

## Case Report

# Histiocytic sarcoma of the lymph node: a rare and aggressive hematolymphoid malignancy



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## Introduction

Histiocytic disorders are thought to be derived from mononuclear phagocytic cells (macrophages and dendritic cells), or histiocytes. This group is divided into Langerhan's cell histiocytes (LCH) and non-LCH. Histiocytic sarcoma (HS) is an extremely rare non-LCH histiocytic malignancy of unknown etiology. It may occur as a sporadic illness or may be clonally related to separate synchronous or metachronous hematologic malignancy, such as follicular lymphoma or acute lymphoblastic leukemia (ALL).<sup>1,2</sup>

## Case

A 47-year-old gentleman noted a slowly enlarging swelling on the left side of his upper neck in March 2017. This was not associated with fever, cough, dysphagia or voice change. A positron emission tomography contrast tomography (PET-CT) scan discovered a fluorodeoxyglucose (FDG) avid mass lesion (standardized uptake value (SUV), max 13.6) in the left cervical region, level II, measuring 46 mm × 52 mm × 53 mm.

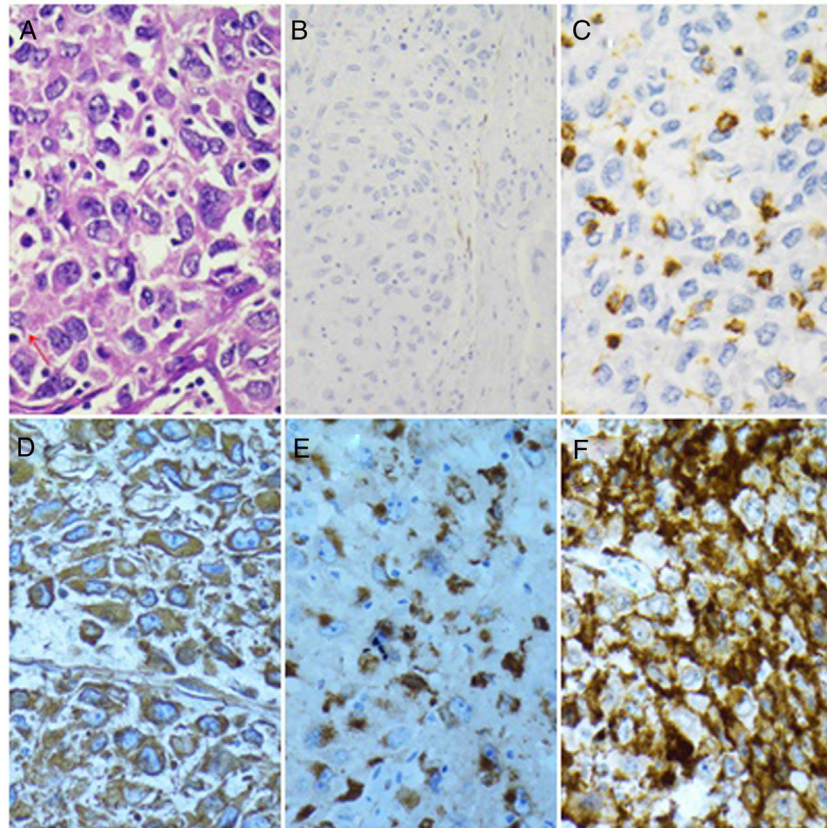
There were areas of enhancement and necrosis. No other FDG avid lesion was noted. He then underwent left extended radical neck dissection (RND) in April 2017. Two out of thirty-four cervical lymph nodes were compromised by the tumor. Extranodal extension was observed. Microscopy revealed diffuse effacement of the nodal architecture by sheets of non-cohesive large round-to-ovoid cells with abundant eosinophilic cytoplasm (Figure 1A). Nuclei were large, folded, eccentrically placed with focal binucleation and multinucleation. Occasional hemophagocytosis was seen (red arrows). A few reactive lymphocytes were seen in the background. Immunohistochemistry (IHC) stains were performed (Figure 1B–F). The cells showed focal variable positivity for CD45 and strong granular cytoplasmic positivity for CD68, CD4 and vimentin. Cells were negative for CK p40 CK7, CK20 napsin A CD56, CD30, CD2, CD3, AFP, Pax8, Pax5, EMA, CD31, S-100, synaptophysin, CD117, SMA, desmin, CD10, chromogranin A, CD34, CD99, ALK-1, CD1a, CD23 and HMB-45. Based on the morphological, immunohistochemical and PET-CT findings, we suggested the diagnosis of histiocytic sarcoma of the lymph node. The patient was advised to undergo chemotherapy (CT), but he refused.

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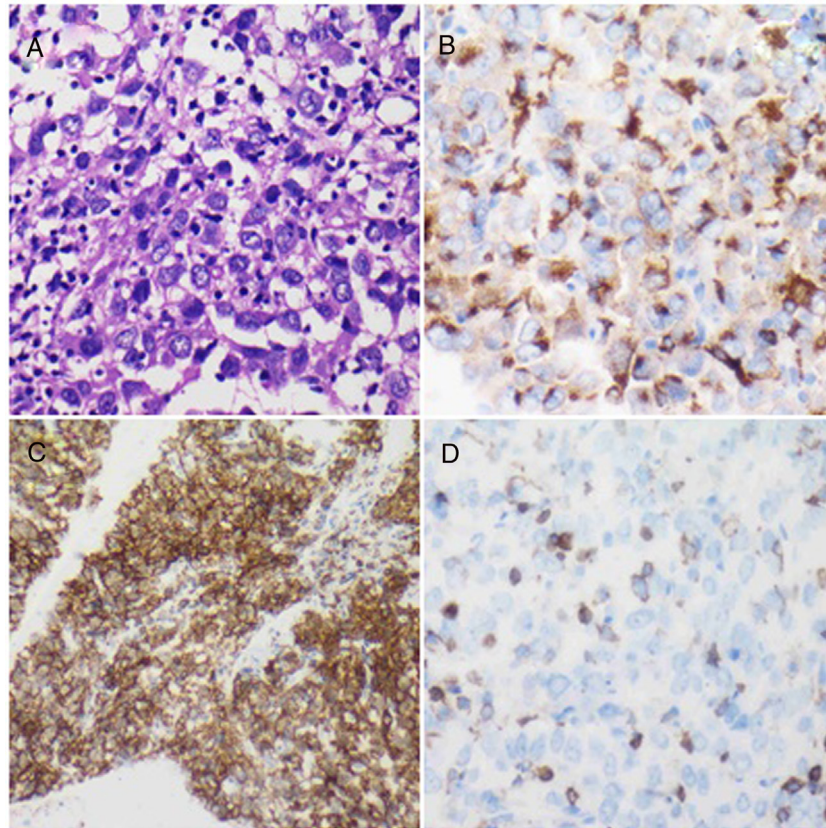
**Figure 1 – (A) Sheets of large non-cohesive cells with occasional hemophagocytosis (red arrows) [LN-H&E X 400]. (B) Tumor cells were immunonegative (CK X 400). (C) Focal positivity in large cells with positivity in background lymphocytes (CD45 X 400). (D) Strong cytoplasmic positivity in large cells (Vimentin X 400). (E) Strong granular positivity in large cells (CD68 X 400). (F) Strong granular positivity in large cells (CD4 X 400).**

After receiving alternative therapy (naturopathy), he presented again to our hospital in September 2018 with complaints of backache and bilateral lower limb weakness for the previous five months. He had no bowel and bladder involvement. On examination, a healed postoperative scar was seen on the neck. Oral and oropharyngeal mucosa were normal, without any palpable lesion. There was a marginal reduction in sensation below the epigastrium (level D5). Power and tone were normal in all four limbs. Deep tendon reflexes (DTRs) were diminished in both upper limbs. He had signs and symptoms indicative of compressive myelopathy at the levels of D4-5 vertebrae. He was re-evaluated with a PET-CT scan. When compared to the previous scan, the large left cervical lymph nodal mass was not observed (operated on). There were new findings: (1) an FDG avid (SUV max: 8.2) lytic destructive lesion was observed in the body of the D4 vertebra, causing the collapse of the vertebra and compression of the cord. (2) FDG avid lytic destructive lesions were seen in the clivus, bilateral occipital condyles (SUV max: 13.3) and neck of the right humerus (SUV max: 10.7). (3) An FDG avid (SUV max: 7.4) lobulated soft tissue density measuring 2.7 cm × 2.5 cm × 1.7 cm in size was observed in the medial segment of the right middle lobe, abutting the mediastinal pleura. No significant FDG avid mediastinal/hilar lymphadenopathy was observed. The biopsy of the paravertebral mass at level D4 showed similar

morphology and IHC profiles (Figure 2A–D). His spinal pain and his gait disturbance remained static after medical decompressive therapy. In view of the stable neurological status with medical decompressive therapy, he was again advised to start systemic CT, while maintaining palliative radiotherapy (RT) in reserve. He did not pursue CT. The follow-up in February 2019 showed stable neurological status, with persistent weakness in both legs.

## Discussion

Tumors of histiocytes are among the rarest tumors affecting lymphoid tissues, probably representing less than 1% of tumors, the majority of cases presenting in extranodal tissues, such as the intestinal tract and skin, followed by the lymph nodes.<sup>3</sup> The HS is a malignant proliferation of cells showing morphologic and immunophenotypic features, similar to those of mature tissue histiocytes. In this case, the patient presented with nodal disease initially, followed by extranodal disease involving the lung, paravertebral region and bones. Multifocality in histiocytic sarcoma has been reported by various authors.<sup>4</sup> In our case, the paravertebral lesion, whether being a metastatic site or a new focal lesion, could not be ascertained, but the development of multiple lytic bony lesions and



**Figure 2 – (A) Sheets of large non-cohesive cells [D4-H&E X 400]. (B) Strong granular positivity in large cells (CD68 X 400). (C) Strong granular positivity in large cells (CD4 X 400). (D) Focal positivity in large cells with positivity in background lymphocytes (CD45 X 400).**

lung lesion after one year likely represents metastatic disease. Kayikcioglu et al. reported two cases of HS in the paravertebral location who died within nine and three months with disease progression after receiving CT.<sup>5</sup>

Based on the morphological appearance, the differential diagnoses of metastatic carcinoma, large cell lymphoma and metastatic melanoma were considered. Markers for carcinoma (CK p40 CK7, CK20, Napsin A, CD56, Pax8, EMA chromogranin A and synaptophysin), markers for melanoma (S-100 and HMB-45), markers for sarcoma (CD34, CD31, CD99, SMA and desmin), markers for large cell lymphoma (CD30, Pax5, ALK-1 and CD10), markers for germ cell tumors (CD30, CD117, CK and AFP) and markers for LCH (CD1a) were all negative. This gave us the clue to consider a rare tumor type, hence we requested CD4 and CD68 investigation, which were highly positive. The CD4 is a T-cell marker, but it is also observed in tissue histiocytes, dendritic cells and Langerhans cells. Among the non-LCH disorders, follicular dendritic cell sarcoma is the closest differential diagnosis. Morphological features of large round-to-ovoid cells, with evidence of hemophagocytosis instead of spindle cells, negativity for the CD23 and positivity for the CD68, favored HS. The CD163 and lysozyme were used, as more specific stains were unavailable.<sup>6</sup> Although CD68 stains a subset of melanomas and carcinomas, other specific markers for both of these entities were negative, hence a diagnosis of HS was suggested.<sup>1</sup>

The HS is usually an aggressive neoplasm, with a poor response to therapy, although some exceptions have been reported. Most patients (60–80%) succumb to progressive disease, reflecting the high clinical stage at presentation (stages III/IV) in the majority (70%) of the patients.<sup>3</sup> The HS is a rare neoplasm and there is still no standardized treatment regimen. These patients are treated like lymphomatous malignancy, with various modalities, such as surgery, CT, RT and bone marrow transplant.<sup>4</sup> Further studies and prospective randomized clinical trials are needed to ascertain the nature and treatment of this rare and aggressive hematological malignancy.

To conclude, the HS is a rare and aggressive hemato-lymphoid malignancy with a wide range of morphological differential diagnoses, especially at the nodal site. It is a diagnosis of exclusion and it is necessary that the reporting pathologist be aware of this pathological entity. Our case illustrates the natural course of this disease, as the patient refused to undergo any kind of conventional treatment.

### Conflicts of interest

The authors declare no conflicts of interest.

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