

Clinically exuberant urticaria pigmentosa in an adult patient*

*Urticária pigmentosa em adulto com apresentação clínica exuberante**

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Abstract: Mastocytosis is a rare, heterogeneous disorder characterized by marked increase in mast cell density in the skin and other organs. A clinically exuberant case of urticaria pigmentosa in an adult woman is presented.

Keywords: Mast cells; Mastocytosis; Urticaria pigmentosa

Resumo: A mastocitose é afecção rara e heterogênea, caracterizada por aumento da densidade dos mastócitos na pele e em outros órgãos, para a qual não há tratamento específico. Descreve-se um caso de urticária pigmentosa em paciente adulta com quadro clínico exuberante.

Palavras-chave: Mastócitos; Mastocitose; Urticária pigmentosa

INTRODUCTION

Mastocytosis is an idiopathic heterogeneous group of conditions characterized by increased number of mast cells in several organs.¹⁻³ The skin is the most frequently affected site,¹⁻⁶ and its incidence ranges from 1:1000 to 1:8000 dermatological patients.^{1,2,6} There is no sex or race preference.²

CASE REPORT

A 44 year-old woman, married, mulatto, housewife, followed-up at the Dermatology Outpatient Clinic of *Hospital das Clínicas* – UFPE, for three years, presented pruriginous skin lesions for about 33 years. On dermatological examination, erythematous papules on the trunk, face, upper and lower limbs, scalp, palms and soles were found (Figure 1),

as well as dermographism (Figure 2). Darier sign was present. No lesions were found in the oral or genital mucosa.

The following tests were performed along the three-year follow-up:

Abdominal ultrasonography: mild periportal fibrosis. Several complete blood counts: all normal. Several liver and renal function tests and lipid profile: normal. Several urine analyses: normal. VDRL: negative. X-ray of long bones: normal.

Two skin biopsies revealed increased number of mast cells in the papillary dermis, especially surrounding the vessels (Figures 3 and 4).

Anti-histamines (anti-H1 and anti-H2) were prescribed and the itching partly improved.

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Conflict of interest: None

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FIGURE 1: Erythematous papules and brownish maculae spread on the trunk

DISCUSSION

Mastocytosis usually affects children, 75% of cases occurring between two and four years of age. If it begins in adulthood, there is an increased risk of systemic involvement, affecting organs such as bones and bone marrow.

The etiology of mast cell hyperproliferation is unknown, but there are reports implicating mutations in the gene of the cell growth factor, c-kit, or of its receptor.^{4,6,7,9}

The cutaneous forms include mastocytoma (solitary nodule,⁵ urticaria pigmentosa (UP), diffuse erythrodermic cutaneous mastocytosis and persistent eruptive macular telangiectasia (PEMT).^{3,4} When other organs are affected, it is called systemic mastocytosis.^{3,5}



FIGURE 2: Papules and maculae disseminated on the dorsum, dermographism in the area corresponding to the bra

sis.^{3,5}

UP is the commonest form of cutaneous mastocytosis¹ and its clinical features include nodules, papules, and reddish-brown plaques.⁵ It may involve any skin or mucosal area. Palms, soles, face and scalp are often spared. Telangiectasias and petechiae may also occur.^{1,5} In teenagers and adults, the lesions are smaller and more numerous. UP usually occurs before the age of two years and it is seldom associated with systemic manifestations. It usually resolves spontaneously in adolescence. When it persists in adulthood, it is usually associated to systemic manifestations and hematological abnormalities.⁴ Additional clinical findings of UP are dermographism,⁵ in extensive disease, itching, rubor and the Darier sign.^{4,5,10} Rubor occurs in 17-36% of patients with UP.¹

Solitary mastocytomas are rare lesions frequently localized in the limbs, sparing palms and soles.¹ They usually start before the age of six months and subside spontaneously.

Diffuse cutaneous mastocytosis presents with edema, erythroderma and skin thickening resembling orange peel or leathery skin.^{1,3,5} The extensive cutaneous infiltration is the result of the generalized presence of mast cells in the dermis, resembling pseudo lichenification. Despite its presentation in early life, this form of mastocytosis resolves between the ages of 15 months and 5 years.³ Secondary complications, such as rubor, bleeding, erythema, severe diarrhea, hypotension, tachycardia, dyspnea and shock, result from mast cell degranulation.^{2,3}

PEMT is a rare type, which occurs in adults and occasionally, in children,¹¹ and it is characterized by diffuse, yet sparse, infiltrate of mast cell in the dermis.⁵ The cutaneous findings include erythematous plaques, telangiectasia and erythematous maculae ranging in size from 2 to 6mm, with sharp and confluent borders.^{1,5} Ten percent of patients present systemic involvement. PEMT is, usually, of difficult diagnosis and refractory to treatments.⁸

Systemic mastocytosis is defined as the proliferation of mast cells in organs, which may include the skin, but not limited to it.⁶ The signs and symptoms of the systemic disease vary with the organs affected.¹ The gastrointestinal tract and the bones are the ones most often affected,⁵ although the blood and lymphatic system, the liver and spleen may also be involved.^{1,5,9} Systemic disease is less common in children,¹ and the patients presenting it have a 30% greater risk of showing malignant transformation.¹ The symptoms of systemic mastocytosis result from mast cell degranulation. The active substances include histamine, chemotactic factors, heparin, prostaglandin D₂, proteases and several leukotrienes.^{2,5} Degranulation may be triggered by immunological mechanisms, physical

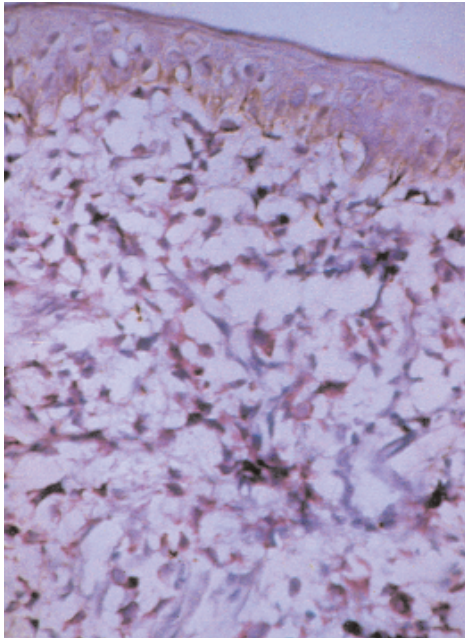


FIGURE 3: Dense infiltrate of mast cells in the papillary and reticular dermis. The epidermis is not affected (100 X)

toxins, snake venom, acarid mite polypeptides, sea food and anaphylatoxins,⁵ chocolate, wine and drugs such as aspirin, alcohol, opioids, polymyxin B, amphotericin B, thiamine, tubocurarin, quinine, radiological contrast, among others. The patients may have fever, chills, night sweats, bone pain, nausea, vomiting, diarrhea, epigastric pain, dysphagia, dyspnea, palpitations, chest pain, syncope, bronchospasm, headache, vertigo, rhinorrhea and hoarseness.^{1,5} These are short-lived episodes lasting from 15 to 30 minutes⁶ and are due to the histaminic shock that may, occasionally, be fatal.⁵

The laboratory tests performed should be chosen according to the symptoms displayed.^{1,3,4} The histological demonstration of increased amount of mast

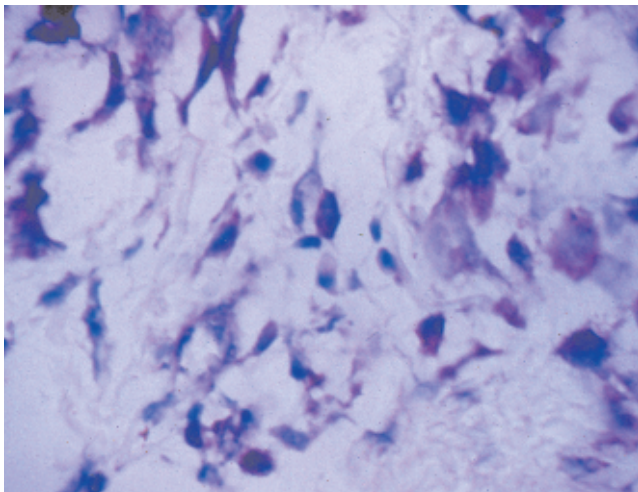


FIGURE 4: Mast cells stained with Giemsa (400 X)

cells in the dermis is usually indicated, although it is not required in some pediatric cases.⁴ In UP, a significant infiltrate of mast cells in the papillary dermis, especially surrounding blood vessels, is found. On histology, the different forms of the disease are alike, whether single or diffuse lesions. The cases of PEMT, however, show a limited number of mast cells in the dermis.⁴ Unfortunately, the skin biopsy results do not predict the risk for systemic involvement.¹ When systemic symptoms do not exist, only physical examination and biopsy are indicated for children.

Complete blood count and liver and renal function tests are usually normal in patients with cutaneous mastocytosis, unless systemic involvement is present. Histamine and its metabolites, methyl-histamine, methyl-imidazolacetic acid, 5-HIAA and prostaglandin D₂ metabolites in 24-hour urine levels are excessive. Nonetheless, the relation between disease activity and urinary excretion of histamine and its metabolites is poor.

In systemic cases, bone marrow aspiration is the gold standard for detecting progression into mast cell hyperplasia and malignancy.¹ Bone lesions may be screened with scintigraphy, including technetium scans.

Up to the present, there is no curative treatment for mastocytosis.^{5,6} H1 antagonists, such as hydroxyzine, are the cornerstone of itching and erythema treatment.⁵ The combination of H1, H2, H3 anti-histamines has been suggested as having a more effective action than H1 alone.^{4,6,10,12} Combined treatments should be started especially in patients with symptoms of gastritis or gastric ulcer secondary to excessive secretion of hydrochloride induced by histamine.⁸ Mast cell membrane stabilizers like ketotifen^{5,12} and sodium chromoglicate^{6,8,10} are recommended.

Psoralens (8-methoxypsoralen) and UVA phototherapy (Puva) have been tested in patients with cutaneous mastocytosis, with good results, although short-lived, the symptoms relapsing three to six months after treatment is completed.^{1,10,13} Puva therapies should be considered when patients do not respond to other treatments and in those in whom the symptoms progress despite the treatment.¹

Puva is indicated for the treatment of childhood diffuse cutaneous mastocytosis because of its efficacy even in low doses, and its low relapse rate.¹³ The mechanism of action of Puva therapy is not completely established;^{2,13} but the decrease in serum and urine levels of histamine metabolites suggest that it interferes in the metabolism of this mediator. Some authors suggest that steroids, either as single or combined to other treatments, may be palliative, with temporary improvement in lesions and symptoms.^{14,15}

temporary improvement in lesions and symptoms.^{14,15} However, none of the treatments mentioned cause definitive regression of the cutaneous or visceral lesions.

The prognosis of patients with cutaneous mastocytosis depends on the existence of systemic involvement and of the age the disease started. UP in

adults has an eight-fold greater chance to evolve to systemic disease than when it starts in childhood.¹ The severity of systemic disease seems to be correlated to late start and to extension of the cutaneous lesions, especially of diffuse and erythrodermic forms. Malignant transformation must be watched in adult patients with UP. □

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