SPMC JHCS

CASE REPORT

Urticaria pigmentosa in a 9-month-old male: case report

Brice P Serquiña,[1] Niña A Gabaton[1]

[1]Department of Dermatology, Southern Philippines Medical Center, JP Laurel Ave, Davao City, Philippines

Correspondence
Brice P Serquiña,
briseisqna@gmail.com

Received
5 April 2022

Accepted
24 March 2023

Published online
31 March 2023

Cite as
Serquiña BP, Gabaton NA. Urticaria pigmentosa in a 9-month-old male: case report. *SPMC J Health Care Serv.* 2023;9(1):3. http://n2t.net/ark:/76951/jhcs8mj38s

ABSTRACT

Urticaria pigmentosa (UP) is the most common form of cutaneous mastocytosis in children. It can be diagnosed clinically, based on the appearance of numerous brownish macules and papules that are symmetrically distributed, mostly on the trunk and the extremities. Skin biopsy is helpful in establishing the diagnosis. Treatment options generally include antihistamines and/or topical corticosteroids. In most cases, pediatric UP tends to disappear spontaneously before puberty. We present the case of a 9-month-old male with a history of multiple brownish patches and plaques, which started when he was four months old. He was diagnosed with UP based on clinical and histopathologic findings, and was prescribed oral antihistamines and emollients for symptomatic treatment.

Keywords. cutaneous mastocytosis, Darier's sign, mast cell degranulation, skin biopsy, histopathology

INTRODUCTION

Urticaria pigmentosa (UP), the most common manifestation of pediatric cutaneous mastocytosis (CM), is generally a benign disease, commonly presenting as erythematous or brown macules, patches and plaques. CM can present as diffuse cutaneous lesions, mastocytomas, or UP.[1-3] UP is caused by various activating mutations in the KIT gene (or the proto-oncogene c-KIT). It is associated with Darier's sign and cutaneous symptoms related to mast cell mediators, such as pruritus, flushing, etc.[1 2] Darier's sign, which is the appearance of a wheal after stroking or rubbing a skin lesion, is pathognomonic of CM.[2 4] Unlike adult forms of mastocytosis, UP rarely has systemic involvement in children.[1] In Southern Philippines Medical Center, a tertiary hospital in Davao City, Philippines, 18 cases of UP were recorded from 2010 to 2020.[5]

The management of UP aims to provide symptomatic relief from pruritus and avoid triggers that can lead to mast cell degranulation.[6] Patients are advised to avoid mast cell degranulation triggers such as spicy foods, dairy, fermented products, alcohol, systemic anesthetic agents, anticholinergic preparations, aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), narcotics, and polymyxin B sulfate.[6 7] Elevated mast cell number during an allergic reaction explains the much higher prevalence of anaphylaxis, which can be severe or fatal at times, among patients with mastocytosis than in the general population.[8] Anaphylaxis is rare in children with UP, unless they have skin lesions affecting larger areas of their skin. However, up to 50% of adults with UP may develop anaphylaxis over their lifetime.[9] Patients can benefit from the chronic administration of H1 antihistamines, which can help reduce cutaneous symptoms. In some cases, a potent topical corticosteroid may be applied under occlusion for 8-12 weeks to alleviate symptoms, although this may not be practical for lesions covering large surface areas.[6]

This case report describes a 9-month-old male who presented with a sudden onset of multiple hyperpigmented macules and plaques during his fourth month of life. The patient was eventually diagnosed with UP and was treated with oral antihistamines and emollients.

CLINICAL FEATURES

A 9-month-old male patient presented at our outpatient clinic with multiple skin lesions on his face, trunk, and extremities. The

IN ESSENCE

Urticaria pigmentosa (UP) is the most common presentation of cutaneous mastocytosis in children that can occur at any age, sex, and race. Diagnosis must rule out systemic involvement and be confirmed by a skin biopsy with special stain to highlight mast cell infiltrates.

In this case report, we describe the case of a 9-month-old male who presented with a sudden onset of multiple brownish macules and patches that began at 4 months old.

The patient's symptoms of pruritus were adequately controlled after a two-year course of symptomatic treatment with antihistamines and hypoallergenic skin care products.

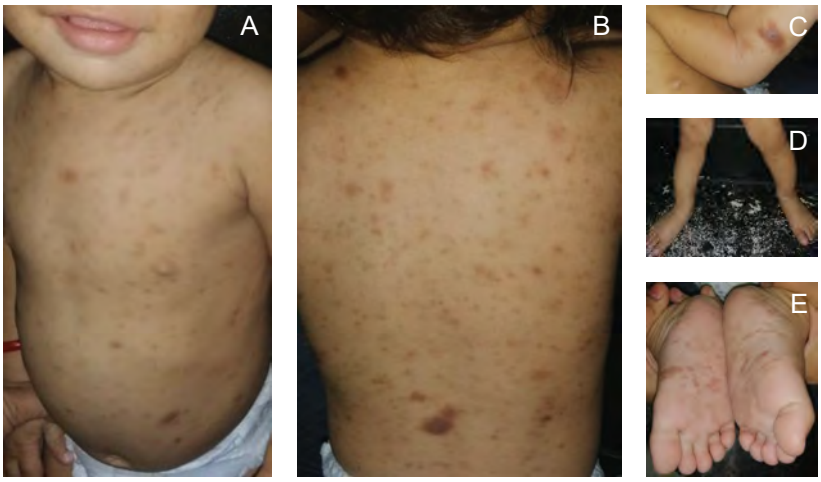

Figure 1 Multiple well-defined, irregularly-shaped, brown macules, patches and plaques on the face (A), anterior and posterior truncal areas (A,B), upper extremities and lower extremities (C,D), and soles (E).

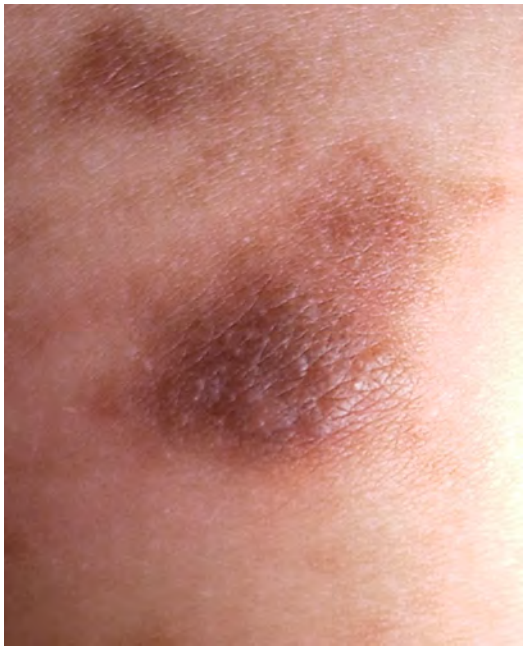

Figure 2 Positive Darier's sign, elicited a few minutes after stroking the skin lesion with a blunt object.

lesions started to appear on his left arm suddenly 5 months prior to the consultation. Some of the lesions observed during onset were flat, brownish discolorations measuring around 0.5 centimeters (cm) in size, while others were reddish and raised, potentially measuring at least 1 cm in size. The patient experienced occasional itching and flushing upon exposure to warm environments in association with these lesions. Two weeks after the skin lesions first appeared, they began to spread to the patient's face, trunk, and extremities, which prompted the patient's parents to seek consultation with a pediatrician. The pediatrician prescribed cetirizine and a hypoallergenic bath soap to manage the cutaneous symptoms, but despite being medicated for over 4 months, the patient's condition did not improve. This prompted the patient to seek further consultation with our department.

The patient did not have fever, cough, colds, or any symptoms related to the cardiac, gastrointestinal, and genitourinary systems. There were no signs of extracutaneous organ involvement. The patient's developmental milestones were at par with his age. There were no similar lesions or known skin conditions in the family.

On physical examination, the patient was alert, active, and had no fever. Multiple, well-defined brown macules, patches, and plaques were observed on the patient's forehead, chin, jaw, neck, anterior and posterior trunk, as well as on both upper and lower extremities, including the palms and soles, covering approximately 68% of the total body surface area. The lesions had irregular shapes and varied in size, ranging from 4 millimeters (mm) to 4 cm in diameter (Figure 1). Upon stroking the patient's lesional skin with a fingernail, wheal formation was observed, indicating a positive Darier's sign (Figure 2). The patient had no dysmorphic features, and the rest of the physical examination findings were unremarkable.

Given the patient's characteristic skin lesions, we were already considering a diagnosis of CM, most probably UP. When the patient exhibited a positive Darier's sign, we eliminated other possible diagnoses, such as Peutz-Jeghers syndrome, neurofibromatosis I, postinflammatory hyperpigmentation, and idiopathic eruptive macular pigmentation, because these conditions do not present with Darier's sign.

DIAGNOSTIC APPROACHES

The diagnosis of UP is established based on characteristic skin findings, as well as skin punch biopsy results that demonstrate increased mast cell infiltrates in the dermis.[2] Serum tryptase levels above 20 ng/mL is a criterion for diagnosing systemic involvement in CM.[10] To confirm our initial diagnosis and rule out possible systemic involvement, we requested a laboratory and histopathological work-up. To determine mast cell burden and risk of systemic involvement,[11] we ordered a serum tryptase

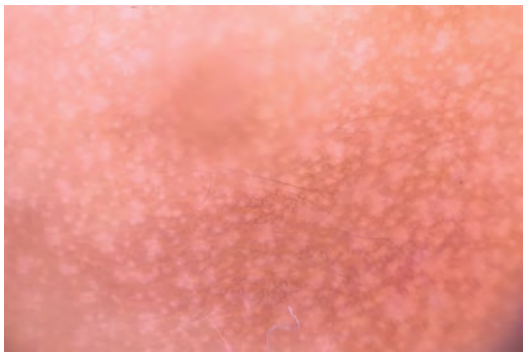

Figure 3 Dermoscopy (x10) of skin lesion showing dark brown pigmentation arranged in a reticular pattern.

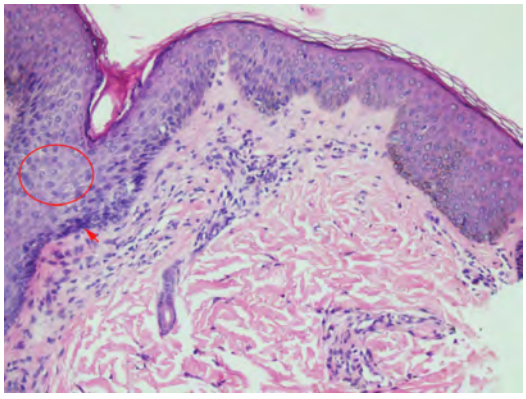

Figure 4 Histopathology of the skin lesion at high power field (hematoxylin-eosin stain, x40), demonstrating a diffuse proliferation of mast cells spanning the dermis. There is basal cell layer hyperpigmentation (red arrow) and mild spongiosis (red ring) in the epidermis.

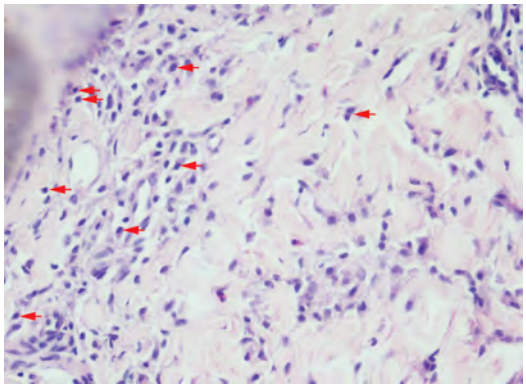

Figure 5 Moderate dense superficial and perivascular inflammatory infiltrates composed of mononuclear cells (red arrows) in the dermis (hematoxylin and eosin, x400).

test, which showed a normal value of 9 μg/L. The patient had additional tests to rule out systemic involvement, which included a complete blood count, liver and kidney function tests, urinalysis, and chest radiography. All the test results were within normal limits.

On dermoscopy of a representative macule, we observed a brown pigment network throughout the lesion (Figure 3). We took a skin punch biopsy sample using a 4-mm instrument on the lesional skin on the patient's right posterior trunk, where the mast cell infiltrates would most likely be found. Histopathology revealed mild spongiosis and basal layer hyperpigmentation in the epidermis, and diffuse proliferation of mast cells in the dermis (Figure 4). The upper dermis had moderately dense superficial and perivascular inflammatory infiltrates consisting of mononuclear cells (Figure 5). Mast cells appeared round in shape, with centrally-located nuclei, taking a "fried-egg" appearance (Figure 6). Immunohistochemistry staining with CD117 (Figure 7) revealed a cluster of brown-staining mast cells in the upper dermis, indicating a positive test result.

THERAPEUTIC APPROACHES

We started the patient on cetirizine oral drops, starting at a dose of 0.25 milligram/kilogram per day, administered at bedtime, whenever pruritus was experienced. We explained the risk of anaphylaxis to the patient's parents. They were counseled regarding the avoidance of certain foods, situations, and medications which can trigger the appearance of cutaneous symptoms. We also advised the parents to use a hypoallergenic bath soap and a mild emollient on the patient.

OUTCOME

The patient came for a follow-up consultation after two years. We observed that the old lesions had flattened out, and there were new inactive macules and patches on the face, trunk, and extremities. During the past two years, the patient's symptoms, such as pruritus, were effectively managed with cetirizine, as well as the hypoallergenic bath soap and emollient that were prescribed.

DISCUSSION

A 9-month-old male infant presented with a 5-month history of brownish macules, patches, and plaques that first appeared on his left arm, and subsequently spread to various parts of his body, including the face, neck, trunk, extremities, palms, and soles. The diagnosis of UP was confirmed by clinical presentation and histopathologic findings. Symptomatic treatment with anti-

histamines and hypoallergenic skin care products was administered for two years, resulting in adequate control of pruritus.

Mastocytosis can occur at birth or at any age, regardless of race or sex. In pediatric cases of CM, 10-15% present with solitary cutaneous mastocytomas,[12] 65-90% with UP,[13] and 5% with diffuse cutaneous involvement.[14] Mastocytosis has a global incidence of 1 in 8000 among patients aged 6 months to 2 years.[3 5 15-19] Most patients do not have a family history of mastocytosis, and only a few familial cases have been reported.[2] At the time we saw our patient—five months after the initial onset of cutaneous symptoms—his laboratory work-up results indicated no systemic involvement, and the histopathology results from a skin biopsy was consistent with UP.

Mast cells come from the bone marrow as agranular, undifferentiated, KIT+ (CD117) pluripotent progenitor cells. KIT is the protein product of the proto-oncogene c-KIT found in the cell membrane of mast cells, melanocytes, primitive hematopoietic stem cells, etc.[5] UP is caused by various activating mutations in the KIT gene.[2 20] Mutations in c-KIT lead to integral activation of KIT causing mast cell proliferation and development. When patients with UP are exposed to mast cell triggers, specific mediators like histamine, eicosanoids, prostaglandins, leukotrienes, heparin, proteases, and cytokines are produced.[2 5] The pathologic increase of mast cells, and their mediators, in the papillary dermis produce the cutaneous symptoms of CM in our patient. After stroking the patient's skin lesion with a blunt object, a wheal formation was observed, which may be attributed to the release of leukotrienes and histamine from cutaneous mast cells.[20] These cells also induce proliferation of melanocytes and production of melanin resulting in the appearance of the brownish pigment network on dermoscopy.[21]

The diagnosis of UP is mainly clinical, with a positive Darier's sign present in the majority of cases.[22] This sign is more pronounced in children than in adults due to the high concentration of mast cells in pediatric skin lesions.[2 4] Our patient presented with a positive Darier's sign, which strongly suggested the diagnosis of UP based on the characteristic and distribution of the lesions. To confirm the diagnosis and aid in further subclassification, we performed dermoscopy, which is a valuable tool for differentiating between melanocytic and non-melanocytic lesions.[23] In UP and in some cases of solitary cutaneous mastocytoma, dermoscopic findings show a brown pigment network throughout the lesion.[24] Skin biopsy is required to confirm the diagnosis.[2] With our patient's skin biopsy results showing an increased amount of mast cells in the dermis—a hallmark finding of UP—as well the characteristic skin lesions and positive Darier's sign, we were able to confirm our initial diagnosis of UP.

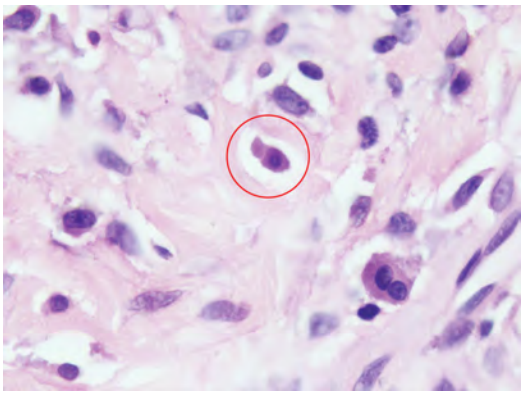

Figure 6 Mast cells with centrally-located nuclei, producing a distinctive "fried-egg" appearance (hematoxylin and eosin, x1000).

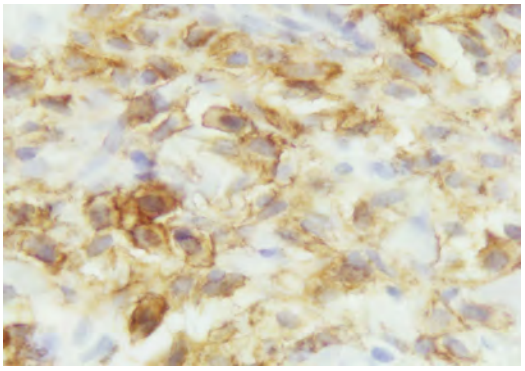

Figure 7 Immunohistochemical staining showing CD117-positive dermal mast cells (x1000).

UP is expected to persist from childhood to adolescence, and then fade away eventually. However, the persistence of lesions and recurrent symptoms (i.e., abdominal pain, diarrhea, serum tryptase greater than 20 µg/L, elevated liver enzymes, abnormal complete blood count) may indicate possible systemic involvement warranting referral to a hematologist for possible bone marrow biopsy.[25] The management of UP mainly involves supportive care. We counseled the patient's family on mast cell degranulation

triggers, provided symptomatic treatment (e.g., itch, flushing), and advised regular follow-up consultations to monitor for any extracutaneous or systemic involvement.

The prognosis of pediatric UP is related to the patient's age of onset. Symptoms of UP may partially or completely resolve by adolescence in 55 to 90% of patients when the disease develops before the age of 10. However, when UP develops after the age of 10, symptoms continue into adulthood in 90% of patients. There is also a greater risk for systemic involvement in 15 to 30% of pediatric patients when UP persists until adulthood.[7 13] Our patient developed UP at the age of four months, and he also presented with a normal baseline tryptase level and generally benign symptoms, indicating a good prognosis.

We saw a male infant who developed multiple skin lesions on his limbs, trunk, and face starting when he was 4 months old. The patient visited our outpatient clinic four times for diagnostic tests, procedures, and treatment. We prescribed an antihistamine, hypoallergenic soap, and emollient for symptomatic management, which has shown adequate control of symptoms after two years. While UP is generally benign, it is crucial for clinicians to be knowledgeable and well-trained to provide substantial support and education to the patients and their families.

Contributors
BPS and NAG contributed to the diagnostic and therapeutic care of the patient in this report. All of them acquired relevant patient data, and searched for and reviewed relevant medical literature used in this report. BPS wrote the original draft, performed the subsequent revisions. All approved the final version, and agreed to be accountable for all aspects of this report.

Acknowledgments
We would like to acknowledge the following consultants from the Department of Dermatology in Southern Philippines Medical Center: Dr Bryan Edgar K Guevara for sharing his expertise in reading and interpreting the histopathology slides of the patient; and Dr Rea T Dapiton and Dr Anna Cristina L Cuenca, our seniors, for helping us in the diagnosis and management of the patient.

Patient consent
Obtained

Reporting guideline used
CARE Checklist
(http://www.care-statement.org/downloads/CAREchecklist-English.pdf)

Article source
Submitted

Peer review
External

Competing interests
None declared

REFERENCES

1. 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. J Allergy Clin Immunol. 2016 Jan;137(1):35-45.

2. Macri A, Cook C. Urticaria Pigmentosa. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482503/?fbclid=IwAR3Zg6VounjmF4xLBJpwFVkHyG6qabd0-EB4tjZqwQgcoPqRGuevGc4A0LI.

3. Allison MA, Schmidt CP. Urticaria pigmentosa. Int Journ Dermatol. 1997 May;36(5):321-325.

4. Southern Philippines Medical Center. Southern Philippines Medical Center Hospital Information System. Davao: Southern Philippines Medical Center.

5. Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, et al. Fitzpatrick's Dermatology. 9th ed. New York: Mcgraw Hill; 2019.

6. Habashy J, Robles DT. Mastocytosis Treatment & Management. 2020 Sep 16 [cited 2023 Mar 28]. In: Medscape. New York: Medscape. c1994-2023. Available from: https://bit.ly/3nylJ5s.

7. Müller UR, Haeberli G. The problem of anaphylaxis and mastocytosis. Curr Allergy Asthma Rep. 2009 Jan;9(1):64-70.

8. British Association of Dermatologists. Urticaria pigmentosa. [cited 2023 Mar 28]. In: British Association of Dermatologists. London: British Association of Dermatologists. c2018. Available from: https://bit.ly/3M51zLC.

9. Lange M, Zawadzka A, Schrörs S, Słomka J, Ługowska-Umer H, Nedoszytko B, Nowicki R. The role of serum tryptase in the diagnosis and monitoring of pediatric mastocytosis: a single-center experience. Postepy Dermatol Alergol. 2017 Aug;34(4):306-312.

10. Seth N, Chinen J, Buheis MG, Chan AJ, Hunt RD, Tuano KTS. Serum Tryptase Levels in 114 Pediatric Patients with Cutaneous Mastocytosis. J Allergy Clin Immunol. 2018 Feb;141(2).

11. Leung AKC, Lam JM, Leong KF. Childhood Solitary Cutaneous Mastocytoma: Clinical Manifestations, Diagnosis, Evaluation, and Management. Curr Pediatr Rev. 2019;15(1):42-46.

12. Hu JC, Takahashi S. Mastocytosis. In: Schwarzenberger K, Werchniak AE, Ko CJ, editors. General Dermatology. Amsterdam: Elsevier; 2009.

13. Nemat K, Abraham S. Cutaneous mastocytosis in childhood. Allergol Select. 2022 Jan 5;6:1-10.

14. Lange M, Niedoszytko M, Renke J, Gleń J, Nedoszytko B. Clinical aspects of paediatric mastocytosis: a review of 101 cases. J Eur Acad Dermatol Venereol. 2013 Jan;27(1):97-102.

15. Méni C, Bruneau J, Georgin-Lavialle S, Le Saché de Peufeilhoux L, Damaj G, Hadj-Rabia S, et al. Paediatric mastocytosis: a systematic review of 1747 cases. Br J Dermatol. 2015 Mar;172(3):642-51.

16. CAPLAN RM. The natural course of urticaria pigmentosa. Analysis and follow-up of 112 cases. Arch Dermatol. 1963 Feb;87:146-57.

17. Heide R, Tank B, Oranje AP. Mastocytosis in childhood. Pediatr Dermatol. 2002 Sep-Oct;19(5):375-81.

18. Jaffe ES, Harris NL, Stein H, Vardiman JW. World Health Organization Classification of Tumours, Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. Lyon: IARC Press; 2001.

19. Castells M, Metcalfe DD, Escribano L. Diagnosis and treatment of cutaneous mastocytosis in children: practical recommendations. Am J Clin Dermatol. 2011 Aug 1;12(4):259-70.

20. Miller MD, Nery NS, Gripp AC, Maceira JP, Nascimento GM. Dermatoscopic findings of urticaria pigmentosa. An Bras Dermatol. 2013 Nov-Dec;88(6):986-8.

21. Varma K, Munshi N, Kumar U. Urticaria pigmentosa: A rare case report. Indian J Clin Exp Dermatol. 2018;4(4):348-49.

22. Goyal T, Kohli S. Darier's Sign. Indian Journal of Paediatric Dermatology. 2018;19(3):277-79.

23. Adya KA, Inamadar AC, Palit A. Dermoscopic Pigment Network: Characteristics in Non-melanocytic Disorders. Indian Dermatol Online J. 2020 Mar 9;11(2):146-153.

24. Nirmal B, Krishnaram AS, Muthu Y, Rajagopal P. Dermatoscopy of Urticaria Pigmentosa with and without Darier's Sign in Skin of Colour. Indian Dermatol Online J. 2019 Aug 28;10(5):577-579.

25. Czarnetzki BM, Kolde G, Schoemann A, Urbanitz S, Urbanitz D. Bone marrow findings in adult patients with urticaria pigmentosa. J Am Acad Dermatol. 1988 Jan;18(1 Pt 1):45-51.

SPMC JHCS OFFICE *Research Utilization and Publication Unit, Acacia Room, Level 3 Outpatient Building, Southern Philippines Medical Center, JP Laurel Avenue, Davao City, Philippines*
Landline *(+6382) 2272731 loc 4127* • ***Website*** *www.spmcjournal.com* • ***Email*** *spmcpapers@gmail.com*