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A Case of Mastocytosis

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Summary: A case of systemic mastocytosis is presented and the relevant literature is reviewed.

Key words: Mastocytosis.

Mastocytosis is an uncommon disease of mast cell proliferation which occurs in cutaneous and systemic forms.It may appear at anytime from birth to middle age. Approximately three_quarters of all cases develop during infancy or early childhood.The etiology is unknown.We present a case of mastocytosis with systemic manifestations.

Case Report

A six month_old boy with severe blister and bullae formation was referred to the Erciyes University Department of Pediatrics.The clinical diagnosis of urticaria pigmentosa was established by documenting an increased number of mast cells by skin biopsy. He was admitted to the hospital at the age of 11 months with history of urticaria, intermittant flushing and diarrhea. Physical examination revealed cutaneous manifestations and hepatosplenomegaly. Laboratory studies consisted of a haemoglobin value 7,5 gr/dl,protombin time 12 seconds,partial tromboplastin time 41 seconds.

Skin biopsy reveaded numerous ovoid mast cells with uniform centrally located nuclei in the superficial dermis. These cells could be difficult to differerentiate form lymhocytes in rutin hematoxyline and eosine stained sections. The sections were stained with toluidine blue, dementrating metachromatic intracytoplasmic granules were obvious. A few cells were elongated and closely simulated fibroblasts and pericyts. Mast cells were limited to upper third of the dermis and surrounding capillary vessels. The overlying epidermis was normal. Increased brown colored pigment in the basal layers of epidermis was melanine (Figure 1)

After the skin biopsy,the liver biopsy was performed.The sections stained with rutin hematoxyline and eosin. Essential hepatic architecture was normal.Periportal diffuse infiltration had consisted of mast cells with Eosinofilic intracytoplasmic granules. These cells had large, pale nuclei and distinct cytoplasmic baundaries.

On staining with toluidine blue, the typical metachromatic cytoplasmic granules could be identified. The portal tracts contained mononuclear cell infiltration. Some hepatocytes showed mild granular

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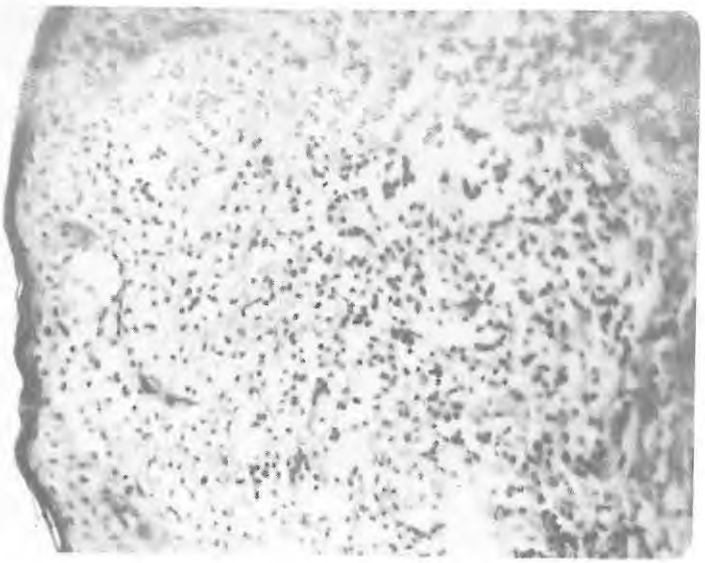

Figure-1 : Mast cells lie closely packed in the upper dermis (HE X 160)

degeneration.The final diagnosis was mastocytosis. The patient was given antiserotonin agents and mast cell stabilizer.

Discussion

Mastocytosis is a term used to describe a group of clinical disorders characterized by the accumulation of mast cells in the skin and at times, generally in adults, other organs of the body.

The clinical spectrum of mastocytosis includes:

1-Single or multiple small cutaneous nodules(solitory mastocytoma)

2-A cutaneous form characterized by multiple hyperpigmented macules or papules(urticaria pigmentosa)

3-A diffuse form in which virtually all of the skin is infiltrated with mast cells (Diffuse cutaneous mastocytosis)

4-Unusual telangiectases of the trunk and extremities usually seen in adults and rarely in children. (Telangiectasia macularis eruptive persistans)

5-Systemic mastocytosis, a condition in which mast cell proliferation occurs in various organ systems, including skin, liver, spleen, lymph nodes, lungs, bones, gastrointestinal tract.

6-Malignant form of mast cell leukemia seen primarily in adults and rarely in children.

Cutaneous manifestations are generally reddish brown, and plaquelike or nodular. Much less common are the telangiectatic and the doughy-feeling erythrodermic forms. When a cutaneous lesion is stroked firmly, it often becomes pruritic and raised with surrounding erythema. Stroked cutaneous lesions of very young children with the disease may vesiculate as it occured in our

patient.[2]

Systemic symptoms of an acute nature reflect a sudden and greatly elevated level of released mast cell mediators.[4] An acute symptomatic systemic episode may focus on the vasculate and presents with headache, flushing, dizziness, tachycardia, hypotension, syncope and even frank shock rarely irreversible and fatal,and/or on the gastrointestinal tract, causing anorexia, nausea, vomiting and diarrhea. Occasionally rhinorrea and rarely, audible wheezing occurs,reminiscent of the signs of rhinitis and asthma,respectively.[2,16] Since the presented case showed hepatic and gastrointestinal system involvement our diagnosis in this case was systemic mastocytosis.

Malabsorption with or without steatorrhea may be due to the chronic release of mediators from mast cells infiltrating small bowel mucosa and lamina propria. Hepatomegaly or hepatosplenomegaly occurs in 5-10 percent of patients and is directly related to the infiltrative disease of these organs.[13] Biopsy specimens may reveal periportal proliferation of mast cells, eosinophil infiltration and fibrosis,and these findings may account for the rare manifestations of portal hypertension and gastroesophageal varices.[14] More than10 percent of all mastocytosis patients have osseous lesions most commonly in the pelvis, ribs, vertebrae, skull and proximal long bones.Anemia, leukopenia, thrombocytopenia, and even mast cell leukemia have been rarely reported in association with severe bone marrow infiltration by mast cells.[15]

Mast cells are abnormal in number in mastocytosis. The cells degranulate in response to physical stimuli such as gentle stroking and moderate heat or cold and the chemical agents known to be histamine releasers such as codeine and radioopaque dye.Once a skin urticates it requires up to 3 days to regenerate adequate granule histamine for the quantification of mast cells in both normal and pathologic sections of skin.Morphomeric counting technique in combination with the conjugated-awidin stain, provides a simple and accurate method 8.

The average plasma histamine concentration is elevated in children with cutaneous or systemic mastocytosis.Plasma levels may indicate possible systemic involvement and provide supportive evidence of progression or regression of the disease.[4] High dermal concentrations of histamine may be responsible for the induction of the skin pigmentary changes associated with local proliferation of mast cells such as urticaria pigmentosa and systemic mastocytosis[9]. The infiltrating mast cells are immature[10].

The heparin released from mastocytons cells has been implicated in the prolonged local bleeding time at the sites of excised lesions.The occasional purpura underlying cutaneous mastocytoma, and the rare incidence of significant gastrointestinal bleeding related to local mast cell infiltration.

The moderate eosinophilia is noted in 10 to 20 percent of patients with mastocytomatoma.[11] Association of tissue eosinophilia with mastocytosis, lesions in bone and periportal spaces reflects the action of eosinophilatactic granule peptides and the generation from arachidonate of

monohydroxyeicosatetraenic acids and leukotriene B_4. The development of porotic and sclerotic osseous lesions may relate to the action of mast cell tryptase and acid hydrolases. Osteoporosis may also be releated to treatment with high dose heparin.[7]

Elevated levels of PGD_2 metabolites have been detected in urine of patients with flushing, hypotermia and schock in the absence of cutaneous lesions.[2] PGD_2 has also been identifed in the blister fluid, from a patient with bullous mastocytosis.Besides PGD_2, histamine and platelet activating factor(PAF) were present in the blister fluid.The interaction between PAF and the inhibitor of platelet aggregation in patients with systemic mastocytosis may provide an explanation for some of the manifestations of the disease in particular the episodic hypotension, cutaneous flushing and pallor.[12]

Treatment of patients with symptomatic cutaneous lesions may be necessary. Pruritis and whealing can be controlled by hydroxyzine. The addition of H_2 blocker cimetidine, has been helpful.[1,2] Drugs known to cause mast cell degranulation such as alcohol, morphine and codeine are to be prohibited. For the gastrointestinal symptoms oral therapy with disodium cromoglycate has been effective.[1]

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