

**Case Report**

# Pulmonary Histiocytic Sarcoma: A Case Report and Literature Review

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**Abstract:** Pulmonary histiocytic sarcoma is a rare, but highly malignant disease. Its low incidence imposes significant difficulties on physicians confronted with affected patients. The reported patient is a 24-year old male with histiocytic sarcoma of the lung. Left lower lobectomy was performed. Histologically, tumor cells had no features of carcinoma. Several entities were raised as differentials: large B or T cell lymphomas, metastatic melanoma, sarcoma, undifferentiated carcinoma, NK cell lymphoma. Immunohistochemically, melanoma, carcinoma, undifferentiated epithelioid sarcoma and also different types of lymphoma were excluded. Therefore, tumors of the histiocytic and dendritic cell lineage had to be considered. Tumors of the dendritic cell lineage were also immunohistochemically excluded, leaving histiocytic sarcoma by exclusion. The patient was followed for six years and six months, with no signs of recurrence of the tumor. Histiocytic sarcomas are tumors of uncertain behavior, with some progressing quickly, and others having a much slower course. As these tumors are rare, there is not much information, although a low number of mitosis might point to a less aggressive course. In the present patient with an unifocal disease, surgical excision was sufficient, without adjuvant radiotherapy and chemotherapy.

**Keywords:** Neoplasms, Histiocytic Sarcoma, Lung, Immunohistochemistry, Surgical Treatment

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## 1. Introduction

Histiocytic sarcoma (HS) is a rare hematological malignant neoplasm composed of cells showing morphologic and immunophenotypic evidence of histiocytic differentiation [1]. HS usually affects the lymph nodes, skin, liver, spleen, soft tissue, and the gastrointestinal tract, whereas HS arising in the lung has very rarely been reported [2]. Reported cases of HS located in the central nervous system (CNS) and bone marrow [3-5] are regarded as aggressive hematopoietic neoplasm with a strong potential for systemic spread and a poor response to therapy [6].

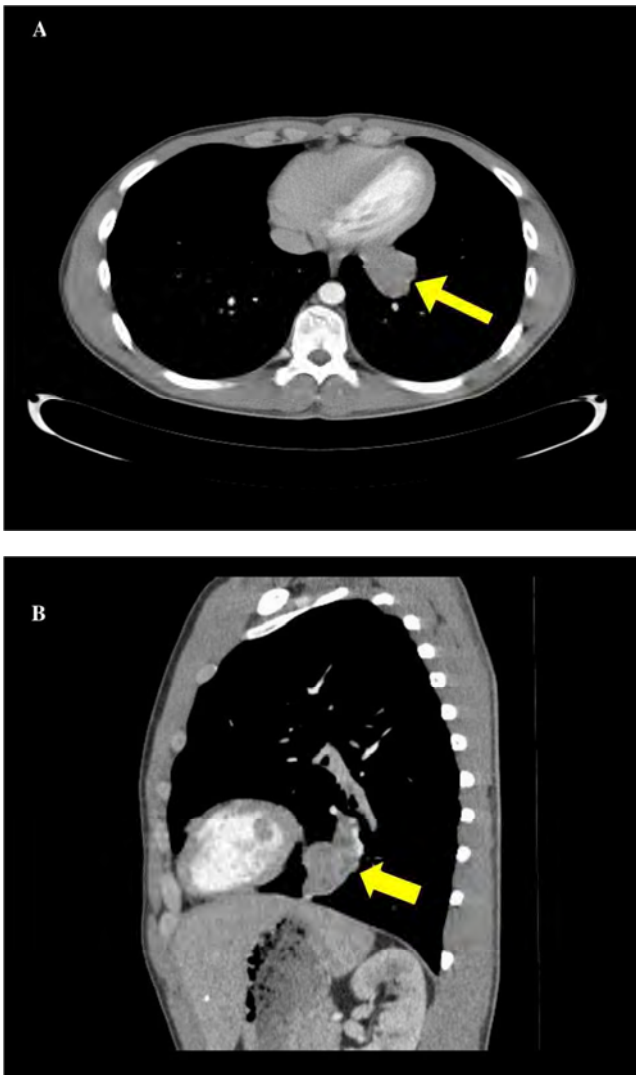
## 2. Case Report

The reported patient is a 24-year old male smoker, until then

healthy, who reported subfebrile temperatures for two months. Physical examination was normal. Erythrocyte sedimentation rate (ESR) was 110 mm/h (reference interval: 2-13 mm/h), a complete blood count showed a leukocyte (WBC) count of 8.9 x10<sup>9</sup>/L (reference interval: 4.0-11.0 x10<sup>9</sup>/L), with normal percentage of particular classes of leukocytes. The hemoglobin was 111 g/L (reference interval: 138-175 g/L), and the platelet count was 607 x10<sup>9</sup>/L (reference interval: 158-424 x10<sup>9</sup>/L). C-reactive protein (CRP) was 158.1 mg/L (reference interval: < 5.0 mg/L). Serum biochemistry revealed an elevated alkaline phosphatase (ALP) level of 248 U/L (reference interval: 60-142 U/L), and gamma glutamyl transferase (GGT) level of 95 U/L (reference interval: 11-55 U/L). The aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LD), and

total bilirubin level were normal. Tumor markers [CA (cancer antigen) 19-9, CA (cancer antigen) 125, CEA (carcinoembryonic antigen), PSA (prostate specific antigen), AFP (alpha-1-phetoprotein), NSE (neuron-specific enolase), CYFRA (cytokeratin 19 fragments) 21-1, B2M (beta-2 microglobulin)] in the serum were normal.

Chest radiography revealed a mass shadow measuring 70 mm in diameter in the left lower lung lobe. Multi slice computed tomography (MSCT) of the chest showed in the central part of the left 9th segment of lung, retrocardially, a well-defined, lobulated solid tumor mass, approximately 60 x 38 x 70 mm in size. The tumor completely obstructed the B9 segmental bronchus (Figure 1). No mediastinal lymph node metastasis or other organ metastases were observed. Bronchoscopy revealed a necrotic tumor obstructing the entry of the left B9 bronchus (Figure 2). Histological and cytological findings of tumor forceps and brush biopsy were not able to establish the diagnosis. The patient underwent open lung biopsy, left lower lobe resection and mediastinal lymphadenectomy.



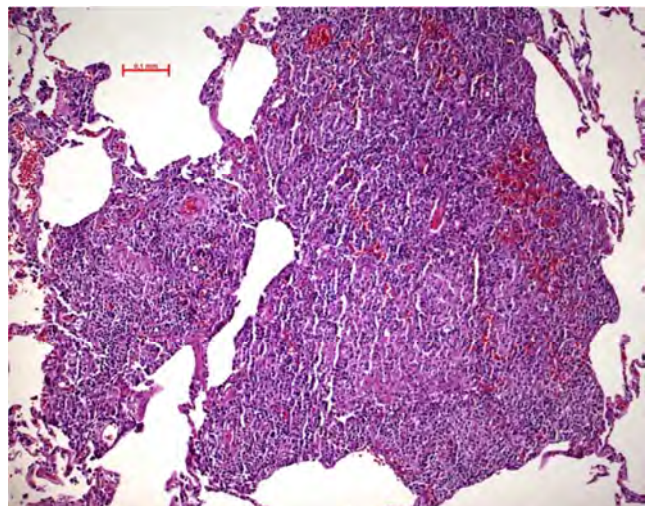
**Figure 1.** Thoracic axial (A) and sagittal (B) MSCT scan showing a left lobulated solid tumor (arrows).



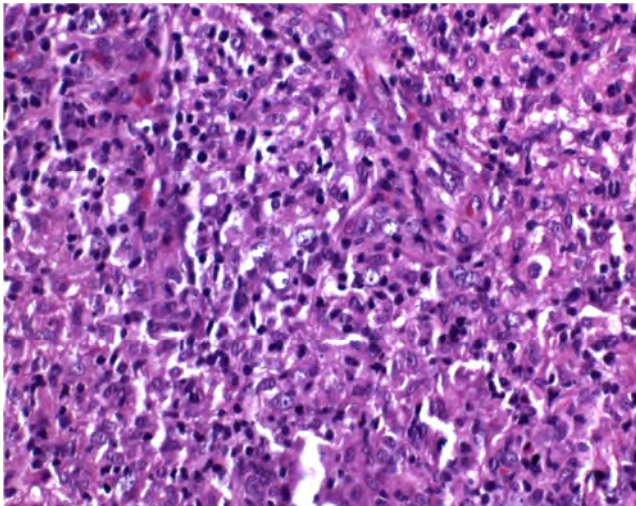
**Figure 2.** Bronchoscopy reveals a necrotic tumor obstructing the entry of left B9 bronchus.

### 2.1. Pathological Findings

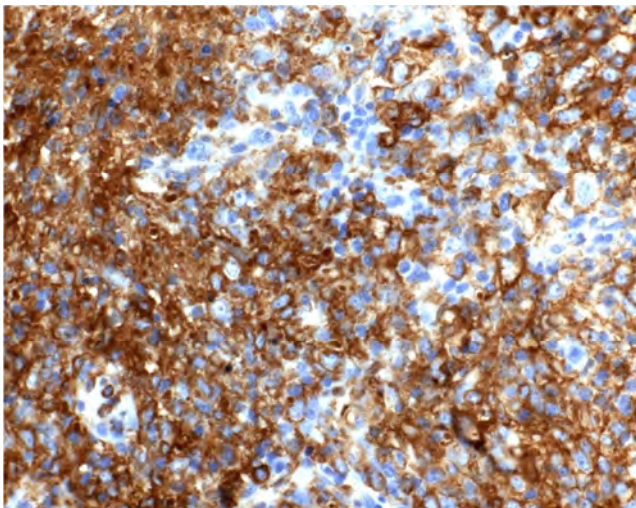
Open lung biopsy showed nodular densities measuring up to 3 cm in diameter. On histology, these nodules showed an infiltration by tumor cells, which did not form epithelial structures, had large polymorphic nuclei with vesicular chromatin, accentuated nuclear membrane staining, and medium-sized nucleoli, usually centrally located within the nucleus (Figure 3). Mitosis was infrequent, but a few atypical mitoses could be seen. In between the tumor cells, lymphocytes were present, in some areas scattered, in other areas forming dense infiltrations obscuring the tumor cells (Figure 4). From the morphologic pattern, several entities had to be differentiated, such as large B or T cell lymphomas, metastatic melanoma, sarcoma, undifferentiated carcinoma, and also NK (natural killer) cell lymphoma. For this reason, immunohistochemical staining was performed.



**Figure 3.** Overview of the tumor showing a dense infiltration by mononuclear cells. Some look like lymphoid cells, other with more eosinophilic cytoplasm might be dendritic or histiocytic cells. The tumor cells are loosely dispersed within the whole tumor. H&E, bar 0.1 mm.



**Figure 4.** High power magnification of the tumor. There are large tumor cells embedded in a lymphocytic background infiltration. The nuclei of the tumor cells are large, have medium-sized nucleoli and a vesicular chromatin. The cytoplasm is eosinophilic. H&E, x400.



**Figure 5.** Immunohistochemistry for CD14 shows positively stained tumor cells, typically membraneous. Magnification x400.

## 2.2. Immunohistochemistry

The tumor cells were positive for CD14 (Figure 5), HLA-DR, CD68, lysozyme, and focally some cells also stained for CD35. The tumor cells were negative for pan-cytokeratin, NCAM, S100 protein, EMA, HMB45, podoplanin, inhibin, CD99, CD117, desmin. Therefore melanoma, carcinoma, undifferentiated epithelioid sarcoma and also different types of lymphoma could be sorted out. With the positive stains, tumors of the histiocytic and dendritic cell lineage had to be considered. Due to the negative staining for S100 protein and the positivity for dendritic/histiocytic cell markers, a diagnosis of histiocytic sarcoma/tumor was rendered. Dendritic cell sarcomas should be either positive for CD35 (follicular) or CD83 (interdigitating) or usually at least focally positive for S100 protein and thus tumors of the dendritic cell lineage could also be excluded, leaving histiocytic tumors by exclusion. The patient has been followed

up on a three- and six-month basis, including clinical examinations, positron emission tomography/computed tomography (PET/CT) and CT scans. The postoperative course has been favorable for six years and six months, without additional treatment. Consent, for the publication for this case report and any additional related information was taken from the patient involved in the study.

## 3. Discussion

Histiocytic sarcoma is a malignant neoplasm recognized by the expression of histiocytic markers. HS is rare; the median age of a patient at the time of diagnosis is usually 55 years [2]. There is no obvious sex predilection. Histologically, the tumor cells are large, round to oval, have rich eosinophilic cytoplasm and are consequently similar to epithelioid histiocytes. These neoplasms usually have large, vesicular nuclei, prominent nucleoli and cytoplasmic vacuoles. Also common are giant multinucleated cells and a conspicuous inflammatory surrounding including plasma cells, lymphocytes, neutrophils, and eosinophils. Mitoses are variably present in HS.

Diagnosis is based on immunophenotypic researches. The neoplasm cells are positive for histiocyte-linked markers such as lysozyme, CD163 and CD68. Histiocytes are likewise frequently positive for HLA-DR, CD45RO and CD45, and can express CD15 and CD4. The proliferation pace as determined by Ki-67 is immensely variable in HS studies, with a mean of 25% [7]. Neoplasm cells are negative for markers of more specialized histiocytes and thus negative for markers linked with interdigitating or follicular dendritic cell markers (CD83, CD35, CD23, CD21) or Langerhans cells (Langerin/CD207 and CD1a). In HS studies, S100 may be expressed, but mostly focally or less intensely than in interdigitating dendritic cell sarcoma. Likewise, myeloid-related cell markers (CD13, CD33) and myeloperoxidase are usually not expressed by the cells of HS. Pan T- or B-cell markers are not expressed by the cells of HS.

HS is treatment-resistant, the prognosis is poor, many cases are progressive, and 60-80% of cases exhibit tumor progression [1]. The prognosis of local small lesions is favorable [2]. The tumor size of the present patient was larger compared with reported cases of HS originating in the lung. It was localized in the lung, completely surgically removed, showing the longest follow up of pulmonary HS so far. Only three cases of HS originating in the lung have previously been reported [2, 6, 7]. In Table 1 are summarized the findings of the three previous published cases as well as the present case. Pulmonary HS can also be a part of multi-organic disease [8].

There is no standardized treatment for patients with HS. For patients with localized disease, the choice of treatment is surgical excision with adjuvant radiotherapy, depending on the location and extent of the disease. For patients with nonresectable, multifocal or aggressive disease, chemotherapy with several chemotherapeutic agents simultaneously is taken into account [9]. Target therapy (imatinib, sorafenib, bevacizumab, alemtuzumab) gives encouraging results [10, 11].

**Table 1. Pulmonary histiocytic sarcoma.**

Case No.	Authors	Published year	Age	Sex	Tumor location	Tumor size
1	Hornick, et al.	2004	63	M	Right lung lower lobe	68 mm
2	Stacher, et al.	2009	23	M	Right lung	4 mm
3	Tomita, et al.	2015	16	M	Right lung (S6)	32 mm
4	Current study		24	M	Left lung (S9)	70 mm

**Table 1. Continued.**

Case No.	Authors	Histology	Therapy	Outcome
1	Hornick, et al.	NA	Chemo	NA
2	Stacher, et al.	Histiocyte-like cells with moderate pleomorphism	Surgical resection	No recurrence within 1 year
3	Tomita, et al.	Spindle cells and foam cells	Surgical resection	No recurrence within 2 years
4	Current study	Single cells with large, polymorphic, vesicular nuclei	Surgical resection	No recurrence within 6.5 years

M, male; NA, not available; Chemo, chemotherapy.

## 4. Conclusion

In conclusion, histiocytic sarcomas are tumors of uncertain behavior, with some progressing quickly, and others having a much slower course. As these tumors are rare, there is not much information, although a low number of mitosis might point to a less aggressive course. In the present patient with an unifocal disease, surgical excision was sufficient, without adjuvant radiotherapy and chemotherapy.

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