullary ependymomas one can achieve a total surgical removal[20], being surgical resection the treatment of choice for extra- and intradural ependymomas.[11] The possibility of a total removal is influenced by the tumor location (only in 42% of the cases located in the conus medullaris *versus* 97% in other locations) and by histology (42% myxopapillary subtype and 97% non-myxopapillary).[21]

The biggest tumors are those linked to higher

neurologic deficits in the pre-operative period and to the worst neurologic prognosis, namely what regards post-operative dysesthesia.[20] Apart of the tumor length, the ratio between the tumor width and the spinal cord maximum width in the tumor region is also a good predictor of the pre-operative clinical condition and the patient neurologic prognosis, it has been verified that values above 0.80 are indicative of a bad prognosis.[20]

Adjuvant therapy is also recommended for rare cases of malignancy, tumor spreading or after a partial tumor resection.[18]

Radiotherapy role in the treatment of intramedullary tumors remain controversial, as post-operative radiotherapy does not influence substantially the local control of the disease nor the survival of patients with medullary ependymoma.[21,22] Although radiotherapy effectiveness has not been definitely proven, its recommendation is frequent in intradural ependymomas where total resection was not possible or when there is a local recurrence or spreading into the CNS.[11,23,24] In patients over 50 years of age, radiotherapy has been very used, but recent studies recommend the aggressive microsurgical resection driven by evoked potential, as benign lesions prognosis after such approach, is excelent.[12] Advanced technology, through stereotactic radiosurgery can, theoretically provide higher doses of radiation to lesions that can not be treated with surgery enabling, on the other hand, to avoid that large areas of the spinal cord would be exposed to radiation.[19]

The treatment of patients with recurrent ependymoma, in which both surgery and radiotherapy have failed, is troublesome. Chemotherapy which does not have in these tumors an important role,[11] is mainly targeted to children, as these are more sensitive to the deleterious effects of radiotherapy.[25] A variety of regimes have been used in recurring intracranial ependymoma including ectoposide, carboplatin, PCV, MOPP, alternating cyclosphosphamide and vincristine with cisplatin and ectoposide and bone marrow autologous transplant,[26-32] but no regimen has shown advantage towards the other and their efficacy was reduced. When the ependymoma has intramedullary location, ectoposide may be a good alternative.[33]

The post-operative functional condition depends on the patient functional condition before the surgery[18,21,34] and the extent of surgical resection,[21] although the latter is not a consensus.[34] On the other hand, the patient´s age seem not to be a worst prognosis indicator.[12,34] Therefore the ependymoma total removal must be always attempted.[21]

The 5 year survival rate in patients with spinal cord ependymoma is 82%, regardless of pre-operative neurologic deficits, but at 20 years of age is only 33 to 50% and it is related with the neurologic dysfunction previous to the surgery.[4]

In spite of the risk of local recurrence and spreading into the CNS, lumbosacral intradural ependymomas have a good prognosis, with a survival rate above 90% at 10 years. Extradural forms have a worst prognosis, highly dependent on its location, with dorsal-sacral tumors with a better prognosis that pre-sacral ones.[11]

To conclude the intramedullary ependymoma, in spite of being a rare CNS neoplasia, is a situation that must be taken into account when establishing the differential diagnosis in patients complaining of pain in the spine or presenting sensory or motor deficits, mainly in young adults. ■

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