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 mastocytosis with an associated haematological disorder and in aggressive 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, vesicles 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 associated with 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/NGF receptor with tyrosine kinase activity; binding of ligand (SCF) induces receptor dimerization, autophosphorylation and signal transduction via molecules containing SH2-domains.
Systemic mast cell disease (SMCD) Larizza L, Beghini A

Atlas Genet Cytogenet Oncol Haematol. 1999; 3(1)

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 AML-M2 with mast cell involvement.
- Asp820Gly in blasts from a patient with aggressive SMCD.
- Asp816Val and Gly560Val have been found in a human mast cell leukemia cell line (HMC1).
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 amino acids containing a proteolytic cleavage site encoded by exon 6 sequences, which is processed, giving rise to an active form (soluble) of 165 amino acids; membrane-bound SCF: 220 amino acids, 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.

References
Nagata H, Worobec AS, Oh CK, Chowdhury BA, Tannenbaum S, Suzuki Y, Metcalfe DD. Identification of a point mutation in the catalytic domain of the protooncogene c-kit in peripheral blood mononuclear cells of patients who have mastocytosis with an associated hematologic disorder. Proc Natl Acad Sci U S A. 1995 Nov 7;92(23):10560-4

This article should be referenced as such: