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Case Report

Urticaria Pigmentosa – A Case Report with a Review of the Literature

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Abstract

Mastocytosis encompasses a rare group of diseases characterized by the accumulation of mast cells, primarily in the skin or internal organs. In the 2016 revised WHO classification, mastocytosis is divided into cutaneous mastocytosis (CM), systemic mastocytosis (CM), and localized mast cell tumor. Cutaneous mastocytosis (CM) includes maculo-papular CM/urticaria pigmentosa (UP), diffuse CM and cutaneous mastocytoma. Urticaria pigmentosa is the most common skin variant. It presents with erythematous brownish macules or papules, often accompanied by pruritus. A case of a 48-year-old woman with disseminated, mildly pruritic, sharply demarcated, livid-brownish macules on the skin of the trunk and extremities is presented. A positive Darier symptom was established. Laboratory tests revealed granulocytosis (73%) and lymphocytosis (19.8%). Serum tryptase and 24-hour urine 5-hydroxyindoleacetic acid were not elevated. The diagnosis of urticaria pigmentosa was confirmed by the histopathological examination revealing perivascular infiltrates of mast cells, mainly in the deep dermis. Screening performed did not detect systemic involvement. Symptomatic treatment with H1 and H2 blockers and topical corticosteroid was carried out. Avoidance of triggers is recommended. The patient's condition has improved. Both a historical review of mastocytosis and a revised classification, as well as the epidemiology, etiology with triggering factors, clinical presentation, laboratory investigations, and management of urticaria pigmentosa are presented.

Keywords

Mastocytosis, Urticaria Pigmentosa, Cutaneous Mastocytosis, Systemic Mastocytosis, KIT Gene Mutations, Symptomatic Treatment

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1. Introduction

Mastocytosis represents a rare and heterogeneous group of conditions characterized by the accumulation of mast cells in the skin and/or internal organs. Typically, the disease manifests with solitary or multiple erythematous-brownish macules or papules, often accompanied by pruritus, appearing either in childhood or adulthood (cutaneous mastocytosis) [1-7]. Due to the variable presentation of skin lesions, diagnosis is frequently delayed. While childhood cases tend to resolve spontaneously before puberty, most adults experience chronicity of the disease with extracutaneous mast cell infiltration (systemic mastocytosis). Hence, a comprehensive evaluation of adult patients with cutaneous mastocytosis is essential [8-11]. This article delineates the symptoms and signs of urticaria pigmentosa and offers management guidelines based on international consensuses. Additionally, it outlines the updated classification of various forms of cutaneous mastocytosis [12, 13].

2. Clinical Case

A 48-year-old female that has noticed red-brown spots scattered on the skin of the trunk and limbs since one year is described. The patient reported mild, fleeting itching, redness and swelling of the spots and isolated episodes of reddening of the skin of the whole body after a warm bath. Clinical examination showed sharply demarcated, livid-brownish macules up to 1.4 cm/d in size, disseminated on her trunk, and extremities (Figure 1, Figure 2). Single excoriations were also observed.

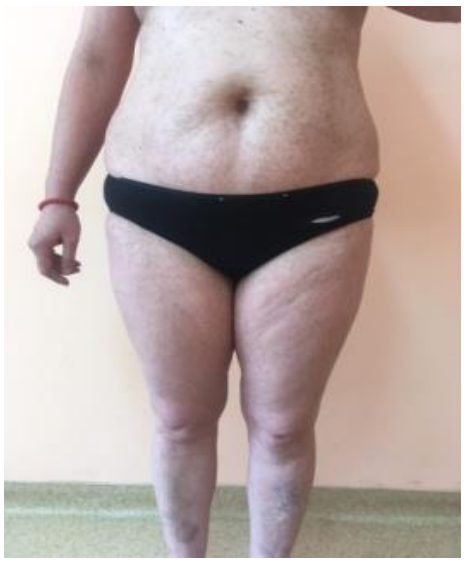

Figure 1. *Disseminated livid-brownish macules on the trunk and extremities of the patient.*

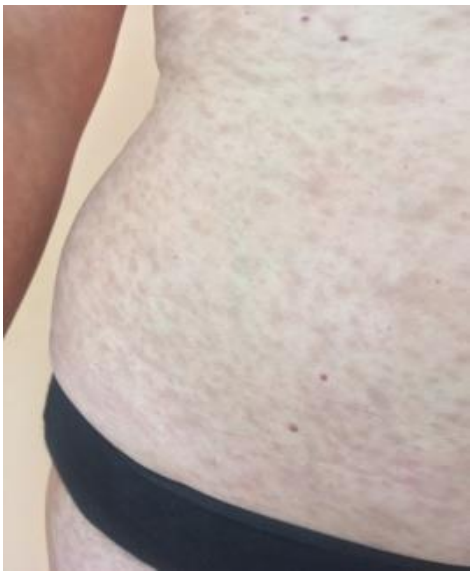

Figure 2. *Sharply demarcated, livid-brownish macules, up to 1.4 cm/d in size, on the trunk of the patient.*

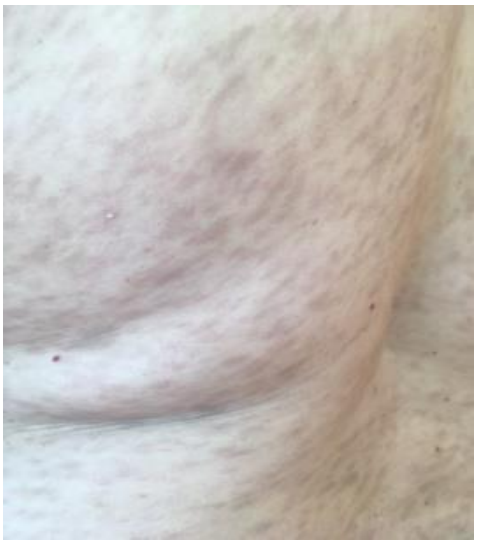

Figure 3. *Positive Darier's sign.*

Darier's symptom was positive (Figure 3). The laboratory findings revealed granulocytosis (73%) and lymphocytosis (19.8%). Serum tryptase and 5-hydroxyindoleacetic acid in 24-hour urine were not elevated. No organomegaly was found on abdominal ultrasonography examination. Consultative examinations with a neurologist, a gastroenterologist and a cardiologist did not reveal any abnormalities.

Histopathological examination showed superficial and deep perivascular infiltrates of mast cells, verified by toluidine blue stain, around the widely dilated venules, predominantly in the deep dermis (Figure 4, Figure 5).

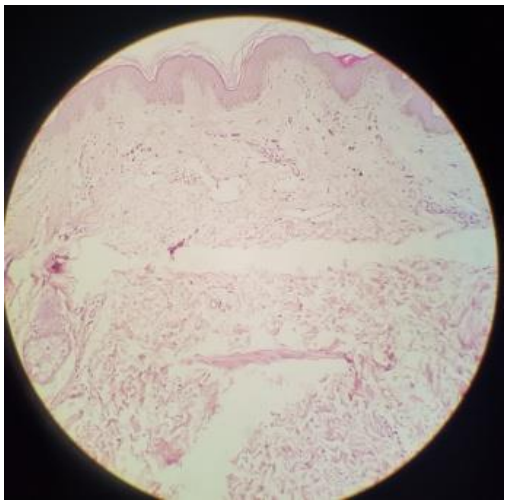

Figure 4. *Histopathological examination showed mild superficial and deep perivascular infiltrates (H&E, x 100).*

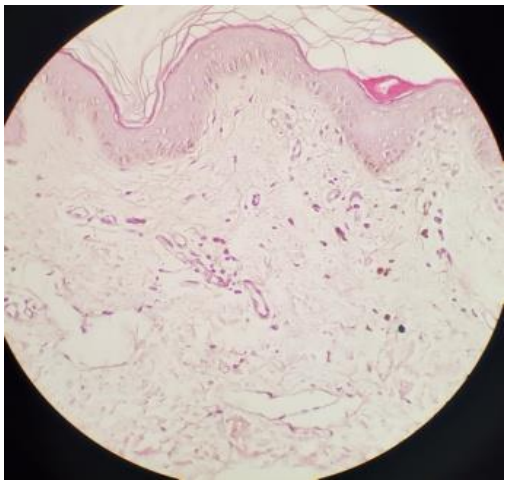

Figure 5. *Oval, kidney-shaped mast cells, arranged around the widely dilated venules (H&E, x 200).*

History, clinical findings and histopathological examination confirmed the diagnosis of urticaria pigmentosa. A trepan biopsy ruled out blood marrow involvement, leading to therapy initiation with cetirizine dihydrochloride, ranitidine, and clobetasol propionate, resulting in a significant clinical response.

3. Discussion

Mastocytosis is a rare disease characterized by the abnormal increase and accumulation of mast cells in one or more organs, most commonly in the skin. Cutaneous mastocytosis was first described by E. Nettleship and W. Tay in 1869 [14]. In 1878 the term "urticaria pigmentosa" was coined. In 1879, P. Ehrlich first discovered mast cells. In 1887, P. Unna found that skin lesions contained a focal accumulation of mast cells [15]. In 1936, French scientists described the systemic form of the disease [16].

In 1953, the term "mastocytosis" was universally recognized. In the revised WHO classification of 2016, mastocytosis is considered an independent, nosological entity, which, according to the affected organs, is divided into cutaneous mastocytosis (CM), systemic mastocytosis (SM), and localized mast cell tumor (17). Cutaneous mastocytosis (CM) includes maculo-papular CM/urticaria pigmentosa (UP), diffuse CM and cutaneous mastocytoma. SM includes indolent SM (ISM), smoldering/slow-progressing SM (TSM), SM associated with hematologic neoplasia (SM-AHN), aggressive SM (ASM), and mast cell leukemia (MCL). A localized mast cell tumor is a mast cell sarcoma (MCS). Approximately 80% of the patients have isolated cutaneous form of the disease [2, 5, 8, 9, 11]. The remaining patients have systemic mastocytosis, as half of them experience specific skin changes as well [10, 11]. In maculo-papular CM/urticaria pigmentosa (UP), lesions range from < 10 to > 100. In diffuse CM, the skin is extensively involved, while in cutaneous mastocytoma, there is only one or a small number (≤ 3) of lesions.

Urticaria pigmentosa, the most prevalent form of cutaneous mastocytosis, typically affects children but can persist into adulthood, necessitating vigilance for systemic involvement. Triggered by activating mutations of the KIT gene, mastocytosis involves the release of various mediators, leading to diverse clinical manifestations.

UP occurs as a result of activating mutations of the KIT gene. In response to certain triggers, mast cells release mediators that cause the typical disease symptoms. Histamine, eicosanoids, prostaglandins, leukotrienes, heparin, proteases, tryptase and cytokines are the most important mediators, while the most common triggers include: physical agents (heat and cold, sudden changes in temperature, sunlight, exercise, friction/pressure/trauma to skin lesions); emotional factors (stress/anxiety, insomnia); medications (narcotics, aspirin and other nonsteroidal anti-inflammatory drugs, morphine, codeine and narcotic derivatives, cough medications, alcohol, local anesthetics, beta-blockers, anticholinergic drugs, vancomycin, amphotericin B, vitamin B1); bites from poisonous insects and snakes; infectious viral and bacterial diseases with fever; others (dental and endoscopic procedures, vaccines, surgical operations, iodine-containing contrast agents); histamine-rich foods/drinks [5, 11, 18]. Some systemic anesthetics can cause anaphylaxis [11].

Mast cell precursor cells express CD34, tyrosine kinase receptor KIT (CD117) and IgG receptor (Fc gamma RII) on their surface. KIT can be activated by its ligand [stem cell factor (SCF)], which induces cell growth, maturation and inhibits apoptosis [11]. Bone marrow stromal cells, keratinocytes, endothelial cells, fibroblasts, Sertoli cells, and granulosa cells produce SCF. The pathogenesis of mastocytosis is due to several mutations in the KIT gene. The most common mutation is an activating mutation at codon 816, where there is a substitution of aspartic acid (AK) with valine (D816V) or another amino acid. These amino acids induce constitutive ligand-dependent activation of the receptor. The

persistent signal leads to uncontrolled proliferation of mast cells. Different point mutations of the KIT-gene lead to a different initial peak of the disease. There are other additional, pathogenetic factors that require further investigation [19-23].

The clinical picture of the disease is not always characteristic. Most often, urticaria pigmentosa presents with disseminated, itchy, sharply demarcated round or oval macular, less often papular, nodular or hemispherical lesions, measuring from a few millimeters to a few centimeters in diameter. About 60% of patients report bullae, which may precede the macules [3, 6, 24]. Rare forms have been described - hemorrhagic, familial bullous, etc. [3, 6, 11]. Lesions may be few or many (from < 10 to > 100). The trunk and limbs are mainly involved, less often the face and scalp and, in extremely rare cases, the oral mucosa, palms and feet [1-4, 6, 11]. A very characteristic sign, especially in childhood, occurring in 90% of cases of UP, is Darier's symptom [25]. It is manifested by itching, edema or urticaria-like appearance of the lesions after rubbing, combing, under the influence of other factors (most often temperature changes) or spontaneously. It usually occurs after 2 to 5 minutes and persists from 30 minutes to several hours. It is due to the impact on hyperactive mast cells and the inflammatory mediators released by them (histamine, prostaglandins, leukotrienes, cytokines, proteases, heparin, etc.). A transient generalized erythema ("flash") is possible in some patients. Pronounced dermographism is characteristic of patients with UP [7, 8, 11].

Extracutaneous involvement is seen in over 50% of patients with UP in adulthood [4, 8, 9, 11]. Gastrointestinal symptoms (abdominal pain, nausea, vomiting, diarrhea, sphincter function disturbances), cardiovascular disorders (tachycardia, hypotension, shock), neurological manifestations (headache, convulsions, loss of consciousness), shortness of breath, rhinorrhea, psychomotor agitation are observed. Death may occur due to massive release of cellular mediators. Night sweats, bone and joint pain, weight loss, and cognitive problems are common. These symptoms, as well as extensive skin lesions, signal the systematization of the disease.

Subjectively there is pruritus in about 50% of patients, which is paroxysmal, spontaneous or caused by triggering factors. UP in early childhood is often presented by light brown macules. At the beginning of the disease, paroxysmal onset, severe itching and urticaria-like appearance of the lesions are noted. In adults, UP usually starts before the age of 20. The macules are permanent, livid-brownish and smaller in size - point-shaped up to 1 cm in diameter. Darier's symptom is positive. Rarely, there is pruritus, formation of bullae and flashes. The evolution of UP is different depending on the age at which the disease started. With onset in childhood, the disease almost always resolves spontaneously, while with onset in adulthood, it persists and may systematize [2, 3, 6, 10, 11].

The diagnosis of urticaria pigmentosa is clinical, but definitive verification requires histopathological examination, with special stains to identify mast cells such as methylene blue (Giemsa), toluidine blue or alcian blue. The most important and characteristic indicator is the increased number of mast cells around the capillaries in the upper dermis [26-29]. The lesions may contain up to 40 times more mast cells compared to normal skin. Mast cells are round or cuboidal in shape. Eosinophils are a common finding in the dermis. Hyperpigmentation of the basal layer may also be observed.

Molecular studies on KIT mutations can be performed on biopsy material. Biopsies from normal skin of patients with mastocytosis do not show elevated mast cells. Therefore, in the absence of skin lesions and suspicion of systemic mastocytosis, a bone marrow biopsy or a biopsy from the gastrointestinal tract is necessary.

An elevated serum tryptase level (above 20 ng/ml) and an increased urinary 5-hydroxyindoleacetic acid level (above 31.2 μmol/dU) are indicative of systemic mastocytosis [2, 28, 29].

The diagnostic criteria for cutaneous mastocytosis are not clearly defined. WHO divides them into major and minor. A diagnosis requires the presence of one major and one minor criterion [17, 28].

Main criterion encompasses the presence of typical skin lesions, while the secondary criteria include typical histology findings (monomorphic, mast cell infiltrate with aggregates of > 15 mast cells per focus or scattered mast cells > 20 per visual field) and molecular verification (detection of KIT-mutation in codon 816 from affected skin).

Bullous impetigo, urticaria, pigmented lichen planus, juvenile xanthogranuloma, insect bites, autoimmune bullous dermatoses are discussed in terms of differential diagnosis.

UP treatment is symptomatic. Systemic therapy is carried out with antihistamine 1 and/or 2 blockers, cell membrane stabilizers (corticosteroids, cromolyn sodium, ketotifen), leukotriene antagonists (block receptors targeting leukotrienes released by mast cells) and aspirin [7, 11, 18, 30-32]. In patients at risk of anaphylactic shock, these medications are recommended for chronic use. Adrenaline/epinephrine is administered subcutaneously in case of anaphylactic reactions. Treatment with a recombinant, monoclonal IgG1k antibody (omalizumab) has also been conducted [32]. A positive but temporary result has been reported from phototherapy (PUVA, NB-UVB and UVA-1) [33, 34]. Corticosteroids and calcineurin inhibitors are applied locally [3, 6, 7, 11, 18, 35].

UP is a benign disease, but the paroxysmal manifestations and the potential for systemic involvement paramount a multidisciplinary care and trigger avoidance strategies [36, 37]. Patients should be provided with both premedication protocols prior to surgery, vaccinations, delivery, and contrast administration, as well as a metered-dose epinephrine auto injector pen [38-41].

4. Conclusions

Mastocytosis includes cutaneous and systemic forms. It is a diagnostic challenge due to its heterogeneous clinical mani-

festations. Urticaria pigmentosa is the most common form of both cutaneous mastocytosis and mastocytosis in general. It presents with characteristic skin lesions and pruritus. The disease is benign, but paroxysmal manifestations and the danger of systematization require a multidisciplinary team of specialists. The etiology of urticaria pigmentosa lies in activating mutations of the KIT gene, causing the release of a mast cell mediators and characteristic symptoms. The disease primarily affects the skin, but extracutaneous involvement may occur, especially in elderly patients, necessitating systemic screening. The diagnosis is based on the clinical picture, histopathological examination and identification of systemic markers, adhering to the WHO criteria. Treatment strategies focus primarily on symptomatic relief and avoidance of mast cell degranulating triggers. A comprehensive understanding of the clinical presentation, diagnostic criteria, and treatment modalities of urticaria pigmentosa is paramount for clinicians to provide effective treatment and optimize patient outcomes. Further research is needed to elucidate its pathophysiology and refine therapeutic approaches to this rare but clinically significant condition.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Caplan R. The natural course of urticaria pigmentosa. Arch Dermatol. 1963; 87: 146–157. https://doi.org/10.1001/archderm.1963.01590140008002

[2] Brockow K, Akin C, Huber M, et al. Assessment of the extent of cutaneous involvement in children and adults with mastocytosis: relationship to symptomatology, tryptase levels, and bone marrow pathology. J Am Acad Dermatol. 2003; 48(4): 508–516. https://doi.org/10.1067/mjd.2003.98

[3] Ben-Amitai D, Metzker A, Cohen HA. Pediatric cutaneous mastocytosis: a review of 180 patients. Isr Med Assoc J. 2005; 7(5): 320-322.

[4] Gonz áez-D áz S, Arias-Cruz A, Mejia K, et al. Urticaria Pigmentosa. Case Report. World Allergy Organ J. 2012; 5(Suppl 2): S203–S204. https://doi.org/10.1097/01.WOX.0000411704.27806.b8

[5] Brockow K. Epidemiology, Prognosis, and Risk Factors in Mastocytosis. Immunol Allergy Clin North America. 2014; 34(2): 283–295. https://doi.org/10.1016/j.iac.2014.01.003

[6] Heinze A, Kuemmet TJ, Chiu YE, et al. Longitudinal Study of Pediatric Urticaria Pigmentosa. Pediatr Dermatol. 2017; 34(2): 144-149. https://doi.org/10.1111/pde.13066

[7] Kayiran MA, Akdeniz N. Diagnosis and treatment of urticaria in primary care. North Clin Istanb. 2019; 6(1): 93-99. https://doi.org/10.14744/nci.2018.75010

[8] Valent P, Escribano L, Broesby-Olsen S, et al. Proposed diagnostic algorithm for patients with suspected mastocytosis: A proposal of the European Competence Network on Mastocytosis. Allergy. 2014; 69(10): 1267–1274. https://doi.org/10.1111/all.12436

[9] Theoharides TC, Valent P, Akin C. Mast Cells, Mastocytosis, and Related Disorders. N Engl J Med. 2015; 373(2): 163–172. https://doi.org/10.1056/NEJMra1409760

[10] Pardanani A. Systemic mastocytosis in adults: 2017 update on diagnosis, risk stratification and management. Am J Hematol. 2016; 91(11): 1146-1159. https://doi.org/10.1002/ajh.24553

[11] Wagner N, Staubach P. Mastocytosis – pathogenesis, clinical manifestation and treatment, 2018 Deutsche Dermatologische Gesellschaft (DDG). Publ John Wiley & Sons Ltd., JDDG. https://doi.org/10.1111/ddg.13418

[12] Hartmann K, Escribano L, Grattan, 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; 137(1): 35-45. https://doi.org/10.1016/j.jaci.2015.08.034

[13] Valent P, Oude Elberink JNG, Gorska A, et al. The Data Registry of the European Competence Network on Mastocytosis (ECNM): Set Up, Projects, and Perspectives. J Allergy Clin Immunol Pract. 2019; 7(1): 81–87. https://doi.org/10.1016/j.jaip.2018.09.024

[14] Nettleship E, Tay W. Reports of Medical and Surgical Practice in the Hospitals of Great Britain. Br Med J. 1869; 2(455): 323–324. https://doi.org/10.1136/bmj.2.455.323

[15] Unna, P. Beitr äge zur Anatomie und Pathogenese der Urticaria simplex und pigmentosa. MSCCH Prakt Dermatol Suppl Dermatol Stud. 1887; 3: 9.

[16] S ézary A, Levy-Coblentz G, Chauvillon P. Dermographisme et mastocytose. Bull Soc Fr Dermatol Syphiligr. 1936; 43: 359–361.

[17] Valent P, Akin C, Metcalfe DD. Mastocytosis: 2016 updated WHO classification and novel emerging treatment concepts. Blood. 2017; 129(11): 1420-1427. https://doi.org/10.1182/blood-2016-09-731893

[18] Castells M, Metcalfe DD, Escribano L. Diagnosis and treatment of cutaneous mastocytosis in children: practical recommendations. Am J Clin Dermatol. 2011; 12(4): 259-270. https://doi.org/10.2165/11588890-000000000-00000

[19] Nagata H, Worobec AS, Oh CK, et al. Identification of a point mutation in the catalytic domain of the protooncogene c-kit in peripheral blood mononuclear cells of patients who have mastocytosis with an associated hematologic disorder. Proc Natl Acad Sci USA. 1995; 92(23): 10560–10564. https://doi.org/10.1073/pnas.92.23.10560

[20] Akin C, Kirschenbaum AS, Semere T, et al. Analysis of the surface expression of c-kit and occurrence of the c-kit Asp816Val activating mutation in T cells, B cells, and myelomono-cytic cells in patients with mastocytosis. Exp Hematol 2000; 28(2): 140–147. https://doi.org/10.1016/s0301-472x(99)00145-9

[21] Sundstrom M, Vliagoftis H, Karlberg P, et al. Functional and phenotypic studies of two variants of a human mast cell line with a distinct set of mutations in the c-kit proto-oncogene. Immunology. 2003; 108(1): 89–97. https://doi.org/10.1046/j.1365-2567.2003.01559.x

[22] Cruse G, Metcalfe DD, Olivera A. Functional Deregulation of KIT. Immunol Allergy Clin North Am. 2014; 34(2): 219–237. https://doi.org/10.1016/j.iac.2014.01.002

[23] Arock M, Sotlar, K, Akin C, et al. KIT mutation analysis in mast cell neoplasms: Recommendations of the European Competence Network on Mastocytosis. Leukemia. 2015; 29(6): 1223–1232. https://doi.org/10.1038/leu.2015.24

[24] Avshalumov K, Pichardo R, Jorizzo JL, et al. Bullous mastocytosis: report of a patient and a brief review of the literature. Am J Dermatopathol. 2008; 30(5): 455-57. https://doi.org/10.1097/DAD.0b013e3181783354

[25] Nirmal B, Krishnaram AS, Muthu Y, et al. Dermatoscopy of Urticaria Pigmentosa with and without Darier's Signin Skin of Colour. Indian Dermatol Online J. 2019; 10(5): 577-579. https://doi.org/10.4103/idoj.IDOJ_501_18

[26] Garriga MM, Friedman MM, Metcalfe DD. A survey of the number and distribution of mast cells in the skin of patients with mast cell disorders. J Allergy Clin Immunol. 1988; 82(3 Pt 1): 425–432. https://doi.org/10.1016/0091-6749(88)90015-2

[27] Horny HP, Sotlar K, Valent P. Mastocytosis: state of the art. Pathobiology. 2007; 74(2): 121–132. https://doi.org/10.1159/000101711

[28] Horny HP, Akin C, Arber D, et al. Mastocytosis. In: WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Eds: Swerdlow SH, Campo E, Harris NL et al..; IARC Press. Lyon, France; 2017: 62–69.

[29] Orlova AS, Shkurlatovskaia KM, Silina EV, et al. Laboratory tests in diagnosis of Mastocytosis: Literature review and case report. 2020; https://doi.org/10.2478/sjecr-2019-0080

[30] Metcalfe DD. The treatment of mastocytosis. J Invest Dermatol 1991; 96(3): 55S–56S. https://doi.org/10.1111/1523-1747.ep12469049.

[31] Arock M, Akin C, Hermine O, et al. Current treatment options in patients with mastocytosis: status in 2015 and future perspectives. Eur J Haematol 2015; 94(6): 474-490. https://doi.org/10.1111/ejh.12544

[32] Valent P, Akin C, Hartmann K, et al. Advances in the Classification and Treatment of Mastocytosis: Current Status and Outlook toward the Future. Cancer Res. 2017; 77(6): 1261-1270. https://doi.org/10.1158/0008-5472.CAN-16-2234

[33] Brazzelli V, Grassi S, Merante S, et al. Narrow-band UVB phototherapy and psoralen-ultraviolet A photochemotherapy in the treatment of cutaneous mastocytosis: a study in 20 patients. Photodermatol Photoimmunol Photomed. 2016; 32(5-6): 238-246. https://doi.org/10.1111/phpp.12248

[34] Pyatilova P, Teplyuk N, Olisova O, et al. Efficacy of PUVA in Russian patients with mastocytosis: A case series and review of literature. Int J Dermatol. 2018; 57(9): e59–e64. https://doi.org/10.1111/ijd.14103

[35] Correia O, Duarte AF, Quirino P, et al. Cutaneous mastocytosis: Two pediatric cases treated with topical pimecrolimus. Dermatol Online J. 2010 May 15; 16(5): 8.

[36] Valent P, Akin C, Gleixner KV, et al. Multidisciplinary Challenges in Mastocytosis and How to Address with Personalized Medicine Approaches. Int J Mol Sci. 2019; 20(12): 1-17. https://doi.org/10.3390/ijms20122976

[37] Broesby-OlsenS, Dybedal I, Gulen T, et al. Multidisciplinary management of mastocytosis: Nordic expert group consensus. Acta Derm Venereol. 2016; 96(5): 602-612. https://doi.org/10.2340/00015555-2325

[38] Dewachter P, Castells MC, Hepner DL, et al. Perioperative management of patients with mastocytosis. Anesthesiology. 2014; 120(3): 753-759. https://doi.org/10.1097/ALN.0000000000000031

[39] Matito A, Morgado JM, SanchezLP, et al. Management of anesthesia in adult and pediatric mastocytosis: A study of the spanish network on mastocytosis (REMA) based on 726 anesthetic procedures. Int Arch Allergy Immunol 2015; 167(1): 47-56. https://doi.org/10.1159/000436969

[40] Zanoni G, Zanotti R, Schena D, et al. Vaccination management in children and adults with mastocytosis. Clin Exp Allergy. 2017; 47(4): 593-596. https://doi.org/10.1111/cea.12882

[41] Turk J, Oates JA, Roberts LJ. Intervention with epinephrine in hypotension associated with mastocytosis. J Allergy Clin Immunol. 1983; 71(2): 189–192. https://doi.org/10.1016/0091-6749(83)90098-2