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Cervical Eosinophilic Granuloma in Adolescents: Case Report and Literature Review

Granuloma eosinofílico cervical en el adolescente: Reporte de un caso y revisión de la literatura

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Abstract

Introduction Eosinophilic granuloma (EG) is a rare, tumor-like lesion, infrequently affecting the cervical spine, particularly in adults. Although vastly described in literature, this pathology mainly affects children, and there is still no consensus on its treatment in older patients. With the goal of contributing to increase the knowledge regarding this infrequent pathology, we present a case of a C3 eosinophilic granuloma in a 16-year-old patient, who was treated conservatively, with good results, including complete return to his previous activities.

Clinical case a 16-year-old male, elite rugby player, presented with a history of persistent neck pain, mainly at night, with no previous trauma. Upon physical examination, he reported neck pain with axial compression of the head, without neurological impairment. Both computed tomography (CT) and magnetic resonance imaging (MRI) scan revealed an aggressive lytic lesion in the C3 vertebral body, a with monostotic presentation on positron emission tomography-computed tomography (PET-CT) compatible with a primary spine tumor. A CT-guided percutaneous biopsy was obtained to establish the diagnosis and provide the proper management. The results were compatible with Langerhans cells. As he presented no symptoms or imaging findings of evident bone instability, as well as no neurological impairment, the patient was treated conservatively, with a cervical brace, oral pain medication and close follow-up. A CT obtained after four months of treatment showed reparative changes of the C3 vertebral body; at this point, the patient reported no neck pain, so he was able to return to his previous activities.

Conclusions Although an EG is rare at this age, it should be considered in the differential diagnosis of primary vertebral aggressive lytic lesions. Imaging and a vertebral biopsy are paramount to confirm the diagnosis. The treatment modality

Keywords
- eosinophilic granuloma
- bone tumor
- cervical
- Langerhans cell histocytosis
- histocytosis X

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depends on the symptoms, the involvement of adjacent structures, and the stability of the affected vertebra. Conservative management including clinical and imaging follow-up is a viable option.

Resumen

Introducción El granuloma eosinofílico (GE) es una patología infrecuente, sobre todo en adultos, que puede afectar la columna cervical. A pesar de la vasta literatura, esta enfermedad afecta principalmente a la población infantil, y no hay un consenso sobre el manejo en adultos. Con el objetivo de aportar conocimiento respecto a esta patología poco frecuente, se presenta un caso clínico de GE cervical en un paciente de 16 años, a quien se trató de manera conservadora, con buenos resultados y retorno completo a sus actividades.

Caso Clínico Un hombre de 16 años, seleccionado de rugby, consultó por dolor cervical axial persistente y nocturno de 6 semanas de evolución, sin trauma evidente. Al examen, destacó dolor a la compresión axial sin compromiso neurológico asociado. Los exámenes de tomografía computarizada (TC) y resonancia magnética (RM) revelaron lesión lítica en el cuerpo de C3 de características agresivas, de presentación monostótica en tomografía por emisión de positrones-tomografía computada (TEP-TC) compatible con tumor primario vertebral. Se decidió realizar biopsia percutánea bajo TC, para definir el diagnóstico y manejo adecuado, la cual fue compatible con células de Langerhans. Al no presentar clínica ni imagenología de inestabilidad ósea evidente o compromiso neurológico, se manejó con tratamiento conservador, inmovilización cervical, analgesia oral, y seguimiento estrecho. A los cuatro meses de evolución, se presentó con una TC con cambios reparativos del cuerpo vertebral y sin dolor, y logró retomar sus actividad habituales.

Conclusiones El diagnóstico de GE es infrecuente a esta edad, y se debe plantear entre diagnósticos diferenciales de lesiones líticas agresivas primarias vertebrales. Es necesario el uso de imágenes, y la biopsia vertebral es fundamental para confirmar el diagnóstico. Su manejo va a depender de la sintomatología, del compromiso de estructuras vecinas, y de la estabilidad de la vértebra afectada. El manejo conservador con seguimiento clínico e imagenológico es una opción viable.

Palabras clave
- granuloma eosinofílico
- tumor óseo
- cervical
- histocitosis de células de Langerhans
- histocitosis X

Introduction

Eosinophilic granuloma (EG) is the most frequent and benign form of Langerhans cell histiocytosis (LCH).[1] It is a pseudotumoral lesion rarely found in the region of the spine, comprising less than 1% of spinal tumors.[2] The most frequently affected skeletal sites are the skull, the pelvis, and the diaphysis of the long bones, involving the spine in 7% to 25% of the cases.[3] It mainly affects the thoracolumbar spine, generally during the first decade of life, and its location in the cervical spine is infrequent.[2,4,5]

The clinical presentation is variable, but it generally begins with neck pain associated or not with stiffness and weakness in the extremities.[2,6,7]

Vertebral lytic destruction is the usual radiological sign, but in certain cases vertebral collapse (vertebra plana) can be observed, mainly in the thoracolumbar spine.[8,9] Computed tomography (CT) is quite helpful in characterizing and determining the extent of the lesion.[10] Some studies[11,12] have shown that magnetic resonance imaging (MRI) increases the diagnostic precision by enabling an evaluation of the intensity in T1 and T2, in addition to enabling the assessment of paravertebral masses and spinal cord involvement. However, the definitive diagnosis is established through biopsy.[13]

Among the differential diagnoses of aggressive vertebral lytic lesions are Ewing sarcoma, multiple myeloma, osteochondritis, tuberculosis, and osteomyelitis, among others, with oncological and surgical treatments that are diametrically different and that can determine their oncological prognosis.[2,9]

The treatment of vertebral eosinophilic granuloma varies from conservative management with immobilization, relative rest and use of anti-inflammatories, to the need for surgery, chemotherapy, radiotherapy, or a combination of both.[2,14,15]

We herein present the case of a 16-year-old boy who, after consulting for neck pain predominantly at night and undergoing a subsequent CT-guided percutaneous biopsy, was

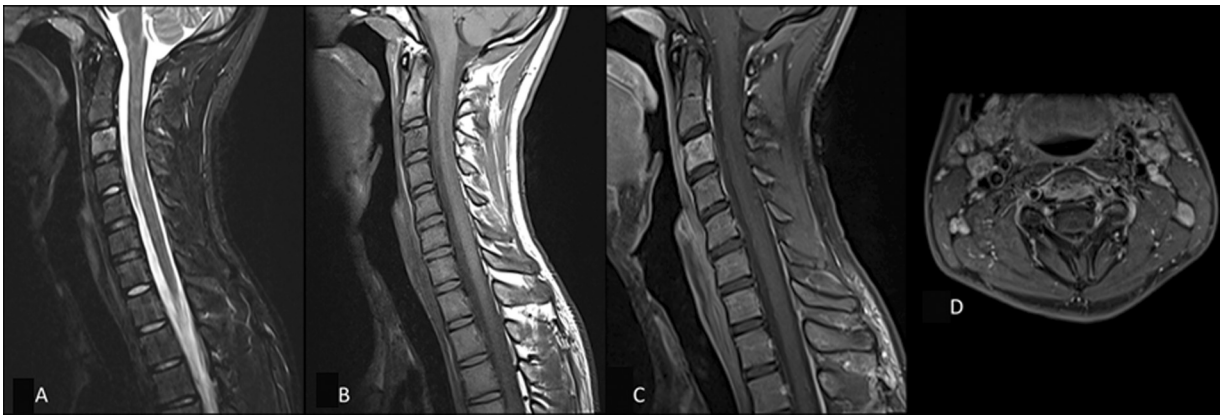

Fig. 1 Cervical spine MRI. Sagittal view in short-tau inversion-recovery (STIR) (**A**) and T1-weighted sequences (**B**). A diffuse increase in the signs of the C3 vertebral body is observed in the STIR sequence and slight hypointensity in the T1-weighted sequence. In sagittal (**C**) and axial (**D**) contrast-enhanced views with fat saturation, the alteration presents contrast uptake, without evident extraosseous involvement.

diagnosed with cervical Langerhans cell histiocytosis, which was managed conservatively. Four months after the diagnosis, the patient felt no pain, had full mobility, and recovery signs in imaging exams.

Clinical case

A 16-year-old male patient, a junior school-level rugby player, with no relevant personal or family history, presented to an outpatient consultation due to persistent and progressive axial cervical pain, that had begun 6 weeks before and was predominantly nocturnal, with no history of weight loss or other red flags. The physical examination revealed pain on axial compression, without stiffness or weakness in the extremities.

An MRI scan was requested, which was complemented with the use of contrast and a CT scan, given the consistent finding of a lytic lesion in the body of C3 with destruction of the posterior cortical bone, associated with bone edema in the left pedicle and no soft tissue compromise (►**Figures 1** and **2**).

The laboratory tests reported a quantitative C-reactive protein of 0.51 mg/dL (normal level: 0.1-0.5 mg/dL). The results of the complete blood count, coagulation tests and biochemical profile were all within normal ranges.

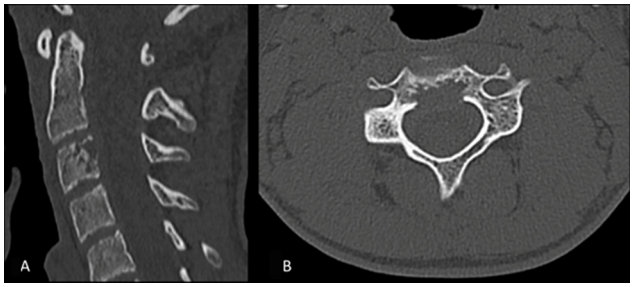

Fig. 2 For a better characterization of the bone compromise, it is complemented with a CT scan. Reconstructions with sagittal (**A**) and axial (**B**) bone algorithm. The C3 body lesion shows a permeative lytic aspect, with poorly-defined margins, with cortical destruction and slight bulging of the posterior wall.

On positron emission tomography-computed tomography (PET-CT), the C3 lesion had a hypermetabolic mass, with signs of local aggressiveness and no evidence of neoplasms or other foci in the rest of the body; thus, a polyostotic presentation was ruled out.

In order to rule out benign-aggressive, malignant or infectious tumor pathologies, to establish the histological diagnosis and define the therapeutic approach, we decided for a posterior biopsy with a percutaneous technique guided by CT performed by an interventional radiologist (at the Memorial Hospital for Cancer and Allied Diseases, in New York, by decision of the relatives).

The anatomicopathological study showed tissue with atypical cells with irregular nuclei and abundant eosinophilic cytoplasm, compatible with Langerhans cells. There was immunohistochemical expression of S100, CD1a, langerin, CD68, and CD45.

Given the presence of bone stability and absence of neurological symptoms, we decided, along with the spinal, neuroimaging and oncology teams in NY, for temporary cessation of sports activities and conservative management with a rigid Philadelphia neck collar (Össur, Reykjavik, Iceland) for 12 weeks, with subsequent progressive removal as per tolerance. At four months of evolution, the patient felt no pain, was able to fully return to his school activities and had undergone a control CT that reported signs of bone regeneration and reparative changes of the lytic lesion of the C3 vertebral body (►**Figure 3**), and a progressive return to sports was authorized. At 12 months of evolution, the patient was asymptomatic, lived a normal life without restrictions regarding sports, and had undergone new cervical CT and MRI scans that reported reparative changes of the cervical lytic lesion of C3 without signs of activity or development of new lesions.

Discussion

Also known as histocytosis X, EG is the benign presentation of Langerhans cell histiocytosis in bone tissue, affecting the

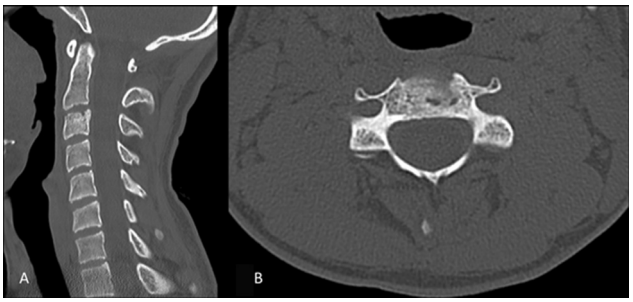

Fig. 3 Control CT of the cervical spine at the fourth month after the biopsy. Reconstructions with sagittal (**A**) and axial (**B**) bone algorithm. Advanced reparative changes of the lytic lesion of the C3 vertebral body are identified, with sclerosis and cortical reconstitution.

reticuloendothelial system, and in which the proliferation of eosinophils and histiocytes is a typical feature.[4,7,11] It is a rare disease that constitutes less than 1% of bone tumors and compromises the spine in 7% to 25% of the cases, affecting the cervical spine in only 0.02% of the cases.[3,8,16] Although it can occur at any age, it generally occurs in children, with 80% of the cases in those under 10 years of age.[4,11] However, among the differential diagnoses to rule out are plasmacytoma, primary sarcomas (especially Ewing sarcoma due to age), multiple myeloma, osteochondritis, tuberculosis, and osteomyelitis. Therefore, clinical suspicion, diagnosis and proper management are of the utmost importance.[2,9] The histological diagnosis is essential to establish a definitive therapeutic approach, which varies radically according to each pathology.

Cervical EG presents with neck pain in 80% of the cases in the pediatric population and in almost 100% of the adult population. The second most common symptom is limited range of motion of the joint, followed by neurological symptoms, which similar in both children and adults.[1,2] Regarding neurological compromise, it is more frequent in cases that affect the thoracic or lumbar spines, since the cervical region presents with pain or stiffness in early stages, which contributes to the establishment of an early diagnosis, prior to the possible collapse and compression of spinal elements.[17,18] However, Prasad and Divya[8] observe that, in the adult population, 61% of the cases present neurological symptoms. In the case herein described, the patient only presented nocturnal neck pain of 6 weeks of evolution, without associated neurological symptoms or limitation of the range of motion of the joint.

Regarding the imaging study, it should start with simple radiographs, with the vertebral lytic lesion being the most common and characteristic sign, regardless of the affected vertebral segment, which can lead to delayed vertebral collapse, also called vertebra plana.[8,11] Although EG is the most common cause of vertebra plana, Ewing sarcoma, lymphoma, tuberculosis, and osteogenesis imperfecta can also cause it.[9] It should be noted that this sign is more common in cases in which the thoracic or lumbar spines are affected, and uncommon in cervical cases, in which the compression forces generated by the axial load are lower.[2,19]

From the radiological point of view, in the differential diagnosis of single spinal injuries several factors must be taken into account, such as the age of the patient, the location of the lesion, and imaging characteristics,[20] which evaluated through the preferred study modalities, which correspond to CT and MRI. Regarding age, in those under 30 years, spinal tumors are infrequent and mostly benign, with some exceptions[20] (Ewing sarcoma, osteosarcoma). Regarding location, the lesions can be grouped into those centered on the vertebral body and those that compromise the posterior elements (with or without extension to another compartment). In the first group, classic malignant pathology is found, except for EG granuloma, giant cell tumor and hemangioma.[20,21] On the other hand, lesions involving the posterior elements include benign lesions such as osteoid osteoma, osteoblastoma, aneurysmal bone cyst, osteochondroma, and sarcomas[20,21] (Ewing sarcoma, osteosarcoma). When analyzing the imaging characteristics, it is important to assess whether the lesion is lytic or sclerotic, the appearance of the margins and the transition zone, the presence of matrix, and other differentiating elements[20] (such as fluid-fluid levels). Considering this particular case, it is possible to limit the differential diagnosis to lytic lesions, which affect patients under 30 years of age and compromise the vertebral body, and the main ones are: EG, chondroblastoma, osteosarcoma and Ewing sarcoma. In 10% to 15% of the cases, EG compromises the spine, and the cervix is the least common location. Regarding imaging, in its classic form it manifests as partial or total collapse of the vertebral body (vertebra plana) with preservation of the pedicles, posterior elements and intervertebral discs, and absence of osteolysis and soft tissue mass. However, osteolysis and soft tissue mass may be present and determine an aggressive appearance.[20–22] Chondroblastomas are benign cartilaginous lesions with a preference for the growing skeleton,[20] which affect the vertebral body and posterior elements. They are frequently lytic lesions with smooth or lobulated margins, sclerotic, with the presence of internal calcifications in 50% to 60% of the cases.[22] Ewing sarcoma as a primary vertebral tumor is uncommon, with a prevalence of 3.5% to 15%, with the cervical spine being the least affected (3.3%).[20,23] In most cases, it manifests as aggressive lytic lesions, with invasion of the spinal canal and a paravertebral soft tissue mass that is usually larger than the bone lesion.[20,23] Only 5% of osteosarcomas originate in the spine, with lumbar and thoracic locations being the most frequent.[21] They preferentially affect the posterior elements, but in up to 17% of the cases they extend to the vertebral body.[23] Conventional osteosarcomas are blastic lesions with variable production of osteoid, cartilage, and fibrous tissue.[20,23] It is not always possible for radiologists to establish a specific diagnosis of a bone lesion. In these cases, however, guidance on the aggressive or non-aggressive aspect of the lesion is expected to support the clinical decision.

The evaluation of the of the paravertebral tissue and posterior elements involvement, which may be associated in 46% of cases, has been made easier thanks to the contribution of CT and MRI.[8]

Eosinophilic granuloma generally presents in isolation, but the literature[8,11,14,24] reports that in 10% to 25% of the cases it can be multifocal, with PET-CT or scintigraphy being very useful to investigate these lesions. In the case herein reported, due to the aggressiveness of the lesion observed on the CT and MRI scans, we decided to perform PET-CT to assess whether the presentation was of a mono- or polyostotic lesion, and the latter was ruled out.

Despite the aforementioned imaging signs, it should be noted that EG can present in various ways, which is why it is known as a great imitator pathology. Although certain studies[18] do not support the routine use of biopsy, especially in isolated cases and with a typical presentation, through the use of CT-guided Tru-cut (Merit Medical, South Jordan, UT, United States) biopsy physicians have been able to obtain samples more safely and with an accuracy between 70-100%;[8,14] therefore, it is considered a first-line tool for diagnosis, commonly used and, for some, essential, despite the lack of consensus on the matter.[9,11,15]

However, cervical spine biopsies are more difficult to obtain due to the anatomy and smaller size of the vertebral elements, as well as the presence of critical neural and vascular structures.[25] There are few publications on the procedural safety and diagnostic performance of CT-guided percutaneous biopsies. In this context, in 2018, Wiesner et al.[25] published a report of 73 patients who underwent CT-guided percutaneous cervical bone biopsies to study suspected infection or tumor pathology. In 96% of the cases, they obtained sufficient samples, without serious complications (there were two cases of vagal reaction). The predominant access route was the posterolateral route, which involves a longer path, but enables the avoidance of the dreaded neurovascular structures. The study[25] shows the usefulness of the technique, as an alternative to open biopsies, for diagnostic confirmation of cervical bone lesions, with good safety parameters and diagnostic performance.

In asymptomatic patients or those who present little pain without associated neurological symptoms, the conservative treatment is indicated, which consists of the temporary cessation of sports activities, immobilization with a rigid collar, and analgesia.[2,4,8,9,15,19] Angelini et al.[9] recommend the use of intralesion methylprednisolone infiltration after biopsy, to reduce the bone edema and relieve pain. In vitro studies[26,27] have shown the production of interleukins and prostaglandins by Langerhans cells, which would induce the bone resorption observed in EG and could explain the benefit provided by the use of corticosteroids. We do not consider their use on a regular basis since there are no protocols regarding the dose to be administered, and, though rare, cases of complications such as osteomyelitis and obstructive hydrocephalus have been described.[28,29]

The surgical treatment is reserved for those cases that present bone instability or neurological deficit, and it ranges from curettage with biopsy, corpectomies associated or not with fusion, to laminectomies.[2,4,7,8]

The conservative treatment with immobilization, complemented with low-dose radiotherapy for mild symptomatic cases, is controversial, since studies[9,30] argue that it can limit both the progression of the disease and bone regeneration itself.

The existing literature on EG is vast, but it is mainly on the pediatric population, especially children between 5 and 10 years of age. There is no consensus regarding management in young adults, and there are many diofferent therapeutic options, none of which has randomized and long-term studies to support them. However, it is of the utmost importance to adequately rule out differential diagnoses, since they vary significantly, both in terms of treatment and of prognosis. Despite the multiple therapies for cervical EG, the results are generally promising, regardless of the procedure applied, with a low rate of recurrence.

We have herein presented the case of a 16-year-old boy with a histological diagnosis of EG, for whom the conservative management with cervical immobilization, rest, and oral analgesia resulted in excellent outcomes, which enabled him to return to his previous activities and provided complete cessation of his symptoms.

Conflict of Interests

The authors have no conflict of interests to declare.

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