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AN ATYPICAL CASE OF NON-HODGKIN'S LYMPHOMA OF MANDIBULAR ALVEOLUS.

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Abstract:

Lymphomas constitute a group of neoplasms of varying degrees of malignancy, which are derived from the basic cells of lymphoid tissue, the lymphocytes and histiocytes in any of their developmental stages. Lymphocytes constitute for 14% of all head and neck cancers. Lymphomas are divided broadly into two categories- Hodgkin's lymphoma and non-Hodgkin's lymphoma. Both the lymphomas are seen in head and neck region, but extra nodal disease with or without lymph node involvement, is more common in non-Hodgkin's lymphoma. Through this article, we would like to report the history, examination findings and laboratory results of a 64-year, old patient diagnosed with non-Hodgkin's lymphoma.

Keywords:

Non-Hodgkin's lymphoma (NHL), Lymphocytes, Immunohistochemistry (IHC), Swelling.

Introduction:

Lymphoma is the overarching concept for a wide variety of lymphoreticular system cancers. Lymphoma of the mouth can be a localized disease, but it's more likely to be part of a larger disease that also affects the lymph nodes in the head and neck. After squamous cell carcinomas and salivary gland tumours, primary lymphomas in the head and neck regions are the second/third most prevalent malignancies, accounting for 2.2 percent of all head-neck malignancies and 3.5 percent of intraoral malignancies[1].

Non-Hodgkin's lymphoma (NHL) is a common hematological malignancy. It is a complex group of malignancies characterized by abnormal T-cell, B-cell, or both clonal growths. The majority of NHLs are B-cell origin, with over 90% of patients expressing the CD20 antigen The age-adjusted incidence rates for NHL in men and women in India are 2.9/100,000 and 1.5/100,000, respectively[2].

The NHLs are collectively ranked fifth among malignant neoplasms in terms of cancer incidence and death in people over 75 years old, and sixth overall among malignant neoplasms. Before the advent of acquired immunodeficiency syndrome [AIDS] epidemic-associated lymphomas, the prevalence was increasing at a pace of 3–4% each year[1]. The case report discussed below was the manifestation of low-grade B-cell NHL of the swelling on the mandibular ridge following the extraction of 44 & 45.

Case report:

A 65 years male patient was referred by a private practioner to our institute. He presented with a chief complaint of swelling in right lower back tooth region and discomfort on eating food since 15 days. The patient first noticed the swelling 3months back which initially started as small as pea size and was associated with the mobility of the teeth. Swelling was gradually increased in size, which aggrevated after the extraction of the mobile teeth to reach to the present size. The past medical, family and personal histories were not significant.

On inspection of extra oral examination, no abnormality was detected in the swelling but on palpation a single lymph node of size 2x2cms was palpable in the right submandibular region which was non tender and firm in consistency. Inspection of intraoral examination revealed a solitary, oval, well-defined diffuse pedunculated swelling which was irregular in shape. The mucosa over the swelling appears reddish pink in colour, lower vestibule was obliterated and enlarged gingiva was seen (Figure 1) in the right mandibular ridge extending from 41 to 45,

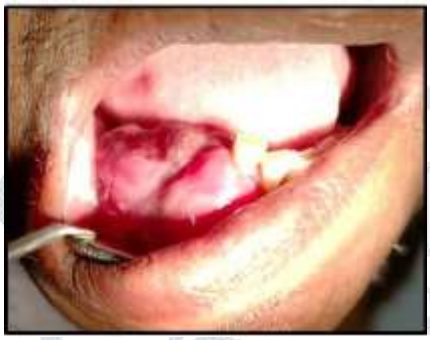

Figure-1 Solitary, oval, well defined intraoral swelling.

labially extending into the vestibule and lingually for 1cm. On palpation, all the inspectory findings were confirmed. Swelling was non tender mass with well-defined borders, sessile base, firm in consistency, and measured approximately 5×4×3cm in size which was fixed to the underlying tissues.

On radiographic investigation. Orthopantogram (OPG) revealed a single unilocular radiolucency with diffused well defined sclerotic border (Figure-2) on right mandible extending anteroposteriorly from 41 to 45, superiorly involving the ridge of the mandible and inferiorly 1cm above the inferior alveolar canal.

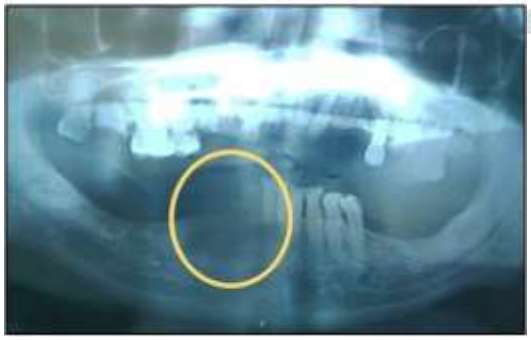

Figure-2 OPG showing radiolucency irt 41 to 45 mandibular ridge.

Based on the clinical and radiographic investigation, a provisional diagnosis of lymphoma was made. After taking an informed written consent, an incisional biopsy was performed under local anesthesia for histopathological and immunohistochemical conformation of the clinical diagnosis.

The biopsy specimen macroscopically appeared as an oval, well-defined soft tissue mass measuring 3 × 2.5cm, creamish brown in colour, and its consistency varied from firm to hard. The soft tissue specimen was cut into 2 halves and sent for processing (figure-3).

Figure-3 Macroscopical appearance of excised specimen.

Formalin fixed paraffin embedded soft tissue section in haematoxylin and eosin staining showed sheets of malignant neoplastic lymphocytes in loose fibro cellular stroma exbhiting altered nuclear cytoplasmic ratio, abnormal mitotic figures, prominent nucleoli, anisocytosis. Connective tissue is composed of diffuse, uniform monotonous proliferation of large-sized lymphocytes (figure-4).

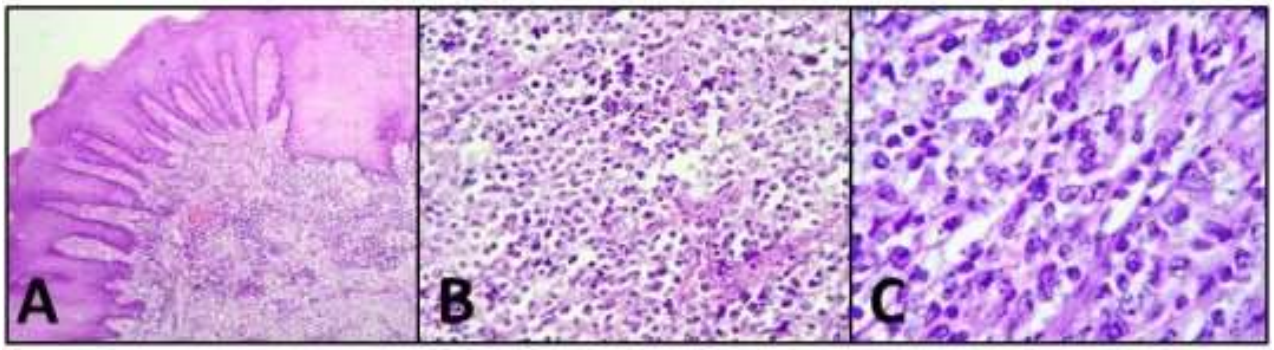

Figure -4 Lymphocytes with altered nuclear cytoplasm ratio, increased mitotic figures.

After the histopathological examination, the impression was Lymphoma. Certain Immunohistochemistry (IHC) markers like Epithelial Membrane Antigen (EMA) and CD 20 were suggested for confirmatory diagnosis.

The lesional tissue section showed positive immunoreactivity to EMA and CD 20 markers (Figure 5 & 6) respectively.

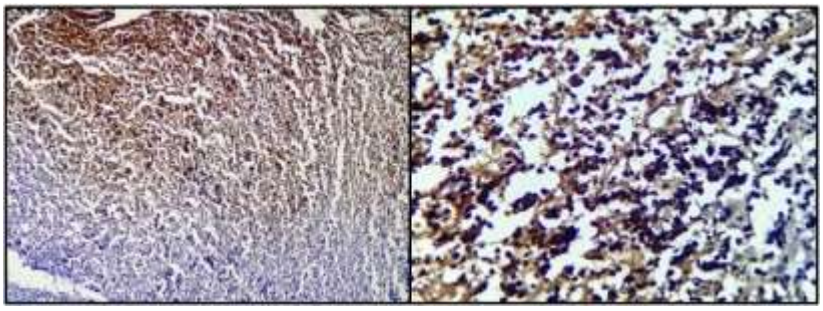

Figure-5 Showing positivity for IHC-Epithelial membrane antigen (EMA).

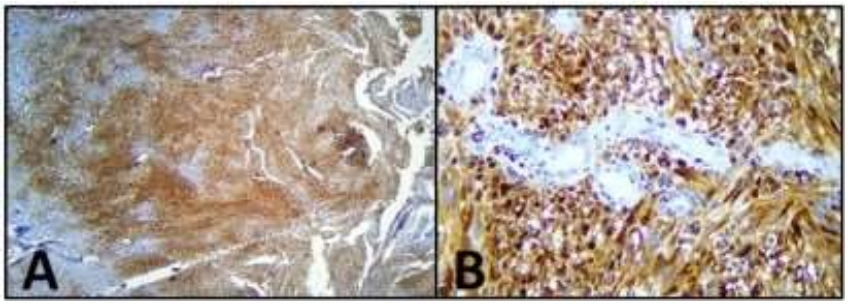

Figure-6 Showing positivity for IHC – CD 20.

Based on both histopathological and immunohistochemical analysis the final diagnosis was given as Diffuse large B-cell lymphoma a variant of Non-Hodgkin's Lymphoma. Under general anesthesia, the lesion was surgically removed, and postoperative radiation and chemotherapy were planned. Patient was kept under observation for periodical review and there was no recurrence on examination after 3 months of follow up.

Discussion:

NHL has long been recognized as a heterogenous group of disorders with varying clinical presentations, morphological appearances, and therapeutic responses. The prognosis is determined by the type of histology, clinical variables, and, more recently, molecular markers.

A group of American pathologists established a classification method known as the working formulation for clinical usage in the early 1980s. Unfortunately, the working formulation's utility and accuracy have been demonstrated to be fairly limited[3]. The International Lymphoma Study Group (ILSG) later codified and published the "Revised European-American lymphoid neoplasms (REAL)" categorization system and the pathologists may employ the R.E.A.L Classification[4], which had higher inter-observer repeatability (>85%) than other classifications. Immunophenotyping was beneficial in some cases but not needed in others. Several improvements were proposed for the WHO version based on years of experience with the REAL classification and input from the committees.

In the year 2008, World Health Organization (WHO)[5] revised a classification system for lymphomas. The neoplasms produced from precursor lymphoid cells are distinguished from those derived from mature lymphoid cells. WHO classification modifications in the year 2016, included a new umbrella category of T-follicular helper cell-derived lymphomas and the evolving recognition of indolent T-cell lymphomas and lymphoproliferative diseases[6].

Several etiological variables have been identified in the etiology of this disease, including Epstein-Barr virus infection, genetic abnormalities in p53 and c-kit, and immunological dysregulation[7]. To validate the diagnosis, chromosomal translocations and molecular rearrangements are commonly used. The translocation of t (14;18) (q 32; q 21), which is present in 85 percent of follicular lymphomas and 28 percent of diffuse large B cell lymphomas, is the most prevalent chromosomal aberration in NHL. Burkitt's lymphoma has t (8;14) or MYC, anaplastic large-cell lymphoma has t (2;5) or anaplastic lymphoma kinase, mantle cell lymphoma has t (11;14) or bcl-1, and marginal zone lymphomas have trisomy 3 or trisomy 18[8]. Human t cell leukemia/lymphoma virus type 1 (HTLV-1) is a blood-borne human retrovirus that has been associated to cause an aggressive form of peripheral T cell lymphoma[3].

Although specific subtypes of NHL, such as Burkitt lymphoma and lymphoblastic lymphoma, have been diagnosed at a younger age, the typical age of diagnosis is about the sixth decade of life[9]. There have been consistent reports of an increase in the incidence of NHL worldwide during the last three decades. Men have an incidence rate that is almost 1.5 times that of women.

In most of the cases the swelling of lymph nodes in the neck, beneath the arms, or in the groin are the common symptoms in both HL and NHL. Fever, nocturnal sweats, exhaustion, abdominal pain, and unexpected weight loss are some of the other symptoms. Lymphomas are normally painless, and lymph nodes may grow in size over time before the patient recognizes. For several weeks, a fever associated with

lymphoma may arise and disappear[8]. But in our case only painless swelling was seen over the mandibular region and palpation of submandibular lymph nodes were recorded with no other signs and symptoms. Since there is only an intraoral nodular growth, it has been difficult to diagnose the case initially.

The oral cavity is frequently the first sign of lymphoma. These can sometimes present as squamous cell carcinoma, which should be taken into account when making a diagnosis[1]. The pain or discomfort caused by bone lymphoma can be ambiguous. This could be misinterpreted as a toothache Particularly with a mandibular lesion, the patient may have paraesthesia (so called numb chin syndrome). Although radiographic alterations may be mild or non-existent in the early stages, radiographs typically show an ill-defined or ragged radiolucency.

Histopathologically, Non-Hodgkin's lymphoma is defined by a proliferation of lymphocytic-appearing cells with varied degrees of differentiation. Low-grade lesions are made up of well-differentiated small lymphocytes, while high-grade lesions are made up of cells that are less differentiated. Lymphomas develop as infiltrative broad sheets of rather homogenous neoplastic cells with little or no evidence of necrosis of the lesional tissue. A semblance of germinal centre formation can be noticed in some lesions, especially those of B-lymphocyte origin[3].

IHC is an important aspect in the diagnosis of lymphoma. IHC with several antibodies determines the lymphoma's lineage and stage of development. B-cell markers (CD20 and CD79a), T-cell markers (CD3 and CD5), Leukocyte common antigen (LCA), and cytoarchitectural pattern other markers such as CD23, bcl-2, CD10, cyclinD1, CD15, CD30, ALK-1, and CD138 are recommended for differential diagnosis (no single marker is specific)[10].

For non-Hodgkin's lymphoma, a basic immunohistochemistry panel is used. CD45 (LCA) expression rules out an epithelial tumour and indicates that the tumour is of hematopoietic origin. NHL is further divided into stages (immature vs. mature) and cell types (immature vs. mature) (B-cell, T-cell, or NK cell). The most extensively used pan-B-cell marker is CD20. The pan-T-cell antigen CD3 is the most widely used. CD4 refers to helper T-cells, CD8 to suppressor cells, and CD57 to natural killer cells (NK cells)[7]. In our case we have done the IHC markers CD20, a surface antigen found on B cells but not T cells and Epithelial Membrane antigen (EMA), which is expressed only in mixed and large cell types, but not in smaller ones. The above both markers were done to confirm the diagnosis of Diffuse large B-cell Lymphoma a variant of Non-Hodgkin's Lymphoma[11].

The Ann Arbor staging is used to manage NHL that affects the head and neck. The Ann Arbor staging system[9] is based on the anatomic extent of involvement, although initially designed to stage Hodgkin's lymphoma, now widely used for NHL. Based on old Arbor method, Lugano's classification has been introduced and this staging includes determination of type and intensity of therapy, overall prognosis of patient, patient complications associated with the disease[12].

Treatment for NHL is determined by the lymphoma's grade (low, middle, or high), its stage, and the patient's age and condition. Low-grade (slow-growing) lymphomas can occasionally be cured with a combination of radiation and chemotherapy in their early stages. Chemotherapy with or without radiation therapy, as well as a bone marrow transplant, can be used to treat advanced-stage, low-grade lymphoma. In recent clinical trials, radioimmunotherapy was used to treat advanced, higher-grade lymphomas or those that recurred following treatment by injecting antibodies with additional radioactive iodine[8].

Conclusion:

The prognosis for NHL is variable, depending on the kind of lymphoma, the extent of progression (staging), and the patient's response to treatment. Patients with B-cell NHL have a higher mortality rate, indicating that they require more care and attention after the diagnosis, which will have an impact on patients and the healthcare system[13]. This case study emphasises the significance of histological immunohistochemistry analysis in addition to clinical and radiographic symptoms in order to make a more accurate diagnosis of this devastating disease**.**

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