

Histiocytic Sarcoma: A Very Rare Tumor in a 97 Year Old-A Case Report

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Abstract

Histiocytic Sarcoma (HS) is an extremely rare tumor with aggressive course and arises in lymph nodes and extra nodal sites. We present a case of HS in a 97-year-old male patient with non-specific clinical features. CT scan revealed left axillary lymph node enlargement and a hypo dense lesion in spleen. On Lymph node biopsy, a diagnosis of HS was made based on the histomorphology and immunopositivity of tumor cells for CD68 and CD 163. Negative markers ruled out the other mimics. Considering his age of 97 years, he was not considered to be suitable for surgery or aggressive therapy. HS is an extremely rare neoplasm and it is a diagnosis of exclusion. The key to diagnosis is immunohistochemistry. Molecular genetic studies have reported a few abnormalities and needs to be confirmed. There is no standard protocol for the management of HS due to its rarity.

Key words: Histiocytic Sarcoma, Lymph node, Spleen, Immunohistochemistry.

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INTRODUCTION

Histiocytic tumors are rarest amongst the tumors affecting lymphoid tissues and accounts for less than 1% of the tumors presenting in lymph nodes and soft tissues [1, 2]. Histiocytic Sarcoma (HS) is a rare neoplasm of mature histiocytes and is considered to be a true hematopoietic neoplasm [3]. It is composed of cells which exhibits immunophenotype and morphology of mature tissue histiocytes [4]. There are very few true cases of HS reported in literature. With the introduction of newer IHC markers, many cases have been diagnosed as HS, which were previously reported as large cell lymphomas [5, 6]. HS is a very aggressive neoplasm. A subset of HS is known to arise from clonal evolution of preexisting hematologic neoplasms [7]. Many case reports have described HS as a secondary event following the primary diagnosis of follicular lymphoma, Acute Monocytic Leukemia, Mantle cell lymphoma, Hairy cell leukemia, MALT type lymphoma, Diffuse large B cell Lymphoma, Large B cell lymphoma, Acute lymphocytic leukemia, Chronic lymphocytic leukemia, Chronic myelomonocytic leukemia, Chronic myeloid leukemia, Mediastinal germ cell tumors, Idiopathic myelofibrosis[2,3,8-11].

A few hundred cases have been reported in literature. The most common site of occurrence is lymph nodes, followed by extra nodal sites like GIT, Spleen, soft tissues and skin [12]. HS is more common in adults and the median age at diagnosis is 51 years [3]. Cells are large, round to oval with abundant eosinophilic, often foamy or vacuolated cytoplasm and focal areas of spindling. Cells show CD163, CD68 and Lysozyme immunoreactivity [8, 12]. Diagnosis of HS is difficult on morphology alone and IHC confirmation is a must [4]. The tumor cells express CD163, CD68, and lysozyme and are negative for CD20, CD30, CD43, CD56, CD57, CD79a, CD5, myeloperoxidase, Mart/Melan A, Alk 1, Perforin, Keratin AE1/3, CK7, CK20, TTF1[4,6]. The term HS was reported by Mathe et al, based on the similarities of the cells to macrophages [13].

Here we present a rare case of HS in a 97 year old male patient. In literature, this case is first of its kind to be reported in such an elderly patient.

CASE REPORT

A 97-year-old male patient presented with complaints of weight loss and generalized weakness since 1 year. Physical examination revealed an enlarged mass in the left axilla. Whole body Computed tomography (CT) was advised. CT showed multiple enlarged lymph nodes in the left axilla and a hypodense lesion measuring 1x1.5 cm in the spleen. Figure 1 is a CT image showing enlarged left axillary lymph nodes and Figure 2 shows CT image showing a hypodense lesion measuring 1x1.5 cm in Spleen. No other findings were present. Based on CT findings, a radiological diagnosis of lymphoma was made. A biopsy was taken from the left axillary group of nodes. Histopathology of biopsied node showed diffuse sheets of large, pleomorphic cells with abundant eosinophilic cytoplasm, atypical nuclei and prominent nucleoli. Large areas of necrosis were present. Scattered tumor giant cells along with many inflammatory cells including eosinophils were seen. Figure 3 Showing large pleomorphic cells with abundant eosinophilic cytoplasm and pleomorphic nuclei and few giant cells(H&E,40X) and figure 4 showing pleomorphic cells with prominent nucleoli and few eosinophils(H &E 40X). Immuno histochemical markers were applied to assist in making a diagnosis. The tumor cells showed diffuse cytoplasmic positivity for CD 68, membranous positivity for CD163 and low scattered positivity for CD4. Figure 5 showing CD68 marker showing diffuse cytoplasmic positivity in tumor cells and giant cells(40X) and Figure 6 showing CD163 marker showing membranous positivity in tumor cells(40X). The cells were negative for CD1a, CD79a, CD5, CD20, CD21, CD19, CD10, CKAE1/AE3, S100, and Melan-A. The complete blood cell counts and peripheral smear were normal. Molecular genetic studies were not done. Based on the morphological and immunohistochemical findings, a diagnosis of Histiocytic Sarcoma of left axillary node was made. The Spleen was left untouched considering the age of the patient. There were no other significant clinical findings. The patient presented with a nonspecific clinical history and multifocal lesions. Due to his age, he was not considered suitable for surgery or aggressive therapy. The best management option decided for this patient was supportive and hospice care. The patient was discharged with an advice for regular follow up.



Fig-1: CT image showing enlarged multiple lymph nodes in the left axilla

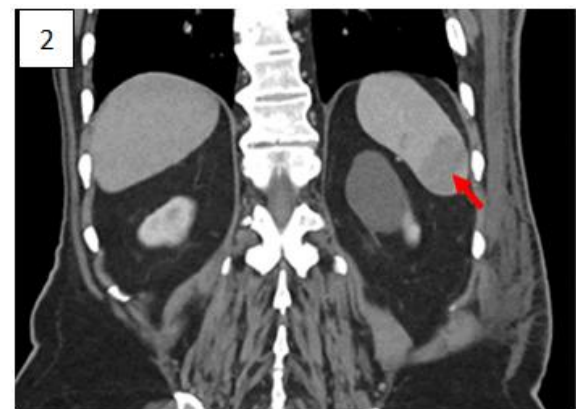


Fig-2: CT image showing a hypodense lesion measuring 1x1.5 cm in Spleen

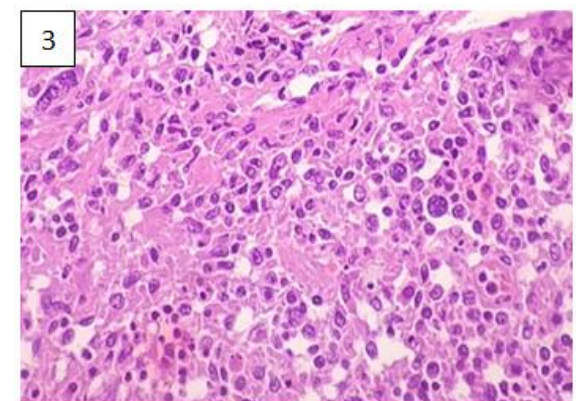


Fig-3: (H & E stain,40x) Showing large pleomorphic cells with abundant eosinophilic cytoplasm and pleomorphic nuclei and few giant cells

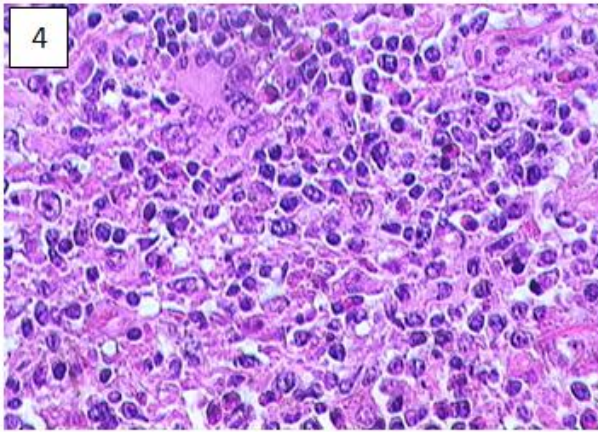


Fig-4: (H & E, 40X) showing pleomorphic cells with prominent nucleoli and few eosinophils

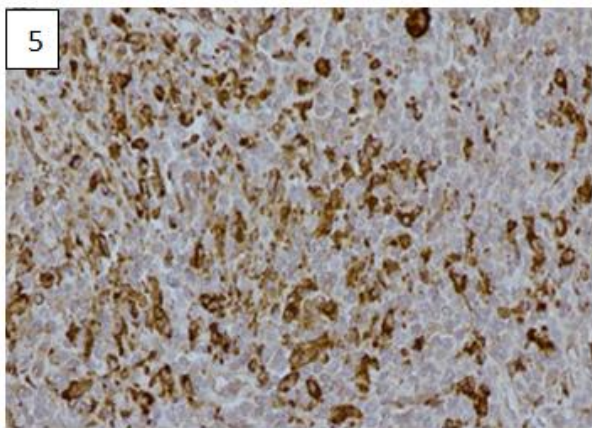


Fig-5: CD68 staining showing diffuse cytoplasmic positivity in tumor cells and giant cells. (40X)

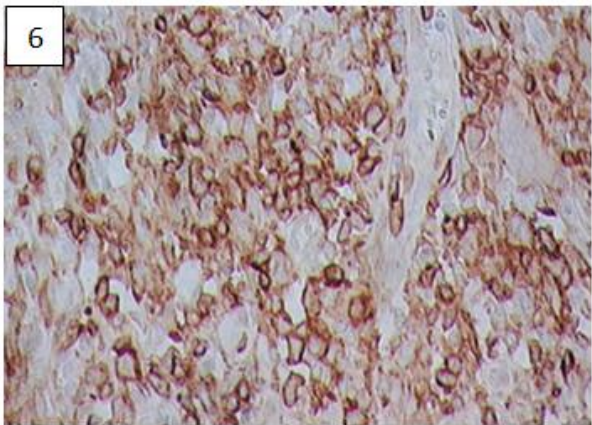


Fig-6: CD163 stain showing membranous positivity in tumor cells.(40X)

DISCUSSION

We present here a case report of a very rare tumor histiocytic sarcoma involving the left axillary lymph nodes and a possibility of splenic involvement. HS is an extremely rare neoplasm with only a few hundred cases reported in literature and to our knowledge, this is the first case of HS to be reported in a patient aged 97 years. HS is a rare neoplasm. Patients usually present in advanced stages with extra nodal involvement and disease usually has an aggressive

clinical course. Many cases were diagnosed as lymphomas prior to the introduction of new IHC markers like CD68 and CD163 specific for histiocytes. The tumor cells are positive for histiocytic markers such as CD68, CD163, CD45, CD4, and lysozyme and negative for other T cell, B cell and dendritic cell markers. S100 may be weakly positive in some tumor cells.

Comprehensive application of immunohistochemistry markers assists in differentiating HS from other lymphomas/sarcomas. A new hemoglobin scavenger receptor CD163 is more specific than CD68 since it is limited to neoplasms of macrophage/histiocytic lineage. Usually, the disease involves single or multiple lymph nodes. Weight loss, pressure symptoms and decreased blood cell counts are seen in patients of HS. CT or a combined PET/CT has to be performed to determine the extent of disease. There is no current consensus on managing this aggressive neoplasm and most patients die within 2 years of diagnosis [8]. The differential diagnosis for HS includes reactive histiocytic proliferations, dendritic cell sarcoma; Langerhans cell histiocytosis, malignant melanoma and large cell lymphomas. IHC confirms HS and also excludes other poorly defined epithelial neoplasms, including large cell lymphomas, melanomas and sarcomas [8]. Some of the histiocytic markers once thought to be specific for histiocytic differentiation like alpha 1 antitrypsin; lysozyme and CD68 are now considered to be of low specificity. Lysozyme can be expressed in NHL and CD68 in a subset of melanoma. CD 163, a new hemoglobin scavenger receptor is more specific than other macrophage/histiocyte markers like CD68 [8, 12]. A newly reported macrophage and B cell transcription factor PU.1 has been reported as specific for HS [14]. HS is defined as a tumor with malignant proliferation of cells showing similarity to histiocytic morphology and immunophenotypic features of histiocytes [13]. There are no distinct molecular abnormalities reported except in cases with a preexisting or prediagnosed hematologic malignancies [3]. Very limited data is available about the molecular and genetic abnormalities associated with HS. A gene, KMT2D/MLL2 involved in chromatin modulation and genesis of lymphoma is reported to be present in HS [14]. RAS-MAPK and PI3K-AKT-MTOR pathway mutations, CDKN2A tumor suppressor gene alteration, BRAF V600E mutations have been reported [7,15]. A report has described cytogenetic alteration like trisomy 8, tetrasomy 8 and translocation t (3;5)(q25;q35), tetrasomy 8, and add(4)(p16), deletion of Chr 3 at q11[16]. Other findings like Genetic and epigenetic inactivation of PTEN, P14ARF and P16 INK4A has been observed in HS [13].

CONCLUSION

HS is an extremely rare neoplasm and it is a diagnosis of exclusion. HS can mimic many other large cell neoplasms on morphology. A wrong diagnosis might affect the treatment modalities and outcome for the patient. The key to diagnosis is

immunohistochemistry. Other diseases need to be ruled out with extensive immunophenotypic analysis before HS is diagnosed. There is no standard protocol for the management of HS due to its rarity. Correct diagnosis at an early stage will help to prolong the patient's disease free survival after surgery. Here we present a very aged patient of 97 years diagnosed with histiocytic sarcoma in left axillary nodes and with no evidence of other hematological malignancies. This patient did not have any cytopenias and has been asked to follow up regularly. HS is a tumor where immunohistochemistry has a very important role in the diagnosis.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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