Clinical Case Report

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Cervical langerhans cell histiocytosis mimicking cervical tuberculosis

A Case report

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Abstract

Rationale: Langerhans cell histiocytosis (LCH) involving adult cervical vertebrae is relatively rare clinically.

Patient concerns: An 18-year-old male patient exhibited a 1-month history of neck pain, restricted neck mobility, and numbness and weakness of both upper limbs. The patient reported no pain at other sites, exhibited no fever or night sweats, and was unable to recall any recent injury.

Diagnoses: On the basis of the radiological features of the lesion and laboratory tests, there was a high possibility that the patient had a tuberculosis lesion. Postoperative GeneXpert and *Mycobacterium tuberculosis* (MTB) culture results showed MTB negative. Postoperative pathological results showed: (Cervical 4 vertebrae) LCH.

Interventions: Our department did an anterior approach operation. The patient was treated with prednisone combined with vincristine after operation.

Outcomes: The patient was discharged from the hospital with complete remission of cervical pain and rapid relief of neurological symptoms.

Lessons: Computed tomography-guided biopsy of lesion tissue must be performed when a suspected infection occurs in young patients. If possible, the lesion tissue obtained during the operation should be cultured and pathologically examined for early diagnosis.

Abbreviations: CT = computed tomography, LCH = langerhans cell histiocytosis, MTB = *Mycobacterium tuberculosis*.

Keywords: adult, case report, cervical tuberculosis, langerhans cell histiocytosis

1. Introduction

Langerhans cell histiocytosis (LCH) is a rare clonal proliferative disease characterized by infiltration of cells similar to langerhans cells (LC) into a single or multiple organs. Among benign and malignant tumors, LCH is more common in children, rare in adults, and the ratio of male to female is 1.2 - 2:1.[1,2] LCH is characterized by marked and abnormal proliferation of bone marrow-derived histiocytes and accompanied by tissue destruction caused by infiltration of a certain number of eosinophils, neutrophils, lymphocytes, plasma cells, and multinucleated giant cells.[3] The clinical symptoms of this disease are not consistent. Currently, there is no effective treatment, and clinical misdiagnosis is common. A case of LCH of the fourth vertebra of the cervical vertebrae was treated in our spinal surgery department and is reported as follows.

2. Case report

An 18-year-old male patient exhibited a 1-month history of neck pain, restricted neck mobility, and numbness and weakness of both upper limbs. The patient reported no pain at other sites, exhibited no fever or night sweats and was unable to recall any recent injury. A physical examination demonstrated localized tenderness over the C4 spinous process, restricted neck mobility, and numbness and weakness of both upper limbs. Laboratory tests, including full blood cell count, serum electrolytes, and renal and liver function tests did not reveal any abnormalities. Erythrocyte sedimentation rate and C-reactive protein were increased to varying degrees. Computed tomography (CT) revealed C4 vertebral bony destruction (Fig. 1A–C). Magnetic resonance imaging revealed C4 osteolytic destruction and corresponding flat spinal cord compression thinning (Fig. 1D). On the basis of the radiological features of the lesion, there was a high possibility that the patient had a tuberculosis lesion. Our department did an anterior approach operation. The position of

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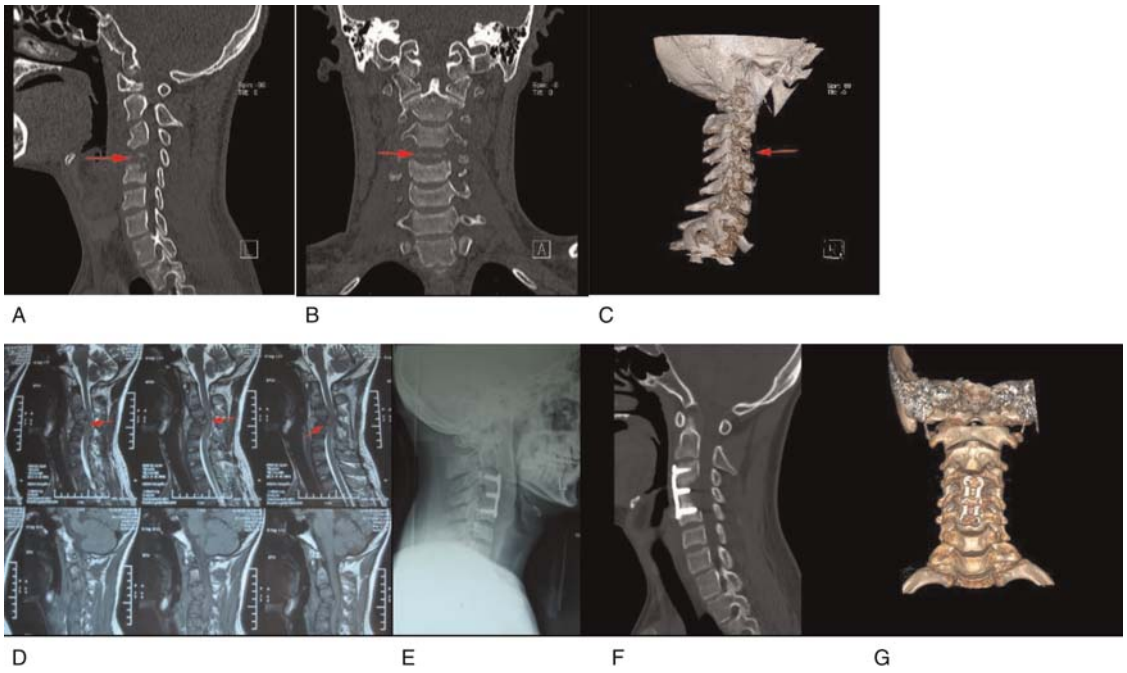

Figure 1. (A–C) CT scan view showing osteolytic destruction of the C4 vertebrae. (D) MRI scan view showing osteolytic destruction of the C4 vertebrae, formation of paravertebral and intraspinal abscess. (E–G) Postoperative imaging study showing that the lesion has been completely removed and that the position of the internal fixation device is satisfactory. Postoperative bone bridge formation is visible in the diseased vertebral body. CT = computed tomography, MRI = magnetic resonance imaging.

the internal fixation was found to be satisfactory by X-ray after operation (Fig. 1E). Postoperative GeneXpert and *Mycobacterium tuberculosis* (MTB) culture results showed MTB negative. Postoperative pathological results showed: (Cervical 4 vertebrae) LCH. Immunohistochemistry showed tumor cells: CD1a (+++); S100 (+); LCA (+); CD68 (KP1) (+); Vimentin (++); Ki-67 (30% +); CD117 (−); CD21(−); CK(−); EMA(−); Lysozyme(+); MPO (−) (Fig. 2). Immunohistochemical staining was positive for

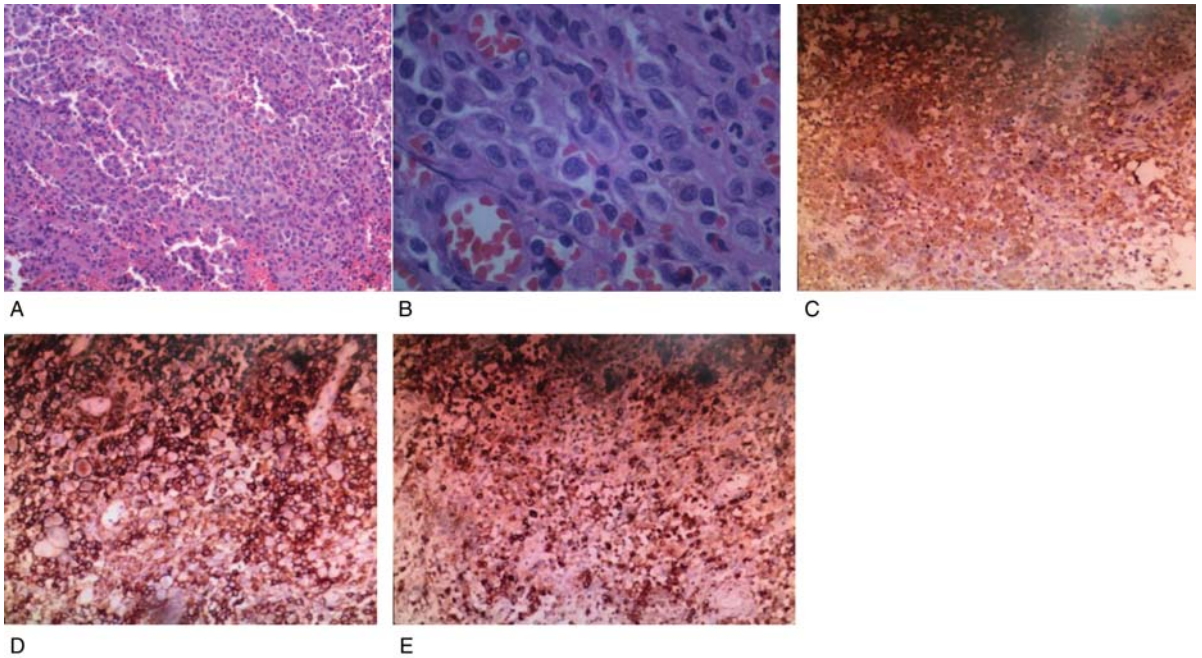

Figure 2. (A) Low magnification (10 × 10) overview of langerhans cells. (B) High magnification (40 × 10) of langerhans cells, with abundant cytoplasm, pale pink cytoplasm, and lobulated or serrated nucleus. (C) Immunohistochemistry showing S100(+) in tumor cells. (D) Immunohistochemistry showing CD1a(+++) in tumor cells. (E) Immunohistochemistry showing CD68 KP1(+) in tumor cells.

CD1a and S-100. No other LCH infiltration was identified in the patient and the patient was treated as suffering from a single-system disease. The patient was treated with prednisone combined with vincristine after operation. There were no serious side effects of the chemotherapy. The patient was discharged from the hospital with complete remission of cervical pain and rapid relief of neurological symptoms. Outside the hospital, the neck was fixed and oral prednisone was continued. Eight months after discharge, the patient returned to our hospital for re-examination. Cervical CT showed that the position of the cervical 3 to 5 vertebral body was satisfactory, and the bone graft area was not collapsed (Fig. 1F and G). The upper limb muscle strength and sensation were the same as those of discharge, and there was no progression in the state of illness.

3. Discussion

LCH is relatively rare clinically. In 2013, the WHO bone tumor classification classified LCH as a tumor with undefined tumor properties (ICD-O code: single-stoke 9752/1, multistoke 9753/1), which is classified as an intermediate (local invasiveness) tumor.[4] The incidence of LCH is approximately 1:1,500,000. The clinical manifestations of LCH vary widely and can involve almost every organ of the body.[5,6] The skeletal lesions of LCH are most common in the skull, femur, mandible, pelvis, and spine.[7] The incidence of spinal involvement is usually 6.5% to 25%. In all spinal lesions, 11% involve the cervical spine.[8] Patients usually have local neck pain, limited range of motion, or neurological dysfunction.[9,10]

The specific pathogenesis of LCH is unclear but may be related to mutations, polymorphisms, and expression changes of susceptibility genes. Satoh found that *B-RAF* gene mutation was as high as 68.8% in the analysis of granuloma samples from LCH patients.[11] In 2010, Badalian–Very et al[12] described the discovery of the BRAF V600E mutation in 40% to 70% of LCH cases, which offers the possibility of targeted therapy for relapsed or rapidly progressing patients. Kim et al[13] found that the P16 protein may play an important role in controlling the cellular mechanism of LC apoptosis and proliferation. Studies have also shown that genetic mechanisms play a role in the pathogenesis of LCH.[14] Chikwava et al[15] found that genetic alterations, especially loss of heterozygosity, increased frequency in high-risk forms of the disease, possibly due to changes in tumor suppressor genes also involved in tumorigenesis, leading to disease progression, which further confirms that genetic mechanisms may be involved in the pathogenesis of LCH.

The clinical symptoms of LCH are not consistent. The histopathological diagnostic criteria require that CD1a and S-100 antigens be expressed on the surface of injured cells for a reaction diagnosis.[16] A pathological biopsy from the patient showed CD1a (+++) and S-100 (+), which is consistent with the above pathological criteria.

The incidence of LCH is low and there is limited experience in treatment. At present, there is no uniform therapeutic opinion in medicine. Treatments include surgery, low-dose radiotherapy, topical corticosteroids with vincristine or vindesine, systemic chemotherapy, and combination therapy, with good response to phototherapy and low-dose methotrexate.[17,18] For patients with LCH who are refractory to treatment or have progressive disease progression, allogeneic hematopoietic stem cell transplantation may provide a certain efficacy.[19,20] In 1992, Greinix et al[21] reported successful treatment of 2 patients with MS-LCH using allogeneic bone marrow transplantation and autologous bone marrow transplantation. Others have reported that using a CD1a monoclonal antibody or an anti-CD52 monoclonal antibody in the treatment of refractory LCH achieves a certain efficacy. Donadieu et al[22,23] conducted an international phase II clinical study and used cladribine and cytarabine to treat 27 patients with refractory LCH. The toxicity during the treatment was heavier, but the overall response rate was 92% and the 5-year survival rate was up to 85%, providing a new idea for the treatment of LCH. In recent years, with the progress of molecular biology techniques, targeted therapies have also provided a new direction for the treatment of LCH. Baumann et al[24] reported that the use of the BRAF multikinase inhibitor sorafenib in combination with imatinib in LCH patients is effective and safe.

The 2 major surgical indications of cervical LCH are kyphosis and neurological deficits. In this case, an adult male patient with cervical nerve defect progressed rapidly, so anterior surgery was performed to remove the lesion, and graft and fusion to reconstruct spinal stability. It is reported that chemotherapy is safe and effective for LCH patients with spinal lesions and may significantly reduce the recurrence rate.[25,26] Therefore, postoperative chemotherapy with vincristine combined with prednisone was performed. No adverse reactions occurred in the course of chemotherapy. Following discharge from the hospital, the patient's muscle strength and sensation of both upper limbs were significantly improved. No aggravation of the lesions was found during follow-up.

Because adult LCH is rare in the clinic, especially involving cervical vertebrae, combined with unclear pathogenesis of LCH and atypical symptoms, it is easy to be misdiagnosed. In this case, the symptoms, signs, and imaging examinations of the patients admitted to hospital were all considered to be cervical bone destruction caused by cervical tuberculosis, with paravertebral abscesses pressing the cervical cord causing both upper limb sensation, and decreased muscle strength. Due to lack of a unified understanding of the treatment of LCH in current medicine, it is clear that symptomatic treatment is the main treatment before diagnosis.

In summary, the clinician should strengthen the understanding of LCH by comprehensive analysis of the patient's symptoms, physical signs, laboratory and imaging examinations, and histopathological examination of the case to avoid misdiagnosis. Due to the relatively few cases reported by LCH in the spine, our department misdiagnosed this patient as "cervical tuberculosis" based on clinical experience, and thus administered the wrong quadruple drug anti-tuberculosis treatment, which delayed the treatment of the patient to some extent. In this case, CT-guided biopsy of the lesion tissue was not performed in time before diagnosis. In the future, CT-guided biopsy of lesion tissue must be performed when a suspected infection occurs in young patients. If possible, the lesion tissue obtained during the operation should be cultured and pathologically examined for early diagnosis. We hope that more spinal surgeons can further explore the pathogenesis and treatment of LCH.

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Author contributions

Methodology: Yuhang Rao.
Resources: Yuqiang Cai.
Software: Chong Wang.
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