Gastrointestinal Manifestations in a Child With Mastocytosis

Gholamhossein Fallahi[1], Parisa Rashtian[1], Majid Aflatoonian[3], Nazanin Babaei[1], Mehdi Gaisari[2], Nima Rezaei[4,5,6]

[1] Department of Pediatric Gastroenterology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

[2] Skin Research Center, Shahid Beheshti University of Medical Sciences, Shohada-e-Tajrish Hospital, Tehran, Iran

[3] Department of Pediatrics, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran

[4] Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

[5] Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

[6] Network of Immunity in Infection, Malignancy, and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), Tehran, Iran

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Abstract- Mastocytosis is characterized by the accumulation of mast cells in different tissues either in the skin or extracutaneous organs. Herein, a 13-year-old girl is presented who suffered from intermittent abdominal pain, nausea, diarrhea with erythematous, and papulous cutaneous lesion. She had a history of same lesions from the age of four years. Since 8 months ago, the patient presented with digestive complaints. The histopathological examination of the cutaneous lesions approved the diagnosis of mastocytosis. H1 and H2 antagonists were prescribed for her, while a mast cell stabilizer for digestive and cutaneous symptoms was also utilized, which improved the signs and symptoms of the patient.

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Introduction

Mastocytosis is a group of disorders, identified by abnormal proliferation and accumulation of mast cells in different tissues either in the skin or extracutaneous organs (1,2,3). This hematopoietic disorder has various manifestations, involving benign skin lesions to highly invasive neoplasms with the involvement of multiple systems. In the cutaneous type of mastocytosis, the mast cell proliferation is restricted to the skin; systemic mastocytosis has been involved in at least one extracutaneous organ, with or without evidence of infiltration of the skin. In systemic mastocytosis patients' bone marrow involvement is almost always present. Other frequently involved organs are spleen, lymph nodes, liver, and gastrointestinal (GI) tract (4).

Symptoms are caused by the release of histamine, and other inflammatory mediators cause flushing, urticaria, itching, diarrhea or to uncontrolled growth and infiltration of clonal mast cells in different organs such as the liver, spleen, and bone marrow (3,5).

In systemic mastocytosis, GI symptoms have been reported in 60-80% of patients such as abdominal pain, diarrhea, nausea, and vomiting (6,7).

Herein, we present a case of systemic mastocytosis with GI involvement.

Case Report

A 13-year-old girl was admitted to the hospital with periodic abdominal pains, accompanied by nausea, vomiting, diarrhea, headache, lightened head with hypotension since eight months ago. At the time of abdominal pain attack, she experienced pallor and hypotension. Frequency and severity of symptoms deteriorated from once a month to once a week within eight months. Abdominal pain was cramping followed by vomiting and loose stool.

She had a history of erythematous cutaneous lesions localized on the extremities and trunk and less on the face, deteriorated by sunlight and pressure since the age of eight. She was under symptomatic treatment with mupirocin and corticosteroids without any improvement. She was lost to follow-up until presenting with GI complaints.

Dermatological examination revealed erythematous maculopapular eruption and papulous and papulonodular hyperpigmented lesions on the back, dorsal site of hands,

Corresponding Author: M. Aflatoonian
Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran
Tel: +98 913 3518107, Fax: +98 21 66929235, E-mail address: aflatoonianm@yahoo.com

and foot (Figure 1A). She was also positive for Darier's sign (Figure 1B). Abdominal examination revealed no tenderness on the palpitation of the abdomen without hepatomegaly or splenomegaly.

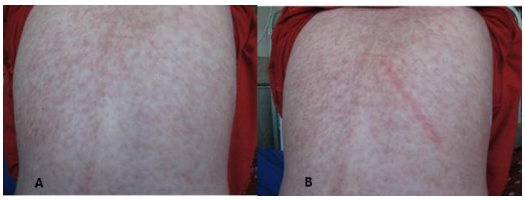

Figure 1. A. Erythematous maculopapular eruption and papulous and papulonodular hyperpigmented lesions on the back. B. Stroking of the lesions and the appearance of an erythema halo, Darier's sign

Laboratory tests showed a normal white blood cell count and biochemistry profile. On ultrasound sonography, the liver appeared with normal echo. The liver span was 130 mm. Spleen span was higher than normal. Jejunum thickness in a 10 cm segment was increased about 4.5 mm. Several mesenteric lymph nodes with a reactive view were seen in the midline periumbilical area. Computed tomography with oral and intravenous contrast showed the disseminated thickness of jejunum, dominant lymph node, and one fixed filling defect in the jejunum wall (Figure 2).

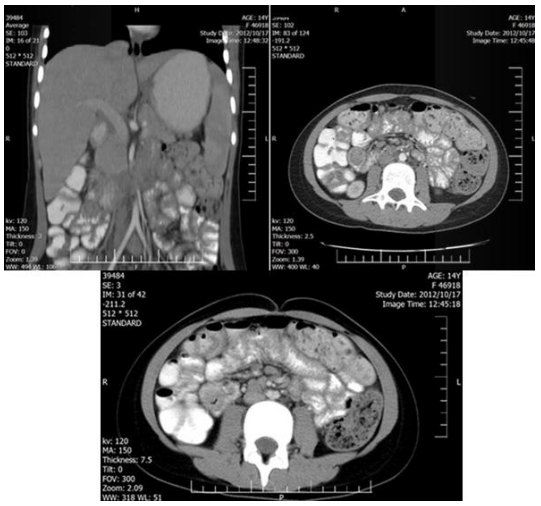

Figure 2. Images of computed tomography with contrast. The disseminated thickness of jejunum, dominant lymph node and a fixed filling defect in the jejunum wall

Upper endoscopy view till the second part of duodenum was normal. Biopsy of antrum revealed some lymphocytes and plasma cells, and on the biopsy of D2 intraepithelial cells, 5/100 was reported. Colonoscopy was done with a normal view, while pathological exams in the taken samples were normal.

Biopsy of skin was done, and microscopic description of skin biopsy reported mild infiltration of mononuclear inflammatory cells mostly, including round to spindle-shaped mast cells with metachromatic granules in toluidine blue staining around superficial and mid-dermal blood vessels or free in between collagen bundles. Mild perivascular and interstitial mast cell infiltrate in dermis was most compatible with clinical diagnosis of cutaneous mastocytosis.

The patient went on treatment with H1 and H2 blocker and mast cell stabilizers. After three months of treatment, she experienced relative improvement.

Discussion

Mastocytosis is a rare disease defined by abnormal growth, proliferation, and infiltration of mast cells in different organs. Mediator-related symptoms are seen in some diseases such as allergies, in different internal disorders such as neurologic or psychiatric diseases, and in other conditions such as myelodysplastic syndromes, primary myelofibrosis, acute myeloid leukemia, acute or chronic basophilic leukemia, and myelomonocytic leukemia (8). Increased number of mast cells in the mucosa of patients with GI diseases have been seen in diseases such as irritable bowel syndrome, mastocytic, enterocolitis, and systemic mastocytosis (9).

There are two main types of mastocytosis based on affected organs: cutaneous mastocytosis, characterized by the existence of lesions limited to the skin, and systemic mastocytosis, a heterogeneous disease in which the extracutaneous organs are affected, with or without skin involvement (**Error! Reference source not found.**,**Error! Reference source not found.Error! Reference source not found.**,**Error! Reference source not found.**,8,**Error! Reference source not found.**). Mastocytosis may present in any age groups. However, approximately 55% of mastocytosis patients develop their disease by 2 years of age, and in another 10%, disease onset occurs between the ages of 2 and 15 years. Thus, most patients are infants or children, and there is a general tendency for the diseases to regress with increasing age (**Error! Reference source not found.**). Most patients are children and present with cutaneous lesions (8). In children, the most common form is benign mastocytosis, generally presenting as solitary mastocytoma, urticaria pigmentosa, or diffuse cutaneous mastocytosis (8). In patients with systemic mastocytosis, bone marrow is the most commonly involved extracutaneous organ (10).

Clinical manifestations in patients with mastocytosis

result from the release of mast cell mediators or infiltration of mast cells in various organs, which may affect the skin, bone marrow, respiratory system, digestive tract, neuropsychiatric and hematologic systems. Mast-cell infiltration can cause organ dysfunction in aggressive type of systemic mastocytosis(7,9).

The clinical feature in systemic mastocytosis is ranging from an asymptomatic course to highly aggressive courses include constitutional signs, mediator-related findings such as flushing, headache, hypotension, syncope, abdominal pain, diarrhea or anaphylaxis and signs related to multisystem involvement with various organ infiltrations such as skin lesions, musculoskeletal disease, bone marrow infiltration, liver, and intestine involvement (2,5,7).

Most patients manifest with classical skin lesions and urticaria pigmentosa, as the most common manifestation of mastocytosis (2,3,7,8,9). The lesion of urticaria pigmentosa appears as scattered small reddish-brown macules or slightly raised papules. Scratching or rubbing the lesions usually causes urtication and erythema around the macules; this is known as Darier's sign (3).

Patients with the systemic disease may present with GI involvement, occurring in 14%-85% of patients and it counts as a second commonest symptom after pruritus (1,6).

GI manifestations include abdominal pain, nausea, vomiting, diarrhea, malabsorption, steatorrhea, hepatomegaly, splenomegaly, portal hypertension, and ascites secondary to portal hypertension. The most common problem is abdominal pain divided into two different types as dyspeptic and cramping. Dyspeptic pain is associated with gastric hypersecretion due to elevated plasma histamine with resultant gastritis and peptic ulcer disease which usually lasts from minutes to hours, whereas cramping pain occurs in waves and persists for several hours to days. Increased production of histamine in systemic mastocytosis can furthermore result in esophagitis, gastric ulcer disease, and intestinal malabsorption (3,6,7,9).

Our patient presented with periodic abdominal pains, accompanied by nausea, vomiting, diarrhea, headache, lightened head with hypotension since eight months ago. Abdominal pain was cramping followed by vomiting and loose stool. These symptoms were in the context of erythematous cutaneous lesions localized on the extremities and trunk and less on the face, deteriorated by sun light and pressure.

Diarrhea is usually episodic and is due to gastric acid hypersecretion; malabsorption is contributed to mucosal injury and edema, released from mast cell derived histamine and prostaglandins, altered bowel motility or tissue infiltration by mast cells (3,6). Vomiting may be due to histamine release with central emetic effect (**Error! Reference source not found.**). Patients with advanced systemic mastocytosis may also present with lymphadenopathy, liver dysfunction, malabsorption, ascites or cytopenia (8).

In our patient, skin lesions were suggestive for mastocytosis; the correct diagnosis was dependent on the detection of mast cells in the intestinal biopsies or skin biopsy (4).

At present, there is no effective therapy for systemic mastocytosis, while management includes the relief of symptoms associated with mast-cell mediator release and improvement of the quality of life. Patients with systemic mastocytosis should avoid triggers for mast cell degranulation as exposure to heat, cold, acute emotional stress, very strenuous exercise, alcohol and nonsteroidal anti-inflammatory drugs (5,9).

Controlling of the symptoms was obtained by treatment with drugs that block the effects of mediators released by mast cells as histamine H1 and H2 receptors antagonists, mast-cell stabilizing drugs such as ketotifen, cromolyn sodium, and anti-leukotriene drugs (1.5).

Treatment of GI disease is directed at controlling peptic symptoms, diarrhea, and malabsorption. Gastric acid hypersecretion leading to peptic symptoms and ulcerations is controlled with H2 antagonists. Diarrhea is difficult to manage, and H2 antagonists are generally not effective. In a patient with severe malabsorption, systemic steroids have shown to be effective (3).

The association of H2 antagonist (ranitidine, nizatidine, loratadine) with mast cell stabilizer (ketotifen) had been beneficial over both the cutaneous manifestations and over the digestive manifestations such as abdominal cramping and diarrhea (3,9). H1 antihistamines can help in controlling flushing and pruritis (9).

Mediator-related symptoms may present with unexpected severe anaphylaxis; therefore prophylactic histamine receptor antagonists are usually suggested, and supplementary glucocorticosteroids may be needed**Error! Reference source not found.**8).

Our patient was treated with combination of H1and H2 antihistamines which had better results, but not complete relief. After three months of treatment with loratadine and ranitidine, the digestive symptoms improved and the cutaneous lesions became less erythematous but hyperpigmented.

Systemic mastocytosis is rare, usually associated with

an urticaria pigmentosa, with difficult diagnosis in its absence. That is why in patients with macular or nodular-pigmented cutaneous lesions appeared in infancy and early childhood, a cutaneous biopsy is necessary (3). Also, physicians should be aware of GI symptoms as a manifestation of systemic mastocytosis. With a low clinical suspicion, the diagnosis is made on biopsy (6).

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