Systemic Mastocytosis:

Recognition, Diagnosis, and Clinical Management

CME Program

Daniel J. DeAngelo, MD, PhD
Chief, Division of Leukemia
Dana-Farber Cancer Institute | Harvard Medical School
Boston, MA

Disclosures

In support of improving patient care, this activity has been planned and implemented by American Academy of CME, Inc. and CheckRare CE. American Academy of CME, Inc. is Jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

American Academy of CME, Inc., designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credits™.* Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Learning Objectives:

- Describe the early symptoms of systemic mastocytosis and its clinical relevance.
- Apply best practices to diagnose systemic mastocytosis more efficiently.

Planner/Faculty Educator Dr. DeAngelo discloses the following relevant financial relationships with ineligible companies:

Consultant: Amgen, Autolos, Blueprint Medicines, Incyte, Jazz, Novartis, Pfizer, and Takeda
Research Support: AbbVie, Glycomimetics, Novartis, and Blueprint Medicines
Data Safety Monitoring Board: Daiichi-Sankyo

Academy and CheckRare CE planners and reviewers for this activity have no relevant financial relationships with any ineligible companies.

All relevant financial relationships listed have been mitigated. This activity will discuss off-label uses and investigational agents.

This accredited continuing education program is supported by an educational grant from Blueprint Medicines Corporation

Section 1: Overview of Systemic Mastocytosis

Pathophysiology · KIT D816V Mutation · Disease Subtypes

What is Systemic Mastocytosis?

A rare, clonal, neoplastic proliferation of mast cells

- Estimated prevalence: ~1 in 10,000 adults
- Driven by activating KIT D816V mutation in ~95% of cases
- Characterized by mast cell infiltration of:
  - Bone marrow (primary site)
  - Skin, liver, spleen, GI tract, lymph nodes
- Highly heterogeneous — ranges from indolent to life-threatening
- **Average time from symptom onset to diagnosis: 9–12 years**

Key Mediators Released:

- Histamine
- Tryptase
- Prostaglandin D2
- Cytokines / TNF-α
- Platelet-activating factor
- Heparin

→ *Mediator symptoms + organ infiltration*

1. Vaes M, et al. Front Med. 2017;4:110. 2. Cohen SS, et al. Br J Haematol. 2014;166:521-528. 3. Jennings SV, et al. Immunol Allergy Clin North Am. 2018;38(3):505-525.

The KIT D816V Mutation: Driver of Disease

Present in ~95% of adults with systemic mastocytosis

- KIT encodes a type III receptor tyrosine kinase
- D816V = substitution of aspartate → valine at position 816 in kinase domain
- Results in:
  - Constitutive (ligand-independent) KIT signaling
  - Uncontrolled mast cell proliferation and survival
- A key WHO diagnostic criterion (minor criterion)
- Quantify mutant allele burden using high-sensitivity ddPCR (<0.1% LOD)
  - **ddPCR detects KIT D816V in peripheral blood: 95% vs 28% with NGS**

KIT Testing Methods

ddPCR	Preferred (sensitivity <0.1%)
NGS	Lower sensitivity; broader panel
ASO-qPCR	Acceptable alternative

Additional High-Risk Mutations

SRSF2 · ASXL1 · RUNX1 · TET2 · CUX1

~25% of non-advanced SM carry ≥1 additional mutation; ~90% of advanced SM

S/A/R mutations = high-risk; inferior OS

1. Komi DEA, et al. Clin Rev Allergy Immunol. 2018;54(3):397-411. 2. George TI, et al. ASH 2020. Abstract 3004. 3. Jawhar M, et al. Leukemia. 2016;30:136-143. 4. Schwaab J, et al. Blood. 2013;122(14):2460-2466 5. DeAngelo D, et al. Nature Med. 2021; 27(12):2183-2191.

WHO Classification: Subtypes of Systemic Mastocytosis

NON-ADVANCED SM (~90%)

Indolent SM (ISM) ~65%

No B- or C-findings; near-normal life expectancy

Smoldering SM (SSM) ~25%

≥2 B-findings; no C-findings; ~9% progression risk

BM Mastocytosis New

SM criteria met; BM-only disease; tryptase often < 125

ADVANCED SM (~10%)

Aggressive SM (ASM) ~1-3%

≥1 C-finding; requires cytoreduction; median OS 5.7 yr

SM-AHN ~7-8%

SM + associated hematologic neoplasm; median OS 2.9 yr

Mast Cell Leukemia ~1%

≥20% MCs in BM aspirate; worst prognosis; OS ~1.9 yr

1. Khoury JD, et al. Leukemia. 2022;36(7):1703-1719. 2. Sperr WR, et al. Lancet Haematol. 2019;6(12):e638-e649. 3. Lim KH, et al. Blood. 2009;113(23):5727-5736.

B-Findings and C-Findings: Determining Subtype

B-findings = organ involvement (borderline) | C-findings = organ damage (cytoreduction required)

B-FINDINGS (Organ Involvement)

1	BM biopsy >30% infiltration by MCs and/or serum tryptase >200 ng/mL
2	Dysplasia or myeloproliferation in non-MC lineage (insufficient for AHN)
3	Hepatomegaly without LFT impairment, palpable splenomegaly, or lymphadenopathy
4	KIT D816V VAF >10% (added in WHO 2022 update)

C-FINDINGS (Organ Damage)

1	BM dysfunction: ANC $<1.0\times10^9$/L, Hb <10 g/dL, or platelets $<100\times10^9$/L
2	Palpable hepatomegaly with liver dysfunction, ascites, and/or portal hypertension
3	Skeletal involvement: large osteolytic lesions and/or pathologic fractures
4	Splenomegaly with hypersplenism; malabsorption with weight loss

1. Valent P, et al. Leuk Res. 2001;25(7):603-625. 2. Khoury JD, et al. Leukemia. 2022;36(7):1703-1719.

Section 2: Suspecting Systemic Mastocytosis

Early Signs & Symptoms · Severity Spectrum · Case Examples

Recognizing SM: Wide Spectrum of Symptoms

Activated mast cells release potent mediators, causing multi-system symptoms

Skin

Urticaria pigmentosa (~80%), flushing, pruritus, Darier's sign

GI Tract

Abdominal pain, diarrhea, nausea/vomiting, peptic ulcer, weight loss

Cardiovascular

Hypotension, syncope, tachycardia, anaphylaxis

Neuropsychiatric

Brain fog, memory loss, anxiety, depression, migraines

Musculoskeletal

Bone pain, osteoporosis, pathologic fractures

Systemic

Fatigue (72–85%), sweating, swelling; >80% limited in daily activities

1. Theoharides TC, et al. N Engl J Med. 2015;373:163-172. 2. Jennings SV, et al. Immunol Allergy Clin North Am. 2018;38(3):505-525. 3. Ustun C et al. Blood Adv. 2025;9(9):2048-2062.

Mast Cell Activation Triggers

Triggers vary by patient and can change over time — avoidance lists should be individualized

Environmental

Heat, cold, temperature changes, weather, pollen, pet dander

Food & Substances

Alcohol, certain foods, NSAIDs, opioids, vancomycin IV

Biological

Insect stings, infections (viral, bacterial, fungal)

Emotional/Physical

Stress, pain, physical exertion, sleep deprivation

Medical

Contrast dyes, surgery, endoscopy/colonoscopy, vaccinations

Mechanical

Friction, vibration, sunlight, skin pressure

1. Theoharides TC, et al. N Engl J Med. 2015;373:163-172. 2. Jennings SV, et al. Immunol Allergy Clin North Am. 2018;38(3):505-525. 3. Ustun C et al. Blood Adv. 2025;9(9):2048-2062.

The Diagnostic Odyssey: Why SM is Missed

9–12 yrs
Avg. time to diagnosis (ISM)

3+
Median specialists before diagnosis

82%
ISM patients troubled by physician's lack of SM knowledge

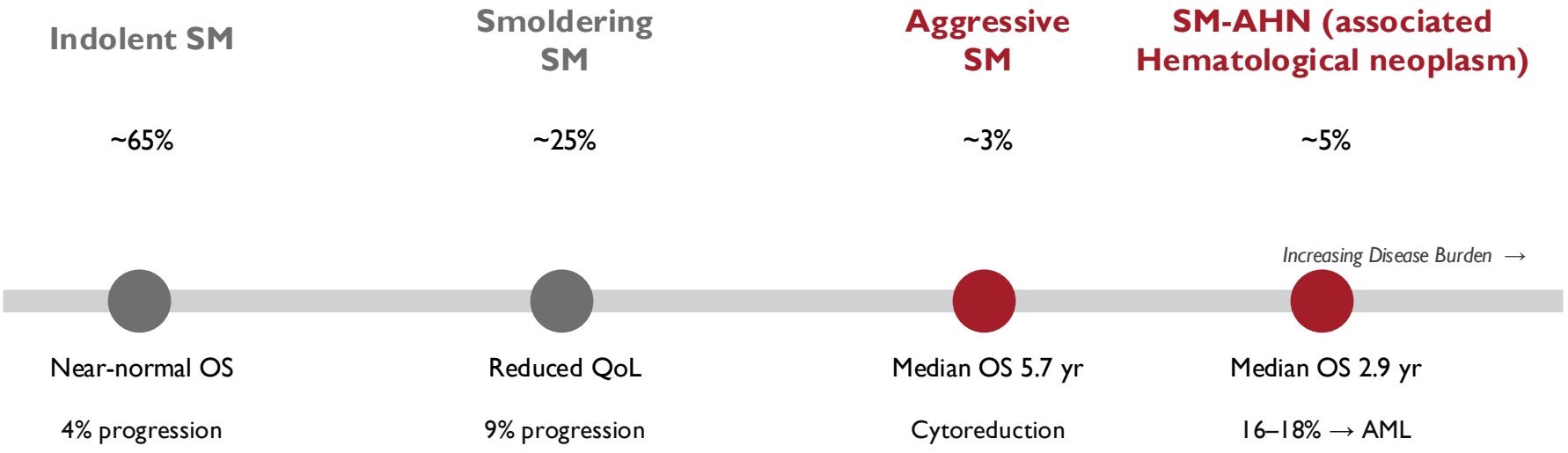
Common Misdiagnoses:

- Irritable bowel syndrome
- Inflammatory bowel disease
- Urticaria / allergic disease
- Idiopathic MCAS
- Myeloproliferative disorders
- Endocrine disorders
- Malabsorption syndromes
- Depression / anxiety

⚠ High index of suspicion needed. Check serum tryptase in any patient with unexplained anaphylaxis, unexplained osteoporosis, or unexplained cytopenias.

1. Pardanani A, et al. Am J Hematol. 2016;91(11):1146-1159. 2. Russell N, et al. J Allergy Clin Immunol Pract. 2019;7:1157-1165. 3. Jennings SV, et al. Immunol Allergy Clin North Am. 2018;38(3):505-525.

Range of Severity: Indolent to Advanced Disease



Indolent SM: despite its name, long-term morbidity includes life-threatening anaphylaxis, frequent GI symptoms, debilitating fatigue, and osteoporosis — patients still suffer significantly.

1. Sperr WR, et al. Lancet Haematol. 2019;6(12):e638-e649. 2. Jennings SV, et al. Immunol Allergy Clin North Am. 2018;38(3):505-525.

Case Example: When Should You Suspect SM?

Case — Illustrative of Diagnostic Delay

44-year-old male truck driver
- Back/leg pain → MRI: T3 compression + prior lumbar fracture
- Osteoporosis (spine) and osteopenia (hip) on DEXA
- Baseline serum tryptase:

21.9 ng/mL

Additional history:
Urticaria pigmentosa ×20 years (increasing) · Diarrhea, abdominal pain · Anaphylaxis ×2 hornet stings (2nd: 3 doses epinephrine) · Brain fog, depression, short-term memory loss

Red Flags for SM

- Unexplained osteoporosis
- Elevated serum tryptase
- Urticaria pigmentosa
- Recurrent anaphylaxis
- Chronic diarrhea
- Brain fog / neuro symptoms
- Darier's sign positive

1. Sperr WR, et al. Lancet Haematol. 2019;6(12):e638-e649. 2. Jennings SV, et al. Immunol Allergy Clin North Am. 2018;38(3):505-525.

Section 3: Diagnosing Systemic Mastocytosis

WHO Criteria · Assessment Tools · Diagnostic Best Practices

WHO 2022 Diagnostic Criteria for SM

Diagnosis requires: 1 Major + ≥1 Minor OR ≥3 Minor criteria

MAJOR CRITERION

Multifocal dense infiltrates of mast cells (≥15 MCs in aggregates) in BM biopsy and/or other extracutaneous organ(s)

MINOR CRITERIA (4 criteria)

1 Atypical Mast Cell Morphology

>25% spindle-shaped or atypical MCs in BM biopsy sections or aspirate smears

2 Activating KIT Mutation

KIT D816V (or other activating mutation) in BM, blood, or extracutaneous organ

3 Aberrant MC Surface Markers

MCs express CD25 ± CD2 ± CD30 (WHO 2022) in addition to normal mast cell markers

4 Elevated Serum Tryptase

Serum tryptase persistently >20 ng/mL (not valid if associated myeloid neoplasm)

1. Khoury JD, et al. Leukemia. 2022;36(7):1703-1719. 2. Arber DA, et al. Blood. 2022;140(11):1200-1228.

Diagnostic Workup: Assessment Tools

Initial Evaluation	Lab & Molecular Testing	BM Biopsy & Pathology
• Complete medical history & physical exam	• Serum tryptase (>20 ng/mL = minor criterion)	• BM biopsy: IHC with tryptase, CD117, CD25, CD2, CD30
• Full-body skin exam (urticaria pigmentosa, Darier's sign)	• CBC with differential; comprehensive metabolic panel	• BM aspirate: MC morphology (>25% atypical = minor)
• Palpation for organomegaly / lymphadenopathy	• KIT D816V by ddPCR in peripheral blood	• Flow cytometry: MC immunophenotype (CD117+/CD25+)
• Neuropsychological evaluation	• NGS panel (SRSF2, ASXL1, RUNX1, TET2); serum IgE; ALP	• Cytogenetics & FISH; MC aggregate quantification

Imaging: CT/ultrasound (organomegaly/LAD); bone densitometry (DEXA); skeletal X-ray or bone scan; endoscopy if GI involvement suspected.

1. Arock M, et al. Leukemia. 2015;29(6):1223-1232. 2. Pardanani A. Am J Hematol. 2019;94(3):363-377.

Serum Tryptase: A Critical Biomarker

Elevated tryptase is a WHO minor criterion AND a key tool for monitoring treatment response

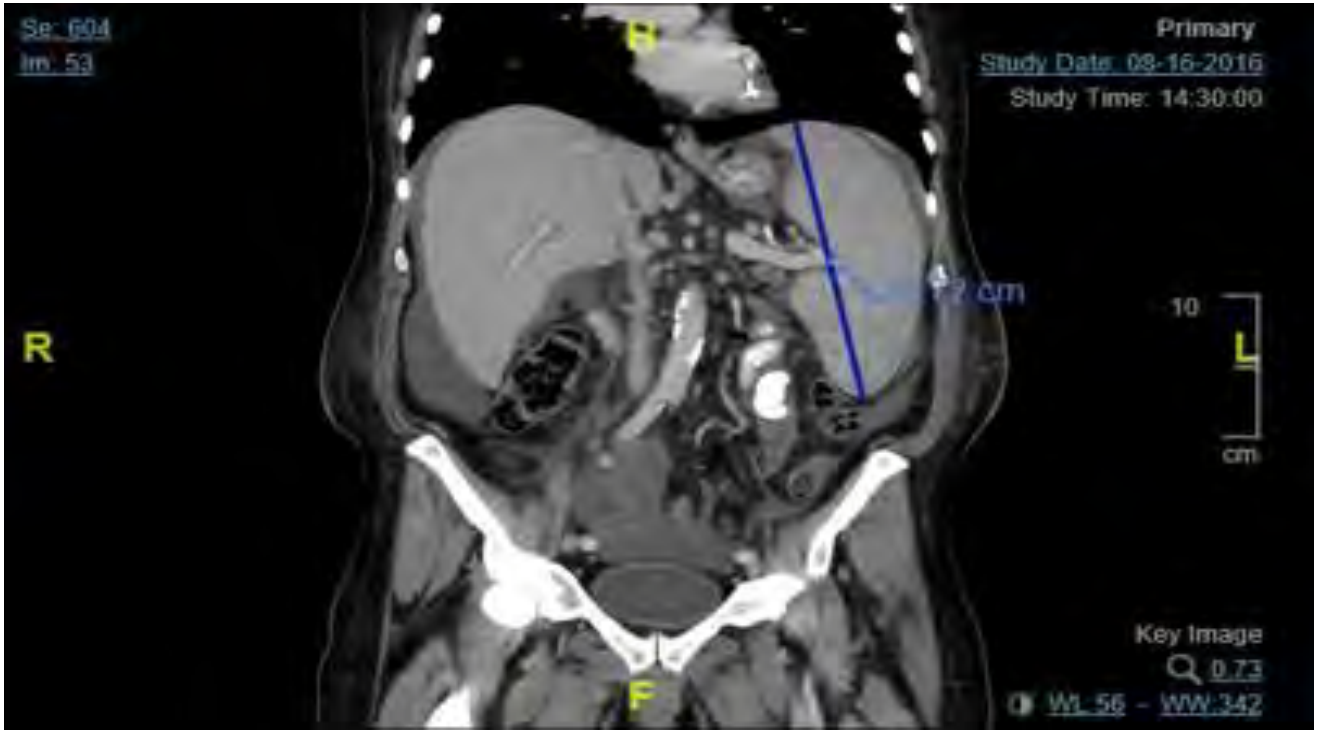
- Normal serum tryptase: <11.5 ng/mL
- **SM diagnostic threshold: >20 ng/mL (minor criterion)**
- Advanced/smoldering SM: commonly >200 ng/mL
- Hereditary Alpha Tryptasemia (HAT) can cause elevated baseline tryptase — consider when:
  - Elevated tryptase without other SM criteria
  - Family history of elevated tryptase; check TPSAB1 copy number
- **Monitor tryptase to assess treatment depth (normalization = deep response)**

Tryptase Reference Points	
<11.5	Normal range
>20	SM minor criterion
>125	Suspect ISM/SSM
>200	B-finding threshold
↓ nl	Deep response on TKI

1. Pardanani A. Am J Hematol. 2019;94(3):363-377. 2. Wu R, et al. Curr Allergy Asthma Rep. 2021;21. 3. Chollet MB, et al. J Allergy Clin Immunol. 2022;149:728-735.

Case 1: CT Scan — Splenomegaly & Ascites

Abdominal CT at presentation demonstrating splenomegaly, ascites, and lymphadenopathy (provided by Dr. DeAngelo)



CT findings: diffuse lymphadenopathy 2–3 cm, small pleural effusion, ascites, and splenomegaly — classic C-findings in SM-AHN.

Gastrointestinal Involvement in Mastocytosis

GI symptoms may occur WITHOUT involvement of other organs — a key diagnostic clue

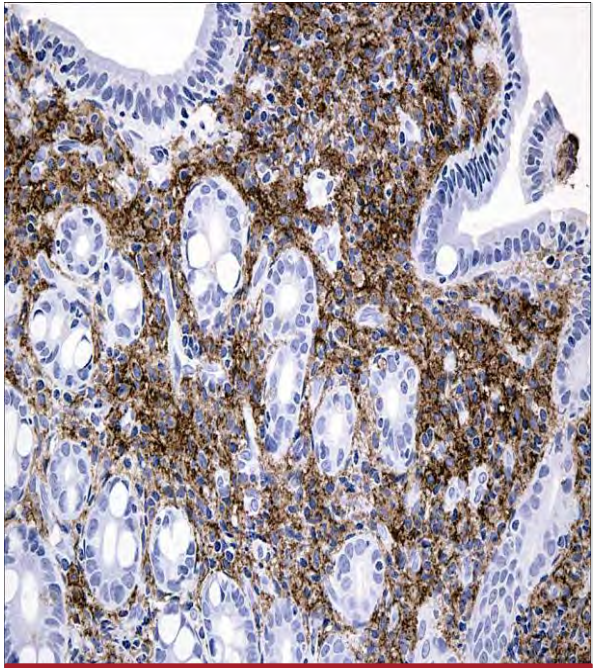
SYMPTOM	PRESUMED ETIOLOGY
Abdominal pain	Altered gut motility — mast cell mediators
Diarrhea	Altered gut motility — mast cell mediators
Nausea / Vomiting	H^+ secretion; delayed stomach emptying
Peptic Ulcer Disease	Histamine-induced H^+ hypersecretion
GI Bleeding	Histamine-induced acid secretion; heparin
Weight loss / Malnutrition	Direct mast cell infiltration of gut

1. Jennings SV, et al. Immunol Allergy Clin North Am. 2018;38(3):505-525. 2. Theoharides TC, et al. N Engl J Med. 2015;373:163-172.

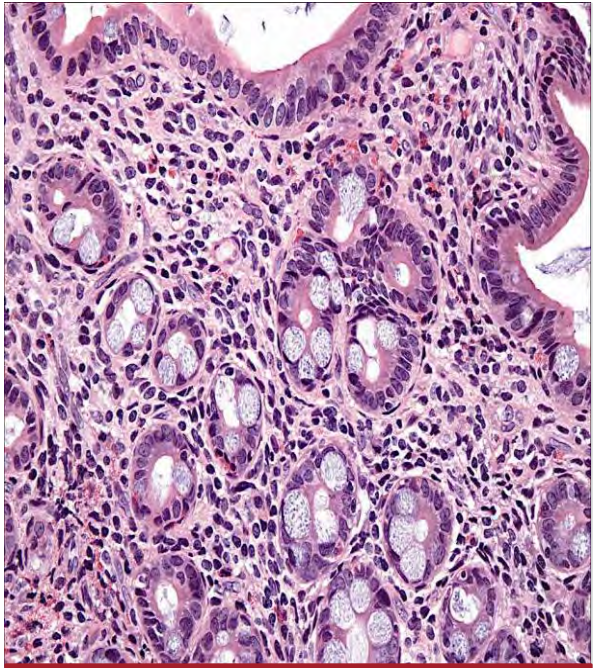
GI Pathology: Small Intestine — Mast Cell Infiltration

Histological evidence of mast cell infiltration in small bowel biopsies. (provided by Dr. DeAngelo)

Small Intestine — H&E



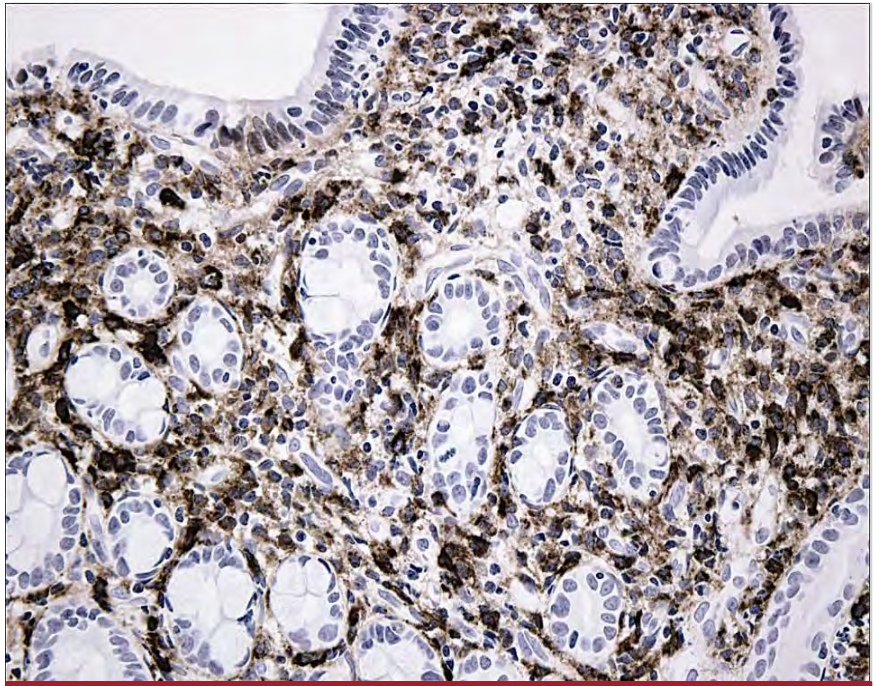
Tryptase IHC



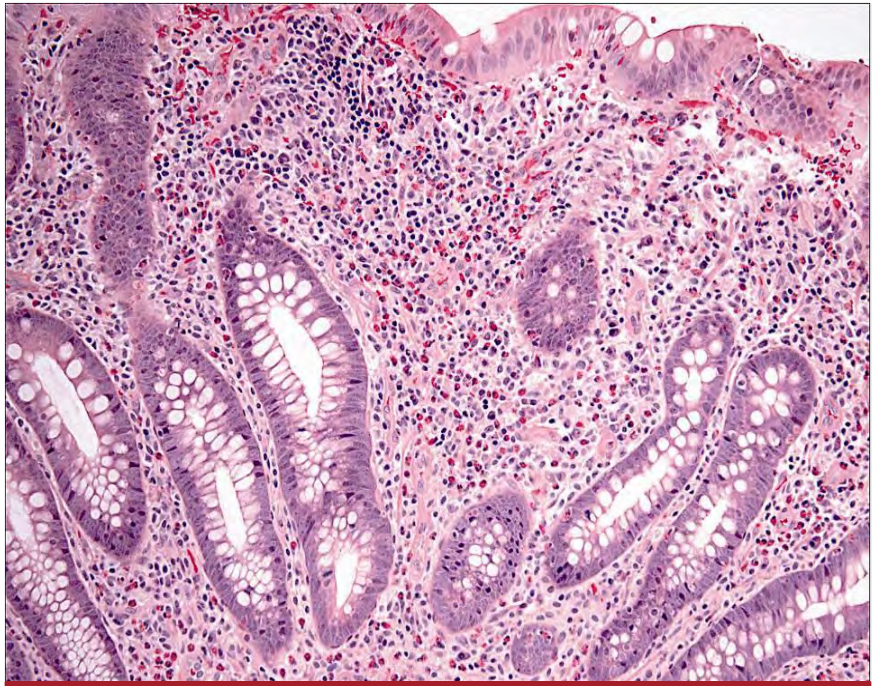
KIT (CD117) IHC

GI Pathology: Colon — Mast Cell Infiltration

Dense mast cell infiltration confirmed by tryptase IHC in colonic biopsies. (provided by Dr. DeAngelo)



Colon — H&E (20×)

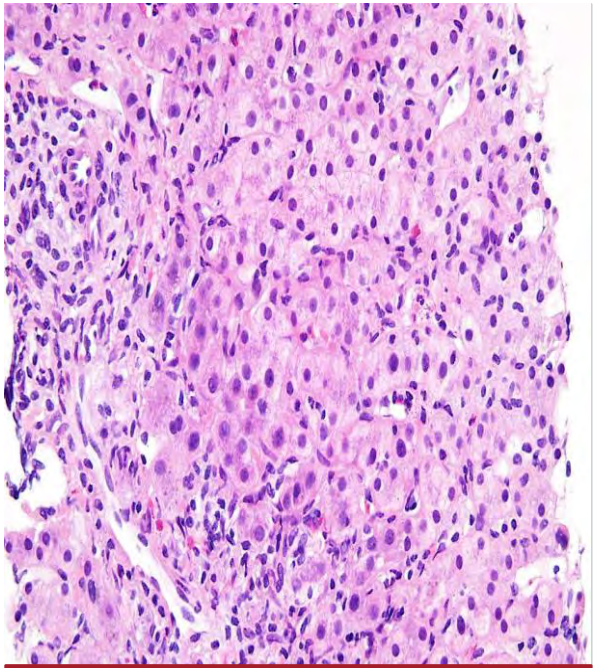


Colon — Tryptase IHC (40×)

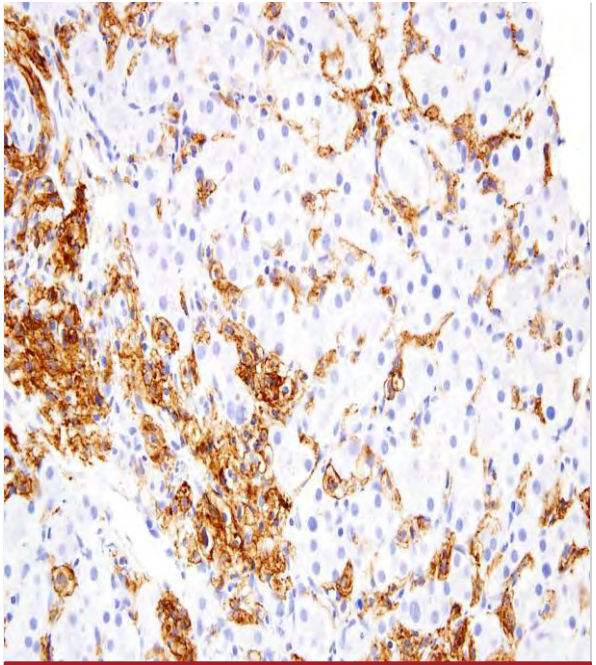
Widespread mucosal mast cell infiltration accounts for the chronic diarrhea, malabsorption, and weight loss seen in SM. Always biopsy with tryptase + CD25 staining.

Hepatic Involvement: Liver Biopsy Pathology

Mast cell infiltration of the liver confirms multi-organ involvement — a C-finding criterion. (provided by Dr. DeAngelo)



Liver — Tryptase IHC



Liver — KIT (CD117) IHC

Multifocal Mast Cell Aggregates in Bone Marrow

The major criterion: ≥15 mast cells in aggregates on BM biopsy

- Mast cells appear spindle-shaped or epithelioid on BM biopsy
- IHC markers for identification:
  - CD117 (KIT): expressed on all mast cells
  - Tryptase: specific for mast cells
  - CD25 ± CD2: aberrant expression in SM (not in normal MCs)
  - CD30: added in WHO 2022; useful when CD25/CD2 negative
- Flow cytometry: CD117+/CD25+ is the hallmark aberrant phenotype
- Dense paratrabecular and perivascular aggregates are typical

Pathology Pearls

1. Request CD25 IHC — not done routinely without clinical suspicion
2. Provide clinical history to pathologist; spindle MCs can be subtle
3. Send peripheral blood for KIT D816V ddPCR simultaneously with BM
4. BM may appear normal in early ISM — don't exclude without tryptase

1. Khoury JD, et al. Leukemia. 2022;36(7):1703-1719. 2. Pardanani A. Am J Hematol. 2019;94(3):363-377.

Section 4: Clinical Cases

Interactive Discussion Across the Disease Spectrum

Case 2: Presentation

75-year-old man | Fatigue, abdominal distention, lower extremity edema ×3 months

WBC	Hgb	Platelets	Tryptase
27 × 10^9/L	**8.2 g/dL**	**64 × 10^9/L**	**187 ng/mL**

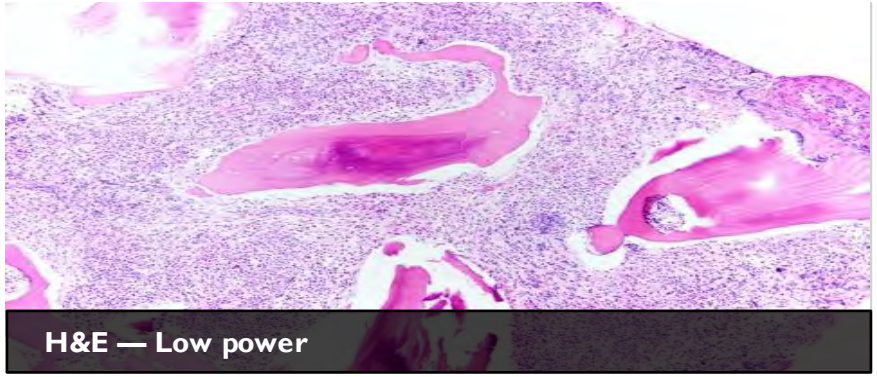
- CT: diffuse lymphadenopathy 2–3 cm, pleural effusion, ascites, splenomegaly
- **BM biopsy: hypercellular, 40% mast cells**
- Flow: MCs expressing CD117 with aberrant CD2 and CD25
- **NGS: KIT D816V + SRSF2, TET2, CUX1 mutations**

CT abdomen — ascites, splenomegaly (provided by Dr. Denagelo)

Discussion: What is the diagnosis? What subtype of SM? What is the best treatment approach?

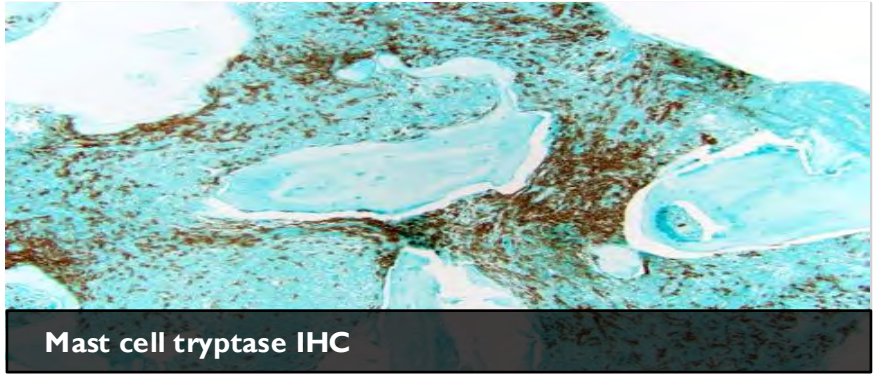
Case 2: Bone Marrow Pathology — 40% Mast Cells

H&E and IHC stains confirming hypercellular marrow with dense mast cell infiltration (provided by Dr. DeAngelo)

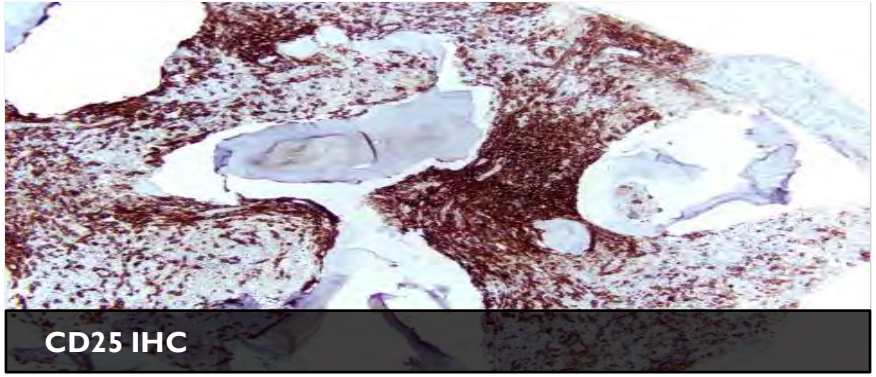


H&E — Low power

H&E — High power



Mast cell tryptase IHC



CD25 IHC

Case 2: Diagnosis & Outcome — SM-AHN (Advanced SM)

Diagnosis: SM with Associated Hematologic Neoplasm (SM-AHN) — Advanced SM

- Meets AdvSM criteria: SM-AHN (KIT D816V + SRSF2/TET2/CUX1 co-mutations)
- **Treatment: Avapritinib 200 mg daily (FDA-approved for AdvSM)**
- Response:
  - Ascites and hepatosplenomegaly resolved
  - Achieved complete remission (CR); BM in remission from SM
  - Tryptase normalized: 187 → 6 ng/mL (nl <11.5)
- Course: AHN transformed to AML (SM still in CR) → AML-directed therapy

Avapritinib in AdvSM EXPLORER / PATHFINDER

75%	ORR all evaluable pts
36%	CR/CRh in EXPLORER
30%	KIT D816V mol. remission
~14 mo	Median DOR

1. DeAngelo DJ, et al. Nat Med. 2021;27(12):2183-2191. 2. Gotlib J, et al. Nat Med. 2021;27(12):2192-2199.

Case 3: Long-Course SM-AHN — Treatment Sequence

46-year-old woman | Chronic diarrhea, weight loss, abdominal distension — 2006 presentation

2006	**Presentation** Tryptase 774, histamine 4777; BM >30% MCs; hepatosplenomegaly, esophageal varices, pan-colonic edema
2006+	**Midostaurin** Started on DFCI protocol. Weaned off TPN after 3 mos. GI symptoms resolved. Remained on treat,emt 12+ yrs.
~2018	**Progression** Progressed on midostaurin after ~10 years. Needed next-line therapy.
Next	**Discussion** What are options after midostaurin failure? Consider avapritinib or clinical trial.

Teaching Point: Midostaurin shows durable responses in AdvSM (ORR 60%, median OS 28.7 mo). Sequential KIT-targeted therapy is feasible after progression. (Expert Opinion)

Gotlib J et al. N Engl J Med. 2016;374(26):2530-2541.

Case 4: Indolent SM — Don't Underestimate the Burden

44-year-old male | Urticaria pigmentosa ×20 years | Tryptase 41.9 ng/mL

- **Spine compression fractures (T3, prior lumbar), osteoporosis, osteopenia**
- GI: GERD, R-sided abdominal pain, cramping, diarrhea with greasy foods/heat/stress/alcohol
- **Anaphylaxis: ×2 hornet stings; 2nd episode required 3 doses of epinephrine**
- Neuro: Brain fog, depression, difficulty concentrating, short-term memory impairment
- Dermatology: Urticaria pigmentosa increasing over time

ISM Management

Anti-mediator: H1+H2 antihistamines, cromolyn sodium, PPI, epinephrine auto-injector (mandatory)

Bone health: Bisphosphonates or denosumab, Ca^{2+}/Vit D, DEXA at diagnosis

KIT-targeted: Avapritinib (FDA-approved ISM 2022) for inadequate symptom control

ISM Teaching Points: (1) Prescribe epinephrine auto-injector to ALL patients. (2) Check DEXA at diagnosis. (3) ~75% of ISM patients require ≥4 drug classes. (4) Avapritinib FDA-approved for ISM with inadequate symptom control.

1. Jennings SV, et al. Immunol Allergy Clin North Am. 2018;38(3):505-525. 2. Hamilton MJ, et al. Front Allergy 2024;5:1401187

Section 5: Clinical Pearls & Practice Takeaways

Key Insights to Enhance Your Clinical Practice

Clinical Pearls: Enhancing SM Diagnosis in Practice

1

Check Tryptase Early

Order serum tryptase in any patient with unexplained anaphylaxis, osteoporosis, or cytopenias. Tryptase >20 ng/mL warrants full SM workup.

2

Tell the Pathologist

Provide clinical history with BM specimens. Request tryptase, CD117, CD25, CD30 IHC. Spindle-shaped MCs and paratrabecular aggregates can be subtle.

3

Prescribe Epinephrine

All patients with mastocytosis are at risk for anaphylaxis. Auto-injectable epinephrine is mandatory. Counsel on avoidance of triggers.

4

Use ddPCR for KIT D816V

Standard NGS detects only 28% of ISM cases in peripheral blood. Digital droplet PCR (ddPCR) detects up to 95% — request ddPCR specifically.

5

Don't Dismiss ISM Symptoms

72–85% of ISM patients have moderate-to-severe fatigue. >80% are limited in daily activities. ISM is NOT 'benign' — treat symptoms aggressively.

6

Refer Early to Specialist

Patients visit a median 3+ specialists over 9–12 years before diagnosis. Early referral with tryptase >20 ng/mL shortens the diagnostic odyssey.

Current KIT-Targeting Therapy Landscape (2026)

KIT inhibition is now a validated, FDA-approved strategy across the SM spectrum

Avapritinib	**FDA-approved AdvSM (2021) and ISM (2023)**	**1L+ in AdvSM (ASM, SM-AHN, MCL)** 200 mg/d starting dose; monitor plt, cognition, edema
Bezuclastinib	**In late-stage development**	Selective KIT D816V inhibitor; SUMMIT trial (nonAdvSM), APEX trial (AdvSM)
Elenestinib	**In late-stage development**	Selective KIT D816V inhibitor; HARBOR trial (ISM and SSM)
Midostaurin	**FDA-approved AdvSM (2017)**	**1L+ in AdvSM; less KIT-selective** ORR 60%, median OS 28.7 mo; 100 mg BID dosing
Imatinib	**FDA-approved 2006 (rare)**	**ASM lacking KIT D816V or unknown KIT status** Exceedingly rare indication; not active against D816V

1. Gotlib J, et al. N Engl J Med. 2016;374:2530-2541. 2. DeAngelo DJ, et al. Nat Med. 2021;27(12):2183-2191. 3. Gotlib J, et al. Nat Med. 2021;27(12):2192-2199. 4. Zhang J et al. J Aller Clin Immunol. 2026;157(2):AB171. 5. DeAngelo DJ et al. Blood 2024; 144 (Suppl 1): 659. 6. Tashi T et al Blood. 2023;142(suppl 1):76.

Treatment Works: Diagnosis Opens the Door

PATHFINDER Study — Avapritinib in Advanced SM: Rapid, Durable Resolution of Symptoms

- Advanced Systemic Mastocytosis-Symptom Assessment Form (AdvSM-SAF): Validated patient-reported outcome tool in AdvSM[a]

Baseline

Cycle 6 day 1

Baseline

Cycle 6 day 1

† Proper diagnosis enables access to targeted, life-changing therapy. Early recognition of SM is the critical first step.

1. Gotlib J, et al. Nat Med. 2021;27(12):2192-2199. (PATHFINDER trial) 2. Taylor F, et al. 2019 ISPOR EU [Poster PRO143].

Summary: Key Takeaways

1. SM is a clonal mast cell neoplasm driven by KIT D816V (~95% of cases). It is underdiagnosed — average time to diagnosis is 9–12 years.

2. Suspect SM in: unexplained anaphylaxis, unexplained osteoporosis, elevated tryptase, chronic urticaria/flushing, and unexplained cytopenias.

3. Diagnosis requires WHO criteria (1 major + 1 minor OR ≥3 minor). Order BM biopsy with CD25 IHC, KIT D816V by ddPCR, and serum tryptase.

4. Even ISM causes significant morbidity — fatigue, GI symptoms, anaphylaxis risk. All patients need epinephrine and bone health management.

5. FDA-approved KIT-targeted therapies are available: avapritinib and midostaurin. Other agents are under investigation: bezuclastinib and elenestinib.

6. Co-mutations (SRSF2, ASXL1, RUNX1) are high-risk prognostic markers — obtain comprehensive NGS panel in all newly diagnosed SM patients.

Systemic Mastocytosis:

Recognition, Diagnosis, and Clinical Management

Thank you for your participation in this CheckRare CME program.
We hope these insights enhance your clinical practice.

Daniel J. DeAngelo, MD, PhD
Chief, Division of Leukemia | Dana-Farber Cancer Institute
Professor of Medicine, Harvard Medical School | Boston, MA