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Leukaemia Section

Mini Review

Systemic mast cell disease (SMCD)

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Identity

Note

Mastocytosis is a heterogeneous clinical entity which is classified into four categories:
1- indolent mastocytosis (the most common form),
2- mastocytosis with an associated hematologic disorder,
3- mast cell leukemia and
4- aggressive mastocytosis.

Clinics and pathology

Phenotype/cell stem origin

Mast cell

Etiology

Involvement of KIT/SCF has been demonstrated in a few cases, but the diversity of the clinical pattern has not yet been elucidated;increased soluble SCF has been reported in the skin of patient with indolent mastocytosis; c-KIT mutations have been identified in patients with all forms of sporadic mastocytosis.

Clinics

Indolent mastocytosis involves the skin, bone marrow and gastrointestinal tract; clinical features range from a single cutaneous nodule to multiple pigmented macules resulting from increased epidermal melanin and papules (urticaria pigmentosa) or diffuse cutaneous involvement; bullae, vescicles and abnormal telangiectasia may be seen; gastrointestinal involvement leads to symptoms such as nausea, vomiting and abdominal pain.

In mastocytosis with an associated hematological disorder the urticaria pigmentosa symptoms are accompanied by a variety of haematological findings due to mast cell infiltrates to bone marrow, spleen, liver and lymph nodes.
Mast cell leukemia is characterized by proliferation and infiltration of immature mast cells in bone marrow, peripheral blood and various extramedullary tissues.
Aggressive mastocytosis is characterized by aggressive involvement of several haematopoietic organs.

Pathology

Accumulation of mast cells in various organs and release of mast cell mediators which are responsible for the different clinical signs.

Prognosis

Highly dependent on the form being severe, often fatal, in all types with the exception of the indolent form.

Genes involved and proteins

KIT

Location

4q12

DNA/RNA

21 exons

Protein

Transmembrane SCF/MGF receptor with tyrosine kinase activity; binding of ligand (SCF) induces receptor dimerization, autophosphorylation and signal transduction via molecules containing SH2- domains.

Somatic mutations

Gly560Val, Asp816Val, Asp816Tyr, Asp820Gly.
Asp816Val in peripheral blood lymphocytes (mastocytosis with an associated hematological disorder: AHD).
Asp816Val in skin and spleen mast cells from patients with aggressive mastocytosis.
Asp816Tyr in blasts from a patient with ANLL-M2 with mast cell involvement.
Asp820 Gly in blasts from a patient with aggressive SMCD.
Asp816Val and Gly560Val have been found in a human mast cell leukemia cell line (HMC1).

Note

All mutations with the exception of Gly560Val cluster to c-kit exon 17. Direct or indirect evidence has been provided that mutations affecting codon 816 promote ligand-independent autophosphorylation of the mutant receptor.

SCF/MGF

Location

12q22

DNA/RNA

9 exons

Protein

Soluble SCF: 248 aminoacids containing a proteolytic cleavage site encoded by exon 6 sequences, which is processed, giving rise to an active form (soluble) of 165 aminoacids; membrane-bound SCF: 220 aminoacids, results from alternative splicing of exon 6.
Note: increased soluble SCF has been detected in the skin of patients with indolent mastocytosis; SCF-specific transcripts are detected by in situ RT-PCR in mast cell infiltrates in papulae from mastocytosis patients.

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