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Case report/Kazuistyka

Mastocytosis – A rare disease complicating pregnancy

Mastocytoza – rzadka choroba komplikująca ciążę

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ABSTRACT

Background: Mastocytosis is a rare disorder characterized by abnormal accumulation of mast cells in various organs. Clinical complaints include pruritus, cutaneous flushing, dyspepsia, and anaphylaxis. Symptoms are usually a result of local and systemic mast cell mediator release. The triggers include drugs, exercise, stress, anxiety, and temperature extremes. **Case:** We report a case of cutaneous mastocytosis in a pregnant woman who achieved a successful pregnancy and delivered a healthy female baby.

In the second case a patient with systemic mastocytosis had an unfavorable course of pregnancy that ended in extremely premature operative delivery due to fetal demise. **Conclusions:** Mastocytosis is perceived as a medical management dilemma because of its potential for unpredictably heightened mast cell activity in response to various physiologic states including pregnancy.

Introduction

Mastocytosis is a myeloproliferative disorder caused by the abnormal proliferation and infiltration of the mast cells in various organs, mainly bone marrow, skin, liver spleen, and lymph nodes. The calculated prevalence of mastocytosis is 13:100 000 inhabitants including all age groups [1]. The disease was classified by WHO into different types, including cutaneous mastocytosis and systemic forms (indolent, aggressive, mast cell leukemia, mast cell sarcoma, mastocytosis associated with non-mast cell associated hematological disease). The systemic mastocytosis is the most common type among adults whereas cutaneous form is typical among

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pediatric patients. The etiology of mastocytosis is still unknown, but *KIT* mutations and gene polymorphisms are seemingly one of the most important underlying molecular factors [2]. Symptomatology of mastocytosis is wide as the mast cells infiltrates may involve different organs. Majority of subjects suffers from skin involvement, recurrent anaphylactic reactions including severe and sometimes fatal ones. The common complaints include gastrointestinal symptoms, osteopenia or osteoporosis, depression and neurological symptoms. The aggressive mastocytosis is a rare disease characterized by the symptoms requiring cytoreductive therapy due to the functional impairment of the affected organs, e.g., cytopenia, liver failure, weight loss and malabsorption.

The most important clinical symptoms in mastocytosis are related to the release of mast cell mediators leading to flush, hypotension and anaphylactic reactions. The causes of the reaction are insect bites, drugs (including NSAIDS, anesthesiological agents, antibiotics), food and physical effort. The disease may also be diagnosed in pregnant women. In such circumstances important questions arise on the safety of both the mother and a child, the treatment which may be used in pregnancy, the delivery and breastfeeding. We describe two patients with mastocytosis treated in the Department of Obstetrics Medical University of Gdansk and discuss the current guidelines on their treatment.

Case 1st

A 27-year-old primipara at 24^{+2} weeks of gestation was admitted to the Obstetrical Department of the Medical University of Gdansk due to pregnancy induced hypertension and edema that did not resolve after treatment.

The patient suffered from urticaria pigmentosa for several years, and indolent systemic mastocytosis was diagnosed in 2005 based on 3 minor WHO criteria (tryptase level 30.2 ng/dl, D816V *KIT* mutation, CD2 and CD25 expression on the bone marrow mast cells). She also suffered from grade 3 anaphylactic reactions according to the Mueller scale caused by food and physical factors.

Her previous treatment included methylprednisolone, methotrexate, prednisone, cetirizine dihydrochloride, alpha methyldopa and metoprolol succinate.

On admission, the patient was in good general and cardiopulmonary condition. Her BMI amounted 32.8 kg/m^2. On laboratory tests, excessive proteinuria, with a concomitant decrease in serum concentration of total protein and albumins, and an increase in both fibrinogen and d-dimer levels were found. Fluctuations in arterial blood pressure, from 140/90 mmHg to 200/120 mmHg, were observed, despite treatment. Preeclampsia was diagnosed and treated both pharmacologically and conservatively with isolation and sensory deprivation. The protein loss was compensated by intravenous infusion of human albumin. Additionally, the patient was administered betamethasone.

Due to mastocytosis, the patient received loratadine and ranitidine hydrochloride before pregnancy. She had no history of hypersensitivity to non-steroidal anti-inflammatory drugs or antibiotics, did not undergo surgeries, and no signs of hypersensitivity were observed during lignocaine anesthesia for bone marrow biopsy.

Due to the high likelihood of preterm cesarean delivery, the patient was consulted by an allergologist in order to assess the potential anesthesia-related risks. Administration of cetirizine dihydrochloride and ranitidine hydrochloride was recommended, as well as premedication with prednisone, cetirizine dihydrochloride and ranitidine hydrochloride given 13, 7 and 1 h prior to the cesarean section.

IUGR was documented on fetal ultrasound. Furthermore, the centralization of fetal circulation was revealed on Doppler ultrasound.

Due to preeclampsia, proteinuria, and the premises for a possible stillbirth, cesarean section was conducted under spinal anesthesia. Clemastine fumarate, hydrocortisone acetate, ranitidine hydrochloride and urapidil; hydrochloride were administered intrapartum. The delivery was uncomplicated, but the pre-term male newborn (580 g, 27 cm) was delivered in poor status.

Early puerperium was complicated by the presence of persistent arterial hypertension and limb edema in the mother. The patient was administered prednisone, ranitidine hydrochloride, alpha methyldopa, urapidil hydrochloride, verapamil hydrochloride, diazepam, nadroparine calcium, cetirizine dihydrochloride and enalapril maleate. Due to poor status of the neonate, lactation was inhibited.

On postoperative day 5 the patient was discharged home on her request, in good general status, with arterial pressure between 150/80 mmHg and 170/120 mmHg, and persistent lower extremity edema. A protein-rich diet was prescribed due to persistently low serum level of albumins (25 g/l).

The neonate died at 22 days of life, due to extreme prematurity, circulatory failure and grade 3 intraventricular hemorrhage.

Case 2nd

A 24-year-old primipara at 31^{+6} week of gestation was admitted to the Obstetrical Department of Medical University of Gdansk due to suspected venous thrombosis of the left lower extremity, manifesting as pain, swelling and limited mobility of the limb (Figs. 1 and 2).

The patient suffered from the juvenile form of cutaneuos mastocytosis. The diagnosis of systemic mastocytosis was performed in 2006; the results were negative. Only mild reactions caused by the physical factors were reported.

The patient was previously treated at the outpatient clinic of the Allergology Department of Medical University of Gdansk due to cutaneous form of mastocytosis. The previous course of the disease was mild, without indications to steroid therapy or any severe manifestations. After confirming pregnancy, antihistaminic treatment was withdrawn due to normal level of mast cell tryptase (13 ng/ml). The patient was prequalified to spontaneous delivery under spinal anesthesia. She had no previous history of anaphylaxis during anesthesia, or drug allergies.

On admission, the patient was in good general and cardiopulmonary condition. Her BMI amounted to 23.8 kg/m^2. The entire skin of the patient was covered with urticaria-like