Identifying and Suspecting Systemic Mastocytosis (SM) in Your Practice

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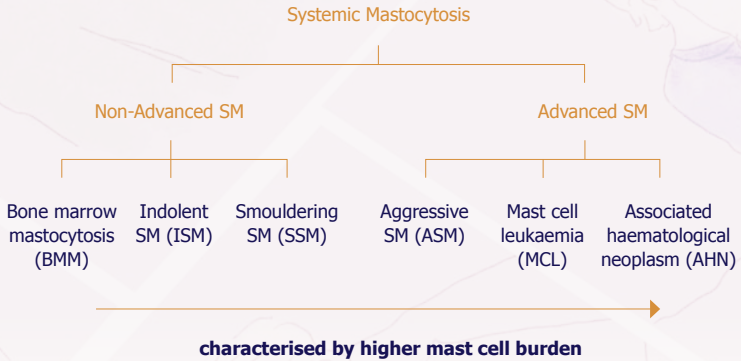
SM, the complex disorder

SM is a genetic disease associated with the uncontrolled proliferation and activation of abnormal mast cells[1–3]

The 2022 World Heath Organization (WHO) diagnostic criteria identify two types of SM, which are classified into six subtypes:[4]



Estimated prevalence

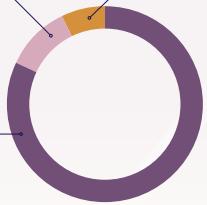
~1 in 10,000

adults have SM[5*]

~11%
SM with unknown subtype

~7%
Advanced SM patients

~82%
ISM patients[†]



*Based on the Cohen 2014 study of 548 adults with SM diagnosed from 1997 to 2010 in linked Danish national health registries, with a 14-year limited-duration prevalence estimated at 9.59 per 100,000 as of 1 January 2011.[5]
†SSM (sometimes considered as a sub-variant of ISM) could not be separated from ISM in this study; the 82% prevalence includes SSM.[5]

Understanding the clinical spectrum: SM is categorised into two main groups

SM can have detrimental long-term effects on patients, regardless of subtype:

Non-Advanced SM

Carries with it a risk of life-threatening anaphylaxis in some cases[2]

Younger at presentation and less likely to manifest constitutional symptoms[3]

Advanced SM

Commonly exhibits mast-cell mediator symptoms, such as maculopapular rash and life-threatening anaphylaxis[6]

Frequently associated with multiorgan failure and related symptoms due to mast cell infiltration[3]

Associated with a poor prognosis and decreased overall survival of 2 months to 3.5 years[2,7]

Suspecting SM is challenging

The median time from symptom onset to diagnosis for SM patients is 7 years[6‡]

97% of adult patients presenting with cutaneous mastocytosis (CM), a form of mastocytosis with only skin involvement, actually have SM[8§]

‡Based on data from 149 patients with self-reported mastocytosis in the Mast Cell Connect registry in the Jennings 2018 study.[6]
§Based on the Berezowska 2014 study with 59 patients with the clinical diagnosis of adult-onset mastocytosis in the skin established between 2004 and 2008.[8]

SM, a heterogeneous disorder with unpredictable symptoms[6]

Early identification of the disease and active management of symptoms, such as life-threatening anaphylaxis, is critical[1]

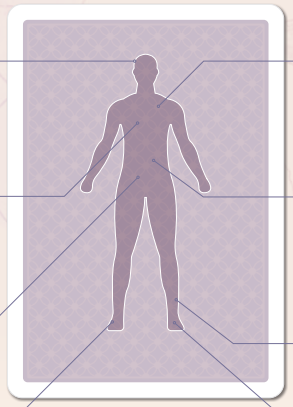
Common symptoms that raise suspicion of SM include skin lesions, anaphylaxis and diarrhoea[6]

For more information on SM symptoms, visit **www.systemicmastocytosis-hcp.com**

Are you missing SM?

Explore the potential clinical consequences across multiple organ systems for SM patients[2,3,6,9]

Not an inclusive list of all symptoms.
The frequency and intensity of any given symptom may vary from person to person.



Neuropsychiatric:
Memory/cognitive impairment, Depression, Migraines, Sleep disturbance

Cardiovascular:
Anaphylaxis with hypotension and syncope, Dizziness, Palpitations

Respiratory:
Dyspnea, Nasal congestion, Throat swelling, Wheezing

Liver/Spleen:
Liver dysfunction, Hypersplenism

Gastrointestinal:
Nausea/vomiting, Diarrhoea, Abdominal pain, Heartburn or reflux

Musculoskeletal:
Bone pain, Myalgia, Osteolytic lesions

Skin:
Pruritus, Flushing, Maculopapular lesions

Systemic:
Fatigue, Weight loss, Anaphylaxis, Malaise

Prominent in advanced SM | Prominent in non-advanced SM | Present in both forms

Recognising common symptoms can raise the suspicion of SM: a combination of diagnostic tests is required due to its heterogeneity

A complete work-up that includes a high-sensitivity *KIT* D816V assay, serum tryptase test and bone marrow biopsy is required for definitive diagnosis:

1 *KIT* D816V peripheral blood

It is recommended by ECNM-AIM to perform high-sensitivity (<1%) *KIT* D816V in patients with suspected SM as a first step[10,11]

2 Serum tryptase

Recommendations for next steps based on serum tryptase level

≥20 ng/mL
Conduct a bone marrow biopsy and screen for *KIT* D816V mutation[9]

<11.5 ng/mL
Mastocytosis unlikely but cannot be ruled out[9]

11.5–20 ng/mL
Systemic mastocytosis possible — screen for *KIT* D816V in peripheral blood with high-sensitivity assay[9]

3 Bone marrow biopsy

ECNM-AIM recommends that patients with MCAS should have a bone marrow examination when they exhibit clear signs of SM such as:
(i) typical skin lesions,
(ii) a *KIT*-activating mutation,
(iii) unexpectedly high / steadily increasing tryptase levels,
(iv) splenomegaly,
(v) unexplained osteoporosis,
(vi) spontaneous anaphylaxis,
(vii) REMA score ≥2,
(viii) blood cell count abnormalities[10]

Recognising severe and recurrent instances of the common symptoms can raise the suspicion of SM: mast cell examination, serum tryptase assessment or high-sensitivity *KIT* D816V mutation testing can help diagnose SM[2,10]

For more information on SM screening options and patients' case studies, visit **www.systemicmastocytosis-hcp.com**

Differentiating CM and SM

Diagnosis of CM and SM both require a bone marrow assessment; when CM is already diagnosed in adults, patients should undergo a complete staging including a bone marrow investigation to confirm or exclude SM[10,12]

ECNM-AIM=European Competence Network on Mastocytosis-American Initiative in Mast Cell Diseases; MCAS=mast cell activation syndrome; REMA= Red Española de Mastocitosis (Spanish Mastocytosis Network)

2022 WHO diagnostic criteria for SM

Diagnosis of SM requires the presence of one major criterion and at least one minor criterion, or at least three minor criteria[12]

MAJOR CRITERION:

Multifocal dense infiltrates of mast cells (≥15 mast cells in aggregates) detected in sections of the bone marrow and/or other extracutaneous organ(s)

MINOR CRITERIA:

1.
>25% of all mast cells are atypical cells
(type I or type II) on bone marrow smears or are spindle-shaped in dense and diffuse mast cell infiltrates in bone marrow or other extracutaneous organ(s)

2.
Activating *KIT* point mutation(s) at codon 816
or in other critical regions of *KIT* in the bone marrow or other extracutaneous organ(s)

3.
Mast cells in bone marrow,
blood or other extracutaneous organ(s) aberrantly express one or more of the following antigens: CD2, CD25, CD30

4.
Baseline serum tryptase concentration >20 ng/mL in the absence of a myeloid AHN. In the case of a known HαT, the tryptase level should be adjusted

'B' findings and 'C' findings are used to determine SM subtype.

For more information, visit
www.systemicmastocytosis-hcp.com

References

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