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Case Report

Bullous mastocytosis: A rare variant of diffuse cutaneous mastocytosis

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Abstract Mastocytosis is an uncommon myeloproliferative disorder characterized by rapid proliferation of mast cells and their accumulation in multiple organs. Skin is solely involved in cutaneous mastocytosis, while on the other hand, internal organs like bone marrow, liver, spleen, and lymph nodes are involved in systemic mastocytosis. We reported a case of a four year old girl who presented in dermatology OPD of Mayo Hospital Lahore with 1 month history of vesiculobullous eruption that gradually evolved to form multiple erythematous to hyper-pigmented papules and plaques with doughy consistency and few papular lesions on forehead as well associated with intense itching with few systemic manifestations. Skin biopsy was performed that showed normal epidermis, sub epidermal blister and papillary dermis contain mixed inflammatory infiltrate composed of mast cells, eosinophils and neutrophils suggestive of "Bullous Mastocytosis." Few such cases have been reported previously. Due to its rarity, pediatricians, dermatologists, and haematologists must remain aware of the different variants of cutaneous mastocytosis.

Key words
Cutaneous mastocytosis; Systemic mastocytosis; Mast cells; Bullous mastocytosis.

Introduction

Mastocytosis is an uncommon myeloproliferative disorder characterized by rapid proliferation of mast cells and their accumulation in multiple organs. Skin is solely involved in cutaneous mastocytosis, while on the other hand, internal organs, specifically bone marrow, liver, spleen, and lymph nodes are involved in systemic mastocytosis.[1,2]

Having a role in immune functions, normal mast cells develop from haematopoietic progenitors. They are activated on binding to an antigen which cross-links antigen specific IgE on the mast cell surface. Multiple triggers such as physical stimuli of stress and pressure, as well as substances such as aspirin, alcohol, anticholinergic drugs, opioids, and radioactive dyes can activate them.[3-5]

Systemic mastocytosis symptoms can result from either release of mediators or tissues being infiltrated by mast cells. Systemic mastocytosis can involve multiple organs and can cause wide range of symptoms depending upon each of these systems: gastrointestinal tract (diarrhea, vomiting), lungs (shortness of breath, wheezing), heart (syncope, tachycardia), musculoskeletal system (bone pain, osteopenia), the skin (rashes, flushing), and nervous system (concentration problems, migraines, depression). General symptoms include fever, malaise, fatigue, and allergic reactions. However anaphylactic reactions are more common in patients of mastocytosis as compared to general population.[6]

Case report

A four-year-old girl was presented in dermatology OPD of Mayo hospital Lahore with

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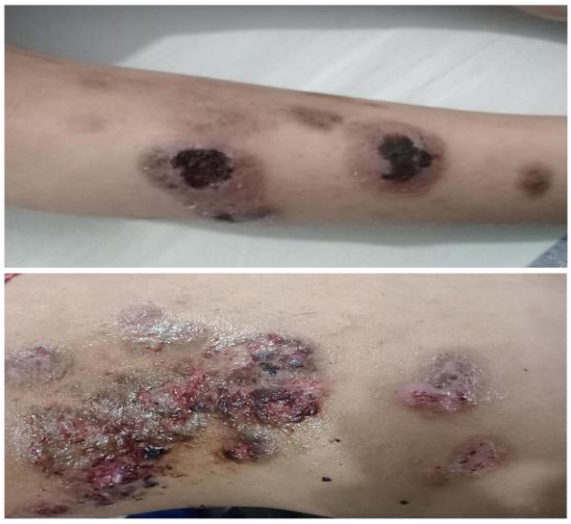

Figure 1 Erythematous to hyper-pigmented plaques on leg and back.

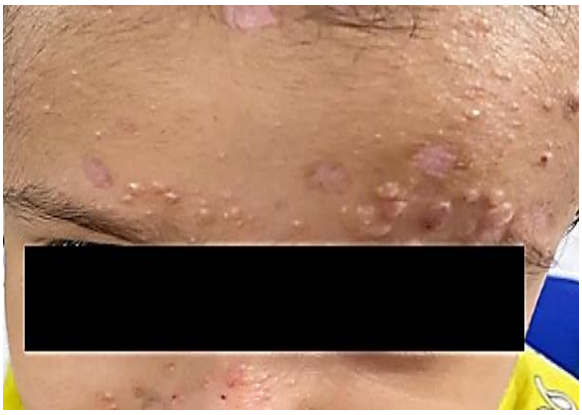

Figure 2 Erythematous papules on forehead.

one month history of vesiculobullous eruption that gradually evolved to form multiple erythematous to hyperpigmented papules and plaques with doughy consistency starting from back and then extended to involve abdomen and lower limb and a few papular lesions on forehead as well, associated with intense itching. Mother of the patient reported low grade intermittent fever and undocumented weight loss for two years; however, there was no history of lymphadenopathy. There was history of occasional oral ulcers involving buccal mucosa. Mother also reported diffuse abdominal pain, recurrent diarrhea, blood in stool and intermittent haematuria for two years. A history of flu, sneezing, and recurrent chest infection since birth was also reported. However there was no history of food allergies, blushing, hypotension, or anaphylactic shock.

Physical examination reveals a young girl with obvious pallor and multiple erythematous to hyper-pigmented plaques on abdomen, back, and lower limbs **(Figure 1)**, and a few erythematous papules on forehead **(Figure 2)**. However, there was no lymphadenopathy, chest and abdominal examination was unremarkable.

Baseline investigation and work up for systemic involvement was done that included complete blood count with peripheral smear which shows HB 8.1 with microcytic hypochromic anemia, ESR 40. Renal function test (RFT), liver function test (LFT), serum electrolytes, and urine complete examinations were normal. However stool for occult blood was positive and X-ray chest showed enlarged cardiac shadow and ultrasound abdomen revealed hepatosplenomegaly. Tzank smears for acantholytic cells and giant cells were done from fresh blisters to rule out other blistering disorders that were negative. Skin biopsy was performed that showed normal epidermis, sub-epidermal blister and papillary dermis composed of mixed inflammatory infiltrate predominantly mast cells with typical fried egg appearance. Sub cutis was normal **(Figure 3)**. Findings were suggestive of "Bullous Mastocytosis". Bone marrow biopsy and CT Abdomen and Chest were planned to determine systemic mastocytosis but parents refused invasive procedure and further work up. Furthermore patient left the ward against medical advice and was lost to follow up so further systemic involvement could not be ruled out.

Patient was started on H1 and H2 receptor blockers, mast cell stabilizer (montileukast), and diluted topical steroid that was advised to apply on lesions showed some improvement in symptoms.

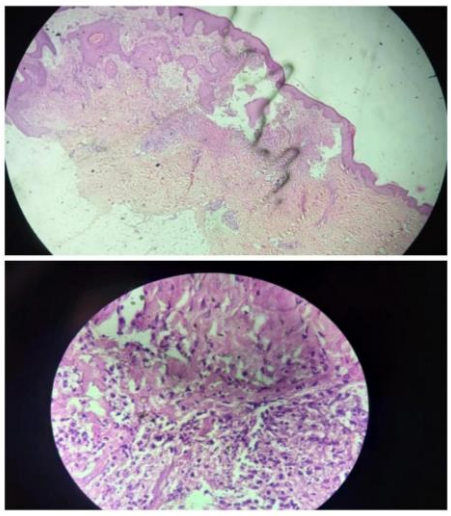

Figure 3 Biopsy shows subepidermal split and dense inflammatory infiltrate predominantly mast cells with typical fried egg appearance.

Discussion

Easily mistaken for other blistering pediatric dermatoses, bullous mastocytosis is often characterized by initial presenting symptoms of vesiculobullous eruption. The mainstay of treatment includes controlling the symptoms caused by de-granulation of mast cells and avoidance of triggering factors. Neonatal onset disease has a relatively poor prognosis, and therefore, recognition of this uncommon form of mastocytosis is important. It is associated with life-threatening complications, including vasodilation, gastrointestinal bleeding, anaphylactic shock, and death.[7]

The prevalence of pediatric mastocytosis has been estimated to be 10 in every 100,000 people. Most childhood cases are benign and present with the cutaneous type of mastocytosis. Urticaria pigmentosa accounts for around 70 to 90% of the cases and the other types including mastocytomas, diffuse cutaneous mastocytosis, and telangiectasia macularis eruptive perstans account for 30% or fewer of the cases. In the present case, the patient presented with an extremely rare bullous variant of diffuse cutaneous mastocytosis. Some researchers have proposed to have a rare occurrence of 1 in 1,000,000 individuals.[8]

Very few cases of bullous mastocytosis with systemic involvement have been reported in literature. Almheiri SK *et al.* reported a similar case of bullous mastocytosis in a child of six months, who presented with generalized blisters on the body.[8] Another case was reported by Asati DP *et al.*, a child presented with generalized eruption of multiple hyper-pigmented macules and plaques, along with a few vesico-pustular lesions.[9] As in our case history, physical examination and baseline investigations were in favor of systemic mastocytosis and other blistering disorders were ruled out by performing Tzanck smears that were negative, and cutaneous biopsy was also suggestive of bullous mastocytosis. However systemic involvement could not be proved further by bone marrow examination and CT scan Abdomen and Chest as patient left the ward against medical advise and was lost to follow up. Clinicians must remain aware of this rare form of mastocytosis as systemic involvement may need aggressive therapy.

The discussion continues regarding different treatment options including aggressive management plans for pediatric mastocytosis. Most cases with only cutaneous manifestations resolve with time and hence can be managed by symptomatic treatment. Only few cases remain persistent, and require repeated bone marrow examination to rule out systemic involvement and need aggressive systemic therapy.[10]

Conclusion

Due to the rarity of bullous mastocytosis, pediatricians, dermatologists, and haematologists must remain aware of the different variants of cutaneous mastocytosis.

Each individual case may require distinctive treatment plan according to the extent of the disease.

Limitations of study Bullous mastocytosis was confirmed on histopathology but extensive work up could not be performed to confirm systemic involvement as patient left the ward against medical advice.

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent.

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Conflict of interest Authors declared no conflict of interest.

Authors' contribution

HA,IH: Diagnosis and management of the case, manuscript writing, has given final approval of the version to be published.

SJ,WS,SS: Identification, diagnosis and management of the case, critical review the manuscript, has given final approval of the version to be published.

NH: Management of the case, manuscript writing, has given final approval of the version to be published.

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