

LETTER TO THE EDITOR

Hypogammaglobulinemias in infants and toddlers with mastocytosis – a new aspect to analyze?

To the Editor,

Mastocytosis, the disease due to the accumulation of mast cells (MC) in one or more organs, affects both adults and children. It is a rare condition as far as the whole population is concerned, but among the patients of dermatological departments and clinics its frequency is higher (1). The occurrence of mastocytosis is sporadic in a great majority of cases; however, more than 50 familial cases and several pairs of monozygotic twins have been described (2). MC accumulate particularly in skin, bone marrow, liver, spleen, and lymph nodes. The clinical manifestation of the disease is due to an unspecific degranulation of MC and action of mediators released. In some cases, degranulation, apart from very intensive local or generalized redness of the skin, may result in dizziness, weakness, hypotension, or even loss of consciousness (3).

Two main categories of the disease have been described – cutaneous mastocytosis (CM) and systemic mastocytosis (SM). In the great majority of affected children, cutaneous form of the disease is diagnosed. CM is considered as benign, limited to the skin, transient disease which is usually associated with MC mediator-related symptoms. WHO distinguishes three major clinical manifestations of CM: maculopapular type (MPCM), diffuse cutaneous mastocytosis (DCM), and solitary mastocytoma of the skin. The most common forms are MPCM (47–75%) and solitary mastocytoma (17–51%). DCM is the most severe, rare form of CM (1–5%) (4). In all the forms of CM, even a mechanical irritation of the lesional skin results in localized reddening and urticarial swelling of different intensity.

Childhood-onset mastocytosis rarely has a very severe course with the presence of frequent incidents of flushing or anaphylaxis, obturation of bronchi, chronic diarrhea, osteoporosis resulting in pathological fractures, gastritis, or different forms of neurophysiological abnormalities (4). SM with bone marrow and internal organs involvement is a rare finding in children (5). Pediatric patients develop the first signs of the disease usually before the age of 2 years, the period of very intensive development. Depending on the extent and activity of the skin lesions, the course of the disease can be more or less affecting everyday life of a child and its family (6).

In our center, a group of 74 infants and toddlers with CM and recurrent infections was analyzed. There were 63 (85.13%) children with MPCM, 9 (12.16%) with DCM, and 2 (2.7%) with solitary mastocytoma. The age of the studied group ranged from 4 months to 3 years, mean age was 1 year and 8/12, and median of age was 22 months. There were 44 boys (59.45%) and 30 girls (40.54%). In none of the patients, serious infections were noted. The levels of main classes of immunoglobulins (Igs) were assessed with the use of immunoturbidimetric method and immunochemical system (Architect, Abbott). The blood samples were taken at the occasion of routine assessments after obtaining parent's informed consent

for clinical examination and blood analysis. The study was approved by the Medical Ethics Committee of the Medical University of Gdańsk and was conducted according to the principles of the Declaration of Helsinki. The levels of all the classes of Ig were interpreted according to the age of patients. In children with abnormal levels of Ig, blood samples were taken twice in a 3-month period.

In 12 (16.21%) young children with different forms of CM in retrospective analysis, we have found different types of hypogammaglobulinemia. There were seven boys and five girls in the immunodeficiency group. In the family history of the patients, there was no data concerning hypogammaglobulinemia. According to ESID Registry – working definitions for clinical diagnosis of primary immunodeficiency, version May 11, 2015, due to the young age of the studied group, what we found was unclassified antibody deficiency. In the group, there were 8 cases (10.81%) with highly probable THI, 3 cases (4.05%) with isolated hypogammaglobulinemia A, and 1 case (1.35%) with isolated hypogammaglobulinemia M. All the patients with hypogammaglobulinemia had normal values of lymphocytosis.

The concentration of serum immunoglobulins varies with age to have practical implications for evaluation and clinical approach. The outcome of hypogammaglobulinemia in children, owing to the heterogeneity in the pattern of clinical presentations, is hard to predict, and in many instances, the diagnosis can be made only retrospectively. Also, transitions between original, fully diagnosed primary immunodeficiencies may occur over time (7). The incidence of hypogammaglobulinemia in our group of infants and toddlers with CM, that constitute a group of intensive prophylaxis programs' realization, was much higher than that reported in the general childhood population, although – at least THI in our personal experience – seems to be more frequent than in available data (8).

A definite classification of observed hypogammaglobulinemias and statement concerning its clinical significance can be made when the immunodeficiency resolves or any other clinical transition appears (9). Even at the absence of serious infections, the high incidence of hypogammaglobulinemia in our group of patients may have its meaning concerning the prophylaxis and the newly reported higher incidence of autoimmune diseases in a group of adult patients with mastocytosis (10).

To our knowledge, this is the first report on higher incidence of hypogammaglobulinemia in a group of childhood-onset mastocytosis patients in comparison with general pediatric population. In conclusion, the results of our study may suggest that further investigation on the subject is required, especially in aspect of immunocompetence. Mastocytosis, particularly the pediatric form of the condition, still remains a not clearly understood disease.

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