DERMATOLOGICAL MANIFESTATIONS OF MAST CELL DISEASE

The Mastocytosis Society Patient/Caregiver Conference
Foster City-San Mateo, CA
May 1-3, 2019

Ana Mósca, M.D.
Pediatrician & Dermatologist

Municipal Jesus Hospital – Rio de Janeiro, Brazil
ALMA – Aliança Latino-Americana em Mastocitose

*No Conflicts of Interest to Declare
Mastocytosis

- Characterized by expansion of clonal mast cells in different organs
  - Caused by activating KIT mutations.

- The organs most frequently involved
  - Skin
  - Bone Marrow

- Traditionally, the disease is divided into:
  - Cutaneous Mastocytosis (CM)
  - Systemic Mastocytosis (SM).

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35-45.
Mastocytosis (CM) Forms

1. **(MPCM)** – MaculoPapular Cutaneous Mastocytosis also known as (UP) Urticaria Pigmentosa

1. **(DCM)** – Diffuse Cutaneous Mastocytosis

1. Mastocytoma of the skin
Maculopapular Cutaneous Mastocytosis (MPCM)

- Most adult patients have small (size), monomorphc spots

- usually associated with SM
  - most often Indolent Systemic Mastocytosis (ISM)

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology. Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35-45.
CM - Adult Onset

- (Rarely Occur) - Larger, polymorphic lesions
- Mastocytomas (Almost Never Occur)
- TMEP - telangiectasia macularis eruptiva perstans
  - Telangiectatic or fixed red macular lesions
    - chest, shoulders, neck, and upper back
    - also seen with maculopapular lesions.
  - Considered diagnosis of MPCM
TMEP - telangiectasia macularis
CM - Adult Onset

- Skin Lesions
  - They are greatly diverse and involve localized and disseminated forms

- Age
  - 20 – 35 years of age
  - 65 – 70 years of age (Late Onset)

- Type
  - small, round, brown or red monomorphic lesions

- Number
  - In beginning, fewer than 10. Evolves to almost universal coverage
  - (Possible) number and coverage corresponds with Systemic Involvement & Tryptase

- Locations:
  - Initiates on thighs, axilla, lower trunk
  - spreading to upper trunk, extremities & neck
Maculopapular Cutaneous Mastocytosis (MPCM)

• Children often present with polymorphism
• larger lesions of variable size and shape pediatric patient
• better prognosis

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology. Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35 - 45
Mastocytosis (CM)

• More than 80% of all patients with mastocytosis exhibit characteristic brown or red skin lesions

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology. *Journal of Allergy and Clinical Immunology*, Volume 137, Issue 1, 35-45
Darier’s sign (+)

- Important Clinical Sign
  - Pathognomonic Diagnosis
    - After mechanical stroking presents by showing urticaria in area of lesions (causes MC degranulation)

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology. Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35-45
Darier’s sign (+)

• A clearly positive Darier’s sign is an important diagnostic finding in patients with mastocytosis.
  • Adults – not always positive
  • Pediatric – always positive

• Important:
  • wait 48 hours after doing the Darier’s sign to perform skin biopsy
    • Friction causes MC degranulation

• After skin biopsy
  • Darier sign is common

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35 - 45
CM - Adult Onset

• Adult with MPCM not showing systemic involvement (Rarely Occurs)
  • Considered true MPCM
• MCPM found in patients with ISM & with advanced SM
  • CM found in SM with associated clonal hematologic non–mast cell lineage disease (SM-AHMCD) or aggressive SM (ASM)
• 95% of patients with ISM exhibit maculopapular skin lesions compared with around 50% of patients with advanced SM.
• <50% of patients with mast cell leukemia present with skin lesions
• Regression of skin lesions
  • Can occur in adults with non-advanced mastocytosis categories

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35 - 45
Mastocytosis

Adult Onset Mastocytosis

• Cutaneous lesions are usually associated with SM, most often indolent systemic mastocytosis (ISM)
• Chronic Condition
• Most have small sized and monomorphic lesions
• 80% carry KIT D816V mutation in exon 17

Pediatric Onset Mastocytosis

• CM without histologically evident involvement of other organs is found in the majority of pediatric patients.
• Spontaneous resolution of disease in adolescence
• Often present with large polymorphic lesions
• Only 35% express KIT D816V;
  • 40% express KIT mutations in exon 8,9 or 11
  • 25% no detectable KIT mutation

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35 - 45
Maculopapular Cutaneous Mastocytosis (MPCM)

Involvement in children is usually more extensive. Cutaneous blisters can be observed.
Blistering in Cutaneous Mastocytosis

Blistering of the skin lesions is seen **exclusively** in children younger than four years of age.
Anaphylaxis in CM

• Frequency:
  • 50% of adults
  • 10% of children

• In children, risk correlates with the severity of skin involvement and Tryptase levels

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35 - 45
Tryptase in CM

Adult Onset

• Levels may vary as according to number of lesions

• correlate with systemic involvement

Pediatric Onset

• Polymorphic lesions
  • tryptase levels are usually within the normal range
  • Sometimes, pronounced cutaneous lesions
    • but usually decrease within 1 to 2 year

• Monomorphc lesions
  • Trypase can be elevated
  • Can continue into adulthood
  • Can be systemic
Criteria for Cutaneous Involvement

1. **Major criterion** - a typical skin lesion and Darier’s sign

2. **Minor criterion** - a histologically confirmed infiltrate of mast cells in the dermis

3. **Minor criterion** - an activating KIT mutation at codon 816 in lesional skin
Maculopapular Cutaneous Mastocytosis (MPCM)
Maculopapular Cutaneous Mastocytosis (MPCM)
Forms of MPCM

- Nodules can present during infancy
- Transform into plaques around 5 to 10 years
- Macules after adolescence
- Disappearance around puberty in many cases (but not all)
- Nodules remain as atrophic lesions with wrinkles similar to anetoderma

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology. Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35 - 45
Forms of MPCM – “Peau orange” – Orange Peel Skin
Maculopapular Cutaneous Mastocytosis (MPCM)

- Variant form with yellow lesions
- Xanthelasmoid CM
Mastocytoma

• Common:
  • A single, elevated brown or yellow lesion.
  • Found early in life.
  • Itching is minimal.
  • Resolves spontaneously with age

• Occasional:
  • A few children may present with more than one lesion
  • Blistering of the lesion.

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology. Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35 - 45
Diffuse Cutaneous Mastocytosis (DCM)

- Symptoms Associated:
  - Itching
  - Blistering
  - Decreased blood pressure (hypotension)
  - Diarrhea
  - Gastrointestinal bleeding
  - Flushing (Reddening of the skin)
  - Anaphylactic shock
  - *(Not recommended testing for Darier’s sign)*
Diffuse cutaneous mastocytosis (DCM)

- Tryptase usually increased
- Most patients without systemic involvement
  - Often resolves with adolescence
  - Prolonged bleeding from skin wounds

Hartmann, Karin et al. Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma & Immunology; and the European Academy of Allergology and Clinical Immunology, Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, 35 - 45.
Diffuse Cutaneous Mastocytosis (DCM)

- Association with pachydermatous skin areas
- Generalized erythema, usually with thickened skin.
- Pronounced and persistent dermographism
- After minimal mechanical irritation.
Rio de Janeiro - Brazil

Thank you very much!

Guanabara's Bay

Pão de Açúcar

Corcovado