

Histiocytic sarcoma associated with Hodgkin's disease

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Abstract

Histiocytic sarcoma is a rare malignant neoplasm. It is well-known the association of Langerhans' cell histiocytosis with Hodgkin's disease but only few cases of histiocytic sarcoma associated with Hodgkin's disease was reported. We present the case of 20-years-old female patient with Hodgkin's disease with a sternal tumor mass which was diagnosed as histiocytic sarcoma. The diagnostic was established immunohistochemically, using a large battery of antibodies (S-100, CD 68, CD 34, CD 15, CD 30, Vim, NFAP) and by electron microscopy which revealed the lack of the Birbeck granules in the malignant proliferated histiocytes.

Keywords: *histiocytic sarcoma, Hodgkin's disease.*

Introduction

Histiocytic sarcoma is a rare malignant neoplasm that occurs in lymph nodes, skin, and the gastrointestinal tract. Many previously published cases were likely misdiagnosed examples of non-Hodgkin lymphoma. Only small numbers of *bona fide* examples exist in the world literature; cases arising primarily at extranodal sites are not well described and often seem to go unrecognized [1, 2].

The etiology of histiocytic sarcoma is unknown. It is a malignant proliferation of neoplastic cells showing immunophenotypic and morphologic features similar to tissue histiocytes [3].

Neoplasms of histiocytes and dendritic cells are rare, and their phenotypic and biological definition is incomplete.

The International Lymphoma Study Group (ILSG), seeking to identify antigens detectable in paraffin-embedded sections that might allow a more complete immunophenotypic classification of histiocytic/dendritic cell neoplasms, established a panel of 15 antibodies including those reactive with histiocytes (CD 68, lysozyme - LYS), Langerhans cells (CD 1a), follicular dendritic cells (CD 21, CD 35) and S-100 protein and designed four groups which include:

- *histiocytic sarcoma*, with the following phenotype: CD 68 (100%), LYS (94%), CD 1a (0%), S-100 (33%), CD 21/35 (0%);

- *Langerhans cell tumour* (LCT), which expressed: CD 68 (96%), LYS (42%), CD 1a (100%), S-100 (100%), CD 21/35 (0%) and present two morphological variants: cytologically typical designated LCT, and cytologically malignant designated Langerhans cell sarcoma (LCS), which is often not easily recognized morphologically as LC-derived, but diagnosed based on CD 1a staining;

- *follicular dendritic cell tumour/sarcoma* (FDCT), which expressed: CD 68 (54%), LYS (8%), CD 1a (0%), S-100 (16%), FDC markers CD 21 / 35 (100%), EMA (40%);

- *interdigitating dendritic cell tumour/sarcoma* (IDCT), which expressed: CD 68 (50%), LYS (25%), CD 1a (0%), S-100 (100%), CD 21/35 (0%).

The ILSG proposed a classification combining immunophenotype and morphology with five categories, including Langerhans cell sarcoma. This simplified scheme is practical for everyday diagnostic use and should provide a framework for additional investigation of these unusual neoplasms [4].

Although an association of lymphoproliferative disease with Langerhans' cell histiocytosis is well described, only sporadic cases with non-Langerhans' dendritic cell proliferation have been published. Indeterminate-cell histiocytosis is associated with a history of low grade B-cell malignancy in 4 of 13 cases (31%) [5].

Association with other hematological disorders, including acute leukemia, lymphoma or myelodysplasia, has been observed in histiocytic sarcomas [3, 6, 7].

Classical Hodgkin's lymphoma is a monoclonal lymphoid neoplasm consisting of mononuclear Hodgkin cells and multinucleated Reed-Sternberg cells residing in an infiltrate containing a variable mixture of non-neoplastic small lymphocytes, eosinophils, neutrophils, histiocytes, plasma cells, fibroblasts and collagen fibers.

Reed-Sternberg cells are positive for CD 30 in nearly all cases and for CD 15 in the majority of cases and are consistently negative for macrophage specific marker CD 68 [8].

We present a case of histiocytic sarcoma which has evolved simultaneously with Hodgkin's lymphoma in a 20 years patient.

☒ Material and methods

The surgical piece came from the Thoracic Surgery Department of the Clinic Hospital for Pulmonary Diseases, Iassy.

The tumoral mass was processed by usual histopathologic technique: paraffin embedded, Haematoxylin-Eosin and Van Gieson stained.

It was also examined in electronic microscopy and immunohistochemical (S-100, CD 68, CD 34, CD 15, CD 30, vimentine, and NFAP).

☒ Results and discussions

A 20-years old female patient referred to the Thoracic Surgery Department of the Clinic Hospital for Pulmonary Diseases in Iassy, because of an ulcerated nodular lesion of the sternum. She was diagnosed with Hodgkin's disease two years before, for which she got six chemotherapeutic cures. At that moment, no adenopathy was detected. The clinical suspicion was of sternal involvement by Hodgkins' disease. Surgical procedure was performed.

Macroscopically, the surgical piece was a relative delimited nodule, with diameter of 10 cm, with suprajacent skin ulcerated. On the cut section the tumor was soft, yellow, with hemorrhagic and necrotic areas.

The light microscopy examination revealed a histiocytic cell population, intermixed with inflammatory cells, eosinophilic abscesses and large areas of necrosis (Figures 1-3).

Morphologically, tumor cells are characterized by abundant eosinophilic cytoplasm. The nuclei are eccentric and round/oval, with atypia varying from mild to pleomorphic. The nucleoli are small and distinct. Binucleated giant cells are common (Figures 4 and 5). No classical Reed Sternberg cell or variants were seen.

Immunohistochemically, tumoral histiocytes are positive for S-100, CD 68 and vimentin (Figures 6-8) and negative for CD 34, CD 15, CD 30, NFAP and desmin.

The ultrastructural features show numerous vacuoles and lysosomes (Figures 9 and 10). Interdigitating cell junctions and Birbeck granules are essentially absent. The latter features distinguish this entity from Langerhans' and dendritic cell tumors, especially when S-100 protein is positive (Figure 11).

The differential diagnosis included inflammatory pseudotumour, interdigitating dendritic cell sarcoma, and follicular dendritic cell sarcoma, malignant Langerhans cell histiocytosis, anaplastic large-cell lymphoma, melanoma, and a range of sarcomas. Tumor cells in Langerhans cell sarcoma have nuclei that are grooved, indented, folded, or lobulate, with fine chromatin and a thin nuclear membrane, features that are absent in histiocytic sarcoma [9].

Immunohistochemically, Langerhans cell sarcoma expresses CD 1a, which is negative in histiocytic sarcoma. A battery of immunostains gave us the possibility to determine whether the cells involved are of B- or T-cell origin.

Considering the wide diversity in morphology of histiocytic sarcoma and the unreliability of histology in

identifying them, positivity with histiocyte-associated antibodies along with the lack of B- or T-antigen expression sustained our diagnostic of histiocytic tumor.

Summarizing the histopathological, immunohistochemical and ultrastructural data, our diagnostic was histiocytic sarcoma which evolves concomitant with Hodgkin's disease.

The malignant tumor in this case corresponded to the definition of histiocytic sarcoma according to the World Health Organization classification [10], that is, a malignant proliferation of cells showing morphologic and immunophenotypic features similar to those of mature tissue histiocytes.

Our question concerning this case was about the moment at the proliferation started inside the sternum. Reviewing the computer tomography aspects we found out that the tumoral proliferation became visible after the 6th cure of chemotherapy and grow up in time, finally involving also the suprajacent skin.

Under the chemotherapy the adenopathic masses disappeared, sign of a good response at oncological therapy.

On the other hand, during the period of surgical procedure the patient did not get oncological treatment and the adenopathy came back.

The histopathological diagnostic of new appeared enlarged lymph node was Hodgkin's disease, nodular sclerosis type.

The patient died 12 month later.

This clinical evolution sustains the idea that the sternal tumor developed secondary and its evolution was in parallel with Hodgkin's lymphoma.

Histiocytic sarcomas run a very aggressive clinical course in most patients. In a study by Kamel *et al.* [11] 6 of 11 patients died of disease within 0.5 to 36 months, and 58% of patients died of disease in the study by Pileri *et al.* [4].

Although histiocytic sarcoma is very rare, its recognition is important for clinical and prognostic reasons.

☒ Conclusions

The case we have presented is one of those complex cases consisting of two malignancies which evolve simultaneously from one moment.

Firstly, the lack of the Reed-Sternberg cells and the abundant histiocytes having large nucleolated nuclei, some multinucleated, admixed with inflammatory cells and eosinophilic abscesses orientated our diagnostic toward a histiocytic tumor.

The immunoeexpression of S-100, CD 68 and vimentin of the proliferated cells and the negativity for CD 15, CD 30 and confirm our first diagnostic.

The ultrastructural study revealed the lack of Birbeck granules and so, the final diagnostic of the sternal tumor is histiocytic sarcoma.

Evaluation of a battery of antibodies in the context of morphology is essential in the workup of histiocytic neoplasms.

Analyses of more cases are required for a better understanding of these tumors.

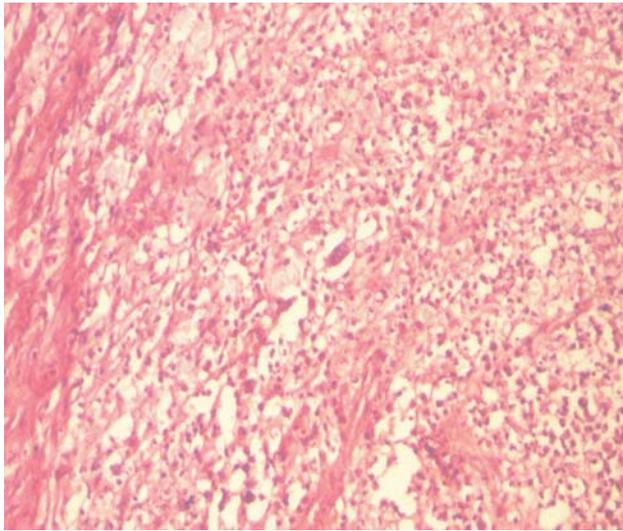


Figure 1 – Histiocytic cell population, intermixed with inflammatory cells (HE staining)

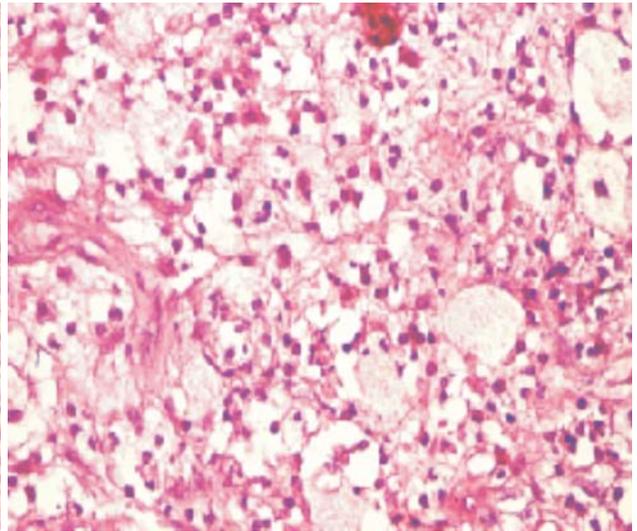


Figure 2 – Histiocytic cell population intermixed with inflammatory cells. Detail (HE staining)

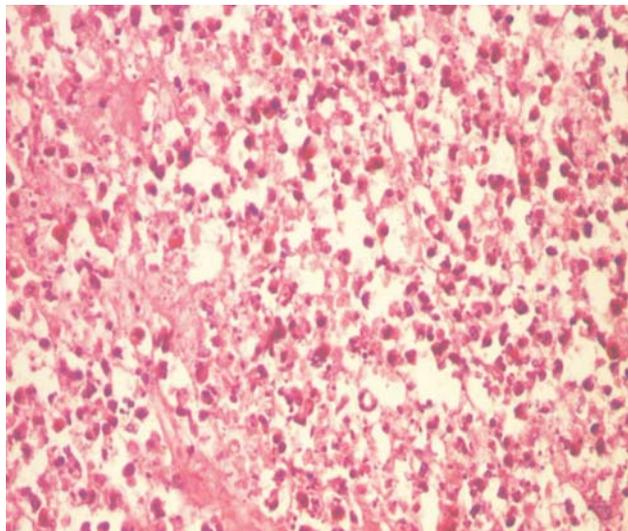


Figure 3 – Eosinophilic abscess (HE staining)

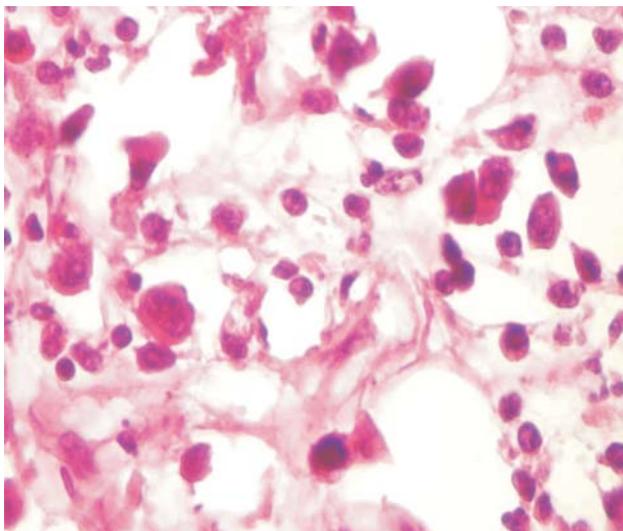


Figure 4 – Tumor cells with abundant eosinophilic cytoplasm and nuclei in various sizes and shapes (HE staining)

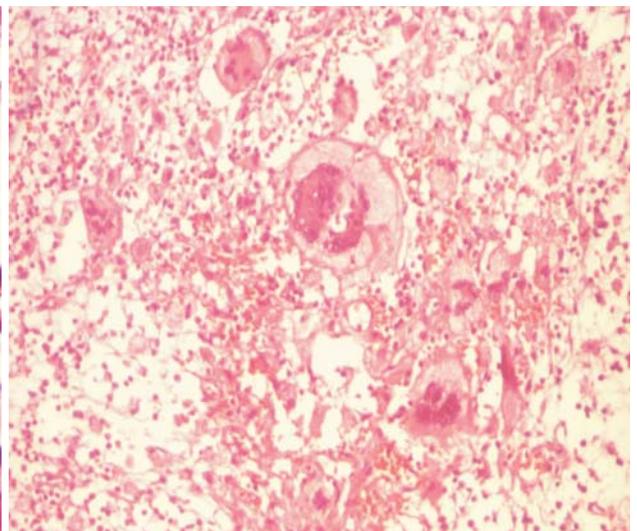


Figure 5 – Tumor cells with abundant clear cytoplasm and nuclei in various sizes and shapes (HE staining)

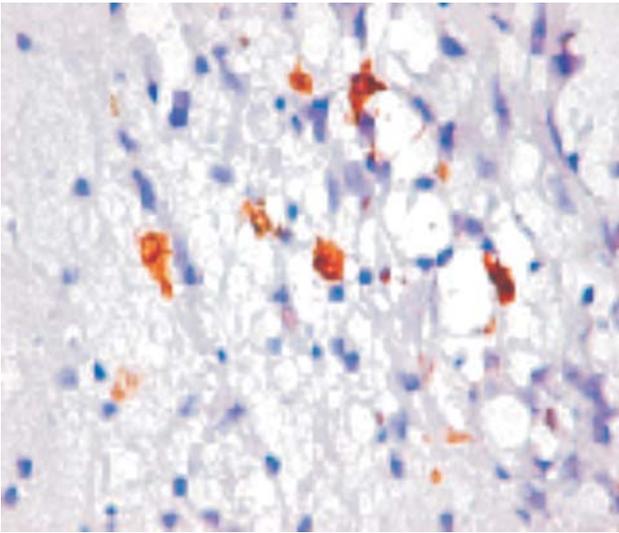


Figure 6 – Tumoral cells positive for S-100 protein

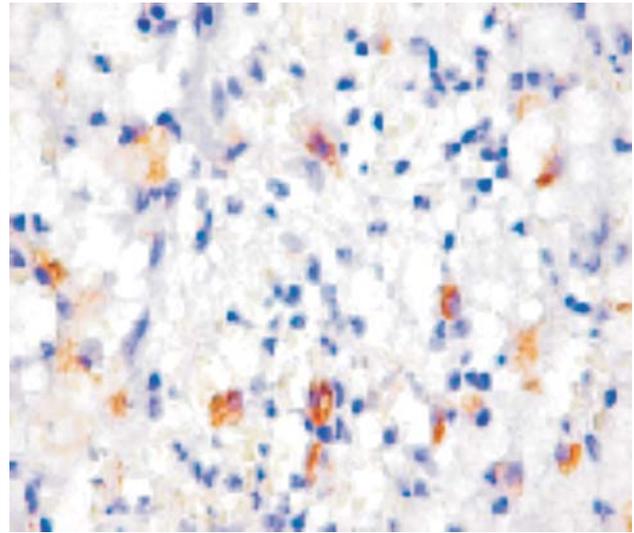


Figure 7 – Tumoral cells positive for CD 68

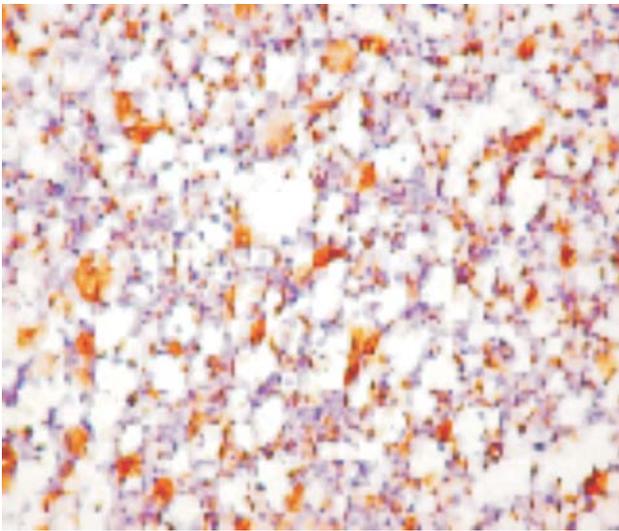


Figure 8 – Tumoral cells positive for vimentin

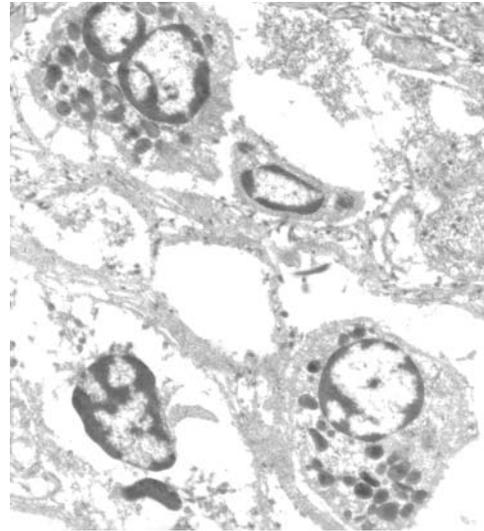


Figure 9 – The neoplastic cells show abundant cytoplasm with numerous lysosomes and no cellular junctions. Electron microscopy

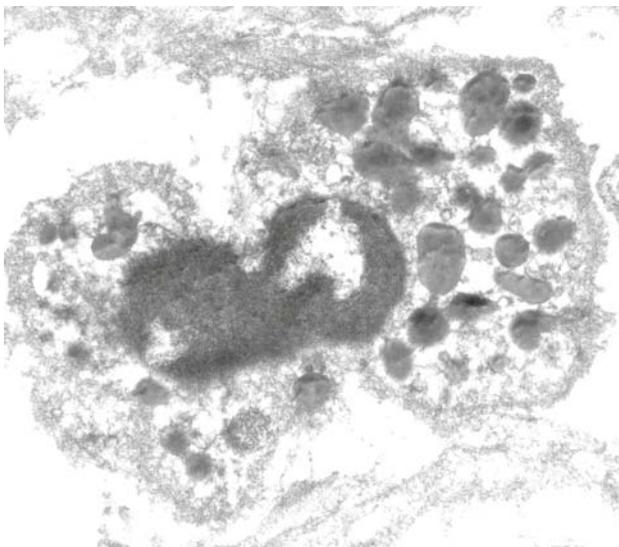


Figure 10 – The electronic microscopy confirmed the histiocytic character of the proliferated cells and the malignant character of the proliferated histiocytes

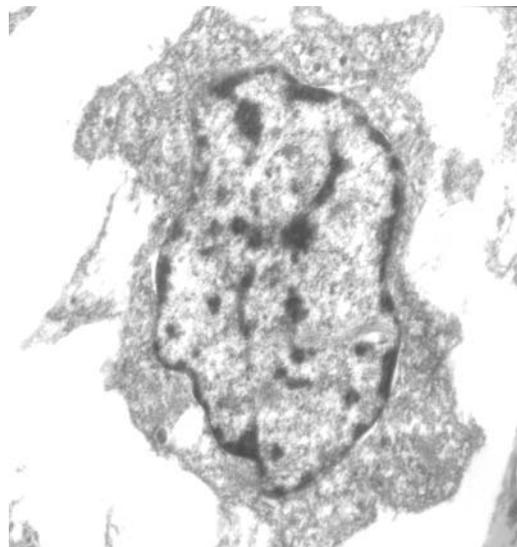


Figure 11 – Malignant histiocyte. Birbeck granules are not seen. Electron microscopy

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