Diffuse Cutaneous mastocytosis (DCM) occurs due to abnormal accumulation of mast cells in the skin. We report an 8-month-old infant presented papulovesicular lesions, predominantly on the trunk. Skin biopsy revealed subepidermal bulla, interspersed with mast cells, eosinophils and neutrophils. Direct immunofluorescence microscopy of perilesional skin revealed nonspecific deposition of IgM in granular pattern along the dermoepidermal junction.

Key Words: Diffuse cutaneous mastocytosis, granular IgM deposition, vesiculobullous lesions

Introduction
Blistering skin eruption in children may pose a diagnostic challenge to the clinician; a variety of hereditary and acquired conditions may manifest with blisters in the pediatric age group. Epidermolysis bullosa tops the list of hereditary cause while the infections (both bacterial and viral) account for the bulk of acquired causes of blistering eruption in a child. Diffuse cutaneous mastocytosis (DCM) is rarely considered in the differential diagnosis of blistering eruption during infancy. We report an infant of DCM who presented with infiltrated papules and vesicular eruptions; perilesional biopsy revealed granular IgM deposition at dermoepidermal junction (DEJ) on direct immunofluorescence (DIF) microscopy.

Case Report
An 8-month-old male infant born of nonconsanguineous marriage presented with itchy lesions all over the body for 3 months. Parents observed itchy, erythematous lesions initially over the scalp; subsequently, the child developed similar lesions all over the body. Parents also observed spontaneous eruption of blisters over the trunk; these would rupture in 3–4 days’ time and heal with postinflammatory depigmentation. There was no history of diarrhea or breathing difficulty. Cutaneous examination revealed erythematous papules and infiltrated plaques with superimposed grouped vesicles on the chest, abdomen, and back [Figure 1]. Gentle stroking of the skin demonstrated erythema and wheals over the area (positive “Darier’s sign”). Areas of hypo- and de-pigmentation were present over the face, neck, and back. Palms, soles, and mucous membrane were spared. A clinical diagnosis of “vesicular” type of DCM was made. Routine hematological, biochemical parameters were within the normal limits. Histopathological study from the lesion on the chest showed subepidermal bulla and numerous mast cells with interspersed eosinophils and neutrophils throughout the dermis [Figure 2]; toluidine blue staining revealed diffuse mast cell infiltration in the dermis and intracellular metachromatic granules [Figure 3]. DIF microscopy from the perilesional skin revealed granular IgM deposition at the DEJ [Figure 4].

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What was known?
• Diffuse cutaneous mastocytosis results from extensive accumulation of mast cells in the skin
• It presents during infancy with blister formation either on normal skin or superimposed on infiltrated papules.

Discussion

Cutaneous mastocytosis (CM) occurs due to abnormal accumulation of mast cells in the skin. It is an uncommon disease with a prevalence of 1 in 25,000–30,000 in the general population.\(^1\) Approximately two-third of cases of CM occur in the childhood; nearly half of these patients have manifestations of disease before the age of 2 years.\(^1\) Pediatric mastocytosis is slightly more common among males in contrast to adult patients where the male to female ratio is almost equal.\(^2\) Although CM is usually sporadic, familial cases with autosomal dominant mode of inheritance have been reported.\(^1\)

Four morphological types of CM have been described: urticaria pigmentosa, solitary mastocytoma, DCM, and telangiectasia macularis eruptiva perstans.\(^3\) DCM is an extremely rare and the most severe clinical presentation of CM, characterized by entire skin infiltration of mast cells.\(^4\) Two clinical variants of DCM have been described in infants.\(^5\) The first variant is characterized by the presence of “large hemorrhagic bullous” lesions that appear early in life. The other subset of patients will have “infiltrative small vesicular” lesions, like the one presented in this report. Tendency for blister formation ceases gradually with time after the age of two and the skin becomes less reactive. In CM, gentle brisk stroking of the skin causes urtication, flare, and sometimes blister formation due to release of histamine from mast cells. This change is referred to as Darier’s sign.\(^6\)

Based on the age of onset of disease, Orkin \textit{et al.} described two forms of presentations of bullous DCM: The neonatal form and the late-onset disease.\(^7\) The former variant has a greater risk of extracutaneous involvement while the latter type (as in our case) shows minimal extracutaneous involvement and has a better prognosis. Pediatric CM is a regressive disease and was previously considered to be nonclonal. However, a recent review of 1747 cases of pediatric CM suggests that it is a clonal disease in 44\% of cases.\(^8\) The typical childhood disease is linked to Glu839Lys c-kit mutation while the adult disease is often linked to Asp816Val c-kit mutation.\(^3\)
The diagnosis of CM requires the triad of typical skin lesions, histological confirmation of focal mast cell infiltrates in the dermis, and the absence of criteria involving systemic involvement. Histopathology is the gold standard for the diagnosis of bullous DCM and shows subepidermal bulla and increased accumulation of the mast cell in the superficial and mid-dermis. The special stains used to detect mast cells in tissues include Giemsa, toluidine blue, and monoclonal antibodies that recognize tryptase or CD117. Serum tryptase level is elevated in pediatric mastocytosis with extensive cutaneous involvement. We could not estimate serum tryptase level in our patient due to financial constraints.

The pathogenesis of bulla formation in DCM is unknown. It is hypothesized that activated mast cells release potent pro-inflammatory cytokines such as interleukin-8 which may initiate intense inflammation along the DEJ leading to blister formation. Mast cell granules and protease–heparin proteoglycan complexes that are released from mast cells may also induce cleavage of the basal membrane components directly or by activation of collagenolytic matrix metalloproteinases leading to the formation of subepidermal bulla.

The presence of granular deposition of IgM along the basement membrane zone (BMZ) is an interesting finding in our case. Granular staining of BMZ with IgM has been reported in heterogeneous group of diseases including systemic lupus erythematosus (SLE). In SLE patients, it usually occurs in conjunction with other immunoreactants, whereas isolated IgM deposition along the BMZ is seen more frequently in non-SLE subgroup of patients. The significance of IgM deposition in DCM is unclear; it could be due to the pronounced inflammation along the DEJ. There was no evidence of systemic involvement or features of autoimmune diseases in our case. Recently, similar finding has been observed by Slavescu et al. in a 6-month-old infant with bullous DCM. Further studies in a large number of patients with DCM are required to confirm this finding.

Majority of cases of pediatric DCM subside partially or completely within 6 years of age. In other patients, the disease presents a stable course or progresses relentlessly. Those children with extensive bullous lesions, early onset of disease and those with symptoms of vasodilatation (flushing or hypotension) are at potential risk of experiencing shock or sudden death. The vast majority of cases require only symptomatic treatment. Drug therapy is aimed to stabilize the mast cell membrane and block the action of inflammatory mediators. The mainstay of treatment is histamine blockers and avoidance of triggering factors (nonsteroidal anti-inflammatory drugs, opioids, and trigger foods which cause degranulation of mast cells). Long-term follow-up of children with DCM is necessary as the disease may have reserved prognosis in at least few patients.

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Nil.

**Conflicts of interest**
There are no conflicts of interest.

**What is new?**
Granular deposition of IgM along the dermoeidermal junction is a unique finding in our case.

**References**