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Case Report

Pathology Section

Histiocytic Sarcoma of Submandibular Gland: A Rare Case Report

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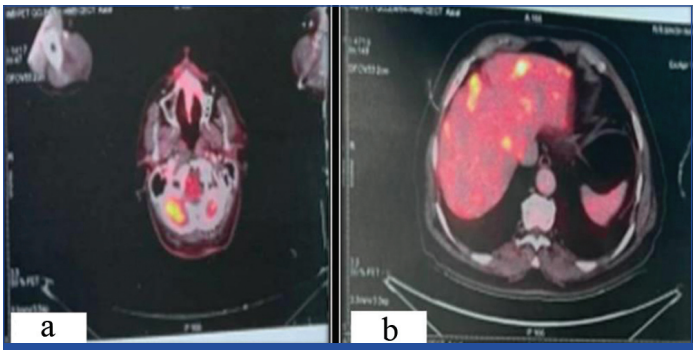
ABSTRACT

Histiocytic Sarcoma (HS) is a rare malignant neoplasm characterised by the neoplastic proliferation of cells showing morphological and immunophenotypic features of mature histiocytes. Majority of the reported cases present in extranodal sites, such as the head and neck, thyroid, duodenum, small intestine, colon, urinary bladder, spleen, and leptomeninges. This report documents a case of primary involvement of the salivary gland by HS. A 77-year-old male patient presented with a firm swelling in the left submandibular region for the last three months. Multiple lymph nodes, along with the presence of lung and liver nodules, were seen. Thus the final diagnosis of HS was made based on histopathology and IHC. Palliative chemotherapy was given to the patient, responded well, and has been well for the last year. The present study is probably the first case of HS involving the submandibular gland.

Keywords: CD 68, Histiocytes, Lymphoma, Salivary gland

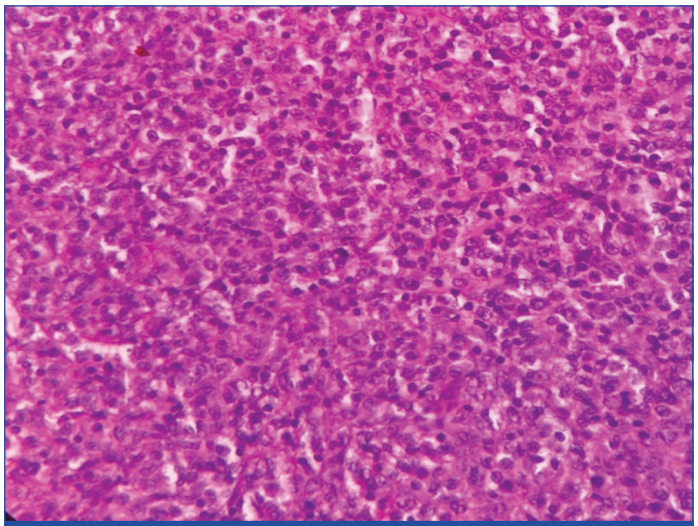
CASE REPORT

A 77-year-old male patient presented to the surgical oncology clinic with complaints of painless left-side neck swelling for the past three months. He had no history of fever, trauma, weight loss, loss of appetite, previous surgery, or any major ailment. Upon examination, a firm, non-tender swelling was found in the left submandibular region measuring 3 cm in its largest dimension. The patient's haematological work-up showed reduced Hb (7 gm/dL), platelet counts (80,000/µL), and slightly raised TLC (12,000/µL) and high Erythrocyte Sedimentation Rate (ESR). Peripheral blood picture showed normocytic normochromic anaemia and a normal differential leucocyte count. On Positron Emission Tomography scan-Computed Tomography (PET-CT), Fludeoxyglucose (FDG) avid metabolically active mitotic disease was seen in the left submandibular gland [Table/Fig-1a]. The left intraparotid, left supraclavicular, left cervical, mediastinal, and abdominal lymph nodes also showed FDG uptake. Additionally, there were multiple lung nodules, liver nodules [Table/Fig-1b], marrow lesions, and spleen lesions. Due to multiple site and organ involvement, neoplastic and infective causes were considered, with lymphoma being the most likely suspect. A biopsy was done on the left submandibular gland lesion.

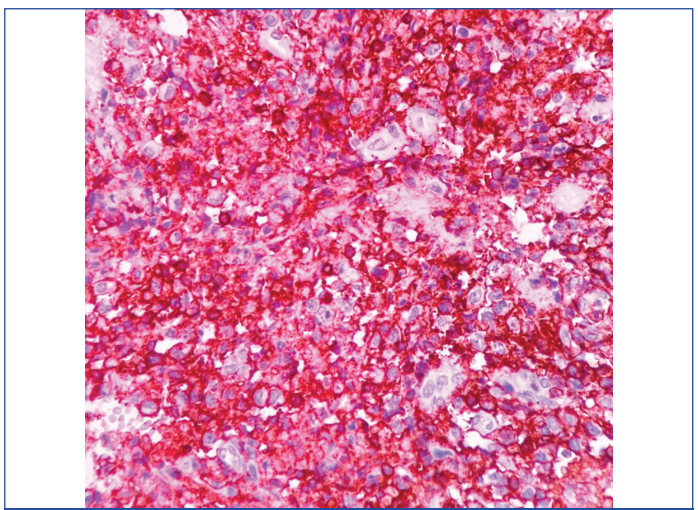


[Table/Fig-1]: a) PET scan showing submandibular swelling increased uptake. b) PET scan showing liver nodules showing increased uptake.

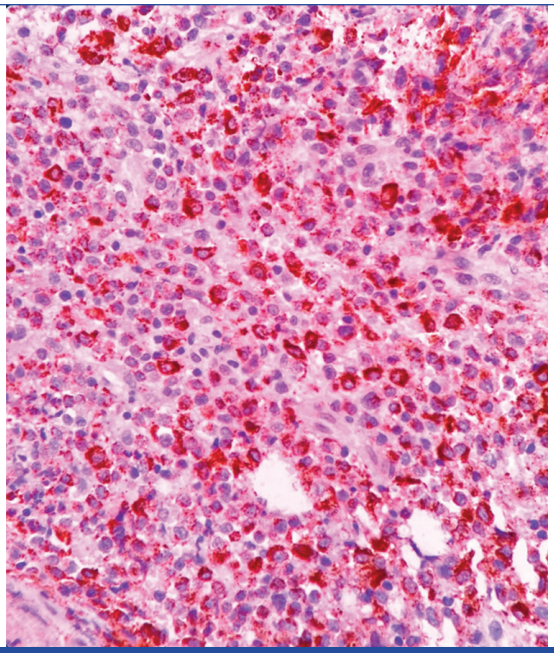
On histopathological examination, the tumour was highly cellular, consisting of sheets of atypical cells with vesicular nuclear chromatin, prominent nucleoli, and abundant clear cytoplasm [Table/Fig-2]. The mitotic rate was high (20-25/10HPF). The tumour cells were infiltrating the peripheral salivary gland tissue. The possibility of a poorly differentiated neoplasm was considered, and an IHC panel of unknown origin was used. On immunohistochemistry, the cells were immunopositive for LCA [Table/Fig-3], CD68 [Table/Fig-4], CD 163, CD4, and CD14. The cells were negative for CD20, CD3, CD30, CD1a, ALK-1, S100p, CK, CD117, BRAF V600E, CD21, and CD23. The Mib 1 labelling index was 30% [Table/Fig-5]. Therefore, a final diagnosis of HS was made based on histopathology and IHC.



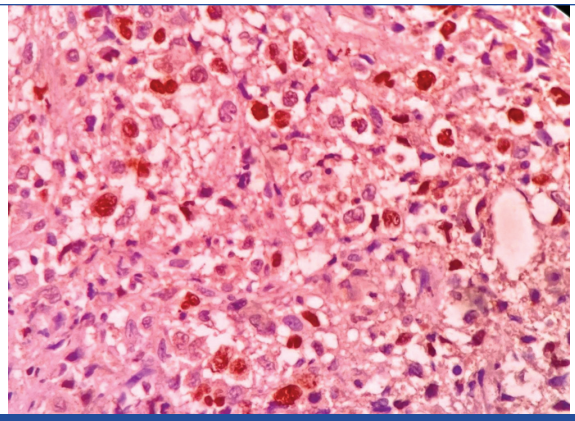
[Table/Fig-2]: H/E 200x showing sheets of atypical cells.



[Table/Fig-3]: IHC 400X showing tumour cells showing diffuse membranous positivity to LCA.



[Table/Fig-4]: IHC 400X showing tumour cells showing membranous and cytoplasmic positivity to CD 68.



[Table/Fig-5]: IHC 400X showing tumour cells showing 30% Mib 1 labelling index.

The patient was given palliative chemotherapy with Ifosfamide and Doxorubicin. He responded well, and PET-CT after four cycles suggested a good metabolic response. After one year of follow-up, the patient was doing well.

DISCUSSION

HS is a rare malignant neoplasm characterised by the neoplastic proliferation of cells showing morphological and immunophenotypic features of mature histiocytes [1]. Majority of the reported cases in the literature present in extranodal sites, such as the head and neck, thyroid, duodenum, small intestine, colon, urinary bladder, spleen, and leptomeninges [2-5]. The presentation of primary HS in the salivary gland is very unusual. Heretofore available literature search suggests only two cases of primary HS of the parotid gland have been reported, while this is the first case involving the submandibular gland [6].

Histiocytic and dendritic cell neoplasms are extremely rare disorders, occurring in approximately 1% of malignant neoplasms in the soft tissues and lymph nodes [1]. According to the recent World Health Organisation (WHO) classification, histiocytic lesions are classified into five groups of diseases: A) Langerhans-related; B) cutaneous and mucocutaneous; C) malignant histiocytoses; D) Rosai-Dorfman disease; and E) haemophagocytic lymphohistiocytosis and macrophage activation syndrome [7]. They arise from mature histiocytic differentiation [8]. The extranodal sites at which HS is reported include the head and neck, thyroid, duodenum and small intestine, colon, urinary bladder, spleen, and leptomeninges. Rarely do they affect lymph nodes also [2-5]. The origin of this disease is still unknown, but certain genetic causes have been postulated, especially in those neoplasms that show transformation from pre-existing low-grade lymphomas [2]. HS constitute <1% of all haematolymphoid neoplasms. HS with head and neck manifestations are particularly rare, and few cases have been presented in the literature [3]. To the best of our knowledge, the present case is the first case of HS involving the submandibular gland. Previously, two cases of HS of the parotid gland have been reported by Akiba J et al. in 2011 and Hussien MT in 2019 [9,10].

Grossly, these tumours have ill-defined infiltrating margins with areas of necrosis. Microscopically, they consist of pleomorphic cells in sheets without any pattern. Cells have irregularly clumped chromatin and prominent nucleoli. Multinucleated tumour giant cells and mitotic activity are easily appreciated. On IHC, histiocytic markers are expressed in these tumour cells, such as CD68, CD163, and lysozyme. They must be negative for B and T cell markers, dendritic cell markers, Langerhans cell markers, S100p, MPO, CD30, Pan CK, and HMB45 [11]. Most commonly, they are often misdiagnosed as non-Hodgkin's lymphoma, especially DLBCL. IHC has a role in differentiating the two. DLBCL will be CD20 positive, while HS is vimentin and CD68, and other histiocytic markers are positive while negative for CD20. Another differential is anaplastic large cell lymphoma, which shows ALK and CD30 positivity while negative for histiocytic markers [2].

Dendritic cell tumours also need to be ruled out by using dendritic cell markers like CD21, CD23, and CD35 while CD68 is usually negative. Other poorly differentiated neoplasms of salivary gland origin can also be ruled out by IHC as they show expression of either epithelial/myoepithelial cell antigens. Myeloid sarcoma should also be excluded in these tumours by using MPO. HS usually lack clonal IgH or T cell receptor rearrangement [12]. Positive BRAF V600E mutation is also seen in a subset of cases [13]. The mean age ofpresentation of HS is 46 years with no apparent gender or hereditary predictors. Most casesof HS follow an aggressive clinical course, with a survival of less than one year. There areno clear guidelines for systemic treatment.

CONCLUSION(S)

The present case is the first case of primary HS in the submandibular gland. It is essential to understand the various morphological, immunophenotypic, and genetic characteristics of HS to obtain a proper and timely diagnosis of this rare entity so that it can be treated appropriately. Also, it should always be kept in the differentials of poorly differentiated neoplasms at these rare sites.

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