CASE REPORT

A histiocytic twist in a tale of GIST

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Received: July 29, 2016 **Accepted:** August 9, 2016 **Online Published:** August 15, 2016
DOI: 10.5430/crcp.v3n4p50 **URL:** http://dx.doi.org/10.5430/crcp.v3n4p50

ABSTRACT

Histiocytic sarcoma (HS) is a rare, non-Langerhan's, malignant histiocytic neoplasm that occurs in lymph nodes and extranodal sites mainly the skin and intestine. Amidst the cases reported so far; majority of the cases previously diagnosed as HS have been Primary T cell lymphomas (PTCL). Cases primarily involving the extranodal sites are rare, with a confusing clinical picture and thus, are often misdiagnosed. Here we report a rare case of extranodal HS in a 54-year-old man, a previously treated case of gastrointestinal stromal tumor (GIST) of the stomach, who now presented with abdominal pain. On imaging, a growth was detected in the small bowel without accompanying lymphadenopathy.

Key Words: Histiocytic sarcoma, Extranodal, Gastrointestinal stromal tumor, Small intestine

1. INTRODUCTION

Histiocytic sarcoma (HS) is a distinct and aggressive lymphohematopoietic malignancy composed of tumor cells of histiocytic origin as revealed by their immuno-morphological character.[1] It mainly affects adults in their 4^{th} and 5^{th} decade with very few cases also reported in the paediatric age group. Isolated lymph node involvement is rare. Majority of cases with extranodal disease involve intestine. The other extranodal sites include skin, spleen, lung, CNS and bone marrow.[2–5] Most patients present with B symptoms (fever, weight loss and night sweats) along with lymphadenopathy, hepatosplenomegaly and peripheral blood cytopenias. Other symptoms vary with the primary site like rashes in cases with skin involvement and pressure symptoms in case of an extranodal disease involving an abdominal organ.[2,5,6] It can occur as an isolated entity or can accompany another hemato-lymphoid malignancy such as Follicular Lymphoma and Acute Lymphoblastic Leukemia due to clonal association.[8] The diagnosis is generally that of exclusion and requires an unequivocal evidence of neoplasia with cells proved to be of monocyte/macrophage lineage.

2. CASE REPORT

A 54-year-old man, a previously treated case of gastrointestinal stromal tumor (GIST) of the stomach (treated two years prior with surgical excision and Imatinib therapy), presented with abdominal pain. On imaging, a lesion was detected in the small bowel. No other lesion was detected in the lymph nodes. Clinico-radiologically, a recurrent GIST was suspected. The patient underwent resection and the specimen was studied for histopathological examination. Grossly, a yellowish-brown, globular, mucoid mass was seen in the wall of the resected segment of the small intestine. The mass predominantly involved the submucosa and muscularis propria. At places it was seen nearly abutting the serosal surface. Areas of necrosis were identified. The intestinal lumen appeared narrowed but the mucosa was unremarkable. Microscopically, the tumor was composed of diffuse sheets of pleomorphic, round to oval cells with abundant eosinophilic cytoplasm having fine granules. The cells had

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vesicular nuclear chromatin with prominent nucleoli and a high mitotic activity with occasional atypical mitosis (see Figures 1-2). The hallmark was extensive emperipolesis (see Figure 3). Background showed polymorphous population comprising of neutrophils, lymphocytes and plasma cells. Abundant multinucleated giant cells were also seen.

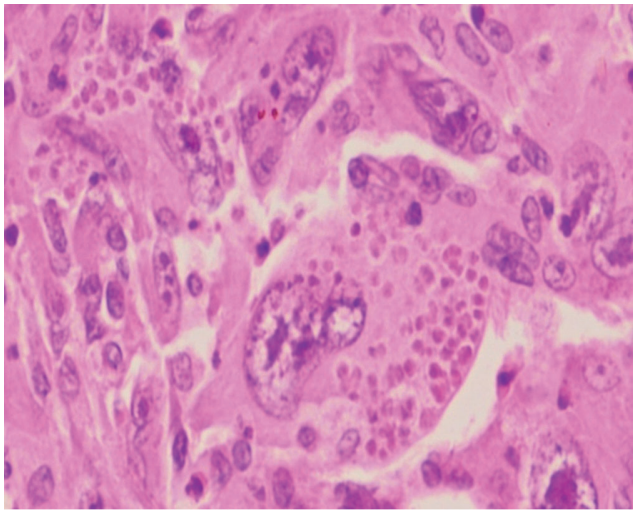

Figure 1. Individual tumor cell with abundant eosinophilic, granular cytoplasm and pleomorphic nucleus with prominent nucleoli

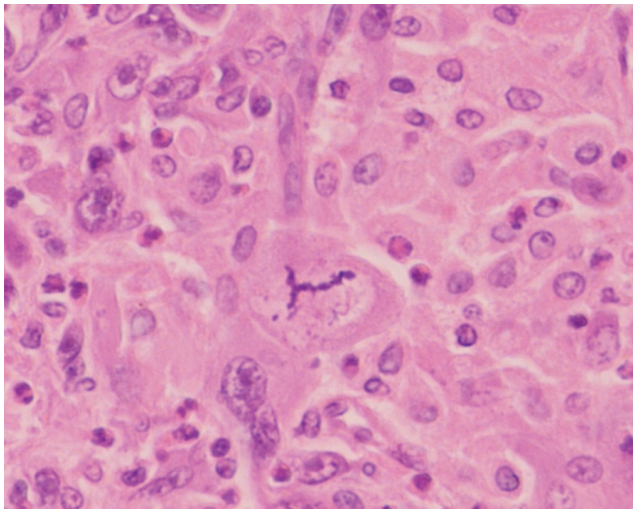

Figure 2. Tumor cell showing atypical mitosis

On Immunohistochemical staining, the tumor cells expressed CD68 (see Figure 4) and LCA. They were immunonegative for pan-CK, MART-1, CD117 (c-kit), DOG-1, SMA and S-100 antigens. Molecular analysis for detection of immunoglobulin heavy chain and rearrangement of TCR-Gamma chain gene was not performed.

Microscopy and immunohistochemistry (IHC) thus, were consistent with a primary extranodal HS. It was imperative to rule out the clinical diagnosis of a recurrent GIST, and thus immunostaining with CD117 and DOG-1 was done, which yielded negative.

The patient did not receive any further treatment at our centre and was lost to follow-up.

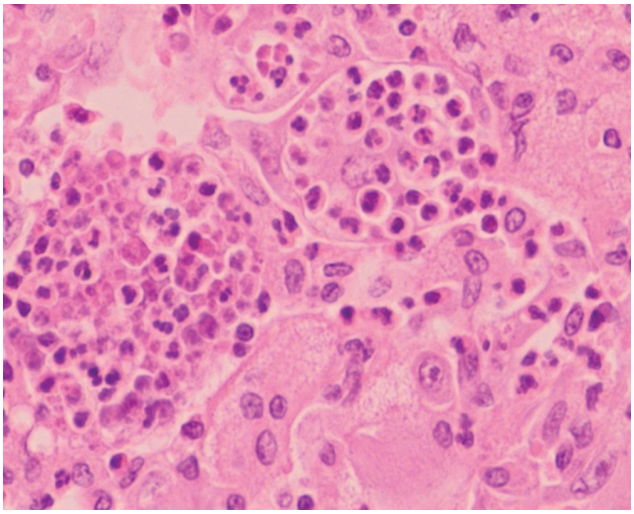

Figure 3. Malignant histiocytes showing emperipolesis

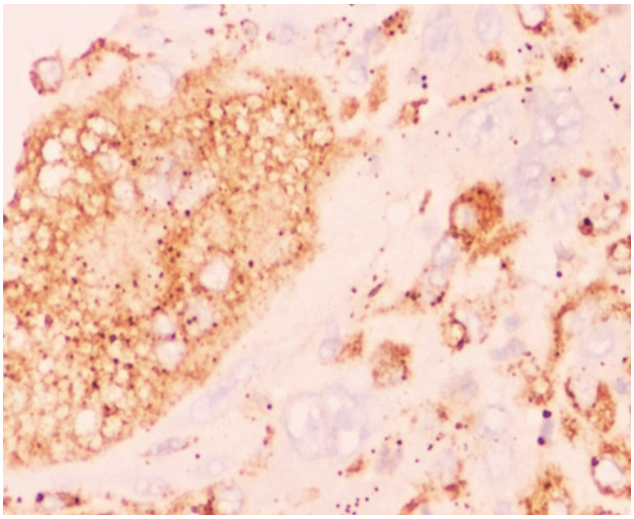

Figure 4. CD68 positive malignant histiocytes

3. Discussion

HS is a rare, but extremely aggressive hematopoietic neoplasm which was first described by Mathé et al. in 1970.[3] It is prudent that reactive histiocytic infiltrates and other malignancies like lymphomas, are carefully ruled out before making a diagnosis of HS. Prognosis is poor given the aggressive progression and relative resistance to therapy. Occasionally, HS may develop as a result of trans-differentiation of a pre-existing B-cell neoplasm.[7]

The most common mode of presentation of cases involving the intestine, is a combination of abdominal pain and intestinal obstruction. Grossly, these are often polypoidal. Microscopically, the tumor shows malignant histiocytes with abundant eosinophilic cytoplasm and pleomorphic, vesicular nuclei with prominent nucleoli. Necrosis is commonly seen. The hallmark of these tumors is extensive and marked emperipolesis. Emperipolesis is different from phagocytosis, as it involves engulfment of a living cell by histiocyte or platelet such that the engulfed cell stays structurally and physiologically viable. Besides HS, it is pathognomically seen in histiocytic disorders like Rosai-Dorfman disease and hemato-lymphoid disorders like Myeloid leukemias and lymphomas.[9] The common morphological differentials in a primary intestinal pathology would include a poorly differentiated carcinoma, malignant melanoma and a large cell lymphosarcoma. Presence of malignant cells showing marked nuclear pleomorphism with atypical mitosis, conspicuous emperipolesis, and immunopositivity of tumor cells for CD68 with immunonegativity for pan-CK and MART-1 clinched the diagnosis in our case, ruling out the other morphological differentials.

In general, combining the results of flow cytometry, immunophenotyping as well as frozen or paraffin section IHC, the neoplastic cells are commonly positive for CD4, CD11c, CD31, CD45 (leukocyte common antigen), CD45RO, CD68, CD163, HLA-DR, lysozyme, fascin, and a_1_antitrypsin. S100 protein can be positive in these neoplasms, but the staining is usually weak or focal.[2] CD163, a hemoglobin scavenger receptor, has recently been described as a novel marker specific for histiocytic lineage and is thus, a valuable tool in the diagnosis of histiocytic tumors.[6]

Ultrastructural features are characterised by extensive surface activity and scattered haloed granules. Birbeck granules are absent.

4. Conclusion

Our case report highlights the need of recognising HS as an important entity even at extranodal sites without any primary nodal involvement. It must be carefully differentiated from other histiocytic lesions and lymphomas especially a large cell Primary T cell lymphomas (PTCL) with sinus growth pattern like ALCL. Our case report also states the importance of keeping other pathologies in mind in a previously known case of a different primary pathology.

Conflicts of Interest Disclosure

The authors declare no conflicts of interest.

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