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Flushing and increase of serum tryptase after mechanical irritation of a solitary mastocytoma

Solitary mastocytomas are infiltrates of mast cells in the upper corium, appearing at any side of the body as brownish-reddish plaques in the first months of life. Their course is benign with a spontaneous regression in most cases. A 5-month-old boy presented a 5 × 3 cm sized brownish-yellow plaque on the back of his right hand. His parents reported repeated episodes of swelling and blistering of the skin lesion as well as recurrent systemic flush-reactions. General laboratory parameters were without pathological findings including a normal serum tryptase (5.5 µg/L). Few minutes after rubbing, the lesion became urticarially swollen and the infant developed a general flush reaction accompanied by a bilateral miosis and asthma-like symptoms which disappeared completely after oral administration of 7 drops of dimetinden. Assessment of the serum tryptase two hours after the provocation revealed a more than 5-fold increase (29.3 µg/L) compared to the basic value. We conclude that uncontrolled stroking of mastocytomas should be avoided in patients with a systemic reaction in their history, since this case demonstrates that despite its limited size, mechanical irritation of a solitary mastocytoma may induce strong systemic symptoms as witnessed by transient increase of the serum tryptase, which to our knowledge has not been described in the literature before.

Key words: flush reaction, mastocytoma, tryptase

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Mastocytomas are infiltrates of mast cells in the upper corium and appear as brownish-reddish maculae or plaques. Together with urticaria pigmentosa mastocytosis, which consists of a diffuse mast cell infiltration of the skin with multiple, ovoid red-brown macules which can involve the entire integument, solitary mastocytomas represent one of the most common forms of cutaneous mastocytosis in childhood. While in adult mastocytosis systemic involvement occurs in 40-90% of the patients, mastocytosis in childhood is limited to the skin in more than 80% of the cases [1, 2] with a tendency to spontaneous resolution before puberty [3]. Solitary mastocytomas usually show up immediately at birth or during the first months of life and only very rarely later [4, 5]. The course is benign and they show spontaneous involution with symptoms and lesions resolving by adolescence in most of the cases [6]. Usually, they measure 0.5-3 cm at the largest diameter and might appear on the trunk, neck, the face or on the extremities. Vesiculation or frank blistering of the lesions occurs very frequently in infancy [7]. Solitary mastocytomas are sometimes associated with flushing and abdominal pain. In addition, there are single reports of convulsions in response to stroking of a mastocytoma or mastocytoma symptoms which resemble seizure disorders [8, 9]. In rare cases a general histamine-flush might appear [10, 11]. Differential diagnoses which need to be considered include xanthomas, juvenile xanthogranulomas or melanocytic naevi, bullous impetigo or epidermolysis bullosa. Physical stimulation of the lesions with a blunt

instrument or rubbing promotes the rapid degranulation of mast cells accompanied by local erythema, oedema and pruritus known as the Darier's sign [12]. Histopathological examinations reveal a dense infiltrate of mast cells in the upper dermis.

Treatment to control flushing or blistering consists of the application of antihistamines, or alternatively hydrocolloid dressings to cover the lesions [10].

Case report

We report the case of a 5-month old boy, who presented a 3 × 5 cm sized, brownish-yellow, shiny infiltrated plaque with a peau d'orange surface on the back of his right hand (*figure 1*). His parents reported the occurrence of swelling and blistering of the lesion about twenty times from the first month of life. Additionally they referred to recurrent severe flushing reactions of unknown origin, which occurred initially every two weeks with a decreasing frequency during the last months. General laboratory examinations did not show any abnormal blood counts besides a mild lymphocytosis. The total serum IgE level was 20.1 kU/L and corresponded to normal age-ranges. There was no allergen-specific IgE detectable. To exclude an occult mastocytosis, we measured the serum tryptase, which was within normal range (5.55 µg/L) at baseline (mean of normal range 5.6 µg/L).

After mechanical irritation of the mastocytoma with a spatula during the examination the boy immediately deve-



Figure 1. Mastocytoma on the back of the right hand.

loped flushing of the head, trunk (*figure 2A, B*) and extremities accompanied by cough and a bilateral miosis. The symptoms disappeared within minutes after oral administration of 7 drops of dimetinden. Two hours after this incident the serum tryptase was measured again and revealed a more than quintuple increase up to a total value of 29.3 $\mu\text{g/L}$.

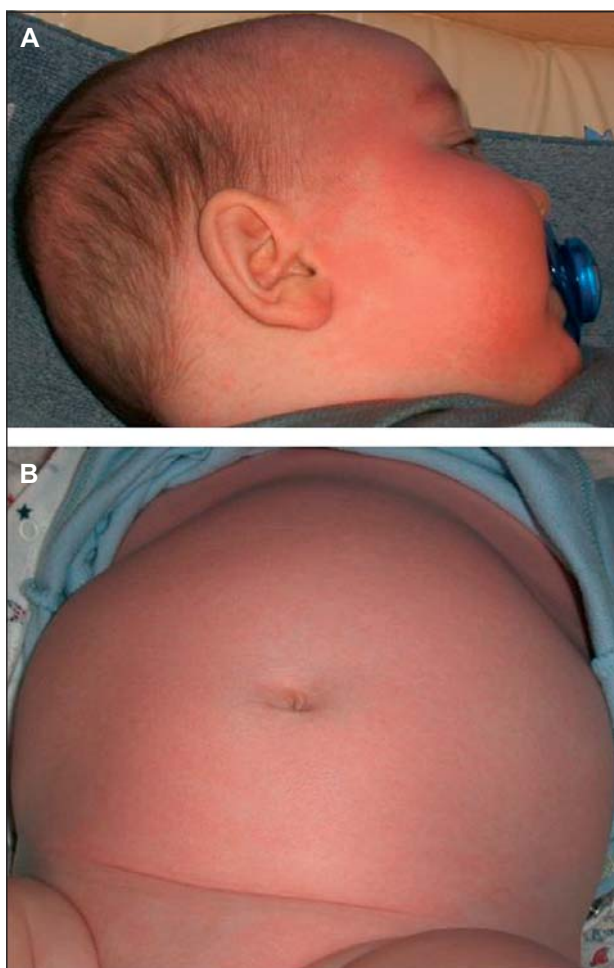


Figure 2. Flush of the head (A) and trunk (B) after mechanical irritation of the mastocytoma.

We diagnosed a solitary mastocytoma with episodes of general flushing. We recommended daily intake of 2.5 mL of dimetinden sirup and the avoidance of mechanical irritation of the skin lesion in order to prevent further episodes of flushing and informed the parents about the potential of histamine liberating drugs as additional trigger factors of flush reactions. Under this treatment the flushing episodes occurred less frequently and in a milder form. In a follow-up control after one year a slight size reduction of the skin lesion was observed.

Discussion

The great increase of serum tryptase after mechanical irritation of the mastocytoma from normal to elevated ranges implicates a strong degranulation of mast cells within the lesion, provoking not only locally restricted, but also systemic effects such as flushing, cough and miosis. Most strikingly, mast cells in a rather small lesion seem to be able to release high amounts of tryptase leading to an increase of the serum tryptase of more than 5-fold the baseline level.

Tryptase, as one of the various mediators derived from activated mast cells, can be used as a specific marker and diagnostic tool to evaluate the degree of mast cell activation [13]. The best described mast cell product is the biogenic amine histamine, which binds to the histamine receptors (H1R-H4R) expressed on different cell types. Among multiple other effects, histamine leads to vasodilatation via the H1-receptor by stimulating endothelial cells to produce vascular smooth muscle relaxants such as prostacycline and nitric oxide, which are assumed to be the main pathophysiological correlates of histamine mediated flush reactions. Histamine provokes bronchospasm and increased peristalsis of smooth muscles of the bronchial and the respiratory tract [14]. In this context, the strong release of histamine and other mediators by mechanically activated mast cells derived from the solitary mastocytoma might be responsible for the flushing and the systemic reactions in our patient. For this reason the prophylactic administration of antihistamines, which block H1R, is necessary and should be strongly recommended to prevent episodes of histamine provoked systemic reactions in severe cases of solitary mastocytoma, as has already been established for the treatment of urticaria pigmentosa [6, 15]. In addition, the administration of mast cell stabilizers [16], topical application or intralesional injection of corticosteroids [17], covering the lesion with hydrocolloid dressings [10, 18] and excision [19] have been described to be effective in the management of solitary mastocytoma.

Physicians should avoid uncontrolled irritation of the mastocytoma in order to provoke the Darier's sign because of the risk of systemic reactions, inform the parents about the connection between the skin lesion and the systemic symptoms and instruct them how to avoid mechanical irritation of the mastocytoma or intake of histamine liberating agents. Furthermore an emergency kit consisting of a liquid or suppository glucocorticosteroid and a liquid H1R blocker should always be recommended and carried along with the child.

Pronounced flushing episodes after irritation of mastocytoma have been described in the literature before [6, 10, 20-24] and have been shown to accompany increased histamine levels in urine after the flush reactions, in some

cases [25]. To our knowledge, this is the first report about increased systemic tryptase levels occurring after mechanical provocation of a solitary mastocytoma. Therefore, measurement of serum tryptase after controlled mechanical irritation of the mastocytoma might represent a helpful diagnostic tool to identify patients with solitary mastocytoma with an increased risk for systemic reactions, who might benefit from transient prophylactic treatment with antihistamines, to avoid recurrent flush reactions. ■

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