NON HODGKIN'S LYMPHOMA – A GROSTESQUE PRESENTATION

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ABSTRACT

Non Hodgkin's lymphomas are heterogonous group of malignancies of lymphoid system, 40% arising from extra nodal sites. Peculiar features include waxing and waning painless lymphadenopathy, swelling of extranodal, endoretiular organs and intraoral swellings. Majority of them are predominantly of B cell lineage. Thorough clinical, biochemical, histopathological, radiological and immunohistochemical evaluation aids in accurate diagnosis and management. A case of terminal stage Non Hodgkin's Large B cell Lymphoma in a 60yr old female patient involving extranodal sites is reported and discussed.

Key Words: *Non Hodgkin's Lymphoma, CD20, B cell Lymphoma*

INTRODUCTION

Lymphomas are malignant neoplasms of Lymphoreticular cells. They have been traditionally divided into Hodgkin's and Non-Hodgkin's lymphoma.[1] Non-Hodgkin's lymphomas are further segregated into B-cell and T-cell type based on cell origin, where the former depict approx 90% and latter approx 10% of all cases. Non Hodgkin's Lymphoma in contrast to Hodgkin's usually manifests outside the lymphoid system involving skin, abdomen, lungs, CNS and oral cavity with 0.1% to 5% incidence in oral cavity.[2] It is the third most common neoplasm of oral cavity and maxillofacial region with most common intraoral sites being palate and tonsil.[3] More aggressive B cell lymphomas present with large abdominal or mediastenal mass.[4]

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CASE REPORT

A 60 year old female reported with multiple painless swellings on both sides of neck and face since one year (fig 1). Initially a small swelling was noted in the right lateral neck region about a year ago which was followed by similar swellings noticed bilaterally in front and back region of neck, around ears and in the underarm region of upper extremities and in groin region which enlarged to present size with no secondary changes.

Within 4 months duration, a swelling over left palatal roof was noted intraorally which gradually increased in size. It was not associated with pain or secondary changes but had caused difficulty in speech and chewing. No history of dysphagia or parasthesia was noted but history of recurrent fever, weight loss and night sweats since 6months was present. She also had history of multiple prior consultations with improper treatments and follow-ups. Her medical and family histories were non contributory.

On general physical examination patient had a lean built, was underweight, undernourished and cachexic. Generalized lymphadenopathy involving submandibular (fig 2), submental (fig 3), preauricular, post auricular, cervical, supra clavicular, occipital (fig 4), axillary (fig 5) and inguinal groups were noted bilaterally with an average size of 8x10cms, non-tender with no secondary changes.

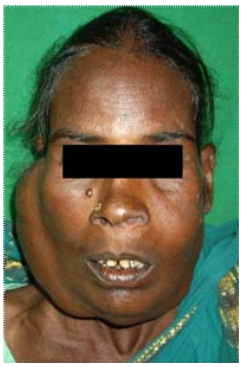

Fig 1: Extraoral swelling of right side of face

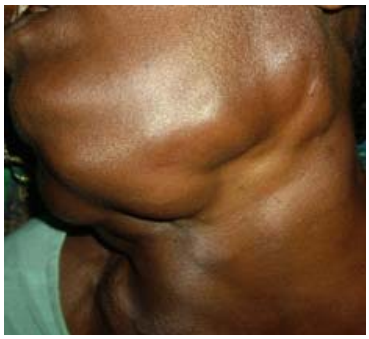

Fig 2: Multiple nodular swellings over left submandibular region

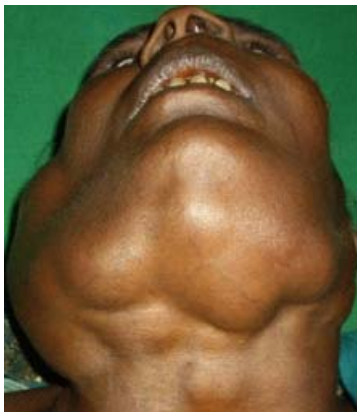

Fig 3: Multiple nodular swellings noted in submental region

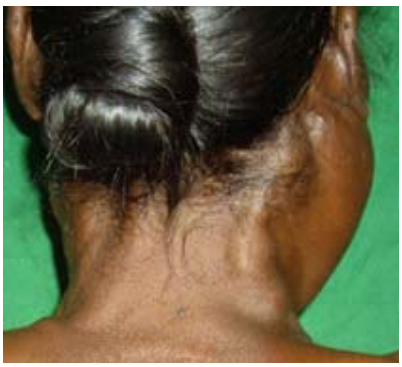

Fig 4: Multiple nodular swellings in the occipital region

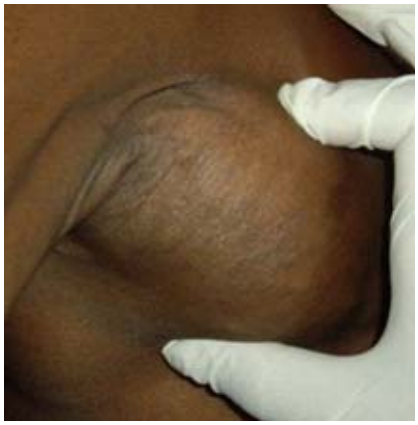

Fig 5: Picture showing large right axillary Lymphnode

Fig 6: Picture showing swelling on right side of face with elevated ear lobe

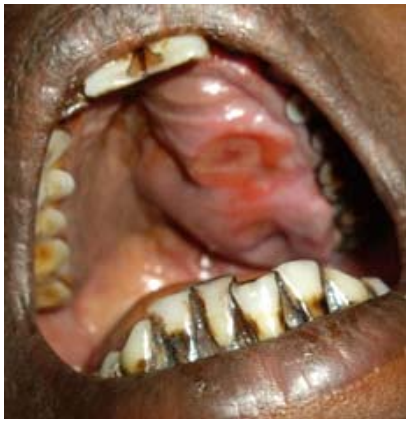

Fig 7: Intraoral swelling of hard palate with superficial ulceration

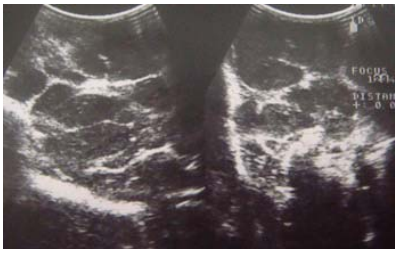

Fig 8: Ultrasound showing multiple homogenous lesions over abdomen

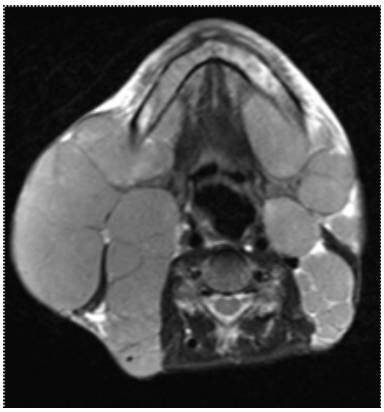

Fig 9A: MRI of head and neck

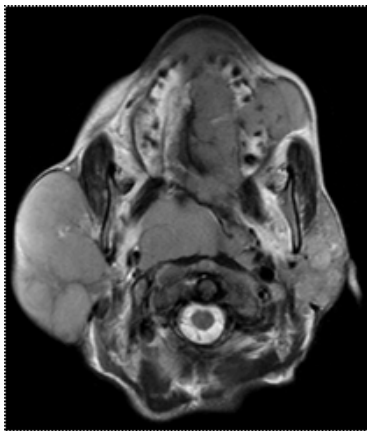

Fig 9B: MRI of head and neck

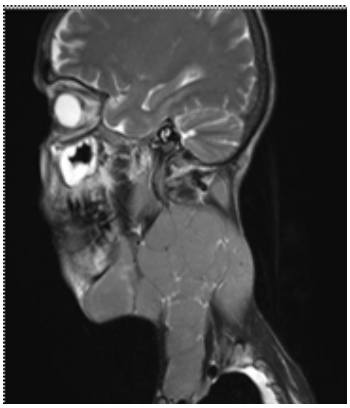

Fig 9C: MRI of head and neck

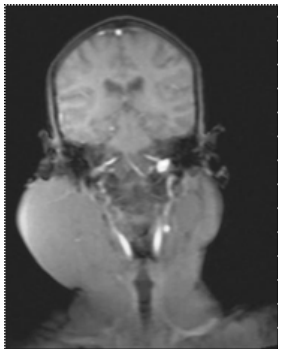

Fig 9D: MRI of head and neck

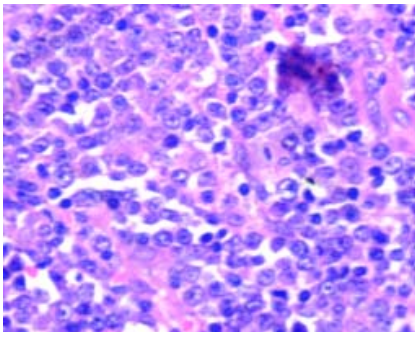

Fig 10: Histopathological picture showing lymphocytes intermixed with large amount of inflammatory cells

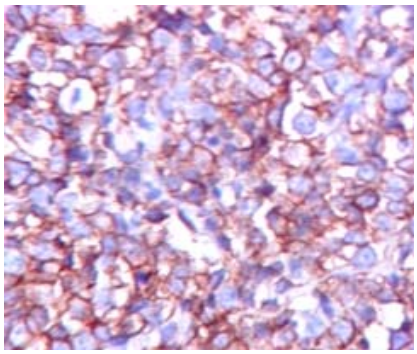

Fig 11: Immuohistochemistry showing tumor cells with CD 20 marker

On extra oral examination gross facial asymmetry was noted on right side involving the parotid and submandibular region causing elevation of ear lobe (fig 6). The swelling was diffuse and lobulated with no secondary changes, no rise in local temperature, non-tender and was firm in consistency. All the regional groups of lymph nodes in head and neck namely preauricular, submandibular, submental, superficial cervical, supraclavicular and occipital groups were enlarged and palpable bilaterally with no secondary changes. They approximately had an average size of about 3x4 cms with occipital lymph nodes being the smallest, about 2 × 2 cm. All the groups of lymph nodes were non-tender, matted and firm in consistency.

On intraoral examination a well defined solitary lobulated swelling was seen in the left side of the palatal region measuring about 6x4cm extending from marginal gingiva of 21,22 up to distal aspect of 28 antero-posteriorly and medio-laterally from midline of palate to the free gingival margin of 24 to 28 region. Surface was smooth with two areas of shallow ulcerations seen measuring approx 1.5cms with sloping edges, surrounded by erythematous areas. On palpation it was tender, soft to firm in consistency (Fig 7). A well defined lobular swelling was also noticed on the tonsillar area.

The thorough clinical examination indicated towards a lesion arising from lymph nodes. Hence, the provisional diagnosis of Non Hodgkin's Lymphoma with clinical staging IV B (Ann Arbor staging) was considered as multiple extra nodal site involvement was seen. Hodgkin's lymphomas, Lymphoblastic leukemia, AIDS associated persistent generalized lymphadenopathy with intraoral neoplasm were enlisted in differentials.

Except raised ESR (110mm/hr) other hematological investigations were normal. Blood glucose levels, serum urea and creatinine levels were estimated to be in normal range. Liver and renal function tests showed no abnormalities. She was seronegative for HIV & HbsAg.

Abdominal ultrasonography (fig 8) revealed multiple non homogenous lesions of varied size and pelvis suggestive of generalized lymphadenopathy and grade-1 renal parenchymal disease along with moderate splenomegaly. MRI of head and neck region was performed in order to assess the various soft tissue involvement, T1and T2 sequences showed involvement of both superficial and deep lobes of right parotid and partial involvement of left parotid glands. Bilateral submandibular salivary glands were also involved and enlarged to greater extent; maxilla revealed an extensive lesion involving the whole left side of palate and also left buccal cortical plate resorption i.r.t 24,25,26,27 with extension of lesion in left vestibule. Extensive enlargement of head and neck lymph nodes, Level 1-6 was noted along with pharyngeal tonsil causing partial obstruction of oropharynx due to elevation of posterior pharyngeal wall. (fig 9A,B,C,D)

Fine needle aspiration cytology of right upper cervical lymph node showed increased cellularity of medium and large lymphocytes having scanty cytoplasm and was suggestive of Non- Hodgkin's lymphoma intermediate grade mixed cellularity type. Biopsy of palatal lesion showed sheets of large lymphocytes intermixed with large amount of inflammatory cells. (fig 10) The diagnosis was validated as CD20 marker was positive on immunohistochemistry. (fig 11)

Final diagnosis of Non Hodgkin's Lymphoma of diffuse large B-cell type was rendered. Patient was referred to cancer institute where 8 cycles of chemotherapy regimen constituting of cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) was planned. The treatment was incomplete as the patient didn't survive after 4 cycles of chemotherapy.

DISCUSSION

Lymphomas are the diverse and complex group of neoplasms affecting lymphoreticular system[5] and are classified based on cell lineage by 'The Revised European American lymphoma' (REAL/WHO) system as : B cell malignancy ,T cell/natural killer malignancy and Hodgkin's lymphoma.[6,7] Hodgkin's lymphoma often presents as nodal disease whereas Non-Hodgkin's may also have an extranodal presentation.[1,6] The exact etiology of lymphomas is unknown however genetic predisposition, immunodeficiency state like HIV, recipients under transplantation and chromosomal translocation has been implicated.[8]

In 2001 Urquhae et al reported a review of 235 cases of head and neck with mean age of 67 years.[9] Various studies imply that it is more common among middle age and elderly (40-80 yrs) with more male predliction and ratio being 3:2.[1] HIV positive patients are 60 times more perlious than general population and around 3% of HIV infected people develop lymphomas.[1] In our case patient was 60yrs old and seronegative for HIV.

B cell Lymphoma are the most common among Non Hodgkin's lymphomas[5] which often present with initial symptoms like painless swelling of lymph nodes, Intraoral boggy swellings, ulcerations along with associated systemic symptoms like fever, night sweats, weight loss etc:[7] Based on associated systemic symptoms NHL patients are further classified as "A" (No symptoms) or "B" (Constitutional symptoms), where "B" constitute systemic signs and symptoms which include fever of unknown origin ,weight loss, drenching night sweats, visceral pain and malaise.[10] About 40% of the new cases are associated with systemic signs and symptoms.[3] In our case painless lymphadenopathy on both sides of neck and face with fever, malaise, weight loss and night sweats were present, hence classified as "B" type.

Intraoral Soft tissue lymphomas usually are misdiagnosed on preliminary examination. A painless lymph node enlargement with submucosal lesion in the junction between hard and soft palate are highly suspicious of Non Hodgkin's Lymphoma.[7]

Clinically and radiographically the manifestation may be similar to squamous cell carcinoma, odontogenic tumor or cyst.[7] Spencer et al reviewed 40 cases out of which 11 cases were sited in palate or maxilla with bone involvement. Eisenbud et al reported 45% occurrence in bone in his review of 31 cases where

Vanderwaal et al reported only a third of their 40 cases in bone. Clinically they may appear as ulceration or mass.[9] Radiographically a well defined radiolucency with bony erosion and lack of cortex, may be observed. In the present case both clinical and radiographic involvement was noted. Radiological studies have proven that large extra osseous soft tissue masses with minimal cortical destruction can be observed on plain radiographs.[11] However computed tomography and magnetic resonance imaging helps in visualizing further changes in case of large lesions with extensive bone destruction.

More aggressive B-cell lymphomas present with large abdominal or mediastenal masses.[4] In our case multiple homogenous lesions of varied size could be seen in the abdomen.The diagnosis is usually based on histopathological findings and advanced investigations like immunohistochemistry and the attributed markers for B cell lymphoma include CD 20, CD79a, MB2, CD30.[6,12] Spencer et al reviewed 40cases where Pan B cell markers (CD20, CD79a) established B cell lineage in 39 cases.[9] In our case immunohistochemistry was positive for CD20 marker and was suggestive of B cell lymphoma.

Various treatment modalities of Non-Hodgkin's Lymphoma include radiotherapy, chemotherapy and surgery in various combinations.[1] However standard modality has been chemotherapy and the regimen includes cyclophosphamide, doxorubicin, oncovin and predinsilone(CHOP).[4] Radiotherapy in the range of 2400-5600cGy (35-40Gy) delivered in 180cGy daily fractions has proven successful in early cases.[8] Radio immunotherapy has been employed as a new therapy for relapse cases. Yttrium90, Iodine131, ibritumomab tiuxetan are the currently used radioimmunoconjugates.[4] Chemotherapy (CHOP) was administered to the present case, however treatment was incomplete after 4 cycles as the patient did not survive.

The prognosis of disease is usually good with estimated 5yr survival rate in 30 % cases after therapy.[1] Survival is excellent in localized diseases, where as less favorable in disseminated cases.[14.]The response of patient population to aggressive chemotherapy in the absence of immunosupression has high efficacy with 65%to85% experiencing a complete survival response and 50-75% attaining long term survival.[1,13] Patients older than 60, with stages 3 and 4 and severe extranodal places of involvement will have an unfavorable prognosis as in our case.

CONCLUSION

The main purpose of this article was to report and focus on the grotesque manifestations of Non Hodgkin's Lymphoma. Awareness and scrupulous knowledge of dentist is essential in such cases for prompt diagnosis and immaculate treatment, all of which will enhance the probability of existence.

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