Case Report

The B-cell non-Hodgkin's lymphoma: An enigma to diagnose

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ABSTRACT

Non-Hodgkin's lymphoma is a heterogeneous group of malignancies characterized by an abnormal clonal proliferation of T-cells, B-cells, or both. Sometimes, tuberculosis and lymphoma presentation can share common symptoms and features. In this case report, we present the case of a 28-year-old female patient who came with a chief complaint of swelling on the right side of the face for the past 6 months. Initially, it was not associated with pain but gradually developed severe pain over the region and reduced salivary flow. The patient was planned for surgery with a differential diagnosis of salivary gland pathology. Post-operatively, the histopathological report showed atypical cells which were diffusely positive for cluster of differentiation (CD)20. Focally positive for CD45 and CD3 which was positive in reactive T lymphocytes. Immunohistochemistry pattern favors the diagnosis of B-cell type NHL. Through this case report, we want to share our experience in treating an aggressive tumor that mimics salivary gland pathology.

Key words: B-cell variant, Cluster of differentiation 20, Fine needle aspiration cytology, Non-Hodgkin's lymphoma

Lymphomas are a heterogeneous group of neoplasms that are broadly classified as Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL) due to their biological, histological, and immunophenotypical differences and clinical behavior patterns. Lukes 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 homogeneous population of a single cell type"[1]. The character of histologic involvement is either diffuse (uniform) or nodular and the distribution of involvement may be regional or systemic (generalized); however, the process is basically multicentric in character [2]. NHLs are a heterogenous group of lymphoproliferative malignancies that are much less predictable than HL and have a far greater predilection to disseminate to extranodal locations. Nearly 25% of NHL cases arise in extranodal locations and most of them are seen involving both nodal and extranodal sites [3].

We present an interesting case of NHL involving the extranodal site of the head-and-neck region which was similar in presentation to a salivary gland pathology. In this case report, we share our experiences and challenges faced in arriving at a diagnosis.

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CASE REPORT

A 28-year-old female patient came with a chief complaint of swelling in relation to the right side of the face for the past 6 months. The patient was apparently asymptomatic 6 months back and after which she developed swelling over the right side of the face which gradually increased in size, attained the present size, and was not associated with pain initially but gradually developed continuous severe pain (Visual Analog Scale-7) for the past 1 month. The patient had difficulty while eating and swallowing along with a dry mouth.

The patient was conscious and oriented to time, place, and person. There was no sign of pallor, icterus, cyanosis, or pedal edema and no nodes in the other regions of the body which are enlarged. On examination, the extraoral inspection findings included facial asymmetry, diffuse swelling in relation to the right side of the face measuring 6×4 cm extending from the lower border of the mandible to the superior end of the neck and from midline to the neck medially and extending up to a layer of the ear. The skin over the swelling appears normal with no evidence of pus discharge or any fistulous tract (Fig. 1). On palpation, all the inspection findings were confirmed and the swelling was tender, warm, immobile, firm, non-pulsatile, and non-compressible measuring 6×4 cm in relation to the right side of the face. The submandibular lymph nodes of the right side were

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tender and palpable. Intraorally, the mouth opening was adequate, the salivary flow was decreased, and dental caries was present on tooth 47 and severely attrited tooth in relation to 46.

Considering the clinical history of chronic swelling, reduced salivary flow, and difficulty in swallowing, the differential diagnosis made was submandibular sialadenitis. Antibiotic therapy was started. Further investigatory tests were done such as fine needle aspiration cytology (FNAC) and magnetic resonance imaging (MRI) of the neck. FNAC report suggested that the submandibular region showed reactive changes in lymph nodes and necrotizing lymphadenitis in the posterior triangle of the neck. MRI neck revealed a well-defined lobulated mass with its epicenter in the right submandibular region with perilesional inflammation and cervical lymphadenopathy (Fig. 2).

Based on the radiological reports, the patient was planned for surgical removal of the submandibular gland and associated lymph nodes. Intraoperatively, an encapsulated mass was seen attached to the submandibular gland. The submandibular gland along with the mass was removed in Toto along with the level I B lymph node (Fig. 3). A part from the encapsulated mass was sent for the frozen section. The frozen section revealed negative for granulomas/epithelial malignancy/tumor deposits. The total sample was sent for histopathological analysis to the department of oral pathology. The gross histopathological report showed a polymorphous lymphoid population suggestive of reactive changes and focally positive for marker cluster of differentiation (CD)45. Marker CD3 was positive in reactive T lymphocytes. The immunohistochemistry report showed atypical cells which were diffusely positive for marker CD20, focally positive for CD45 and CD3 positive in reactive T-lymphocytes. The histopathological report and immunohistochemistry pattern favor the diagnosis of diffuse large B-cell non-Hodgkin lymphoma (DLBCL) (Fig. 4).

The patient and attenders were counseled after the final diagnosis of the DLBCL tumor and the possible chances of recurrence since the B cell type is the most aggressive form of NHL. Post-discharge, she was referred for chemotherapy and has completed chemotherapy treatment outside the hospital. The patient is still in follow-up after 2 years and is doing good without any signs of recurrence.

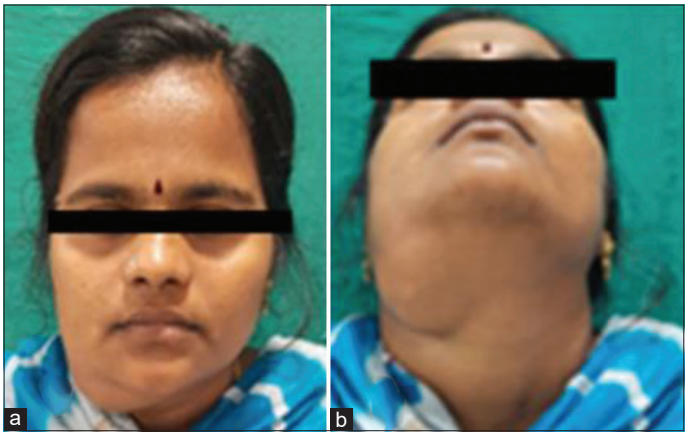

Figure 1: Pre-operative images of the patient

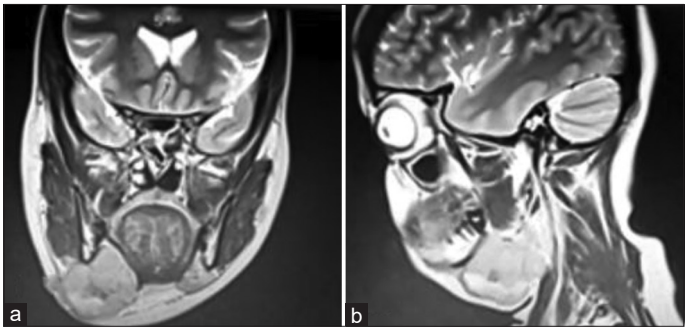

Figure 2: Pre-operative magnetic resonance imaging of the patient

DISCUSSION

NHL constitutes approximately 5% of all head-and-neck malignancies and shows a wide range of features that are comparable to that of Hodgkin's disease [4]. One of the characteristics is extranodal disease, with or without lymph node involvement which is more common among NHL patients. The three types of NHL are Burkitt's lymphoma, Mantle type, and the B-cell type. The B-cell variant is the most aggressive variant of the NHL.

NHL may be associated with various factors, including infections, environmental factors, immunodeficiency states, and chronic inflammation [5]. Various infectious agents have been attributed to different types of NHL. Epstein–Barr virus, a deoxyribonucleic acid virus, is associated with the causation of certain types of NHL, including an endemic variant of Burkitt's lymphoma. Human T-cell leukemia virus type 1 causes adult T-cell lymphoma. It induces chronic antigenic stimulation and cytokine dysregulation, resulting in uncontrolled B-or T-cell stimulation and proliferation. Hepatitis C virus (HCV) results in

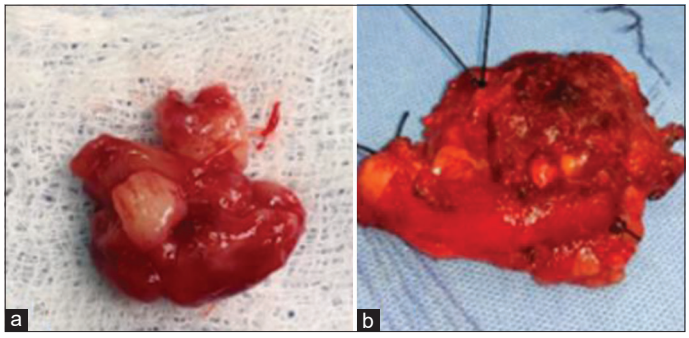

Figure 3: (a) Level II B lymph node and (b) Excised specimen

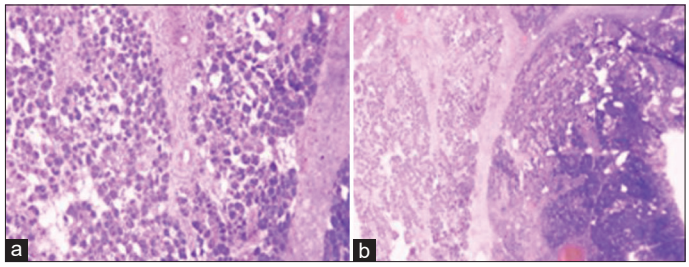

Figure 4: (a and b) Histopathological image (Pic Courtesy: Department of Oral and Maxillofacial Pathology)

clonal B-cell expansions. Splenic marginal zone lymphoma and diffuse large B-cell lymphoma are some subtypes of NHL due to the HCV. Human herpesvirus 8 is associated with primary effusion lymphoma and is a rare high-grade B-cell NHL associated with Kaposi sarcoma. *Helicobacter pylori* infection is associated with an increased risk of gastric mucosa-associated lymphoid tissue lymphomas, a primary gastrointestinal lymphoma [6].

Histologically, diffuse large B-cell lymphoma contains a large number of lymphoid cells with abundant cytoplasm and nuclei, which are larger than reactive histiocytes. According to Ann-arbor staging, NHL has been classified into four stages. For confirmation of diagnosis, the following pan-B cell marker, including PAX5 (paired box containing B cell 5), CD79, and CD20, should be expressed in diffused large B-cell lymphoma. CD20 is classified under the pan-B cell marker, and its presence on benign and neoplastic lymphocytes is considered specific for B-cell lineage [7]. PAX5 is a member of the paired box transcription factors involved in the development and is expressed in hematopoietic malignancies of B-cell lineage and is used as an adjunct marker in the diagnosis of HL and NHL [8].

Delay in diagnosis and treatment makes the estimated mortality rate high. Improper diagnosis and inappropriate or suboptimal treatment may be one of the contributory possible reasons for the poorer outcome. Treatment of NHL is based on the type, stage, histopathological features, and symptoms [9]. The most common treatment includes chemotherapy, radiotherapy, immunotherapy, stem cell transplant, and in rare cases, surgery. Chemoimmunotherapy, i.e., rituximab, in combination with chemotherapy, is most commonly used [10]. Radiation is the main treatment for early stages (I and II). Stage II with bulky disease, Stage III, and Stage IV are treated with chemotherapy along with immunotherapy, targeted therapy, and in some cases, radiation therapy [1].

Kumar *et al*. reported a case of diffuse large B-cell lymphoma and concluded that diagnostic criteria and differential diagnosis of each lymphoid tumor should be correlated with morphology, molecular genetics, and clinical history to confirm the diagnostic impression [11]. In another study by Singh *et al*., they have described that diagnosis should be done by correlating the histopathological features of these entities which will tell the malignant nature and prognosis of different forms of lymphomas [12], while Narang *et al*. did a case report on NHL misdiagnosed as tuberculosis. They concluded that NHL should be kept in mind as a differential diagnosis in patients not responding to antitubercular treatment [13]. Karadwal *et al.* reported a case of diffuse mixed B-cell NHL of the mandible and found that team effort by clinicians and histopathologists along with an understanding of the condition can help in timely diagnosis and treatment which can reduce morbidity [14].

In this case, radiological investigations such as FNAC and MRI neck do not give any conclusive diagnosis and are not relevant to clinical history. Frozen sections also showed negative for malignancy. Post-operative final histopathological report and immunohistochemistry only favored the diagnosis of DLBCL. This case report highlights the challenges faced in arriving a definitive diagnosis.

CONCLUSION

NHL requires a proper clinical examination and very importantly, a detailed histopathological, as well as, radiological evaluation. This was a perfect example of a case with a diagnostic dilemma in which the clinical history seemed to be a salivary gland pathology but further radiological investigations showed a hidden mass in the gland which later turned out to be an aggressive life-threatening tumor. It is always said that there is much more to a diagnosis than just a clinical examination.

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