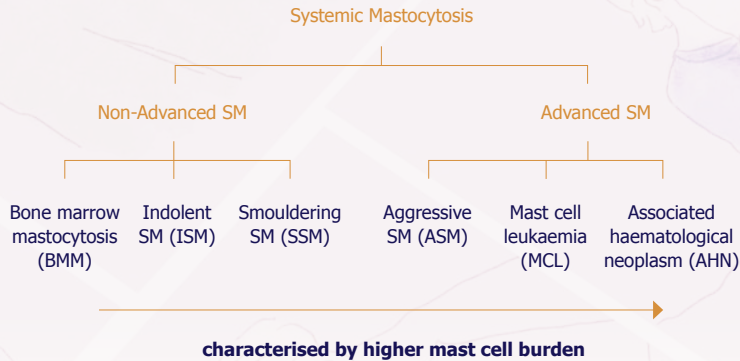

Identifying and Suspecting Systemic Mastocytosis (SM) in Your Practice



SM, the complex disorder

SM is a genetic disease associated with the uncontrolled proliferation and activation of abnormal mast cells¹⁻³

The 2022 World Health 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%

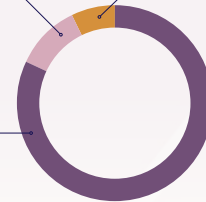
SM with unknown subtype

~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 cases²

Younger at presentation and less likely to manifest constitutional symptoms³

Advanced SM

Commonly exhibits mast-cell mediator symptoms, such as maculopapular rash and life-threatening anaphylaxis⁶

Frequently associated with multiorgan failure and related symptoms due to mast cell infiltration³

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 symptoms⁶

Early identification of the disease and active management of symptoms, such as life-threatening anaphylaxis, is critical¹

Common symptoms that raise suspicion of SM include skin lesions, anaphylaxis and diarrhoea⁶



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



Respiratory:

Dyspnea, Nasal congestion, Throat swelling, Wheezing



Gastrointestinal:

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



Skin:

Pruritus, Flushing, Maculopapular lesions



Cardiovascular:

Anaphylaxis with hypotension and syncope, Dizziness, Palpitations



Liver/Spleen:

Liver dysfunction, Hypersplenism



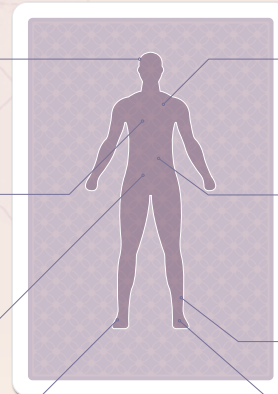
Musculoskeletal:

Bone pain, Myalgia, Osteolytic 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}

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

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 mutation⁹

<11.5 ng/mL

Mastocytosis unlikely but cannot be ruled out⁹

11.5–20 ng/mL

Systemic mastocytosis possible — screen for *KIT* D816V in peripheral blood with high-sensitivity assay⁹

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 abnormalities¹⁰

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}

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}

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 criteria¹²

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 HaT, the tryptase level should be adjusted**



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

‘B’ findings and ‘C’ findings are used to determine SM subtype.

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