Review Article

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Surgical Treatment of Langerhans Cell Histiocytosis of Cervical Spine: Case-Report and Systematic Review of Literature

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Background: Langerhans cell histiocytosis (LCH) is a rare disease involving the cervical spine. This condition is present firstly in the thoracic spine, commonest, followed by the lumbar spine and cervical spine. In Langerhans cell histiocytosis there is excessive proliferation of pathologic Langerhans cells. It is commonly found in males with a ratio of 2.5:1. The etiology of LCH is unknown. There are three defined entities classified on their severities. Letterer-Siwe disease involves multiple organs, Hand-Schuller-Christian disease presents with bony lesions and endocrine abnormalities, and eosinophilic granuloma (EG) presents with isolated bony lesions. We describe a case-report a girl with Langerhans cell histiocytosis in cervical vertebrae.The objective of this study is to show the rare case of Cervical Spine Langerhans Cell Histiocytosis.

Method: We were a literature review with inclusion and exclusion criteria and we described a case-report.

Case-Report: A 9-month-old girl had neck pain associated with right upper limb weakness. Imaging showed infiltrative and expansive lesions in the vertebral body from C1 to C6 with spinal cord and root compression. The patient underwent a laminectomy from C2 to C5. Histopathological was suggestive of LCH.

Conclusion: Despite the rarity of the disease, Langerhans cell histiocytosis can be treated with a surgical approach when neurologic deficits are present.

Keywords: Langerhans cell Histiocytosis, Cervical Spine, Extradural Tumor, Neurosurgery, Pediatric Neurosurgery

INTRODUCTION

Langerhans cell histiocytosis (LCH), formerly known as Histiocytosis X, is a rare non-neoplastic bone disease that can affect the spine. It is more commonly found in males, with a reported male-to-female ratio of 2.5:1. The incidence of LCH is approximately 1 in 1,500,000 individuals. The etiology remains unknown. The pathophysiology involves the excessive clonal proliferation of pathological Langerhans cells, which originate from the monocyte-macrophage lineage.

Bunch [4] summarized the most common sites of LCH involvement as follows: 27% in the skull, 15% in the femur, and only 6.5% in the spine. LCH can present in three clinical forms: Letterer-Siwe (LW), Hand-Schüller-Christian disease (HSCD), and Eosinophilic Granuloma (EG). Hand-Schüller-Christian disease is characterized by eosinophilic granuloma lytic bone lesions, diabetes insipidus, and exophthalmos. Letterer-Siwe disease is an aggressive and typically fatal systemic condition that involves infiltration of the skin, liver, spleen, and bone marrow by reticuloendothelial cells.

In the spine, the vertebral bodies are most commonly affected, while the posterior elements are generally spared. Among spinal sites, the thoracic region is the most frequently involved, followed by the lumbar and cervical regions. LCH of the thoracic spine was first described by Compere [1] et al., while Macnab [2] et al. later reported eosinophilic granuloma in the cervical spine. Bertram [3] et al. conducted a comprehensive literature review and identified 53 cases of cervical eosinophilic granuloma, 43 of which occurred in children. Notably, approximately 60% of cervical spinal lesions in pediatric LCH patients affect the C3-C5 levels [3].

The clinical manifestations of LCH are variable. Lesions in the cervical spine typically present with neck pain and stiffness, often without any history of trauma. Neurological examination findings can range from normal to significant deficits, including radiculopathy or myelopathy.

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The objective of this study is to present a rare case of LCH in the cervical spine of a baby girl and to conduct a literature review on this disease.

MATERIALS AND METHODS

Literature Search Strategy

The literature review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, while the case report adhered to the CARE (Case Report) protocol. For the literature review, the authors utilized databases including PubMed, MEDLINE, and EMBASE, employing recursive literature searches covering the period from 1987 to 2024. The key search terms were “Langerhans cell histiocytosis” AND “Cervical vertebrae” AND “Epidural neoplasms”.

Study Selection

The studies were submitted inclusion and exclusion criteria. The inclusion criteria were: 1) The studies were original research articles. 2) Study design were clinical trial, systematic review with and without meta-analyses, randomized controlled trial and review of literature. 3) Only Pediatric population. 4) The studies selected was just English-written. Exclusion criteria: 1) Studies non-english-written. 2) Cases of LCH in adult population and non-cervical spine or other bony involvement. 3) Duplicate records were removed (figure 1)

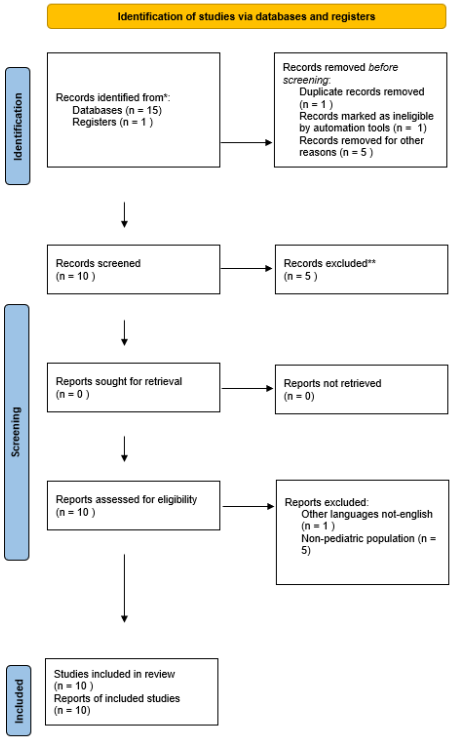

Figure 1- PRISMA flowchart; representative of the criteria for identification, screening, eligibility, and inclusion and exclusion of the systematic review.

RESULTS

Case-Report

A 9-month-old girl weighing 6 kg was referred for evaluation due to a two-week history of neck pain and torticollis, with no history of trauma. The pregnancy and childbirth were uneventful. Neurological examination revealed mild hemiparesis (Grade IV on the MRC scale) in the right upper limb. Laboratory findings, including erythrocyte sedimentation rate and C-reactive protein levels, were all within normal limits. The child underwent an MRI of the skull and cervical spine (Figures 2, 3, and 4).

The patient was admitted to the hospital for a possible biopsy and excision of the lesion. She was taken to the operating room (OR) under general anesthesia. The chosen approach was posterior cervical, with the patient in a prone position and under neurophysiological monitoring. A midline incision was made from the external occipital prominence to C7. Blood loss was minimal, mitigating the risk of hypovolemia. Exposure of the posterior cervical spine revealed soft laminae, allowing for easy dissection. The laminae of C3 and C4 were excised without fluoroscopic guidance and sent for histopathological examination. Additionally, the intracanal lesion was directly excised.

The patient was discharged three days after surgery. Approximately two weeks postoperatively, the histopathological exam confirmed the diagnosis of Langerhans cell histiocytosis (LCH). Unfortunately, the patient passed away two months after initiating chemotherapy due to infectious complications.

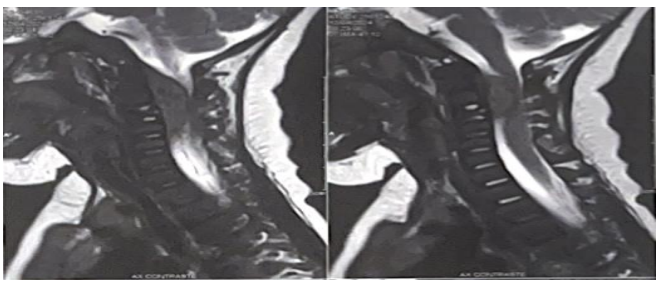

Figure 2 - Sagittal T2-weighted MRI scan show the lesion at the level C2 to C5 with spinal cord compression

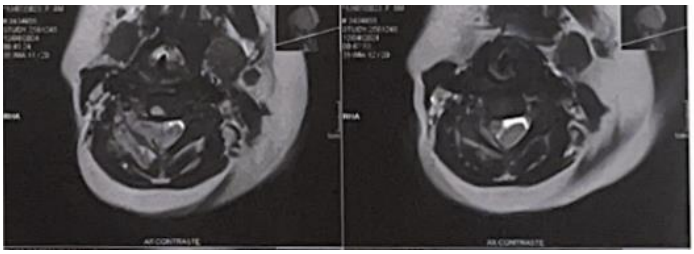

Figure 3 - Axial T2-weighted MRI scan show the lesion within the foramen C3-C4

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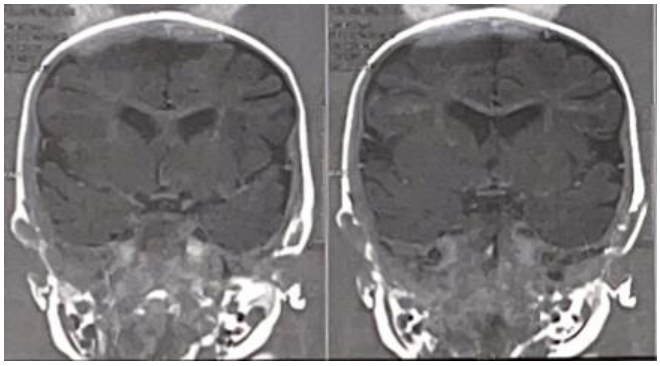

Figure 4- Coronal IR-weighted MRI scan evidencing intracranial lesion in bilateral frontoparietal bone

DISCUSSION

Children with Langerhans cell histiocytosis (LCH) of the cervical spine generally present with sudden-onset cervical pain, stiffness, and torticollis. Patients with LCH in the thoracic and lumbar spine exhibit more neurological symptoms compared to those with cervical spine involvement, which predominantly manifests as muscular symptoms, such as restricted neck motion or torticollis.

The etiology of LCH remains unknown. The pathophysiology involves excessive clonal proliferation of pathological Langerhans cells, which are derived from the monocyte-macrophage lineage.

Involvement of the cervical spine in children with LCH is rare, with the C3-C5 region being the most commonly affected site. It typically involves the vertebral bodies, while the posterior elements are less frequently affected. Vertebral plana occurs when there is a complete collapse of the vertebral body.

Several differential diagnoses for cervical pain must be considered, including benign fibrous histiocytoma, osteoid osteoma, osteoblastoma, giant-cell tumor, aneurysmal bone cyst, hemangioma, non-ossifying fibroma, vertebral infection, and malignant neoplasms such as osteosarcoma and Ewing sarcoma.

The treatment of cervical spine LCH has been highly variable, ranging from conservative observation and prolonged immobilization to systemic chemotherapy and surgical intervention. Reported outcomes for cervical LCH are generally favorable, regardless of the treatment modality. However, the literature lacks formal guidelines regarding the use of orthoses, the necessity for arthrodesis, or evidence of reossification.

Puigdevall [6] reported a case of a five-year-old girl in whom postoperative orthosis was recommended. Sadashiva [8] performed an anterior cervical approach (ACA) with C5 corpectomy, decompression of a soft tissue component, interbody fusion with a titanium cage filled with autologous iliac crest bone graft, and fixation using plates and screws (ACDF), followed by two months of rigid cervical collar use. Per [9] described a case involving an anterior cervical approach with C6 corpectomy, excision of the lateral mass, and anterior fixation using autograft bone with a 2-mm-thick anterior plate and screws, followed by one month of cervical collar immobilization. Scarpinati [7] similarly recommended the use of a cervical collar for two months.

Radiation therapy (RT) is not considered a first-line treatment due to the risk of secondary malignancies and radiation myelitis. Additionally, RT can damage the mucosa of the trachea and esophagus. In pediatric populations, RT poses a particular risk of destroying the growth plates of bones. However, RT may be necessary in cases where the disease continues to progress despite other treatments.

In our case, surgical treatment was chosen because the patient presented with hemiparesis and neck pain, in addition to requiring an anatomopathological diagnosis. Additional chemotherapy was proposed. The Histiocyte Society LCH III Trial recommends prednisolone and vinblastine for patients with single-system "multifocal bone disease." Table 1 summarizes the main findings from clinical cases andtheir follow-up strategies.

The limitations of our study include the lack of randomized clinical trials (RCTs) and systematic reviews with or without meta-analyses on Langerhans cell histiocytosis in children. Most of the available literature consists of case reports and case series, particularly in the pediatric population.

CONCLUSION

Langerhans cell histiocytosis is a rare bone disease characterized by the excessive clonal proliferation of Langerhans histiocytes, which may affect the spine. In the pediatric population, the thoracic spine is most frequently involved, followed by the lumbar and cervical regions. The primary clinical manifestations are neck pain and stiffness, though neurological symptoms can vary from mild to severe, potentially leading to spinal cord compression in advanced cases.

Magnetic resonance imaging or computed tomography are the diagnostic modalities of choice. Management can range from clinical observation to surgical intervention, depending on the presence and severity of neurological deficits.

Further studies on LCH in the pediatric population are necessary, as there is no consensus on optimal management or surgical approaches. Questions remain regarding whether re-ossification occurs after biopsy or surgical intervention, and whether anterior or posterior corpectomy with fixation using autografts and screws is the preferred method. Additionally, the ideal duration of follow-up is yet to be established. These open questions underscore the need for continued research to provide clearer answers and improve outcomes.

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Table 1 - Clinical summary of cases-reports of the management and approach for Langerhans-Cell Histiocytosis

Author	Age	Sex	Symptoms	CT	MRI	Location	Treatment	Follow-up
Scarpinati (1995)	13-years-old	Male	Cervical burning pain irradiating to the internal side of the right upper limb associated deficit of strength to the four limbs. Physical examination neck stiffness, mild spastic tetraparesis and bilateral weakness of bicipital jerks	-	Lesion of the C5 vertebral body protruding in the spinal canal and compressing the cord	C5	Surgery	3-years
Ngu (2003)	3.5 years-old	Male	Neck pain and torticollis	Lytic lesion in the left lateral mass of the C1	Post-gadolinium T1-weighted showed enhancement, and T2-weighted demonstrate hyperintensity involving a portion of the lateral mass of C1 with extension into the left perivertebral soft tissues of C1-C2	C1-C2	Biopsy + chemotherapy	14-months
Per (2008)	5 years-old	Male	Severe neck pain, torticollis, left arm pain	Destruction of the C6 body and invasion of the left lateral mass	Destruction of the C6 body and invasion of the left lateral mass	Cervical (C5 to C7)	Surgical (Anterior Cervical Corpectomy and excision of the lateral mass)	18-months
Puigdevall (2008)	10-years-old	Male	Neck pain associated with slight restriction of the head rotation	Osteolytic lesion in the left lateral mass	-	Upper Cervical Spine	Biopsy + chemotherapy	6-years
	5 years-old	Female	Neck pain and torticollis	Lytic lesion in the left lateral mass of the atlas. Complete collapse of the T4 vertebral body, and a	-	Upper cervical spine, thoracic and lumbar	Biopsy + chemotherapy	14-months

				lytic lesion at L1.				
Ha (2012)	6-years-old	Male	Severe back pain and limited neck motion. Neurological examinatio was normal	Osteolytic lesion with pathological fracture of the odontoid process, and associated destruction of the C2 body with posterior displacement	-	C2	Biopsy + chemotherapy	2-years
Sadashiva (2015)	9-years-old	Female	Neck pain associated progressive neck tilt, painful restriction of movements and left upper limb weakness	Reduced C5 body height > 90%	T2-weighted hyperintense and the intervertebral disc were spared	C5	Surgery (Anterior Cervical Approach C5 Corpectomy, decompression of soft tissue componentwhich was yellowish firm and avascular, interbody fusion with titanium cage filled with autologous iliac crest bone graft, fixation using plates and screws)	18-months

DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the local Ethics Committee, number: Comite de Ética e Pesquisa - 35

Consent to participate

The patients gave consent to use their information and images for research purposes. *Consent for publication*

Conflict of interest

None

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CONTRIBUTIONS

-**Breno Barbosa**: Conceptualization, Writing – original draft
-**Paulo Ronaldo Jube Ribeiro**: Writing – original draft, Writing – review & editing

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