CASE REPORT

Brown Macules, Papules, and Nodules in A Filipino Infant: A Case Report of Polymorphic Maculopapular Cutaneous Mastocytosis

Krystel Angela A. Olano[1]*, Johannes F. Dayrit[1]

[1]Department of Dermatology, Research Institute for Tropical Medicine, Alabang, Muntinlupa City, Metro Manila, Philippines

Correspondence: Krystel Angela A. Olano; Department of Dermatology, Research Institute for Tropical Medicine, Alabang, Muntinlupa City, Metro Manila, Philippines; Email: krystelangela.a.olano@gmail.com

Received: 25 February 2025; Accepted: 30 May 2025; Published: 30 September 2025

Abstract: Polymorphic maculopapular cutaneous mastocytosis (pMPCM) is the most common form of cutaneous mastocytosis (CM) in children, characterized by polymorphic brown to red oval lesions, plaques, and nodules that often appear asymmetrically. Although primarily confined to the skin, it may present with a range of clinical manifestations. These lesions can be mistaken for other hyperpigmentation disorders, such as café-au-lait spots, drug eruptions, or idiopathic eruptive macular pigmentation. Here, we report a case of pMPCM in a Filipino infant, highlighting the diagnostic challenges and emphasizing the clinical, histopathological, and therapeutic aspects of the disease. This case illustrates practical diagnostic and clinical approaches that may aid clinicians in identifying pediatric mastocytosis, even in resource-limited settings where advanced testing is unavailable.

Keywords: Polymorphic maculopapular cutaneous mastocytosis; Mastocytosis in children; CD117 immunohistochemistry; Pediatric hyperpigmentation disorders

Introduction

Polymorphic maculopapular cutaneous mastocytosis (pMPCM) is the most common form of cutaneous mastocytosis (CM) in children, typically appearing within the first few weeks to six months of life as brown-red macules, plaques, and nodules of varying shapes and sizes. Unlike the monomorphic variant, which appears later in childhood with smaller lesions predominantly on the trunk, pMPCM is more variable in presentation. It involves clonal mast cell proliferation confined to the skin, with a generally favorable prognosis. Mutations of the KIT gene have been associated with CM, but studies have found them to be less common in children than in adults [1]. Lesions may change over time, with blistering commonly observed in infancy and typically resolving by early childhood. While most cases regress by adolescence, some may evolve into residual anetoderma-like lesions following lesion involution [2].

From 2011 to 2023, the Philippine Dermatological Society Health Information Systems recorded only four cases of CM in infants

under one year of age, and 24 cases in children aged 1 to 10 years. None were specifically identified as pMPCM, highlighting the rarity of this variant in Filipino children. This report presents a case of pMPCM in a Filipino infant, emphasizing the clinical, histopathological, and therapeutic aspects, as well as the diagnostic challenges posed by limited access to diagnostic tools such as serum tryptase testing, immunohistochemistry, and genetic analysis in the Philippines.

Case Presentation

A 1-year-and-9-month-old Filipino male presented with widespread cutaneous lesions, including macules, patches, papules, and plaques. He was born full-term via spontaneous vaginal delivery but was admitted for neonatal sepsis due to prolonged rupture of membranes. At 4 months of age, brown macules appeared on his extremities, gradually progressing into papules and plaques by the age of one, involving the face, trunk, and limbs. Some lesions developed into bullae, which ruptured and left residual scars. The patient had been prescribed cetirizine 5 mg once daily; however, this was associated with a further increase in lesions, although these typically subsided within a few days. No other triggers were identified, and an allergy workup was not performed due to limited accessibility. No topical treatments were used at the time. The patient experienced an episode of acute gastroenteritis with mild dehydration at 7 months of age but had no history of systemic allergic reactions, anaphylaxis, or symptoms suggestive of systemic mast cell activation. There was no family history of similar dermatologic conditions.

Dermatologic examination revealed multiple brown macules, patches, papules, plaques, vesicles, and bullae—some of which were ruptured—with residual scarring over the face, trunk, and limbs, as shown in **Figure 1**. The Darier sign was positive, indicating mast cell mediator release, and is considered pathognomonic for CM [2]. The presence of a positive Darier sign, along with the characteristic skin lesions, fulfills the major diagnostic criteria for CM [3]. No hepatosplenomegaly, lymphadenopathy, or other systemic abnormalities were observed.

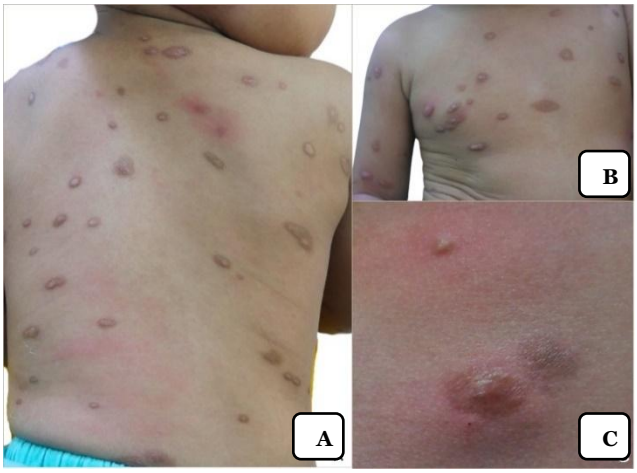

Figure 1. Cutaneous examination showing: (A) hyperpigmented and erythematous macules, patches, and plaques with a positive Darier's sign; (B) hyperpigmented and erythematous macules, patches, and plaques; and (C) a papule and a ruptured bulla on an erythematous background.

Hematoxylin and eosin (H&E) staining and immunohistochemistry were performed on the skin biopsy sample. The findings revealed a dense, pandermal infiltrate of round mast cells with predominant perimembrane CD117 staining, as shown in **Figure 2**, confirming the diagnosis of pMPCM. Additional immunohisto-chemical markers, such as CD2, CD25, and CD30, were not assessed, as CD2 and CD25, in particular, are not readily available in the Philippines. Laboratory investigations, along with abdominal ultrasonography, ruled out extracutaneous involvement.

The patient was treated with loratadine 5 mg taken once daily, desonide cream 0.05% applied twice daily to macules and patches, and clobetasol cream 0.05% applied twice daily to plaques and nodules. As previously noted, the lesions flared with cetirizine 5 mg, prompting a

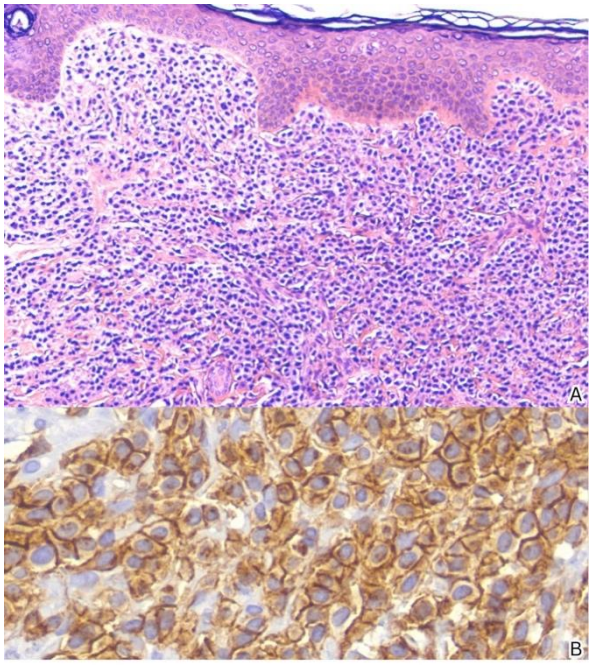

Figure 2. (A) Histopathology showing very dense infiltrate of round shape mast cells (H & E x 200) and (B) predominant perimembrane c-KIT immunohistochemical staining of the mast cells (CD 117 x 400).

switch to loratadine. After 8 months, the patient showed significant improvement, with reduced lesion size and fewer episodes of blistering. He remains under close monitoring through monthly skin examinations and assessments for signs of systemic involvement. At 2 years and 5 months of age, the patient exhibits residual hyperpigmentation with no new lesions. A speech delay has also been noted, warranting further evaluation.

Discussion

pMPCM presents a diagnostic challenge due to its diverse clinical manifestations and potential overlap with other dermatologic conditions, especially disorders of hyperpigmentation in children such as café au lait macules, drug eruptions and idiopathic eruptive macular pigmentation.

Serum tryptase testing and peripheral blood KIT mutation analysis (e.g., KIT D816V) are recommended tools for assessing disease burden and the risk of systemic involvement in children with CM. Elevated tryptase levels (>20 ng/mL) may indicate an increased mast cell burden, systemic involvement, or other conditions such as anaphylaxis or hereditary alpha-tryptasemia. Detection of the KIT D816V mutation helps identify patients who may require further evaluation and monitoring. Bone marrow (BM) biopsy is reserved for those presenting with organomegaly, significant peripheral blood abnormalities, markedly elevated or rising tryptase levels, or gastrointestinal symptoms, to confirm systemic mastocytosis or to detect other myeloid neoplasms. Elevated tryptase levels alone are insufficient to warrant a BM biopsy for further confirmation of the diagnosis [2-4].

Given the limited availability of serum tryptase testing and genetic analysis locally, clinicians must rely on alternative diagnostic strategies to confirm the diagnosis of pMPCM. This underscores the critical importance of comprehensive clinical assessment and histopathologic evaluation in establishing the diagnosis. Since pediatric mastocytosis is typically limited to the skin and lacks systemic or hematologic involvement, diagnosis can be made based on clinical assessment. This includes careful evaluation of lesion morphology, number, size, color, distribution, and the presence of a positive Darier's sign [3]. The characteristic Darier sign—a wheal-and-flare reaction elicited by rubbing a lesion—serves as an important clinical clue for the diagnosis of CM [2].

When available, histopathologic stains such as toluidine blue, Giemsa, and CD117 immunohistochemistry can confirm mast cell infiltration and further support the diagnosis [4]. Histologically, pMPCM typically demonstrates a dense infiltrate of round or cuboidal mast cells, whereas monomorphic CM is characterized by fewer, spindle-shaped mast cells. Staining with toluidine blue, Giemsa, and antibodies against CD117 or tryptase aids in identifying subtle mast cell infiltrates. CD2 and CD25—markers associated with systemic mastocytosis—are often

negative in cutaneous mast cells. CD30, although frequently positive in childhood-onset CM and systemic mastocytosis, does not correlate with clinical subtype or disease progression [4].

Most cases of childhood pMPCM have a favorable prognosis [5], with spontaneous regression of lesions typically occurring by puberty [6]. However, the presence of blistering during infancy, widespread lesion distribution, and systemic symptoms may indicate a more severe disease course [7]. In the present case, the absence of extracutaneous involvement suggests a cutaneous-limited form of the disease, with symptomatic management remaining the primary therapeutic goal.

Management of pMPCM centers on minimizing mast cell degranulation, alleviating pruritus, and avoiding known triggers such as heat, friction, and certain medications—including NSAIDs, dextromethorphan, opioids, and muscle relaxants [4]. This is because, in mastocytosis, mast cell activation—often via IgE receptors or triggered by stimuli like heat, stress, or specific drugs—leads to the release of mediators responsible for symptoms such as pruritus, flushing, and blistering. Therefore, avoiding these triggers is essential to minimize mast cell degranulation and reduce symptom flares [2]. Other treatment options include oral H1 antihistamines to relieve itching and flushing, H2 antihistamines to manage gastrointestinal symptoms [6], and oral cromolyn sodium for gastrointestinal involvement [4]. In more severe cases, such as diffuse bullous disease or life-threatening forms, oral methoxypsoralen combined with long-wave ultraviolet A (PUVA) therapy may be considered [8]. Additionally, high-potency topical corticosteroids and calcineurin inhibitors can help reduce cutaneous inflammation [4,9].

Long-term follow-up is essential for monitoring disease progression and identifying potential systemic involvement, as approximately 10% of pediatric mastocytosis cases persisting beyond adolescence may develop into systemic disease. Risk factors warranting further evaluation include monomorphic lesion morphology, persistence of cutaneous lesions after puberty, late onset, lymphadenopathy, hepatosplenomegaly, and abnormal laboratory findings [9].

In this case, the lesions flared following the intake of cetirizine during a previous treatment course. Cetirizine contains methyl parahydroxybenzoate (methyl paraben), which has been shown to sensitize mast cells by increasing intracellular calcium levels, thereby promoting degranulation [10]. Additionally, it activates transient receptor potential ankyrin 1 (TRPA1) channels, exacerbating neurogenic inflammation and pruritus [11]. Similar to certain local anesthetics, parabens may trigger mast cell activation and inflammation [12], likely explaining the patient's paradoxical lesion flare despite antihistamine therapy.

A speech delay was also noted in this patient, prompting further evaluation in light of reports suggesting potential neurodevelopmental impacts in pediatric CM. Although a direct causal relationship has not been established, some cases have reported motor and intellectual delays associated with GNB1 mutations [13], as well as MRI findings indicative of delayed myelination [14]. These observations raise the possibility of neurodevelopmental involvement in a subset of patients. However, in this case, no neuroimaging or genetic testing has been performed to date, underscoring the need for further assessment.

Conclusion

This case highlights the polymorphic presentation of CM in a Filipino infant—an underreported population—underscoring the importance of recognizing its diverse morphology to ensure accurate diagnosis and management. Despite a delayed diagnosis at 1 year and 9 months of age, individualized treatment resulted in significant clinical improvement, emphasizing the importance of

tailored care even when diagnosis is not made during early infancy. The unexpected exacerbation of lesions with cetirizine intake also brings attention to the potential impact of excipients in pediatric patients with mast cell disorders. Additionally, the observed speech delay raises important questions about possible neurodevelopmental associations, warranting further investigation.

This case demonstrates that an accurate diagnosis of pediatric CM is achievable even in resource-limited settings through detailed clinical assessment, recognition of characteristic lesions, and histopathologic confirmation, highlighting the critical role of clinical expertise. Furthermore, this case contributes to the limited local data on pediatric mastocytosis and underscores the need for improved access to diagnostic tools, as well as longitudinal studies to better understand clinical outcomes, refine diagnostic criteria, and guide evidence-based management across diverse pediatric populations.

Acknowledgement

Special thanks to the co-author of this case report, Dr. Johannes F. Dayrit, for his invaluable guidance and encouragement throughout the preparation of this manuscript. I also extend my sincere gratitude to Dr. Antonio Torrelo (Niño Jesús University Children's Hospital, Madrid, Spain) for his expert contribution to the diagnostic evaluation.

Potential Conflict of Interest

The authors declare no potential conflicts of interest.

References

1. Nemat K, Abraham S. Cutaneous mastocytosis in childhood. Allergologie Select. 2022;6:1-10.
2. Ługowska-Umer H, Czarny J, Rydz A, Nowicki RJ, Lange M. Current challenges in the diagnosis of pediatric cutaneous mastocytosis. Diagnostics. 2023;13(23):3583.
3. Giona F. Pediatric mastocytosis: an update. Mediterranean Journal of Hematology and Infectious Diseases. 2021;13(1):e2021069.
4. Schaffer JV. Pediatric mastocytosis: recognition and management. American Journal of Clinical Dermatology. 2021;22(2):205-20.
5. Wiechers T, Rabenhorst A, Schick T, Preussner LM, Förster A, Valent P, et al. Large maculopapular cutaneous lesions are associated with favorable outcome in childhood-onset mastocytosis. Journal of Allergy and Clinical Immunology. 2015;136(6):1581-90.e3.
6. Hartmann K, Escribano L, Grattan C, Brockow K, Carter MC, Alvarez-Twose I, 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. 2016;137(1):35-45.
7. Brockow K, Ring J, Alvarez-Twose I, Orfao A, Escribano L. Extensive blistering is a predictor for severe complications in children with mastocytosis. Allergy. 2012;67(10):1323-4.
8. Escribano L, García-Belmonte D, Hernández-González A, Otheo E, Núñez-Lopez R, Vázquez JL, et al. Successful management of a case of diffuse cutaneous mastocytosis with recurrent anaphylactoid episodes and hypertension. Journal of Allergy and Clinical Immunology. 2004;113(2 Supplement):S335.
9. Sandru F, Petca RC, Costescu M, Dumitraşcu MC, Popa A, Petca A, et al. Cutaneous mastocytosis in childhood—update from the

literature. Journal of Clinical Medicine. 2021;10(7):1474.
10. Fukugasako S, Ito S, Ikemoto Y. Effects of methyl p-hydroxybenzoate (methyl paraben) on Ca2+ concentration and histamine release in rat peritoneal mast cells. British Journal of Pharmacology. 2003;139(2):381-7.
11. Fujita F, Moriyama T, Higashi T, Shima A, Tominaga M. Methyl p-hydroxybenzoate causes pain sensation through activation of TRPA1 channels. British Journal of Pharmacology. 2007;151(1):134-41.
12. Rama TA, Castells M. Triggers of anaphylaxis in mastocytosis patients: evidence of the current drug-avoidance recommendation. Current Treatment Options in Allergy. 2023;10(4):442-57.
13. Szczałuba K, Biernacka A, Szymańska K, Gasperowicz P, Kosińska J, Rydzanicz M, et al. Novel GNB1 de novo mutation in a patient with neurodevelopmental disorder and cutaneous mastocytosis: Clinical report and literature review. European Journal of Medical Genetics. 2018;61(3):157-60.
14. Watanabe Y, Morichi S, Takamatsu T, Ito T, Yamanaka G, Yusuke W, et al. Pediatric Cutaneous Mastocytosis with Motor and Intellectual Delay. Cureus. 2023;15(2):e34536.