

A case of Langerhans' cell histiocytosis in a child

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ABSTRACT

Langerhans' Cell Histiocytosis(LCH) in children constitutes a diverse group of disorders which are rare but may be severe in their clinical expression. We report the case of a four year old boy who presented with complaints of pain in upper and lower jaws associated with recurrent loss of teeth. Thorough evaluation showed a multisystem involvement which was suggestive of LCH. There are no specific guidelines for treatment of LCH but sound knowledge of etiology, pathogenesis, signs-symptoms, investigations and treatment of LCH is essential for early diagnosis and accurate timely management of this disorder.

Keywords: Langerhans' Cell Histiocytosis, Hand Schüller Christian disease, Histiocytosis – X

INTRODUCTION

Langerhans' Cell Histiocytosis(LCH) is a rare disorder that primarily affects children. It was first described in medical literature around the turn of twentieth century. Patients with LCH have too many histiocytes. These cells accumulate in different organs and can result in variety of symptoms.¹

Histiocytes include dendritic cells and those of the monocyte-macrophage series. There is evidence that cytokines can modulate the cells to behave as one or the other line. The current classification divides the disorders into those of varied (and often unpredictable) biological behavior and those that are frankly malignant. Each of these is subdivided into diseases of the dendritic cells and macrophage-related conditions. Thus, immature Langerhans-type dendritic cells are the *sine qua non* of Langerhans cell disease.²

LCH is also known as Histiocytosis-X, which includes eosinophilic granuloma, lateral Letterer-Siwe disease, Hand Schüller Christian disease. LCH may present locally or as a multifocal disease that affects only the skeletal system or other tissues and organs such as lungs, liver and skin. The aim of this article is to describe a case of multisystem involvement in LCH in pediatric age group.³

CASE REPORT

A four year old boy presented with pain in upper and lower jaws associated with recurrent fall of teeth in molar and premolar regions of both upper and lower jaws. The pain was so severe that it has affected his daily activities including sleep of the child. On examination the child had clubbing. X-ray of mandible and upper jaw showed the appearance of floating teeth with localised osteolytic lesions. The rest of the skeleton was normal on radiography. CBC, urine examinations, renal function tests, liver function tests (LFTs) and coagulation profiles were normal. USG abdomen showed the hyperechoic lesions in right lobe of liver with mild haepatomegaly. HRCT skull, thorax, abdomen showed irregular lytic areas in molar region of mandible on both sides with floating teeth (Fig. 1); mild enlargement of both optic nerves; multiple tiny discrete variable sized cysts scattered throughout both lung parenchyma, suggestive of Honey-comb appearance (Fig. 2); and multiple ill-defined hypodense lesions throughout the liver suggestive of Langerhans' Cell Histiocytosis with Hand Schüller Christian disease.

Biopsy from bone and gums was taken and sent for electron microscopy and immunofluorescence studies to look for *sine qua non* Birbeck granules, Langerhans' cells and CD 1a positivity respectively.

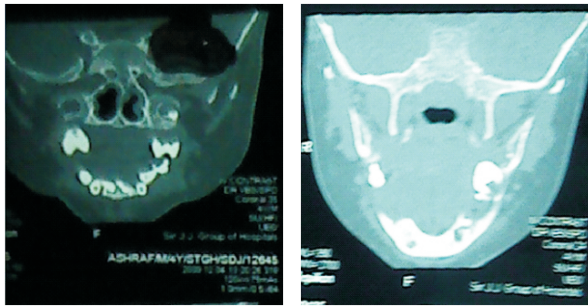


Figure 1. Irregular lytic areas in molar region of mandible on both sides with floating teeth.

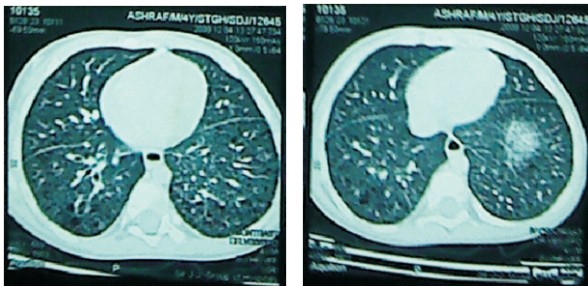


Figure 2. Multiple tiny discrete variable sized cysts scattered throughout both lung parenchyma, suggestive of Honey-comb appearance.

DISCUSSION

Histiocytosis encompasses a group of diverse disorders characterized by the accumulation and infiltration of monocytes, macrophages and dendritic cells in the affected tissues. Normal histiocytes originate from pluripotent stem cells which are found in bone marrow. Under the influence of various cytokines, these precursor cells can become committed and differentiate to become a specific group of specialised cells. Any imbalance in the above pathway leads to the pathology of histiocytosis.

The incidence of LCH is 4-5.4 per million populations. The overall M:F ratio is 1.5:1. The M:F ratio in individuals who have a single organ system involvement is 1.3:1; and in individuals with multisystem disease is 1.9:1. The disease can occur in any age group. The incidence peaks in children between 1-3 years.

The presentations of these disorders are varied based on the site of involvement. Bone involvement is observed in 78% patients, which often involves the axillary skeleton. Maxillary, mandibular and gingival disease may cause loss of

teeth, haemorrhagic gums, mucosal ulcerations and bleeding. Pulmonary involvement is observed in 20-40% of patients and may result in respiratory symptoms such as cough, tachypnoea, dyspnoea, pneumothorax and clubbing. Diffuse cystic changes, nodular infiltrate, pleural effusion, and pneumothorax are known to occur. Imaging studies may reveal cysts and micronodular infiltrates. Pulmonary function tests may reveal restrictive lung disease with decreased pulmonary volume.

The optimal treatment is not yet established. The aim of the therapy is to relieve clinical symptoms and prevent complications of the disease. For single system disease, no therapy or only local therapy may be necessary although further treatment may be needed in certain circumstances.

Topical therapy in the form of topical corticosteroids is preferred in children. Extemporaneously prepared topical 0.02% nitrogen mustard has also been advocated. Single agent therapy with Purine analogs with activity for treatment of Langerhans cell histiocytosis (LCH) include 2-chlorodeoxyadenosine (2CdA; cladribine [Leustatin]) and 2-deoxycytosine (2CDF; pentostatin [Nipent]); 2CdA has been found to be particularly toxic to histiocytes. As a single agent, cyclosporine has been used in pretreated patients with advanced LCH. Pamidronate, a bisphosphonate agent, has been reported to induce response or result in disease stability in a very small group of patients. Multi-agent therapy uses of a combination of cytarabine arabinoside (Ara-C), vincristine, and prednisolone to treat disseminated LCH with organ dysfunction has been reported. Different chemotherapeutic agents are still under trial.

Radiation therapy (doses ranging from 750-1500 cGy) can result in good local control of a solitary lesion, or metastasis occurring in critical areas. Fractionated doses of radiotherapy have also been used.

When the multiple lesions are present and are refractory, systemic therapy may be required.

When patients do not have an early response to vinblastine, corticosteroids, methotrexate, 6-mercaptopurine, or even etoposide, alternate therapies should be administered. Although several immunomodulatory agents, such as cyclosporine, have been used in patients with refractory disease, the results have been inconsistent. Cytotoxic chemotherapy often needs to be administered as well. 2CdA is both lympholytic and monolytic, making it a potentially ideal drug to use in LCH. Response rates to 2CdA have been particularly good in patients with extensive skin and bone disease, and in some patients with pulmonary involvement.

CONCLUSION

LCH possess a wide spectrum of clinical manifestations, and hence, a high index of suspicion, combined with a sound knowledge of

the disease process, is vital for its diagnosis. A definitive diagnosis is made on histological and immunohistochemical assessment with radiology confined to understanding the extent of the lesion. Treatment options include surgery, radiotherapy, and chemotherapy, alone, or in combination.

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