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Case Report

An Infrequent Case of Sudden Flushing: Infantile Cutaneous Mastocytosis

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Abstract ***Introduction:*** Sudden flushing is a common symptom in infants but it can be a manifestation of life-threatening disease, therefore differential diagnosis is crucial for an infant with flushing. ***Case Description:*** Here, we describe a two-month-old boy who presented to the Paediatric Emergency Department with four sudden attacks of flushing with accompanying fatigue, especially after feedings. Upon physical examination, a 5x7 cm brown lesion on his left hypochondra was noted. His laboratory tests were unremarkable. Pathological examination of a biopsy of the lesion revealed diffuse mast cell infiltration. The patient was diagnosed with cutaneous mastocytosis. ***Conclusion:*** This case underscores the importance of the detailed examination of children with sudden attacks of flushing to make a correct diagnosis and to prevent future life-threatening complications of infrequent clinical entities.

Key words *Children; Cutaneous; Flushing; Mastocytosis*

Introduction

Sudden colour change is a common and important cause of paediatric emergency visits for infants. Underlying reasons may be innocent, such as regurgitation, or life-threatening, such as congenital heart disease or seizures. It is therefore crucial to diagnose the patients correctly.

Flushing in infants is a common form of colour change and appears as reddening of the skin, especially the face and neck, mainly due to the dilatation of cutaneous vasculature.[1] Flushing can be episodic or persistent. There can be many underlying reasons for it; these include benign reasons, such as rosacea, fever, emotional distress, and temperature change and more serious reasons, such as neuroendocrine disorders, intoxication, carcinoid syndrome, pheochromocytoma, mastocytosis, anaphylaxis, medullary thyroid cancer, renal cell carcinoma, inborn errors of metabolism such as Fabry disease, and autonomic dysfunction. In addition, flushing can mimic an epileptic event.[1-3] Here, we present the case of a patient who presented to the Paediatric Emergency Department (PED) with brief flushing episodes and who was diagnosed with cutaneous mastocytosis (CM).

Case Description

A two-month-old boy presented to the PED with the complaint of sudden attacks of flushing. The first attack

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occurred when he was one month old. The attacks recurred four times with the last two attacks occurring in the 12 hours before presenting to the PED. Flushing occurred suddenly, especially during or after feeding. The episodes lasted approximately for 20 minutes and the patient recovered spontaneously. During the attacks, the patient looked tired and was less active but did not have any other symptoms during or after the attacks. He also had a hyper pigmented lesion on the left upper portion of the abdomen and one brown maculae on his back since birth. He was hospitalised in a local hospital one month ago because a bulla formed on the hyper pigmented lesion. Bullous cellulitis was presumed, and the patient was given intravenous antibiotics and examined for other dermatological disorders, such as epidermolysis bullosa. However, he was discharged 10 days later without a definite diagnosis. His other medical history was insignificant.

The patient was not febrile upon arrival at the PED. His heart rate was 136/min, his respiratory rate was 30/min, his oxygen saturation was 97% and his arterial pressure was 80/50 mmHg. A dermatological examination revealed a 7x5 cm sized irregularly bordered reddish-brown patch with a partial peau d'orange appearance, and bullae was observed on the patient's flank (Figure 1). Darier's sign was demonstrated. Family pointed out that the bulla formation was recurrent and concurrent with flushing attacks. Another similar but smaller patch was detected on the patient's back. His cardiovascular and neurological examinations were normal.

Laboratory tests showed a normal haemoglobin level and normal leukocyte and platelet counts with normal peripheral smear. Renal and liver function tests, including serum electrolytes, were within normal limits. A plain chest X-ray showed no abnormalities. In order to rule out possible cardiovascular abnormalities, electrocardiography and echocardiography were performed and were within normal limits. Electroencephalography showed no epileptic discharge. The patient's abdominal ultrasound was also normal. A punch biopsy was taken from the hyper pigmented dermal lesion showing diffuse mast cell infiltration (Figure 2a). Immunohistochemically, mast cell tryptase positivity was seen in the neoplastic cells (Figure 2b). In light of the aforementioned clinicopathological findings, the patient was diagnosed with CM. Serum tryptase was 2.4 µ/L (N: <11.5).

The patient's mother was asked to list his diet and attacks, and his diet was arranged to eliminate the triggering foods. Hydroxyzine treatment was started and the family was informed about triggering factors, anaphylaxis and the emergency use of epinephrine injections. The patient had only one attack in the subsequent two months, which was brief and resolved spontaneously.

Discussion

Mastocytosis is a mast cell proliferation disorder that presents with many different clinical signs ranging from asymptomatic rash or itching to diarrhoea and anaphylaxis.[4] It is classified as CM and systemic mastocytosis (SM); while CM is restricted to the skin, SM is a haematologically clonal disease (it is sub-classified as indolent (ISM), aggressive (ASM), or SM with an associated clonal haematological non-mast cell lineage disease (SM-AHNMD).[5] Although skin involvement can be encountered in ISM and sometimes in ASM, in SM at least one extra cutaneous tissue/organ is involved, bone marrow almost always being present.[5,6] In children, however, disease is often limited to the skin and systemic involvement is rare.[5] Our patient was diagnosed with CM because he did not have any organomegaly, organ dysfunction, or cytopenia, which are suggestive of SM. Moreover, bone marrow examination is not recommended

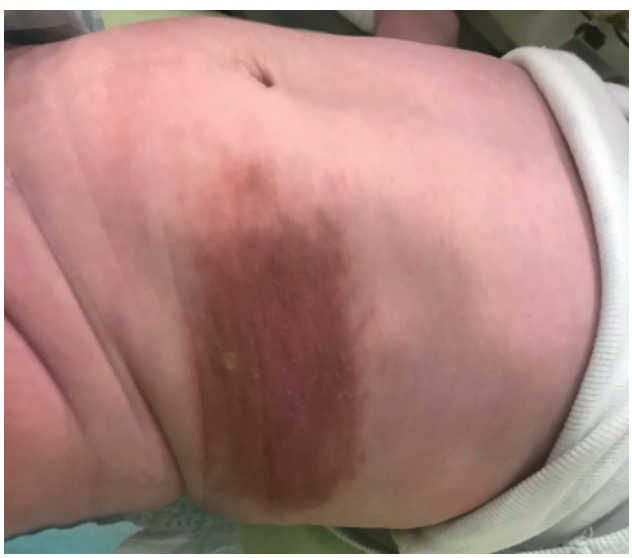

Figure 1 7x5 cm sized irregular bordered reddish brown patch with partially peau d'orange appear and bullae observed on his flank.

for patients with tryptase <100 μ/L; therefore, a bone marrow examination was not performed for our patient.[6]

CM is also sub-classified as 1) mastocytoma, 2) urticaria pigmentosa, or 3) diffuse cutaneous mastocytosis.[4,7,8] Our patient had urticaria pigmentosa, which accounts for most cases of paediatric cutaneous mastocytomas (70-90% of cases). It consists of red-brown maculae, papules, or plaques, sometimes bulla and blistering that can cause systemic symptoms, such as flushing or hypotension, when a patient is traumatised.[7-10] Systemic symptoms develop as a result of the sudden degranulation of mast cells and the release of mediators due to an activating mutation of a transmembrane tyrosine kinase receptor, KIT, resulting in increased mast cells in tissues.[4,7,8] Increased mast cells release several mediators, such as histamine, heparin, tryptase, leukotrienes, prostaglandin D2, platelet activating factor, and interleukins. This causes a wide range of clinical symptoms, such as itching, increased vascular permeability, gastric hyper secretion, bronchial constriction and local anticoagulation.[4,7,8] The rubbing of skin can cause blistering, but in severe cases blistering can occur spontaneously if there are enough mediators.[4,7] Blistering of bulla in our patient showed sudden degranulation of mast cells which also resulted in sudden flushing attacks with accompanying fatigue.

Bulla formation on hyper pigmented lesions is seen only in paediatric onset CM, mostly in the first few years of life.[7] Bulla are tense and sometimes haemorrhagic; they may be formed after rubbing (Darier's sign) or in severe cases may form spontaneously.[4,7,8] In childhood mastocytosis, bullous lesions may rarely be associated with sudden collapse and death with/without systemic involvement.[8,9] Our patient had repeated bulla formation on a hyper pigmented lesion, but a correct diagnosis could not be made when he was hospitalised for examination. Therefore, it is very important to consider CM in the differential diagnosis of bullous diseases in childhood.

Certain foods can trigger systemic symptoms in childhood, which can explain the occurrence of attacks after feeding in our patient.[4] Other triggers of systemic symptoms are a sudden change in temperature, fever, certain drugs (non-steroidal anti-inflammatory drugs, narcotic analgesics, cough medications, and radiographic dyes), irritability and teething. Therefore, children with sudden flushing episodes in these circumstances should be evaluated for CM.[4]

The treatment of CM involves antihistamines for flushing and itching and the avoidance of triggers, such as some commonly used drugs and chemicals, physical stimuli (heat, sudden changes of temperature, rubbing, sunlight), emotional factors (stress, anxiety, or emotional deprivation), viral infections, dental procedures, vaccinations and surgery.[7,10] In addition, paediatricians should warn parents about the small but significant risk of anaphylaxis and should prepare them for emergency treatment for anaphylaxis, especially for patients with bullous lesions.[4-10]

The prognosis is generally favourable for childhood CM, especially urticaria pigmentosa. It usually fades in adolescence without systemic involvement. However, these patients should still be followed for the possibility of bone marrow involvement and the development of haematological malignancy. Follow-up is usually clinical,

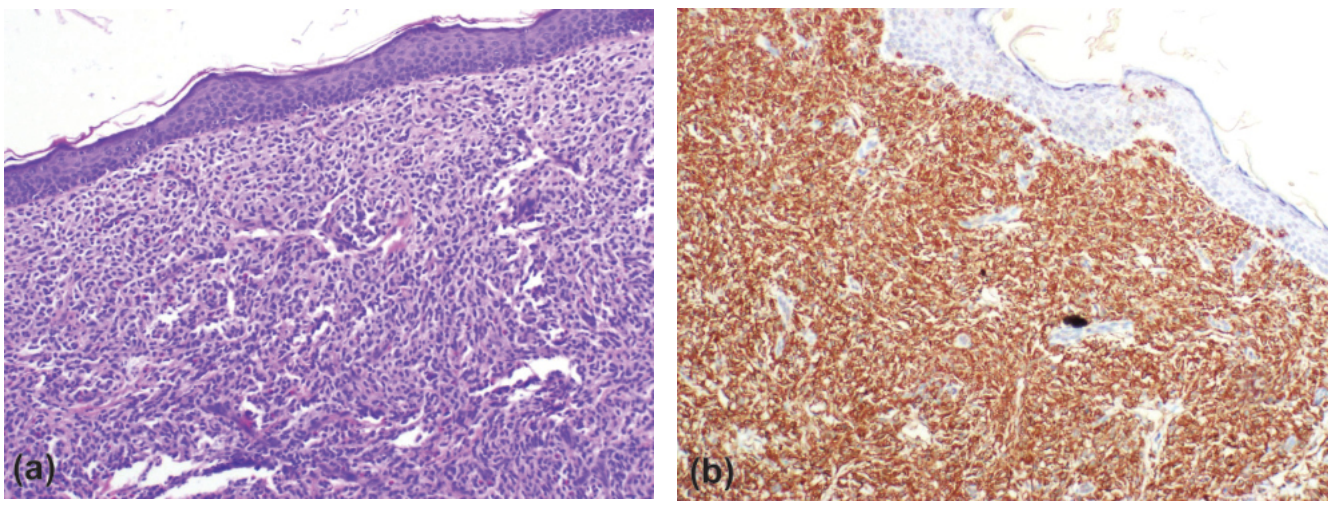

Figure 2 (a) Punch biopsy taken from the hyperpigmented lesion dermal showing diffuse mast cell infiltration. (b) Immunohistochemically mast cell tyrptase positivity seen in the neoplastic cells.

and bone marrow biopsy is rarely necessary.[4,7,8] Low concentration of serum tryptase (<20 μ/L) is a good prognostic sign indicating a low risk of systemic involvement.[8] Therefore, the long-term prognosis of our patient is expected to be good, unless a sudden discharge from the bullous lesion causes anaphylaxis or sudden collapse. Consequently, close follow-up was planned, possible complications were carefully explained to the parents, and urgent adrenalin intervention was explained in detail.

Sudden colour changes in infancy are common and have many underlying causes. A detailed history and a physical examination of infants who present to PEDs with sudden colour change are crucial to diagnose uncommon clinical entities, such as mastocytosis, to anticipate complications of the disease in a timely manner, and to treat the patients accordingly. Therefore, paediatric emergency physicians should be aware of these kinds of infrequent but specific clinical disorders of childhood.

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Conflict of Interest

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