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Langerhans Cell Histiocytosis in the Oral Cavity

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ABSTRACT

Background: Langerhans cell histiocytosis (LCH) is a rare hematological malignancy. The incidence of this disease is only 1% of soft tissue and lymph node cancer. Clinical manifestations and organ involvement vary widely. Lesions in the oral cavity are rare. LCH occurs more often in children, 10 times more often than in young adults. **Case presentation:** A 20-year-old male came with the main complaint of a lump on the roof of the mouth and the right inner cheek. Physical examination of the face and oral cavity found a mass attached to the palate 1x1x1 cm with the same color as the surrounding tissue, flat surface, soft consistency, could be moved, and a mass was found in the left buccal 2x2x2 cm, with the same color as the surrounding tissue, flat surface, cystic consistency, not fixed and can be moved. Hematology laboratory examination was within normal limits, so no examination was carried out for bone marrow puncture (BMP). From the results of a CT scan of the head and neck, a solid mass was found with a hypodense part in it in the right buccal area attached to m. right masseter, and in the left hard palate area, which was suggestive of Langerhans cell histiocytosis. The results of histopathological examination of the lesion which underwent an incisional biopsy showed positive S100 and CD1a, this patient was diagnosed with Langerhans cell histiocytosis LCH. Next, this patient was treated with excision of the mass in the palate and buccal area. The patient was treated in the surgical inpatient department for 2 days, and the postoperative wound was in good condition. **Conclusion:** Cases of Langerhans cell histiocytosis (LCH) are very rare cases that have different clinical symptoms depending on the organs involved, so it is important to understand this disease better. In this case, it was unilocal LCH without the involvement of other organs, so only local therapy was carried out in the form of surgical excision and observation was carried out after 3 months after surgery with the results of the wound improving without any new lumps appearing.

1. Introduction

Histiocytosis is a term applied to a group of rare diseases of the reticuloendothelial system. Even though the clinical symptoms that appear are different, the histological picture remains the same, including the picture of abnormal proliferation in

histiocyte cells, which is a feature of Langerhans cells. The disease is known as Langerhans cell histiocytosis (LCH), formerly histiocytosis X.^{1,2} Langerhans cell histiocytosis (LCH) is characterized by clonal proliferation of atypical Langerhans cells in various organs. Organs that may be involved are bones, lungs,

liver, lymph nodes, spleen, hematopoietic system, and possibly mucocutaneous. The clinical picture is polymorphous, so therapy and prognosis may differ. The spectrum ranges from fulminant to benign and self-limited. The local variant of LCH usually presents as solitary or multiple bone lesions, sometimes with the involvement of the overlying mucosa. Isolated lesions of the oral mucosa without bone involvement are rare cases.³

Possible etiology is a neonatal infection, no history of vaccination in children, history of exposure to radiation, and thyroid disease. However, this disease is also associated with acute lymphoblastic leukemia and lymphoma. LCH is often found in children and adults. In children, it often occurs between the ages of 1-3 years and can sometimes be found in newborns. Children between the ages of 5 and 15 years usually present with isolated lesions on the bones. The incidence of LCH is 0.4 in 100,000 children up to 15 years of age. Boys are twice as likely as girls, and in adults, the ratio is reversed.⁴ The organs frequently involved in adults are the lungs, bones, and skin. Isolated lesions in the oral cavity occur in approximately 5% of cases and are accompanied by bone involvement. In the soft tissues of the oral cavity, the most frequent locations are the gingiva, maxilla, and hard palate.¹ In this case report, we report a 20-year-old man with Langerhans histiocyte cells on the roof of the oral cavity and this is a rare case in the surgical oncology service at Dr. Hasan Sadikin General Hospital, Bandung.

2. Case Presentation

A 20-year-old man came in complaining of a lump in his mouth on the wall of the roof of his mouth and right cheek for 3 years. The lump initially was only the size of a marble, then grew bigger and bigger as a ping pong ball over time and was accompanied by pain. Complaints accompanied by decreased appetite. The lump that is felt does not cause any other symptoms. The patient's family did not experience the same disease. Based on the results of the physical examination, the vital signs were within normal limits.

The patient weighed 55 kg and was 156 cm tall. On examination of the face and oral cavity, it was found to be present. A mass attached to the palate 1x1x1 cm with the same color as the surrounding tissue, flat surface, and soft consistency, and a mass was found in the buccal dextra 2x2x2 cm, with the same color as the surrounding tissue, flat surface, cystic consistency, not fixed and movable. Not found KGB enlargement in the right and left neck. An incisional biopsy was performed on both lesions, and the results of histopathological examination and CPI showed CD1 (+)/S100(+), showing Langerhans cell histiocytosis. From the results of a CT scan of the head and neck, a solid mass with a hypodense part in it was found in the right buccal area attached to m. masseter dextra, and in the area of the left hard palate, which was suggestive of Langerhans cell histiocytosis. There is no indication of bone marrow in this patient. Next, this patient was treated with excision of the mass in the palate and buccal area. Intraoperatively, a mass was found on the palate measuring 2x1x1 cm with a rubbery and brittle consistency with firm boundaries, and an encapsulated mass was found on the right buccal with a size of 2.5 cmx2x1 cm with a rubbery consistency and filled with fluid. The patient was treated in the surgical inpatient department of Dr. Hasan Sadikin General Hospital for 2 days, and the post-operative wound was in good condition. The patient was re-examined after two weeks after surgery with good wounds and post-operative histopathology results of Langerhans cell histiocytosis on palate region preparations.

3. Discussion

These Langerhans cell histiocytosis (LCH) cover a wide spectrum of clinical manifestations in children and adults, ranging from self-limiting to life-threatening lesions. The diagnosis of LCH is based on clinical and radiological findings in combination with histopathological analysis, namely the presence of histiocyte infiltration with ultrastructure or proven by immunophenotype to assess the characteristics of these Langerhans cells.



Figure 1. Clinically, the patient appears to have lesions on the wall of the palate and right cheek.

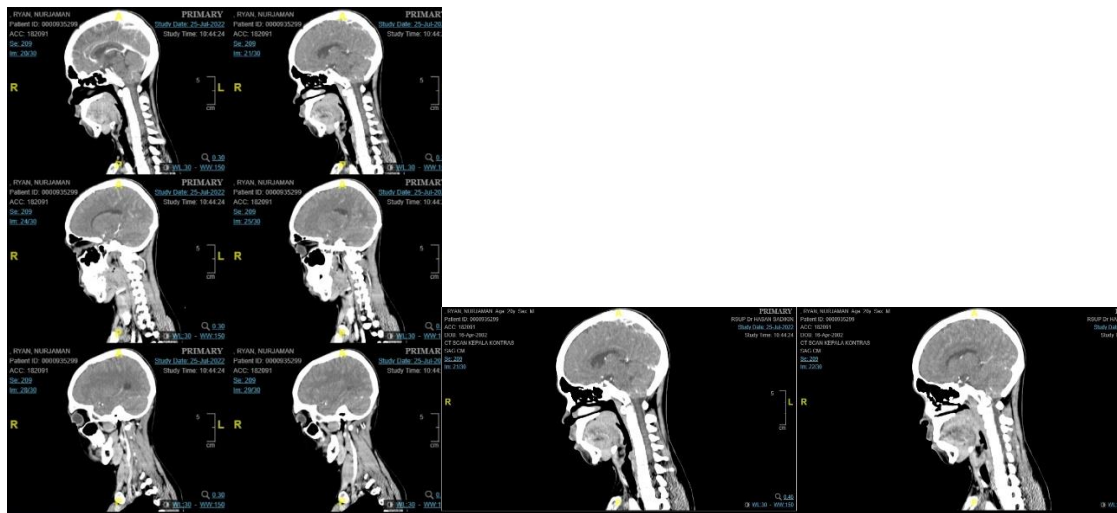


Figure 2. From the head CT scan, a solid mass was found with a hypodense part in the right buccal area attached to m. right masseter, and in the area of the left hard palate suggestive of Langerhans cell histiocytosis.



Figure 3. Intraoperative findings.

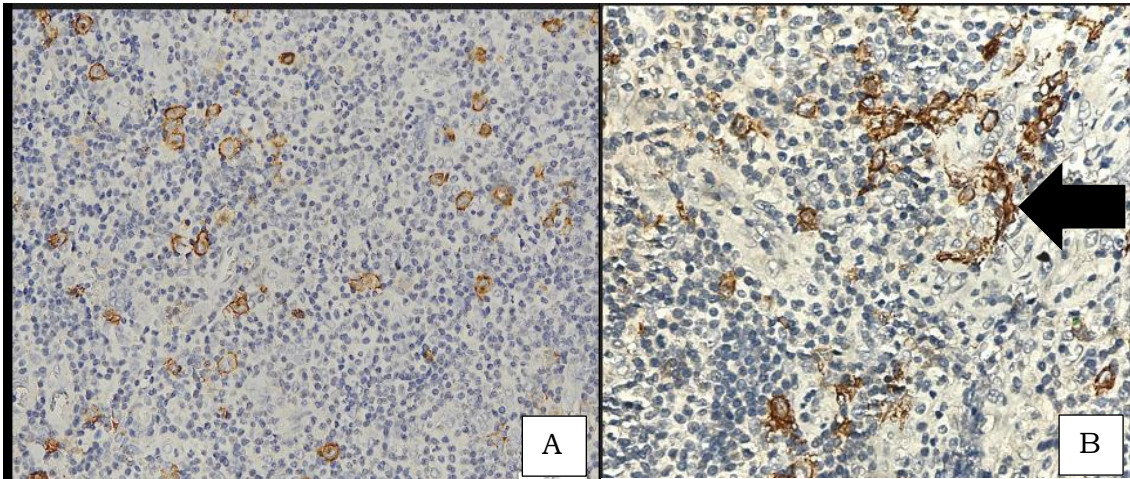


Figure 4. Positive CD1 immunohistochemistry. A. 100x magnification; B. 400x magnification.

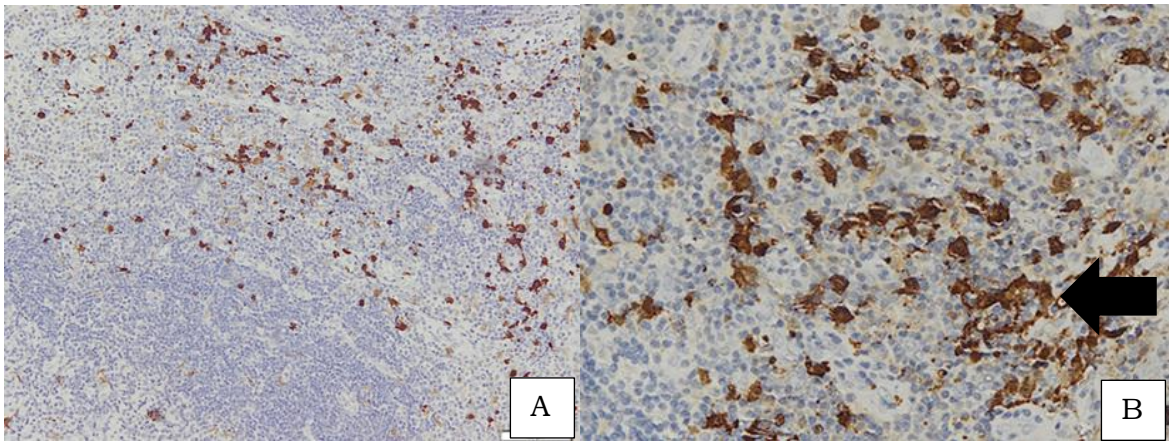


Figure 5. Positive S100 immunohistochemistry. A. 100x magnification; B. 400x magnification.

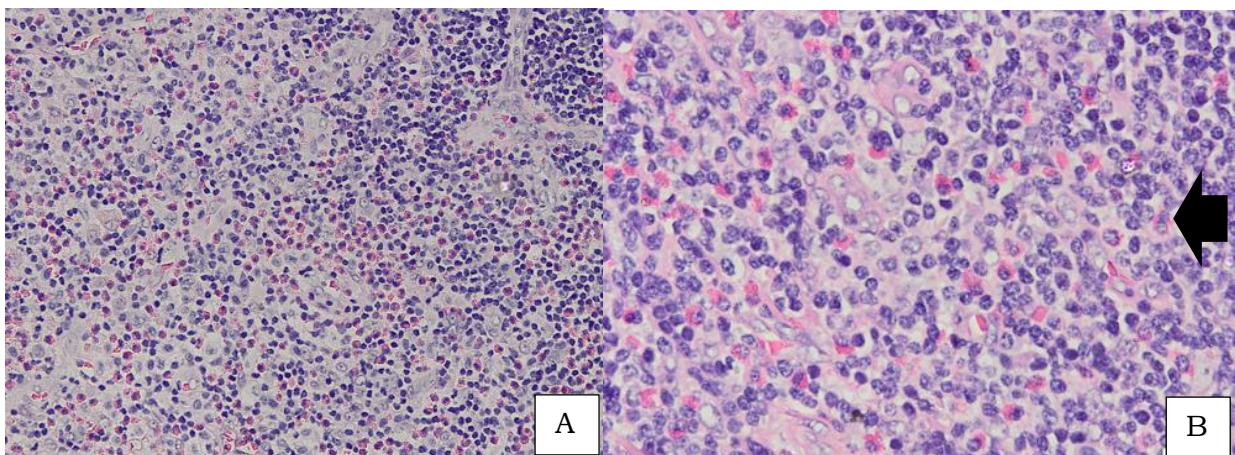


Figure 6. Histological features of hematoxylin-eosin (HE) staining. A. 100x magnification; B. 400x magnification.

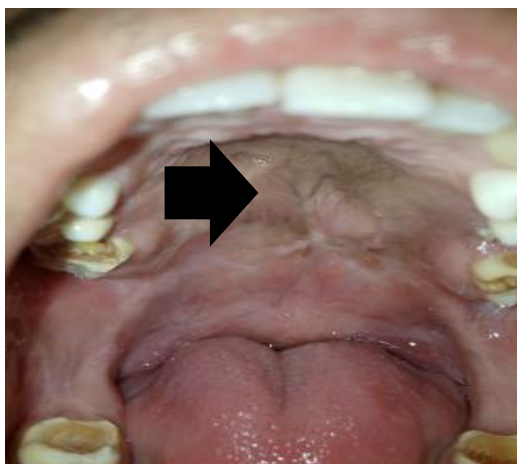


Figure 7. Control photo after 3 months after surgery, it appears that the surgical wound is closing well without any complaints of lumps in the same place.

It is strongly recommended that a biopsy to confirm suspected LCH be performed in all cases, especially for patients requiring therapy.⁵ Langerhans disease of histiocyte cells is characterized by the accumulation of cells thought to originate from dendritic cells (DC) or macrophages. There are more than 100 subtypes of histiocytosis. The original classification of histiocytic neoplasms by the Working Group of the Histiocyte Society, which was published in 1987, consists of Langerhans cells, non-Langerhans cells, and malignant histiocytosis cells. However, in 2016, the Histiocyte Society classified based on clinical, radiographic, histological, phenotypic, and other molecular into 5 disease groups: (1) Langerhans-related; (2) cutaneous and mucocutaneous; (3) malignant histiocytosis; (4) Rosai-Dorfman disease (RDD); and (5) hemophagocytic lymphohistiocytosis and macrophage activation syndrome.⁶

Estimates of the prevalence of LCH vary widely (e.g., from approximately 1:50,000 to 1:200,000). The incidence is 5 to 8 cases/million children. All patients with LCH had evidence of activation of the RAS-RAF-MEK-ERK signaling pathway. The presence of the BRAFV600E mutation is identified in 50 to 60% of patients suffering from LCH. This mutation is monoallelic and acts as a factor in oncogenesis. Approximately 10 -15% of patients have MAP2K mutations. Because of these mutations, LCH is now

considered an oncogene-driven myeloid-inducing oncogene. In LCH, abnormally proliferating dendritic cells infiltrate one or more organs. Bones, skin, teeth, gingival tissue, ears, endocrine organs, lungs, liver, spleen, lymph nodes, and bone marrow may be involved. Organs can be affected by infiltration, causing dysfunction, or by compression from nearby enlarged structures. In about half of patients, more than one organ is involved.⁷

The diagnosis of Langerhans cell histiocytosis is based on clinical and radiological findings and tumor tissue biopsy results. Initial diagnosis depends on clinical symptoms. Typical symptoms and physical examination that must be carried out start from the head, eyes, ears, nose, and throat (HEENT); and examination of the cardiovascular, pulmonary, musculoskeletal, lymphatic, gastrointestinal, endocrine, and neurological systems should also be performed.⁶

Definitive diagnosis of LCH requires the presence of CD 68/ 163 β histiocytes that are positive for CD1a and/or langerin (CD207) on immunohistochemical (IHC) staining. Previously, an electron microscope examination was needed to show Birbeck granules. Apart from a definite diagnosis of this disease, it has not been used since its existence inspection IHC.⁹ These cells were identified by pathologists experienced in the diagnosis of LCH according to characteristics

from immunohistochemistry, which included cell surface CD1a, CD207 (langerin), and S-100 (although nonspecific).⁸ The histopathological picture of LCH tumors shows the presence of neoplastic histiocytes mixed with inflammatory cell infiltration. On hematoxylin and eosin (H&E) staining, neoplastic LCH cells will be depicted as mononucleations with characteristic signs of coffee bean-shaped, Abundant eosinophils and multinucleated giant cells.⁶ Laboratory tests should include complete blood count, blood chemistry, coagulation studies, thyroid-stimulating hormone, free T4, urine analysis, C-reactive protein, and morning serum cortisol with adrenocorticotrophic hormone. Examination of prolactin and IGF-1 levels should be considered in certain patients. Examination of FSH / LH, testosterone, and estradiol levels can be carried out if clinical symptoms are found. Bone marrow examination should be performed in all patients with abnormal blood test results to rule out LCH involvement in the bone marrow and concomitant myeloid neoplasm. Tumor tissue biopsy is recommended in all cases.⁸

The NCCN's management of histiocyte neoplasms includes recommendations for how to diagnose and manage Langerhans cell histiocytes (LCH), ECD (Erdheim-Chester disease (ECD)), and RDD (Rosai-Dorfman disease) (although WHO has not officially recognized RDD as a neoplasm). Evidence supporting the management of histiocyte neoplasms in adults is largely based on small retrospective studies, case series, and case reports due to the lack of prospective studies in adults. In addition, some diagnostic and treatment recommendations for adults with histiocyte neoplasms are, of course, extrapolated from prospective studies in children and young adults, unless otherwise stated.⁶ Several treatment modalities for Langerhans cells histiocyte (LCH) have been discovered including clinical observation, surgical curettage, high dose local and systemic corticosteroid injections, low dose radiotherapy, chemotherapy and bone marrow transplantation as well as administration of antibody therapy for resistant cases.

Patients with Langerhans cell histiocytosis who progress despite standard therapy usually respond to more aggressive chemotherapy. Recent studies documenting mutations in the BRAF and MAP2K1 genes may revolutionize the prevalent therapeutic regimen and pave the way for targeted therapy in LCH, resulting in a better prognosis.⁷

Histiocytic Langerhans cells affecting the mucosa of the hard palate without bone infiltration, as in our case, is a rare case and often causes a delay in diagnosis. In this case, a palate mass was found, which from positive S100 and CD1a immunohistochemical staining was found to provide a final diagnosis of Langerhans cell histiocytes. Based on the NCCN guidelines, which state that in patients with Langerhans histiocytes in the mucosa isolated on the palatal mucosa without involvement of bones or other organs, local therapy can be carried out, namely surgical excision.⁶ Then, the patient was followed up for 3 months after surgery. The patient did not complain of any new lumps in the same location. An isolated lesion of the mucosa may occur in approximately 5% of all cases of Langerhans cell histiocytes. For the oral cavity, the sites most frequently involved are the gingiva, followed by the maxilla and hard palate¹. LCH should be considered in the differential diagnosis of intraoral lesions. Early diagnosis of LCH is important because curative treatment is available, and symptoms can be reduced if it is treated early.⁹

4. Conclusion

Langerhans cell histiocytosis (LCH) is a rare disorder of the reticuloendothelial system with unknown etiology. Early detection of LCH plays an important role in prognosis, which is closely related to age, number of organs involved, and degree of functional lesions.

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