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Pediatric Mandibular Langerhans Cell Histiocytosis with Upper Airway Compromise: A Case Report

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ABSTRACT

Background: Langerhans cell histiocytosis (LCH) is a category of poorly understood disorders characterized by the abnormal growth and accumulation of Langerhans cells (LC) and eosinophils in various organs. The exact cause of LCH remains unknown, but it can result from alteration to the immune system, modifications in genetics, or an infectious process. LCH can be present in localized and systemic forms, affecting different organs depending on the patient's age, disease extent, and systemic involvement. Treatment modalities for LCH could be used individually or in combination, such as surgery, chemotherapy, radiotherapy, or even steroid injections. Also, a few reported cases of the localized subtype showed a spontaneous recovery.

Objective: We aimed to delineate the diagnostic approach and treatment modalities for cases with Mandibular (LCH) that might have airway compromise.

Subjects and methods: A 4-year-old girl, previously healthy, presented to the Emergency Department (ED) with a history of swelling over the mandible for the last 3 weeks.

Results: Results: Symptoms started as toothache that was not interfering with eating or limiting her activity. No swelling or change in color over the jaw were observed. Jaw swelling started to appear, increased in size and interfered with eating. She was diagnosed provisionally as dental abscess formation and received other antibiotics for 5 days, but unfortunately her condition was complicated with bleeding from the swelling and drooling of saliva and yellowish discharge as well so visited our ED. She lost one kilogram during this time. LCH was confirmed with transoral tissue biopsy.

Conclusion: Mandibular Lngerhans Cell Histocytosis is one of the differential diagnosis of Osteolytic lesions that need diagnostic approaches and modalities of treatment with paying attention to upper airy way involvement.

Keywords: Pediatric, Mandibular, Langerhans cell histiocytosis, Upper airway.

INTRODUCTION

Langerhans cell histiocytosis (LCH) is an uncommon condition represented by a collection of excessive histiocytic cells proliferation. It was labeled as Langerhans cell histiocytosis in 1985, after it was initially discovered by Alfred Hand in 1893 [1,2]. LCH is categorized clinically based on the system involvement to either one organ or multiple organs to be affected, hence the name single-cell LCH (SS-LCH) which involve one system/organ, or multisystem LCH (MS-LCH) with two or more organs/system to be involved [3].

Annually around 2 patients per million have been reported to have LCH, with vast majority of those patients having a single-system involvement 70% [4].

While only 50% of them had more the one organ to be affected. However, only minority out of the patients had multisystem LCH (30%). It is more evident Among the pediatric age group, especially males which carry a higher risk when it comes to gender (1.6–1.7times more than females) [5]. Although it can occur in any age group the peak was found to be the greatest around 3.5 years, but in general, most patients are younger than 15 years [1,2].

In our case, we are going to delineate the diagnostic approach and treatment modalities in 4-year-old child that was presented with SS-LCH located in the jaw bones, with challenges in the pediatric intensive care unit (PICU) course.

Clinical course:

A 4-year-old girl, previously healthy, presented to the Emergency Department (ED)with a history of swelling over the mandible for the last 3 weeks. The symptoms started as toothache that was not interfering with eating or limiting her activity. No swelling or change in color over the jaw were observed.

She sought medical advice in another clinic since jaw swelling started to appear, increased in size and interfered with eating (Figure 1). Oral analgesic and antibiotics were prescribed, but visited another healthcare facility for a second opinion, as the patient did not improve. She was diagnosed provisionally as dental abscess formation and received other antibiotics for 5 days, but unfortunately her condition was complicated with bleeding from the swelling and drooling of saliva and yellowish discharge as well so visited our ED. She lost one kilogram of her weight during this time.

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She had no significant past history suggestive of having dental or upper airway problem. The family history showed that one of her siblings had leukemia when he was one year old, now he is three-year-old healthy and alive.

On physical examination, she looked well developed vitally stable, not in distress and afebrile. In general, the examination was unremarkable, besides the head and neck region showed clear large left mandibular swelling. While her laboratory findings were within normal limits such as blood biochemistry including LDH and uric acid, and complete blood count.

The findings of the Computerized tomography (CT) showed an eroded, lytic, solid lesion that completely destroyed the lower jaw (Figure 2). Pan CT and MRI head and neck (Figure 3) were highly suggestive of malignancy. Mild hepatosplenomegaly and cervical lymphadenopathy were found as well, but without distant metastasis. The provisional diagnoses were Langerhans cell histiocytosis, osteomyelitis, lymphoma Ewing sarcoma.

Due to drooling saliva and recurrent oral bleeding with potential airway compromise, she was admitted to the PICU for close monitoring. The patient was covered with a broad-spectrum antibiotic including ceftriaxone and clindamycin for five days to ensure the coverage for gram positive, gram negative, aerobe and anaerobe treating possible osteomyelitis, until this diagnosis was excluded.

Tissue biopsy was obtained under general anesthesia, without difficulty of endotracheal intubation during the procedure. Oral excisional biopsy of deep tissue and bone was taken in addition to extraction of the lower left mandibular primary second molar and the floated teeth. Histopathology showed Langerhans cell histiocytosis (LCH).

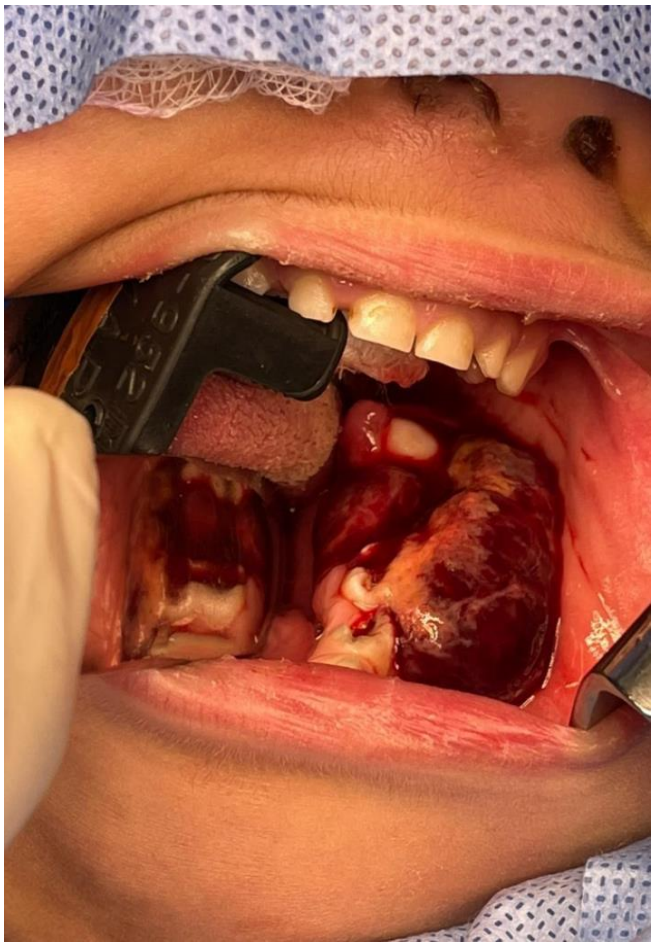

Figure (1): The mandibular mass bulging in the left side of the mouth cavity with floating teeth.

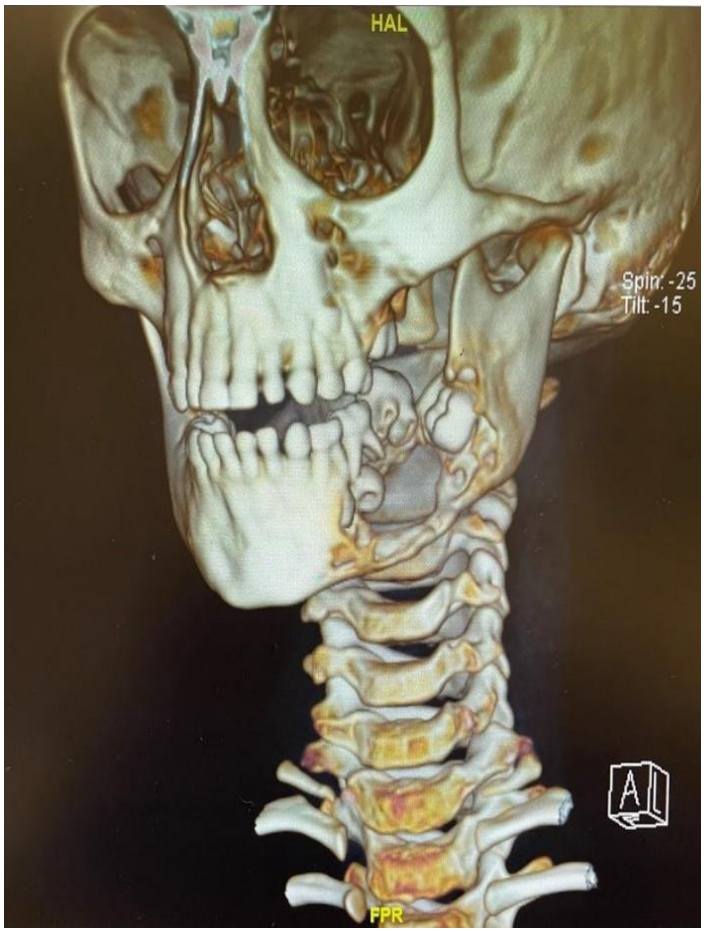

Figure (2): Three dimensional CT of the head and neck showed osseous lesion affecting the left side of the mandible with floating of the left lower second primary molar tooth and the secondary molars.

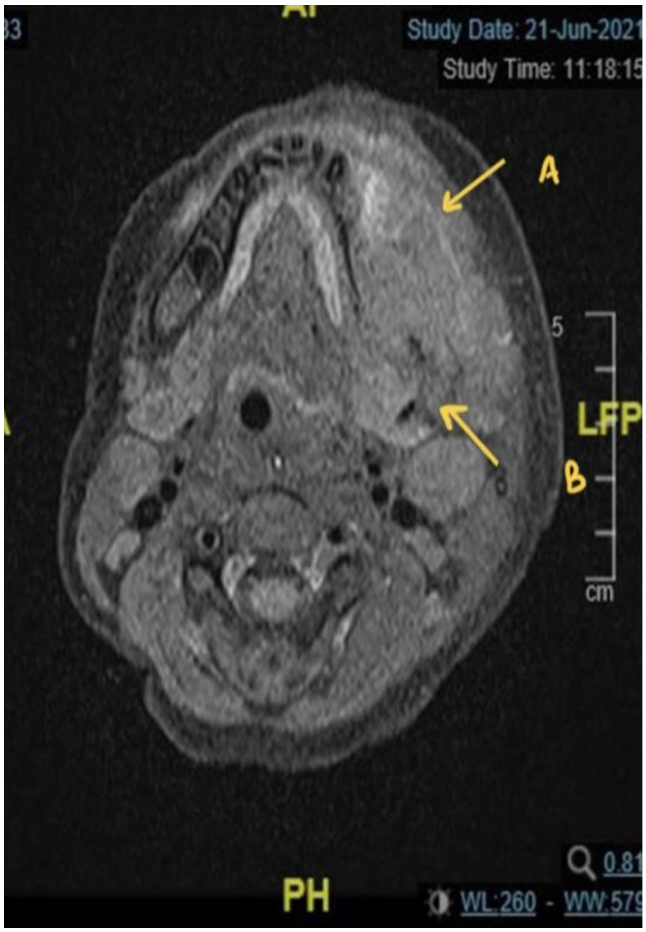

Figure (2): MRI head showed Left mandibular destructive and aggressive-looking lesion [A] and infiltrative soft tissue changes in the left submandibular and masticator spaces [B] as well as left level Ib and II lymphadenopathy

The pediatric oncology tumor board-initiated chemotherapy with vinblastine as per protocol, completed the initial course 1 and 2, and planned to go for continuation arm A. The patient received a total of 52 weeks chemotherapy with an excellent result. The MRI showed a complete resolution of the left mandibular LCH, with no soft tissue component or enhancement appreciated. A follow up with facial CT scan within three months was scheduled.

DISCUSSION

The etiology and progression of LCH have been studied for several years but its exact cause remains the subject of debate [(6)]. Recently, advancements in research have made a great impact on the discovery of a clonal myeloid origin of the LCH cells and detected a number of activating mutations alongside the MAPK signal transduction pathway [(7)]. However, the diagnosis of LCH is distinct and can't be misinterpreted with other conditions just by observing Birbeck granules in electron microscopy and immunohistochemistry is positive for S100, CD1a, and CD 207[(8)].

The clinical presentation of LCH can broadly be classified as first, (unifocal disease) which affects single site only. Second, (multifocal uni-system) disease which results in multiple sites involvement in the same single organ system. Third, (multifocal multisystem disease) which is diffuse throughout the body. The majority of maxillofacial LCH cases present as unifocal single system involvement, while the other two classes constitute almost 50% of the remaining [(9)]. It was found that bony parts of the jaw tend to be two times involved more than soft tissues. Although Systemic sign, like lethargy and fever might be present, however it is not specific as it might be seen in both with a single system or multisystem involvement. The mandible is more likely to be involved than the maxilla 3:1, especially the posterior regions [(10)].

Several symptoms may overlap with other conditions, but it is important to be taken into consideration such as alteration of the level of consciousness, dizziness, neurological changes, growth failure, poor weight gain, tachycardia, tachypnoea, cough, alteration to the bowl habits, jaundice, polyuria, polydipsia, pain, swelling, fever, skin rashes and ulcerations. Oral conditions may present as bleeding, gingivitis, periodontitis, halitosis, mucosal swelling, ulceration, excessive mobile teeth, floating teeth, loss of teeth, and rarely as pathologic jaw fractures.

A predominant feature is the punched out lytic bone lesions which lead to alveolar bone loss and floating teeth. The differential diagnosis for similar presentation includes osteomyelitis, juvenile periodontitis, non-specific periodontitis, Ewing's sarcoma, lymphoma, leukemia, multiple myeloma plasmacytoma, and giant cell tumor.

The most common complaint to be reported is pain. [(11)] but Chugh A.et al. [(12)] found that although the majority of the patients had pain 60%, some of them had swelling of the same region as well 40%. However, when it comes to the laryngeal involvement it is almost rare as only five cases have been reported in Zahou AS et al. [(13)]. Among those, two were in children and three were in adults.

In each, the clinical symptoms of LCH as it affects the larynx included dyspnea, and dysphonia which could be obvious as seen in this patient and another case that was reported in the literature [14]. However, the severity and the duration vary from one patient to another and may last several weeks. sub or supraglottic mass may be the Findings on the laryngoscopy, which may protrude into the glottic lumen and ultimately result in airway obstruction. This is the mechanism in which the symptoms develop such as hoarseness, dyspnea, stridor, edema, and loss of the vocal mobility [(13)].

Unlike many other infiltrative bone diseases, LCH does not have a specific laboratory finding that distinguishes it from other conditions. Despite the lack of difference, the laboratory investigations must be done to rule out other conditions. However, due to the absence of pathognomonic features on the Laboratory findings, the diagnosis can only be determined by the tissue biopsy [(14)].

For this patient, the differential diagnosis included osteomyelitis, LCH, eosinophilic granuloma, lymphoma, and Ewing sarcoma. As our patient had only left mandibular involvement and no other systemic involvement, so eosinophilic granuloma was the first possible diagnosis. The second differential diagnosis was Ewing sarcoma related to the CT findings, as both LCH and Ewing sarcoma causes similar lesions radiologically when flat bones are involved.

However, Ewing sarcoma is well known to affect the long types of bones, rather than affecting the jaw. Though Burkit lymphoma affects children, but it usually involves the maxilla instead of the mandible. In regards to osteomyelitis although there were no history of trauma exposure or infectious processes to the teeth, still, the treating team decided to cover with

empirical antibiotics until the culture results were negative and LCH was confirmed with transoral tissue biopsy.

Histopathological characteristics of the lesion include multiplication of Langerhans cells, which was pinpointed immunohistochemically by the identification of the antigens S100 and CD1a.

There are various modalities of treatment for LCH depending on the case presentation and based on the extent of the lesion itself. The treatment options include Surgical curettage, and radiation whether chemotherapy or radiotherapy which can be used alone or in combination [(15)]. However, in this case the patient received chemotherapy only including vinblastine, 6 mercaptopurine, in addition to prednisolone, as she was of multifocal involvement and systemic disease. Different treatment regimens along with various locations in which the lesion can occur, impact the Recurrence that ranges from 1.6% to 25% [(16)]. Patients with LCH are at greater risk for second malignancies, including solid tumors and hematopoietic conditions, so physicians should be vigilant of those patients and arrange follow ups with them frequently.

CONCLUSION

Langerhans cell histiocytosis is a rare disease, and oro-dental symptoms may be the first complaint of the disease, which cause patients to seek treatment. Careful clinical examination and good diagnostic and management approach could increase survival chances with minimal deformity. Careful evaluation and monitoring for upper airway is essential.

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