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HIGH GRADE B CELL LYMPHOMA- A CASE REPORT

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ABSTRACT
Introduction: High grade B-cell lymphoma is a type of Non-Hodgkin's Lymphoma which can involve lymph nodes and extranodal organs. The various types of non-Hodgkin's lymphoma are divided into high grade and low grade.Case report: An 8 year old male patient reported with complain of swelling and scar over right side of lower jaw. History revealed similar swelling 3 years back at the same site for which the patient underwent surgery through an extra-oral approach. Patient reported with an extraoral scar resembling a keloid and a diffuse swelling measuring 10cmX6cm extending from posterior border of ramus to submandibular region. Swelling was hard, fixed and tender on palpation. Incisional biopsy of the jaw lesion on routine histopathology showed large round cells with a centrally placed hyperchromatic nuclei resembling lymphocytes giving a picture of a hematolymphoid neoplasm. The tumor cells were positive for LCA, CD20 & PAX5, with a ki67 index >80% and BCL2 focally positive. No immunoreactivity noted for MPO, MyoD1, Tdt and synaptophysin.Conclusion: Based on histopathological and immunohistochemical findings, a final diagnosis of High grade B-cell lymphoma and extraoral keloid was given.

INTRODUCTION

Lukes has defined malignant lymphoma as "a neoplastic proliferative process of the lymphopoietic portion of the reticuloendothelial system that involves cells of either the lymphocytic or histiocytic series in varying degrees of differentiation and occurs in an essentially homogenous population of single cell type".[1] Lymphomas have been divided into Hodgkin's lymphoma and non Hodgkin's lymphoma.[2] Hodgkin's lymphoma usually occurs in lymph nodes while the non-Hodgkin's lymphoma can involve both lymphnodes and extranodal sites.[3]

The working classification of lymphoma classifies Non-hodgkin's lymphoma into low, intermediate and high grade varieties.[4] High grade lymphomas usually involve large lymphoblastic and small noncleaved cells.[1] The other classification systems used for lymphomas are Rapaport, REAL and WHO classification. WHO classification is currently the gold standard for classification and divides lymphoma into B cells, T cells/ NK cells and Hodgkin's lymphoma.[5] When lymphoma involves a single bone leaving visceral organs or lymph nodes, it is known as primary intraosseous lymphoma.[6] It is rare and makes for 3.1% of malignant bone tumor.[7]

Here we present a case of high grade B cell lymphoma in the jaw of an eight year old child with the consent of his guardians.

CASE DESCRIPTION AND RESULTS:

An eight year old male patient presented to Department of Pedodontics with a chief complaint of swelling and scar in the right side of the face since 1 year. Patient gives history of surgery at a local hospital 3 years back for the swelling in the lower jaw, the reports of which couldn't be availed. Following the surgery scar and swelling has gradually increased in size. Extraoral examination revealed a keloid measuring 10X5cms extending from right ear lobe till angle of the mandible. A diffuse swelling extending from posterior border of

mandible to submandibular region is also noted (Figure 1). On intraoral examination obliteration of buccal vestibule extending from anterior border of ramus to deciduous 1st molar was present. Buccal cortical plate expansion was observed while lingual cortical plate appeared normal. On palpation the swelling was hard and tender and the keloid firm and non tender. Due to the swelling asymmetry of face was noted with no altered sensation and secondary changes on overlying skin. Family history was not contributory. OPG revealed a lytic lesion involving the body and ramus of the mandible (Figure 2). A provisional diagnosis of odontogenic tumor was given.

FNAC from the lesion showed scattered non-cohesive large round cells with round uniform coarse chromatin and nucleoli (Figure 3). Differential diagnosis of round cell tumor of childhood, peripheral neuroectodermal tumor (PNET), rhabdomyosarcoma and hematolymphoid malignancy were given. After routine blood investigations were done incisional biopsy was carried out for both keloid and jaw lesion. The microscopic examination of H & E stained section of biopsy revealed connective tissue stroma containing sheets of intermediate and large sized round cells (Figure 4). These cells showed open faced nuclei and some showed centrally placed nuclei resembling lymphocytes. Nuclear pleomorhism and cells with multilobulated coarse nuclei were also seen. The section showed features of a hematolymphoid neoplasm, hence subjected for further IHC investigations. IHC showed cells which are LCA (Leukocyte Common Antigen- specific marker for lymphocytes), CD20 (highly reliable B cell marker) and PAX5 ((B-cell-specific activator protein) positive, with a Ki67 (proliferation marker) index of >80%. No immunoreactivity for MPO (myeloperoxidase marker specific for myeloid cells), MyoD1 (muscle marker), Tdt (terminal deoxynucleotidyl transferase- enzyme expressed by acute leukemia cells) and synoptophysin (neurosecretory associated protein). Very few reactive CD3 (marker for T cells and natural killer cells) positive T cells were noted and BCL2 (antiapoptotic protein) appeared focally positive (Figure 5).

Correlating with IHC, it was suggestive of a high grade B cell neoplasm. The microscopic examination of keloid showed non keratinised stratified squamous epithelium and sub-epithelial connective tissue. At areas the epithelium displayed atrophy. Basal cell layer showed presence of melanin pigment. The underlying connective tissue revealed haphazardly arranged thick bundles of collagen giving a glassy appearance, numerous spindle shaped fibroblasts and endothelial lined capillaries which suggested of keloid (Figure 6). Patient underwent surgical and chemotherapeutic treatment following the diagnosis.

Figure 1: Image showing extraoral keloid and swelling of the jaw on the right side of the face.

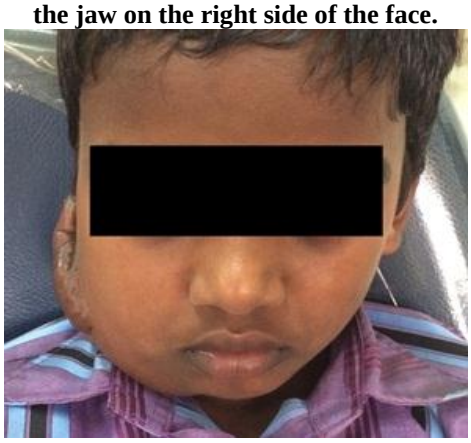


Figure 2: Diffuse radiolucency noted on the right side of mandible involving lower border.

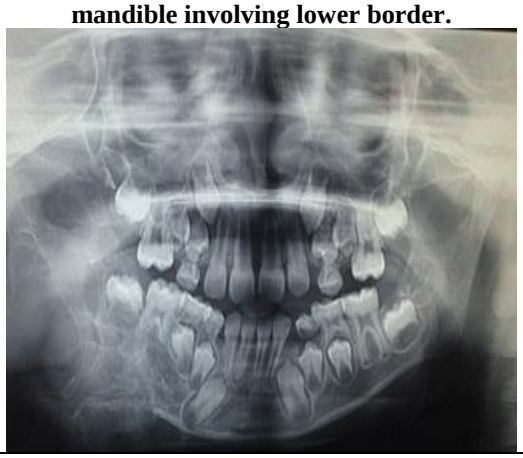


Figure 3: Non-cohesive large cells with round uniform coarse chromatin and nucleoli seen in FNAC (Leishman stain)

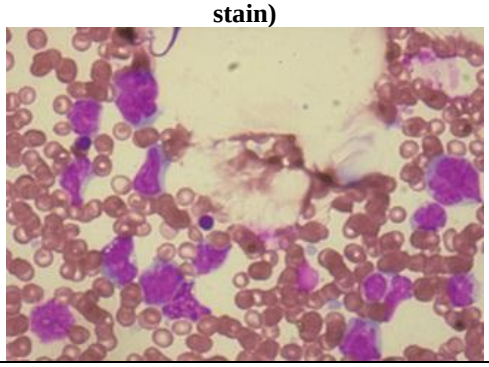


Figure 4: H & E stained tissue revealing cellular stroma consisting of round cells

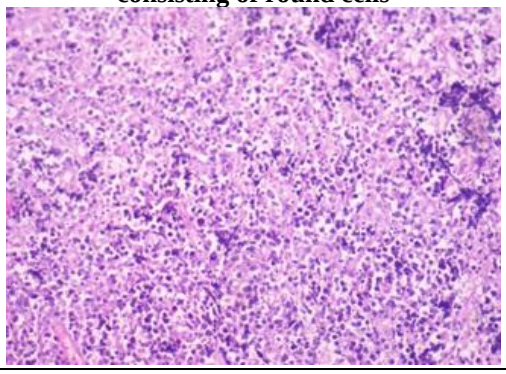


Figure 5: IHC- LCA, CD20, BCL2 positive. Ki67 index : >80%. CD3 is focally positive. MYO D1, SYNAPTOPHYSIN and TdT showing no immunoreactivity.

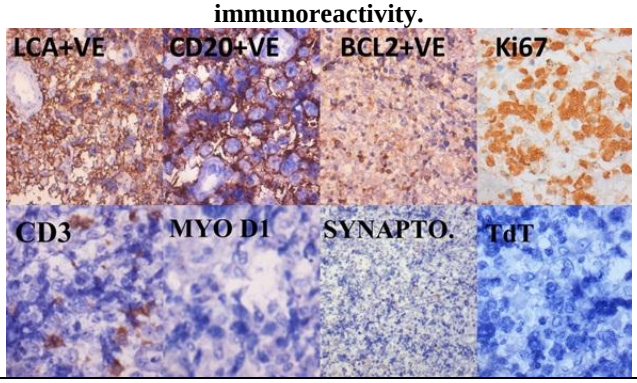
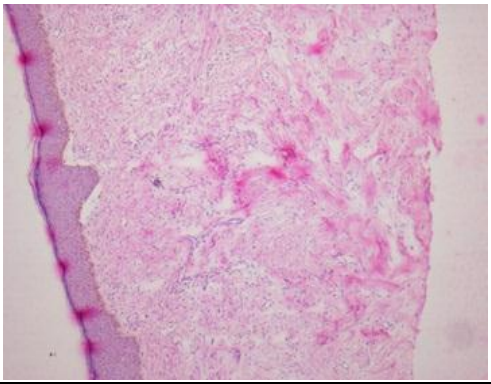


Figure 6: H & E stained section showing dense mature collagen bundle in the connective tissue, characteristic of keloid.



DISCUSSION:

NHLs occur by a multistep accumulation of genetic aberration. During B cell differentiation recurrent translocation can occur which can be the initial step in malignant transformation[8]. These translocations can lead to dysregulation of cell proliferation, survival and differentiation. Secondary genetic alterations are often required as these translocations are not sufficient to induce malignant transformations. B cell lymphoma can occur at various stages of B lymphocyte development if the controlled process of cell maturation is altered.[8] Somatic hypermutation (SHM) and class switch recombination (CSR) are the DNA modifications required during germinal centre reaction, if any aberration occurs during these critical steps it can lead to lymphomas. t(14;18), t(11;14) and deregulation of BCL2 gene is noted in follicular lymphoma and diffuse large B cell lymphoma (DLBCL).[9]

Even though lymphoma is the second most common neoplasm in the head and neck region it rarely occurs in the oral cavity.[10] In the oral cavity, NHL can occur within soft tissue or bone, affecting the paranasal sinuses, gingiva, floor of the mouth, buccal sulcus, salivary gland, or cheek. The more commonly affected sites are the Waldeyer's ring and the palate.[11] Primary intraosseous lymphomas of the jaw are rare and clinically and radiographically mimic odontogenic infections, cysts or tumors which can results in delayed diagnosis and treatment.[7] Usually malignant NHL of jaws affects adults in the 4th–5th decades with a male to female ratio of approximately 3:2, although some reports have suggested a female predilection.[12] In the present case mandible is involved which is not a very common site for lymphoma also the child is eight year old which makes it a rare entity. Many a times the first symptoms of large B-cell lymphoma of the oral cavity are painless swelling of the neck, fever, sweats, and weight loss.[7] There are no pathognomonic radiographic findings. Radiographic features are usually that of non-specific osteolysis. Panoramic films can show widening of the mental foramen, loss of cortical definition or widening of the mandibular canal, loss of lamina dura, or widening of periodontal ligament[13]. CT scan is necessary to exclude visceral or nodal involvement.[14] Histopathology of NHL usually shows proliferation of neoplastic cells as infiltrative broad sheets. Extralymphatic lymphomas can infiltrate adjacent normal tissue and destroy it.[15]

IHC can be done for confirmatory diagnosis of lymphomas and to determine the type of lymphoma. LCA can distinguish between lymphoid and nonlymphoid tissues. Diffuse large B cell lymphoma commonly stains positive for CD20 and CD79a.[16] CD3 is a marker for T cells and NK cells while Ki67 is commonly used as a proliferative marker.[10] In the present case a panel of IHC was done. MyoD1 and synaptophysin negativity excluded muscular and neural lesions respectively. TdT which is an enzyme expressed by acute leukemic cells is negative which excludes leukemia. IHC showed positivity for LCA, CD20 and PAX5 with focal positivity for BCL2 which confirmed the lesion as B cell lymphoma. The high Ki67 index indicates towards the aggressiveness of the lesion.

Recent advances like immunophenotyping, detection of IgH at the DNA level by use of polymerase chain reaction (PCR) to assess monoclonality and microarray are very useful diagnostic tools to detect lymphoma. Efforts should be made to diagnose this disease as rapidly as possible, since prognosis is directly related to disease staging recorded at the time of patient's admission.[17]

NHL can be managed by chemotherapy, radiotherapy and surgery in various combinations.[2] Cyclophosphamide, Doxorubicine, Vincristine, and prednisone (CHOP) regimen is the therapy for most cases.[16] Many clinicians choose wait and watch strategy for low grade lymphomas as the median survival rate without treatment is 8-10 years and they tend to recur despite chemotherapy.[15] For localized intermediate grade and high grade lymphomas treatment is chemotherapy plus radiotherapy. Early diagnosis will improve the prognosis. However patients older than 60, with immunodeficiency and several extranodal places of

involvement will have a nonfavorable prognosis. Over the past 25 years the prognosis of advanced B cell lymphoma in children and adolescents has improved dramatically (30–40% to 80–90% 5-year event-free survival) with intensive chemotherapy.[18] The initial response to treatment is good but this entity shows a prolonged course with remissions and exacerbations. The disease may progress into a leukemia.[7] Although lymphomas of the oral cavity and maxillofacial region are rare, it is important to describe the complete manifestation of their natural history in order to provide knowledge of their development.

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