Chapter 11 Other Neoplasms of Myeloid Origin: Histiocytic/Dendritic-Cell and Mast Cell Neoplasms

ABSTRACT

Other rare neoplasms may arise from myeloid progenitors, including Histiocytic/ Dendritic Neoplasms and mast cell neoplasms. The Classification of both categories in the 5th edition of WHO has some modifications with newly introduced entities. Histiocytic neoplasms exhibit diverse somatic oncogenic alterations. Their clinical presentation ranges from incidental findings to critical illness with severe organ dysfunction. Each subtype has distinct morphologic and immunophenotypic features. However, some overlap exists between the different subtypes. Mastocytosis involves abnormal mast cells accumulating in various organs. It develops as a clonal expansion of mast cells derived by constitutive activation of the KIT receptor. The clinical course varies from asymptomatic to diffuse systemic involvement with comorbidities mainly related to mediators' release.

INTRODUCTION

Histiocytic and mast cell neoplasms are two rare categories of myeloid origin. Each encompasses a spectrum of subtypes with heterogeneous clinical courses, pathological features, and prognoses. Histiocyte/ dendritic neoplasms have an accumulation of macrophages, monocytes, dendritic cells, interdigitating reticulum cells, or Langerhans cells in affected tissues. (*Durham, 2019*).

*T*he molecular landscape of histiocytosis often involves the MAPK/ERK pathway (RAS-RAF-MEK-ERK) and correlates with phenotypes of various entities. (*Tzankov et al., 2018*)

Mastocytosis results from abnormal mast cells accumulating in various organs. It develops as a clonal expansion of mast cells derived by constitutive activation of the KIT receptor. The clinical course varies from asymptomatic to diffuse systemic involvement with comorbidities mainly related to mediators' release.

The diagnostic approach to both categories integrates pertinent clinical features, morphology, immunohistochemistry of tissue lesions, molecular analysis, and risk assessment. The broad differential diagnosis of each category includes several reactive and neoplastic disorders.

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HISTIOCYTIC/DENDRITIC NEOPLASMS

Systemic histiocytic neoplasms originate from hematopoietic stem/progenitor cells (HSPCs) and may be associated with hematological malignancies bearing the same genetic alteration(s).

Pathogenesis and Molecular Landscape of Dendritic Cell and Histiocytic Neoplasms

Driver mutations in particular genes (e.g., N/KRAS) may predispose to an additional clonally related hematological malignancy or secondary histiocytic neoplasm. A multipotent HSPC origin emphasizes the importance of adequate bone marrow staging, molecular analysis, and long-term follow-up of all histiocytosis patients. (Kemps et al., 2021)

Histiocytic neoplasms exhibit diverse somatic oncogenic alterations (*Figure 1*), often involving the MAPK/ERK pathway (RAS-RAF-MEK-ERK) and potentially other pathogenic mechanisms in certain subtypes which provide essential diagnostic and therapeutic channels. (*Durham, 2019*).

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