Systemic Mastocytosis with Unusual Cell Morphology: A Case Report

Delgado-Colón D, MD1, Vélez R, MD1, Ramos-Lamboy V, MD2, Fernández, A, MD2.
University of Puerto Rico- Medical Sciences Campus, School of Medicine, Department of Pathology and Laboratory Medicine1 and Department of Hematology-Oncology2, Administración de Servicios Médicos de Puerto Rico.

Introduction:
Mast cell disorders comprise an heterogeneous spectrum that ranges from cutaneous mastocytosis to aggressive systemic mastocytosis and mast cell leukemia. Systemic mastocytosis is a clonal neoplastic proliferation of mast cells that accumulate in one or more organ systems, almost always including the bone marrow. The presentation of mastocytosis in the bone marrow is highly variable and ranges from small aggregates of round and spindle cells to diffuse involvement of the bone marrow admixed variably with eosinophils and fibrosis. Morphologically, mast cell disorders presenting as atypical infiltrates in the bone marrow may simulate and be confused with a myriad of hematological and nonhematological diseases which can present a diagnostic challenge, as in our case. We report a case of an atypical morphological presentation of systemic mastocytosis infiltrating the bone marrow, for which immunostains were crucial for diagnosis.

Case Report:
This is the case of a 77 year old man who presented with shortness of breath on exertion, general malaise, early satiety and weight loss (30 pounds in 1 month). Physical examination showed a lean, chronically ill male with normal vital signs and no skin lesions or rashes. He had abdominal distention with ascites, splenomegaly and bilateral leg pitting edema. A chest and abdomino-pelvic CT scans showed mediastinal adenopathy, ascites, splenomegaly, portal hypertension, and thickening of gallbladder, transverse and ascending colon walls. Bone survey described a permeative pattern in the proximal humerus, most likely related to an infiltrating process. A peripheral smear showed moderate normocytic normochromic anemia, leukocytosis with eosinophilia and moderate thrombocytopenia.

A previous bone marrow biopsy performed at another institution was diagnosed as Acute Myelogenous Leukemia. After referral, a new bone marrow biopsy and aspiration were performed at our institution. The bone marrow showed multifocal infiltrates of neoplastic cells distorting the normal bone marrow architecture with predominance of perivascular and paratrabecular distribution, some of them with spindle shape (Fig. 1). The aspirate revealed atypical cells with abundant eosinophilic cytoplasm of unknown origin, some with few eosinophilic granules, some agranular and some binucleated cells (Fig. 2). The peripheral smear revealed agranular neoplastic cells with eosinophilic cytoplasm (Fig. 3). Flow cytometry analysis was not diagnostic. Immunohistochemistry evaluation of the bone marrow biopsy highlighted the infiltrate of neoplastic cells, that were positive for CD117 (Fig. 4) and CD68 (Fig. 5), but negative to myeloperoxidase and CD15. This combination along with morphology lead to a suspicion of mastocytosis and metachromatic granules were performed. Giemsa and toluidine blue (Fig.6) highlighted the granules, which confirmed the diagnosis. The case was consulted with the National Institutes of Health (NIH) which performed additional immunostains.

The neoplastic cells were positive for mast cell tryptase, CD2 and CD25, classic markers of mast cell neoplasias, which supported our diagnosis of systemic mastocytosis. The possible treatment alternatives were discussed with the patient, but due to his poor performance status and multiple factors affecting his poor prognosis, supportive care was started. The patient regained his appetite, started gaining weight, and increased his activity levels. His blood counts have remained stable without need for further transfusions. The patient is currently stable without worsening of symptoms.

Discussion:
This case represents a difficult diagnosis of systemic mastocytosis in which immunohistochemistry was essential for the diagnosis. According to the World Health Organization (WHO) the diagnosis of systemic mastocytosis requires one major criterion and one of four minor criteria to be met. This patient had the major criterion of dense infiltrates of aggregates of mast cells and two minor criteria (immunophenotype and atypical morphology), but due to the atypical morphology, the identification of the neoplastic cells as mast cells was difficult. Morphologically, in aggressive and leukemic variants of systemic mastocytosis, mast cells may be atypical and devoid of metachromatic granules, such as this case which had a large population of agranular mast cells. This can make the identification of mast cells difficult by morphology alone and can lead to misdiagnosis. A high grade of suspicion and a careful evaluation by the hematologist and pathologist with immunohistochemistry are pivotal in the diagnosis of this elusive entity.

References: