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Case report

Urticaria pigmentosa presenting as cardiac emergency

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ABSTRACT

Introduction: Urticaria pigmentosa is a common type of mastocytosis. It is a disease that needs to be treated by doctors of many specialties.
Aim: We present a case report based discussion concerning the approach to a patient with this disease including treatment, prophylaxis of degranulation and anesthesia in affected patients.
Case study: A 57-year-old male patient was admitted for diagnosis of maculopapular lesions that first occurred about 10 years before. He presented massive maculopapular lesion covering his trunk and legs with positive Darier's sign. The punch biopsy revealed mastocytosis, the tryptase level was slightly elevated – 22 μg/L ($N < 20$ μg/L) and the trepanobiopsy revealed no involvement of the disease in bone marrow. We started PUVA therapy with improvement.
Results and discussion: Patient was not diagnosed before although he had many serious symptoms of the disease which were ignored by both, doctors and the patient (fainting, the cardiorespiratory arrest and the seizures during the anesthesia, recurring diarrhea). After last incident, when the skin lesion was already covering almost whole trunk and legs he was sent to the Department of Dermatology for further diagnosis that was described in beginning.
Conclusions: Mastocytosis is a disease that is not easy to diagnose, classify and treat for doctors. But it is crucial that patients know the disease well and are informed on how to cope with the symptoms.

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1. Introduction

Mastocytosis is a disease defined by excessive accumulation of mastocytes in tissues. It is a disease that may affect either skin or both skin and internal organs. Skin and bone marrow are the organs that are affected most frequently. The disease can be divided in two types: the systemic mastocytosis and the cutaneous mastocytosis. Patients with systemic mastocytosis often also have the skin symptoms of the disease. Most adults present the systemic form of the disorder. Darier's sign, which is defined by whealing and reddening of lesions after mechanical stroking or rubbing, is usually observed.

Mastocytosis is a heterogeneous group. In was classified by macroscopic features of skin lesions, their localization and the age of onset.[1–3] The current World Health Organization (WHO) classification subdivides mastocytosis into seven major categories: (1) cutaneous mastocytosis, (2) indolent systemic mastocytosis, (3) systemic mastocytosis with associated clonal, hematological non-mast-cell lineage disease, (4) aggressive systemic mastocytosis, (5) mast cell leukemia, (6) mast cell sarcoma, and (7) extracutaneous mastocytoma. An accepted approach to classification of cutaneous mastocytosis is to divide cutaneous mastocytosis into (1) maculopapular cutaneous mastocytosis, also known as urticaria pigmentosa; (2) diffuse cutaneous mastocytosis; and (3) mastocytoma of the skin.[4–6]

2. Aim

We present a case report of a patient with maculopapular mastocytosis and discussion concerning dermatological approach to this disease.

3. Case study

A 57-year-old male patient was admitted to the Department of Dermatology Sexually Transmitted Diseases and Clinical Immunology for diagnosis of maculopapular lesions (Figs. 1, 2) that first occurred about 10 years before. Patient was not diagnosed nor treated before his first visit to dermatologist about 2 months before admission. Then the punch biopsy was performed and the histopathological examination revealed mastocytosis. Physical examination shown no abnormalities despite the skin lesions. He presented massive maculopapular lesions covering his trunk and legs with positive Darier's sign (Figs. 3, 4). Ultrasonographic examination of abdomen was normal. The tryptase level was slightly elevated – 22 μg/L ($N < 20$ μg/L) The treatment for skin maculopapular mastocytosis was started with PUVA (psoralen + UVA phototherapy) while waiting for trepanobiopsy. During this treatment patient observed significant improvement in skin condition but also remitting exacerbations. Afterwards the trepanobiopsy revealed no involvement of the disease in bone marrow.

Before the diagnosis was settled patient had many serious symptoms of the disease which were ignored by both, doctors and the patient. In 1998 he had the pacemaker implantation because of the diagnosis of vasovagal syndrome. No documentation of the diagnosing is available. Patient claimed he had a history of fainting. In 2001 he had a cholecystectomy. During the anesthesia he had the cardiorespiratory arrest of unknown reason. In September 2015 patient was hospitalized in department of gastroenterology in order to perform the colonoscopy because of recurring diarrhea for 4 years.

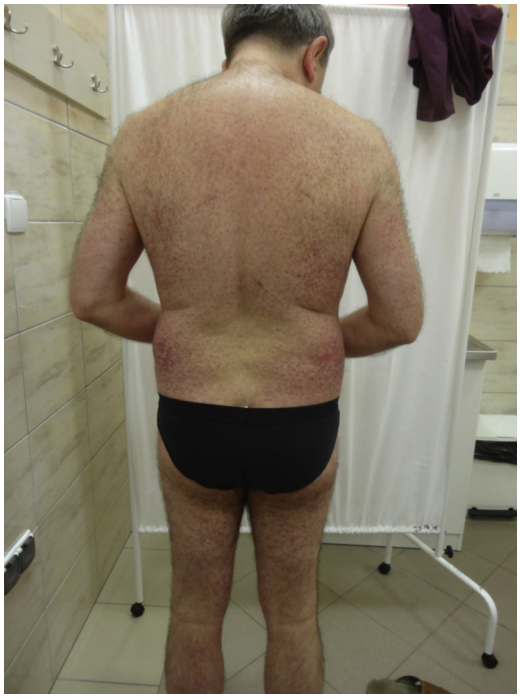

Fig. 1 – The massive maculopapular lesions covering trunk and legs of patient.

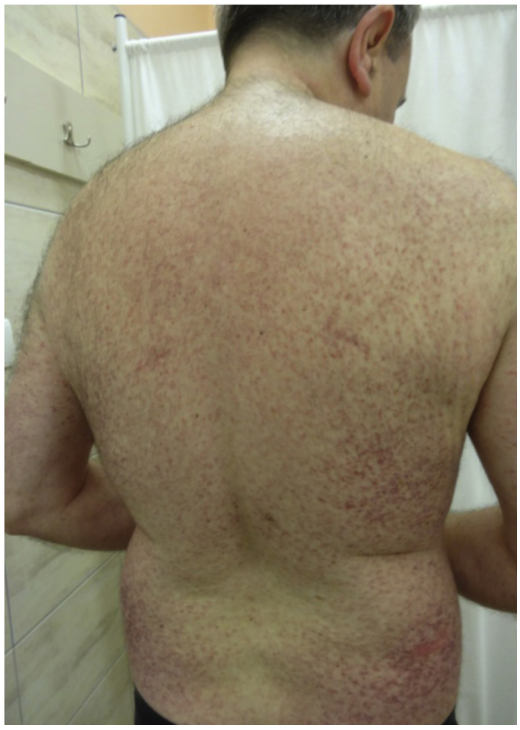

Fig. 2 – The maculopapular lesions on the trunk.

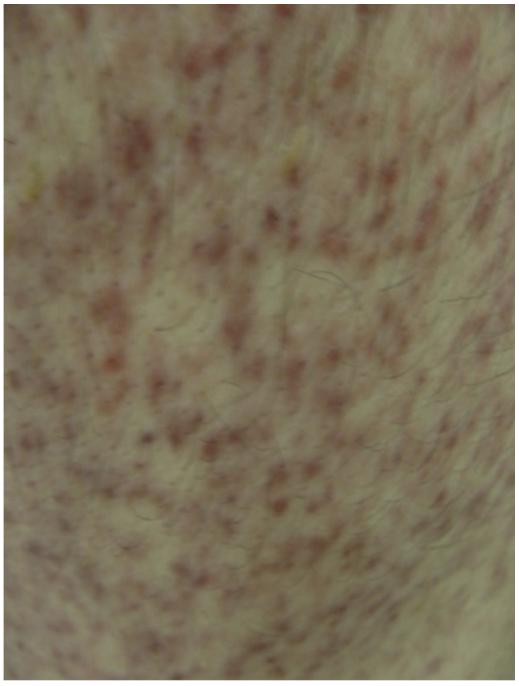

Fig. 3 – The maculopapular lesions before mechanical rubbing.

After the anesthetics were injected (Propofol 150 mg and Fentanil 0.1 mg) intravenously patient presented seizures. Because of loss of saturation to 30% he was intubated and needed external ventilation. During this incidence the sudden deterioration of skin lesions was observed including urticaria. Afterwards patient got better, was extubated and was breathing efficiently. Later the endoscopic examination of colon was performed without anesthesia revealing microscopic colitis. After last incident, when the skin lesion was already covering almost whole trunk and legs he was sent to the Department of Dermatology for further diagnosis that was described in beginning.

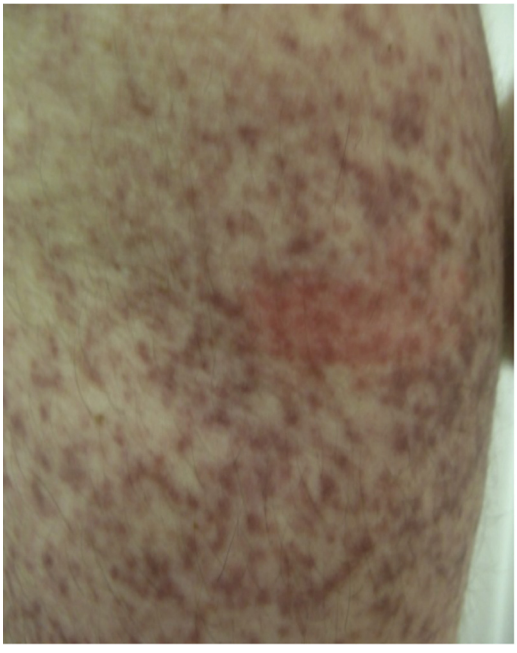

Fig. 4 – The positive Darier's sign – whealing and reddening of lesions after mechanical rubbing.

4. Results and discussion

Majority of adult patients most often develop mastocytosis between 20 to 35 years of age, however it is possible at any age. Most often they present maculopapular lesion the type of disease also known before as urticaria pigmentosa. However this name is not any more accepted according to the European Union–US consensus group. Great majority of patients with maculopapular lesion develop the bone marrow infiltration which leads to diagnosis of systemic mastocytosis.[7–9] Therefore, adult patients with maculopapular lesion in most cases must have the trepanobiopsy performed to differentiate between systemic mastocytosis and cutaneous mastocytosis.

In order to diagnose the systemic mastocytosis it is helpful to use the WHO criteria. There is one major criterion: multifocal, dense aggregates of mast cells (15 or more) detected in sections of bone marrow and confirmed by tryptase immunohistochemistry or other special stains and four minor criteria:

(1) in biopsy section, more than 25% of the masts cells in the infiltrate have atypical morphology, or of all the mast cells in the aspirate smear, more than 25% are immature or atypical,
(2) mast cells co-express CD117 with CD2 and/or CD25,
(3) detection of KIT point mutation at codon 816 in bone marrow, blood, or other extracutaneous organs,
(4) serum total tryptase persistently is more than 20 ng/mL (nevertheless, many centers consider the normal range as being more than 11.4 ng/mL (cut off provided by company) or even more than 10 ng/mL). There are not valid criteria in cases of systemic mastocytosis with associated clonal hematologic non-mast-cell lineage disease. Diagnosis may be rendered if one major plus one minor or three minor criteria are fulfilled.[10,11]

Further hematological examination helps to decide on which type of systemic mastocytosis does the patient suffer from. Once the diagnosis is settled it is important to choose the most efficient method of treatment. Treatment of systemic mastocytosis consists of hematological treatment of infiltrated tissues, treatment of acute mastocytes degranulation, treatment of chronic mastocytes degranulation and avoiding agents triggering mastocytes degranulation. Whereas indolent systemic mastocytosis is directed on controlling symptoms associated with mastocytes activation.

Hematological treatment is recommended only in systemic mastocytosis patients (tyrosine kinase inhibitors, cladribine). In some cases, mostly the most aggressive form of systemic mastocytosis the hematopoietic stem cell transplantation is the only potentially curative treatment.[12]

When a patient is already diagnosed and given proper treatment he has to be tough how to live with the disease safely. Not only his doctor needs to know which drugs to avoid but also the patient himself has to be aware of how to cope with mastocytosis. First of all he needs to be aware of what the symptoms related to mast cell mediator release could be. Acute degranulation may be presented by flushing, urticaria, headache, vascular instability and could lead to cardiorespiratory arrest. Mostly the skin lesions that were present before get worse or the new ones appear. It is crucial o recognize this symptoms as soon as possible because the reaction may be very fast and massive. Chronic degranulation of mastocytes could give symptoms such as headaches, diarrhea, and hypertension.[4,7,9,12]

Both acute and chronic degranulation can usually be controlled by antihistamine drugs. Sometimes, more severe symptoms need to be treated with glucocorticosteroids or even adrenalin. Therefore it is suggested that patients with mastocytosis are equipped with adrenaline injector.

PUVA treatment (the oral administration of methoxypsoralen plus ultraviolet A) has resulted in a decrease in itching and wheal formation in patients with urticaria pigmentosa with or without systemic disease.[13] PUVA can protect mastocytes cells against degranulation under the influence of triggering factors.[14] This method can quickly control of the disease, but it occurs relapses 3–6 months after cessation of therapy.[13] Moreover after PUVA a decreasing levels of urine and blood mediators are observed.[13,15] This is the most popular method of dermatological treatment with good tolerance and security. In the newest study Maiorino et al., the development of melanoma in psoriatic patients does not seem to be increased after a mean of 7.1 years of follow-up, even in patients exposed to more than 250 PUVA sessions. Although the literature data report cases of melanoma in patients treated with PUVA, the correlation between the UVA exposure and malignant transformation seems to be controversial.[16] In the literature we can find only one case report about a development a malignant melanoma in a female patient treated with UVA1 and bath PUVA therapy for urticaria pigmentosa.[17]

Another very important aspect of taking care of the patient with mastocytosis is the life style modification. Patient should be aware of all the potential triggers of the mast cell degranulation. Drugs, physical stimuli and food ingredients should be discussed. Other agents that can trigger the mastocytes degranulation are bites of insects, heat, cold, sunlight, alcohol, emotional stress, exercise. Patient with mastocytosis can also have the concomitant allergy. The test for drug allergy (not only intradermal tests) is advised in patients who had symptoms of drug allergy in medical history. Symptoms of exposition to those allergens may lead to severe anaphylactic reaction due to massive mastocytes activation.

There are many drugs that can lead to activation of mastocytes: amfotericin B, quinine and many drugs used in anesthesia. Planning anesthesia in patients is troublesome. Both the anesthesiologist and surgeon should know that the patient that is going to be operated suffers from mastocytosis. However, it is not a contraindication to anesthesia. It is advised that before the anesthesia subcutaneous tests for hypersensitivity to the drug are run. Moreover patient should be premedicated with H1 and H2 histamine receptor blockers. Atracurium and mivacurium should be avoided because they cause mast cell degranulation. Rocuronium, vecuronium and cisatracurium seem to be suitable alternatives. Succinylcholine (suxamethonium) is unlikely to cause non-allergic mast cell degranulation but it seems to be the most common cause of allergic anaphylaxis during anesthesia. It should be avoided if possible because, if allergic anaphylaxis occurs in a patient with mastocytosis, the reaction is likely to be more severe. Propofol is a commonly-used induction drug and it is said to be suitable in patients with mastocytosis. Sevoflurane, isoflurane and desflurane do not cause mast cell degranulation and are therefore safe. Codeine and morphine have both been shown to cause histamine release.[18] There is no particular reason to avoid benzodiazepines such as diazepam, temazepam and midazolam. There is no evidence that local anesthetics of the common amide type should be avoided (lidocaine, bupivacaine, levobupivacaine, ropivacaine, prilocaine) but the reaction differs within patients. Amethocaine, an ester local anesthetic found in EMLA cream (contains lidocaine and prilocaine), seems to be safe. It seems that there is no reason to avoid epidural or spinal anesthesia, or local anesthetic nerve blocks.[19–23]

5. Conclusions

Mastocytosis is a disease that is not easy to diagnose, classify and treat for doctors. But it is crucial that patients know the disease well and are informed on how to cope with the symptoms. Sometimes situations that lead to degranulation of mastocytes is difficult to be avoided (for example insect bites). That is why patients with history of serious incidents of degranulation of mastocytes should use the pharmacological prophylactic especially carefully during the periods of higher risk (for example summer holiday). Such patients should take anti-histamine drugs (both H1 and H2) and always have the adrenalin injector. Moreover it is important that family members are educated on how to behave if the symptoms of activation of mastocytes occur.[24]

Conflict of interest

None declared.

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