Diffuse Cutaneous Mastocytosis in a Filipino Newborn: A Case Report*

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ABSTRACT

INTRODUCTION: Cutaneous mastocytosis is the accumulation of mast cells in the skin. Diffuse cutaneous mastocytosis is a rare variant accounting for only 1.74% of al mastocytosis cases reported. Ninety percent of cases are seen in children presenting with multiple erythematous to yellow-tan papules and plaques with leathery texture. The pathogenesis is in the structure and activity of kit receptor expressed on mast cells, melanocytes and other cells.

CASE SUMMARY: This is a female neonate born to an 18 year old mother, G1P1 via vaginal delivery at 37 weeks age of gestation. Patient presented with a generalized involvement of multiple, well defined, indurated, leathery, brown papules and confluent plaques. Darier sign was positive. Histopathological examination revealed diffuse involvement of the dermis with mast cells. Giemsa stain was positive. Patient was diagnosed both clinically and histopathologically with diffuse cutaneous mastocytosis without systemic involvement. She was treated with H1 antihistamines and topical glucocorticoids.

CONCLUSION: Diffuse cutaneous mastocytosis can be diagnosed both clinically and histopathologically. Treatment is mostly symptomatic. It is always prudent to inform co-managing physicians, the patient, and their families of potential mast cell degranulating stimuli and to watch out for signs and symptoms for systemic involvement.

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INTRODUCTION

Mastocytosis is a sporadic disease characterized by pathologically increased number of mast cells predominantly in the skin, bone marrow, liver, spleen, lymph nodes and gastrointestinal tract. There are seven variants of mastocytosis according to the World Health Organization (WHO) classification: cutaneous mastocytosis, indolent systemic mastocytosis, systemic mastocytosis with associated clonal hematological non-mast cell-lineage disease, mast cell leukemia, extracutaneousmastocytosis, mast cell sarcoma and aggressive systemic mastocytosis.[1]

In our country, based on the data from Philippine Pediatric Society, mastocytosis in general presents in 6 out of 2,598,210 patients aged 0-18 year old seen from May 2006 to present.[2]

Cutaneous mastocytosis (CM) represents over 90% of all mastocytosis cases and is the most common presentation with a predilection for the pediatric age group. CM is made up of three major variants: urticariapigmentosa (UP), mastocytoma and diffuse cutaneousmastocytosis (DCM). Approximately 58-90% of patients have the UP subtype, and 10-40% have mastocytoma. Diffuse cutaneous mastocytosis is the rarest variant accounting for only 1.74%.[3]

In Europe, 71 children with cutaneous mastocytosis were analyzed. 53 (75%) cases present with urticariapigmentosa, 12 (17%) with mastocytoma and 6 (8%) with diffuse cutaneous mastocytosis.[4] A study was done in Israel wherein they conducted a retrospective chart review of all pediatric cases diagnosed with cutaneous mastocytosis over the last 20 years. Of the 180 patients identified, 117 (65%) were diagnosed with urticarial pigmentosa, 62 (34.4%) with mastocytoma and only 1 (0.6%) with diffuse cutaneous mastocytosis.[5]

CASE REPORT

A female neonate with an APGAR score of 8,9 was born with leathery skin and brown nodules all over the body. The patient was born to non-consanguineous parents via vaginal delivery at 37 weeks AOG to an 18 year old, G1P1 (1001) mother. Mother had six prenatal check-ups at a local health center and was prescribed with multivitamins and ferrous sulfate. No systemic illness was noted during the course of pregnancy. Syphilis and HBsAg were both non reactive. No complications were encountered during delivery. No family history of any congenital anomalies or dermatologic disease was elicited on both the maternal and paternal side of the patient.

Physical examination revealed generalized involvement, with lesions consisting of multiple, well defined, indurated, leathery, brown papules and confluent plaques (Figure 1). No vesicles and bullae seen at that time. Darier sign was positive. A clinical diagnosis of diffuse cutaneous mastocytosis was made by the Dermatology service. The mother was advised regarding the condition. The patient's caregivers were instructed to keep the patient in a cool, comfortable environment, and to limit intense rubbing or manipulation of the patient's skin. Caution on giving mast cell degranulating agents such as anticholinergic preparations, aspirin and other NSAIDS, narcotics, polymyxin B sulfate, systemic anesthetics and certain food were also discussed with the people directly involved in the patient's care.

Skin punch biopsy (3mm) was done with consent and sent for H&E and Giemsa stains. Liver enzymes and clotting indices were increased, prompting referral to Pediatric Gastroenterology, Hematology and Oncology respectively, to evaluate for possibility of systemic involvement and rule out systemic mastocytosis. Additional hepatobiliary tree ultrasound, x-ray of skull, chest and pelvis and peripheral blood smear were requested.

New vesicles, bullae and crusted lesion were noted starting on the 8th DOL (Figure 2). Normal saline solution compresses on crusted areas was advised. Mometasone furoate cream was also applied to new bullous lesions.

Histopathological examination revealed diffuse infiltration of mast cells on the entire dermis. Giemsa stain was positive for mast cells. H1 antihistamine, Hydroxyzine was prescribed at 1.2-2 mg/kg TID to mitigate excess histamine release.

At 12th DOL, patient was observed to be less irritable, still with elevated liver enzymes, and no progression of cutaneous lesions were noted (Fig3).

DISCUSSION

Diffuse cutaneous is encountered almost exclusively in infants, rarely in neonates, and may persist into adult life. It has been associated with systemic mastocytosis particularly the indolent type. Deaths associated with extensive mast cell mediator release in both children and adults are rare but have been reported.[3]

The pathogenesis of mastocytosis reveals changes in the structure and activity of kit receptor expressed on mast cells (MC), melanocytes, and other cells. Stem cell factor (SCF) is the ligand for the transmembrane tyrosine kinase receptor c-kit, and is an important growth factor for the final maturation and development of mast cells. Uncontrolled proliferation of mast cells in mastocytosis seems to be secondary to abnormalities of ligand-receptor (c-kit ligand).[5]

Patients presenting with childhood CM may complain of pruritus and flushing, often exacerbated by exercise, heat or local trauma to skin lesions. They may also experience abdominal pain, diarrhea, palpitations, dizziness and syncope. When there is extracutaneous involvement, patients may present with fever, night sweats, malaise, weight loss, bone pain, epigastric distress, and cognitive disorganization. It is to be noted that in mastocytosis, there is a relative absence of pulmonary symptoms.[3]

Cutaneous presentation of diffuse cutaneous mastocytosis includes multiple erythematous to yellow-tan papules and plaques with leathery texture.[5] Some may describe it as peaud'orange appearance on the skin surface (Figure 4). cutaneous mastocytosis and urticariapigmentosa are associated with a non-scarring bullous eruption. The vesicles and bullae usually resolve when patient is about 3 to 5 years of age.[6] DCM presenting with generalized bullae has a relatively poorer prognosis and has been observed to have a higher rate of transformation to systemic mastocytosis (SM).[3] The blisters are believed to be due to serine proteases that are released from mast cells.

Basically, the diagnosis of childhood CM is based on the clinical presentation of the cutaneous lesions, a positive Darier sign and the presence of significant mast cell hyperplasia on histologic study.

Darier sign is the development of an urticarial wheal after firmly rubbing a characteristic lesion. The sign is more apparent in childhood urticarial pigmentosa and mastocytomas rather than in adult mastocytosis. This is elucidated by the fact that there is a 40 to 150 fold greater mast cell concentrations in childhood UP and mastocytomas than normal skin as compared to 8-fold greater content in adult mastocytosis.[6] Stains used to detect mast cells in tissues include Giemsa, toluidine blue, Leder, and monoclonal antibodies that recognize tryptase or CD117.[3]

Treatment for cutaneous mastocytosis is conservative and symptomatic. The goal is alleviation of symptoms using anti-mediator drugs such as antihistamines, cromolyn sodium, acetyl salicylic acid and ketotifen. The importance of emollients should be emphasized. To decrease histamine release associated pruritus, flushing and wheal formation, intake of H1 antihistamines such as hydroxyzine, cetirizine and fexofenadine is effective. H2 antihistamines for management of excess gastric secretion such as cimetidine and ranitidine can then be combined to H1 blocker to support control of symptoms of mastocytosis.[7,8]

Patients and their family members should be informed of potential mast cell degranulating stimuli such as ingested alcohol, anticholinergic preparations, aspirin and other NSAIDS, narcotics, polymyxin B sulfate, systemic anesthetics, heat and friction. A number of systemic anesthetic agents have been directly and indirectly linked in precipitating symptoms of mastocytosis. It is recommended to monitor patients 24 hours post operatively after undergoing surgery with general anesthesia to watch out for delayed anaphylaxis, although, injections of lidocaine can be used safely in these cases. Foods such as crawfish, lobster, spices, cheese and hot beverages should also be avoided.

Case reports showed good cutaneous response to application of psoralen plus PUVA, local corticosteroids with occlusion or intralesional triamcinolone acetonide injections.2 Under occlusion potent topical glucocorticoids for 8 h/day for 8-12

weeks decreases the number of lesional skin mast cells. However this method can cause skin atrophy and when the treatment is discontinued, recurrence of lesions are expected within the year. 1-2 months treatment of methoxypsoralen with ultraviolet A (PUVA) light given four times a week can aid in the pruritus and appearance of wheals of CM patients. Though, within 3-6 months of discontinuation of PUVA pruritus often reappears.

Prognosis of diffuse cutaneous mastocytosis is variable, though most bullous lesions spontaneously resolve before 5 years of age. DCM is also linked to have an increased risk of systemic involvement. Mast cell leukemia has been reported in persistence of diffuse cutaneous mastocytosis in adulthood that has developed to indolent systemic mastocytosis.

CONCLUSION

Diffuse cutaneous mastocytosis occurs most exclusive in infants but is rarely seen in neonates such as the case presented. Cutaneous presentation ranges from leathery papules and plaques as well as vesicles and bullae. Physicians and family members should be informed of the potential mast cell degranulating stimuli and also of the signs and symptoms for systemic involvement. Mainstay of treatment remains to be application emollients, and topical glucocorticosteroids plus addition of H1 with or without H2 antihistamines.

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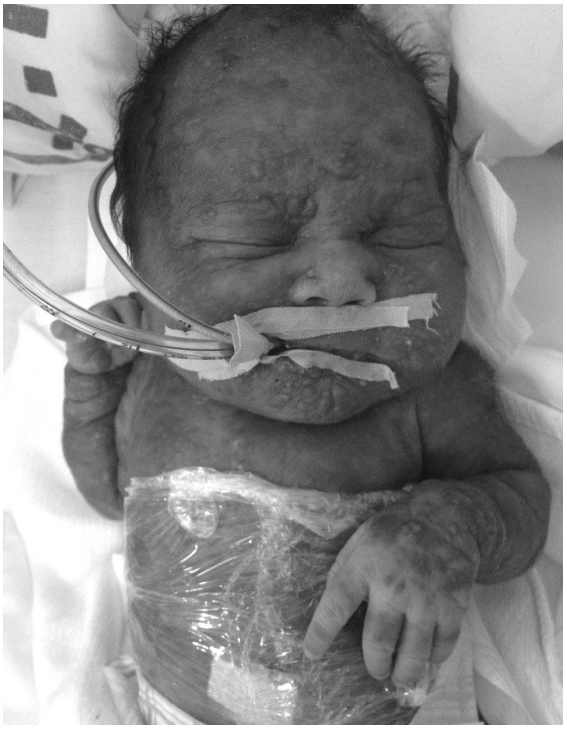
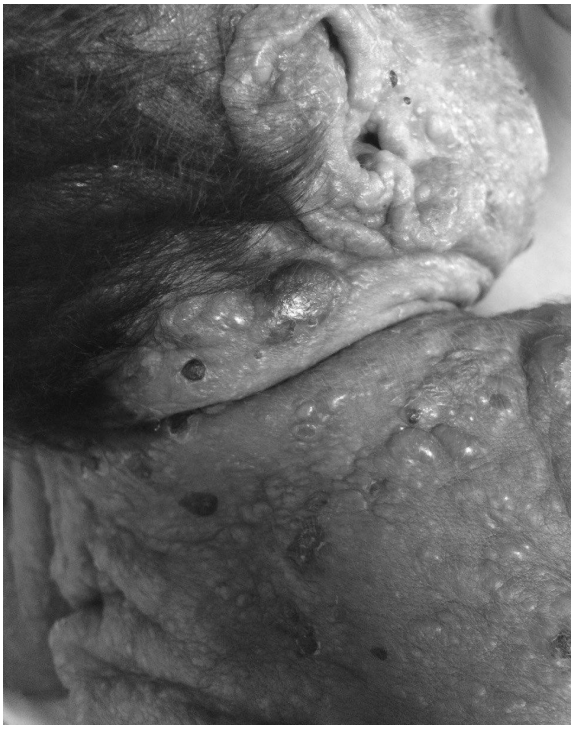


Figure 1



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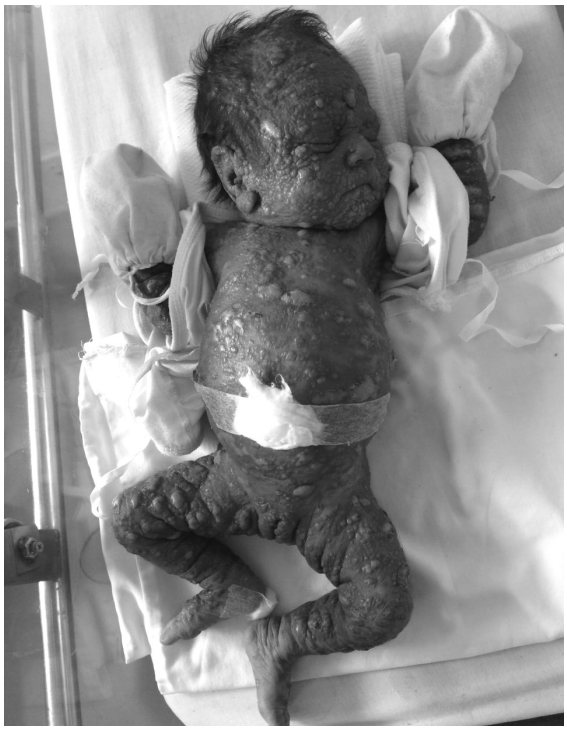

Figure 3

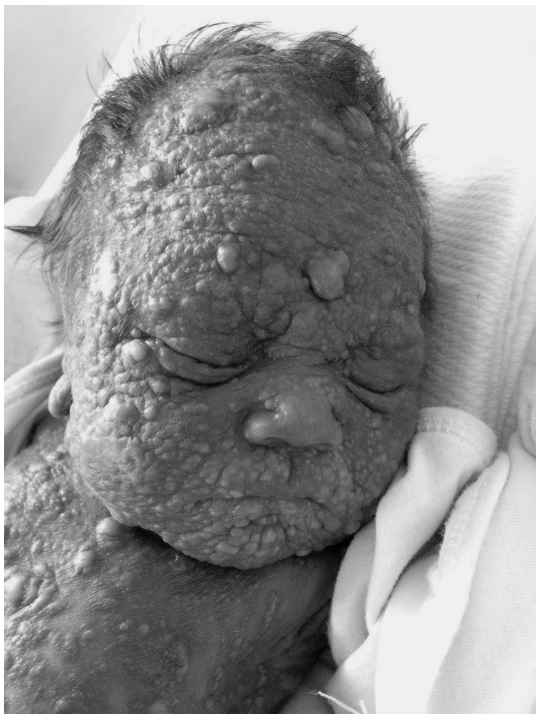

Figure 4