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Case Report

Pathology Section

Syncytial Variant of Nodular Sclerosis Hodgkin Lymphoma: A Case Report on Histological Medley of Morphological Variants

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ABSTRACT

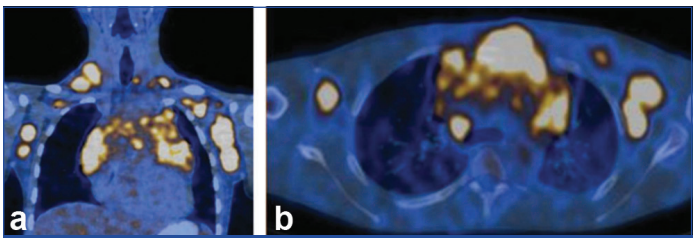
There are several histological and morphological subtypes of Hodgkin Lymphoma (HL), a malignant lymphoproliferative disease, and each has distinct prognostic consequences. Syncytial Variants is an unique, uncommon morphological type of Nodular Sclerosis Hodgkin Lymphoma (SV-NSHL). Unlike other subtypes of classical HL, which exhibit a male preponderance, it is more prevalent in females. The most often affected lymph nodes, which can exhibit contiguous spread, are the cervical or mediastinal lymph nodes, or both. Hereby, the authors present a case report of an 18-year-old male patient who has been experiencing intermittent fever, weight loss, neck pain, and gradual enlargement of the neck and axillary lymph nodes over the past two months presented to the Outpatient Department (OPD). Clinical examnation and radiological assessment using plain Computed Tomography (CT) of chest scan showed several enlarged lymph nodes in the mediastinum and anterior chest wall, along with sternum erosion. This led to a differential diagnosis of lymphoma, sarcoidosis, and atypical tuberculosis. Histological analysis {Haematoxylin and Eosin (H&E)} and immunohistochemical profiling of an excised left supraclavicular lymph node rendered the diagnosis of classic HL, and a very rare variant, the SV-NSHL. The present case is being reported for its extreme rarity, diagnostic challenges, and distinct clinicopathological correlation.

Keywords: Complications, Diagnosis, Histopathology, Therapy

CASE REPORT

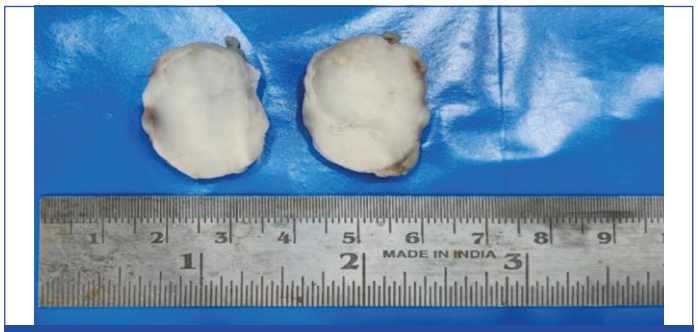
An 18-year-old male presented to the OPD complaining of neck pain and progressive enlargement of lymph nodes, particularly in the mediastinal and supraclavicular regions, over the past two months, accompanied by significant weight loss. Laboratory investigations showed severe anaemia, with haemoglobin level of 7 g/dL (Reference range: 13.8 g/dL to 17.2 g/dL), and total White Blood Cell (WBC) count of 21,000/µL (Reference range: 4,000-11,000 cells/µL). Radiological investigations revealed multiple enlarged conglomerate lymph nodes noted in left anterior chest wall, upper paratracheal, prevascular, para-aortic, and hilar lymph node, largest measuring 4×3 cm in left axilla, 3×2 cm in right upper paratracheal area, and 2×1 cm in prevascular region. The differential diagnosis on radiology included lymphoma, atypical tuberculosis, and sarcoidosis.

A Positron Emission Tomography-Computed Tomography (PET-CT) scan revealed [Table/Fig-1a,b] increased Fluorodeoxyglucose (FDG) uptake and increased metabolic activity in the above group of enlarged lymph nodes and mediastinal mass, suggestive of a malignant lymphoproliferative disorder or lymphoma.



[Table/Fig-1]: a) PET-CT Scan image: Sagittal section shows enlarged nodes with increased Fluorodeoxyglucose (FDG) uptake and increased metabolic activity in left anterior chest wall, upper paratracheal and hilar lymph nodes; b) Coronal section of the thorax of the same patient shows increased FDG uptake and increased metabolic activity in the mediastinal mass. (Images from left to right)

A nodular mass measuring 2.8×1.8×1 cm was received. The external surface was grey-white, and cut surface showed a grey-white, solid, and homogenous appearance [Table/Fig-2].



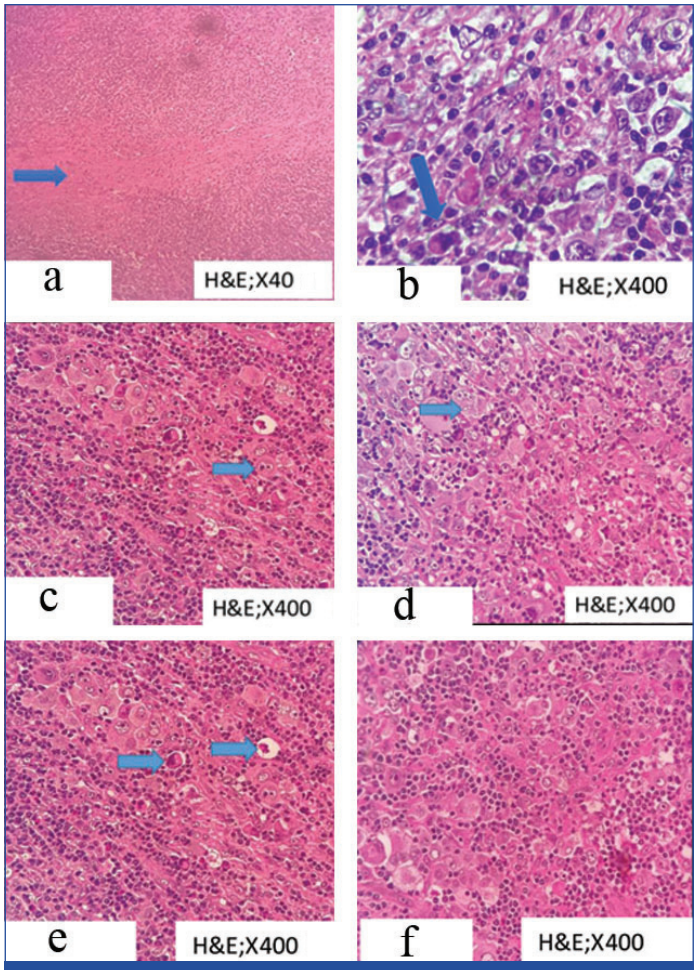
[Table/Fig-2]: Gross pathology- showing excised lymph node mass, cut surface revealed a grey-white, solid homogenous area.

Histopathological evaluation [Table/Fig-3a-f] of multiple sections studied from excised supraclavicular lymph node showed complete effacement of architecture revealing a polymorphous population of lymphoid cells and lymph node parenchyma divided into vague nodules separated by fibrous septae.

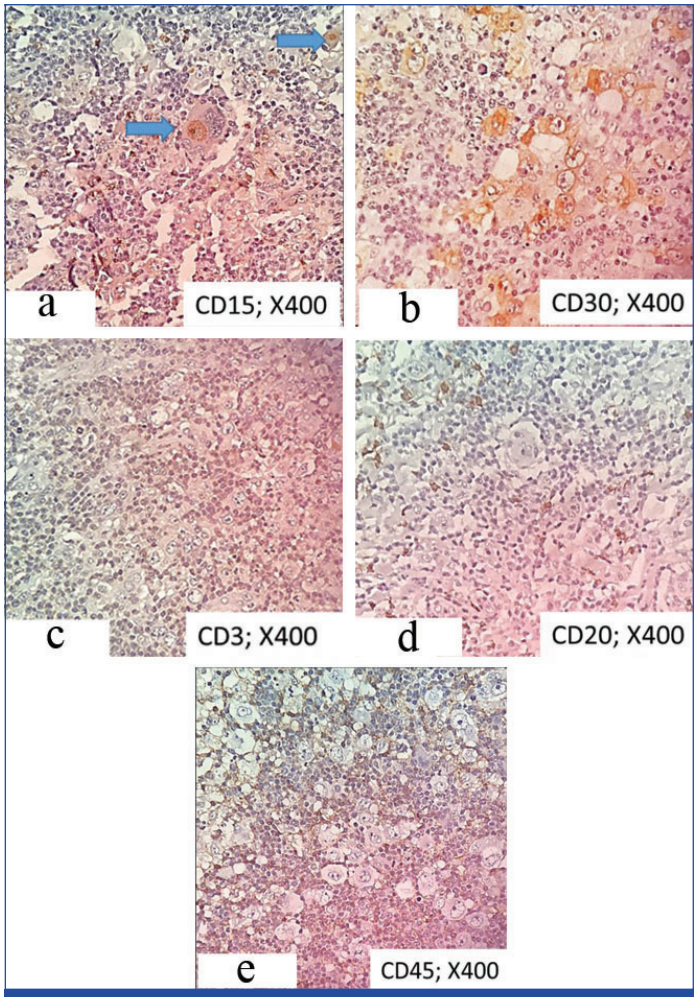
The polymorphous lymphoid population consisted of large number of tumour cells arranged in many areas in a sheet-like/syncytial pattern, which composed of all morphological cell variants noted in HL {mononuclear Hodgkin cells, binucleate Hodgkin/Reed-Sternberg cells (HRS), many lacunar cells, mummified cells, and multi-lobated large lymphohistiocytic cells or "popcorn cells." The background exhibited a mixed inflammatory infiltrate with increased eosinophils, neutrophils, mature small lymphocytes, and histiocytes. Focal area of necrosis and occasional mitotic figures were noted. No evidence of granulomas were noted.

Immunohistochemistry Results

The tumour cells were diffusely and strong to moderately positive (membranous and cytoplasmic) for CD30 and diffusely and moderate to weakly positive (membranous and cytoplasmic) for CD15. The tumour cells were negative for CD45, CD20, and CD3 [Table/Fig-4a-e]. (Pictures are represented in collage format below as per reviewer instructions).



[Table/Fig-3]: a) Collagenous bands of fibrosis and sclerosis (blue arrow) dividing the tumour into nodules of varying sizes; b) Mummified cell variant of Hodgkin Lymphoma highlighted in blue arrow and mononuclear Hodgkin cells (highlighted in white arrow); c) Binucleated Reed-Sternberg cells (blue arrow) of Hodgkin lymphoma; d) Multilobated large cells or "lymphohistiocytic" variant or "popcorn cells" of Hodgkin lymphoma; e) Lacunar cell (blue arrow) variant of Hodgkin lymphoma; f) Sheet-like or syncytial pattern of arrangement of tumour cells comprising of various morphological variants of Hodgkin lymphoma arranged in sheets within a mixed inflammatory background.



[Table/Fig-4]: a) Tumour cells (blue arrow) show moderate to weak positivity for CD15; b) Tumour cells (blue arrow) show strong to moderate positivity for CD30; c) Tumour cells are negative for CD3; d) Tumour cells are negative for CD20; e) Tumour cells are negative for CD45.

The histopathological and immunohistochemical findings confirmed the diagnosis of classical HL, nodular sclerosis subtype. The presence of a sheet-like pattern of tumour cells (all morphological variants of HL) with focal necrosis rendered a more specific diagnosis of SV-NSHL.

The patient underwent chemotherapy Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone regimen (CHOP), adjuvant therapy, recovered well, in good health, and pursuing his education and in constant periodic follow-up with the oncologist.

DISCUSSION

Approximately 10% of all lymphoma cases are classified as HL, a malignant condition originating from germinal center B cells within the lymph nodes [1]. The overall five-year survival rate for people with early-stage cancer is more than 95%, whereas for those with advanced-stage disease, it is around 85%. As classified by World Health Organisation (WHO) [2,3], HL has two pathological subtypes: (i) Nodular Lymphocyte Predominant HL and (ii) Classic HL. Classic HL is further categorised into four subtypes: (a) Nodular Sclerosis; (b) Lymphocyte Rich; (c) Mixed Cellularity; and (d) Lymphocyte Depleted [2,3]. In the context of HL, inflammatory cells form the main bulk of tumour nodules, with scant population of neoplastic cells like lacunar cells, HRS cells, and mummified cells.

The NSHL predominantly affecting young age patients, makes up 70% of all classical HL [4]. The syncytial variant of NSHL, as observed in our reported case, has been relatively unexplored in the literature. Lukes RJ and Butler JJ had been the first to analyse cases of non sclerosing HL, characterised by the abnormal proliferation of lymphoid tissue consisting of HRS cells that form cohesive clusters separated by interlacing collagenous bands, leading to the formation of cellular nodules [5,6]. The diagnosis is based on three characteristic features: lacunar cells, diagnostic HRS cells, and bands of fibrosis between neoplastic cells, often associated with necrosis. At least two out of three features should be present to validate the diagnosis [5]. It also requires the presence of lacunar cells, identified as large pleomorphic cells with abundant clear cytoplasm condensed around perinuclear region within a lacuna-like space, typically identified by CD30 positivity [7]. The degree of fibrosis is extensively variable across multiple foci of same lymph node.

Patients with HL, more common in young adults, often presents with painless lymphadenopathy located above the diaphragm, accompanied by B symptoms such as significant weight loss, persistent high fever, and profuse night sweats [8]. Nodular sclerosis subtype of HL more commonly associated with supraclavicular lymphadenopathy as most common extramediastinal site of involvement [9].

The prognostic evaluation of NSHL is classified using The British National Lymphoma Investigation (BNLI) grading system. As per BNLI, NSHL is categorised into Grade 1 and Grade 2. More than 75% of nodules showing scattered HRS cells in a lymphocyte-rich mixed cellularity background. is seen in Grade 2 More than 25% of the nodules showing sheets of HRS cell showing pleomorphism and lymphocyte depletion.

Since, most Grade 2 cases are not syncytial variants, but the majority of syncytial variant patients are Grade-2 due to the presence of atypical cells, the BNLI grading by itself does not

accurately represent the clinicopathological characteristics of this illness [10].

The SV-NSHL is concluded as an aggressive subtype with poor prognostic outcomes. In research conducted by Sethi T et al., 167 patients with NSHL were analysed, of which 43 cases were identified as syncytial variants based on morphological and immunophenotypical criteria [11]. The study demonstrated patients with syncytial variants had poorer complete response to standard induction therapy compared to typical NSHL cases. Furthermore, during the 49-month follow-up period in the study mentioned, the syncytial variants was related to greater relapse rates and shorter progression-free survival. Within the classical NSHL category, the results highlights the syncytial variants as a high-risk category [11].

CONCLUSION(S)

The SV-NSHL as confirmed by histopathological features has been strongly associated with specific clinical features like younger age group, male prepoderance (as observed in our case with an 18-year-old male), presence of a mediastinal lymph node enlargement, and high clinical tumour staging. These were also observed in our case, the patient having generalised lymphadenopathy and mediastinal lymph node enlargement eroding the sternum. The present case has been reported due to its extreme rarity, diagnostic challenges it posed and its association with poorer prognostic parameters compared to other histological types of HL. SV-NSHL, which has distinct histopathological features that pathologists should be aware of and warrants reporting in the medical literature. In the era of precision medicine and precision oncology, accurate diagnosis and subtyping such as this very rare variant, with prognostic significance, will be invaluable for further patient treatment options, reduced morbidity and side effects, and remission or increased disease-free survival.

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