Mastocytosis is a group of diseases characterised by accumulation of mast cells in one or more organs including skin, bone marrow, liver, spleen and lymph nodes, skin being the most frequent site of organ involvement. Symptoms are related to continuous activation of mast cells and causes pruritus, flushing, diarrhoea, abdominal pain, musculoskeletal pain, vascular instability, headaches and neuropsychiatric symptoms (1, 2). In children the disease is usually confined to the skin and mostly resolves spontaneously before onset of puberty, whereas in adults, mastocytosis is usually systemic and persist for the lifetime of the patient (1, 2).

Anaphylaxis is a recognised feature of mastocytosis, and symptoms are in both cases related to excessive mast cell mediator release, especially of histamine (3). Here, we present a case concerning a patient with indolent systemic mastocytosis (SM) and recurrent idiopathic anaphylaxis, with full remission of anaphylaxis after onset of treatment with anti-IgE (omalizumab).

CASE REPORT

A 31-year-old man was referred to our outpatient clinic on suspicion of urticaria pigmentosa (UP). For the last 5 years he had noticed a chronically evolving red to brownish macular symmetric exanthema on his trunk and extremities. Physical stimuli, such as heat, resulted in flare-ups with elevation and more intense colour of the elements. Within the last 2 years he had been admitted 3 times to an intensive care unit due to anaphylaxis of unknown cause. Symptoms prior to all episodes were uneasiness, abdominal pain, urge, dizziness and unconsciousness within 10 min. When admitted he presented with hypotension (systolic blood pressure: 75 mmHg), tachycardia, generalised flushing but no urticaria or angioedema. He was treated with standardised anaphylactic regimens and inotropic support until stabilisation. The patient had no previous history of other diseases; no drug abuse and allergies were only described as allergic rhinitis to grass and birch. The patient was equipped with glucocorticoids, antihistamine and epinephrine for future emergency use.

The dermatological examination showed positive Darier’s sign and the diagnosis UP was further confirmed by histology. On suspicion of SM, baseline tryptase was estimated a month after his last anaphylactic reaction, being 50.9 µg/l (normal < 12.0 µg/l). Additionally, the patient was referred to the Department of Haematology, where a bone marrow biopsy was performed. It showed accumulation of mast cells (10%), and D816V point mutation in the c-kit gene in 0.5% of all cells. A previous CT-scan of thorax, abdomen and pelvis had shown a borderline enlarged spleen and an ultrasound examination had detected one enlarged inguinal lymph node (2.1 cm in diameter), clinically indicating mast cell accumulation in these organs. The inguinal lymph node showed spontaneous regression, and to this date no other clinical findings have indicated further diagnostic imaging examinations. The presence of dense infiltrates of mast cells in the bone marrow (major criteria of SM), combined with detection of the c-kit mutation and elevated serum tryptase value (2 out of 4 minor criterions of SM) and absence of B- and C-findings lead to the diagnosis: indolent SM.

In September 2011 the patient was admitted to the emergency ward with his 4th episode of anaphylaxis, in spite of self-administered epinephrine, glucocorticoids and antihistamine in relation to the attack. This was his 3rd episode within one and a half month, in spite of treatment with high-dosage glucocorticoids, continuous non-sedating (ns) H1-antihistamine TID, H2-antihistamine and leukotriene antagonists. Because of recurrent life threatening events, treatment with omalizumab was initiated. Dosage was calculated from baseline IgE on 25 IU and weight: 106 kg, corresponding to 300 mg every 4th week. During the 15 months in which the patient has received omalizumab, he has experienced no anaphylactic events, and adjuvant treatment has now been reduced to ns-H1-antihistamine once daily. Omalizumab has been well tolerated, and no adverse effects have been reported. Serum tryptase is continuously elevated (74.1–9.13 µg/l) and on haematological indication supplemental treatment (interferon) has been considered but not instituted.

DISCUSSION

The mast cell is the pivotal cell in both mastocytosis and anaphylaxis. Previous studies have emphasised this common pathological precursor, suggesting a clinical correlation between mastocytosis and anaphylaxis (3–6). However, anaphylaxis-like symptoms in patients with mastocytosis often arise spontaneously,
or is triggered by external stimuli such as heat, exercise, drugs or hymenoptera venoms (4). Urticaria and angioedema, normally present in non-mastocytotic anaphylaxis, are often absent (3, 4, 7, 8).

In mastocytosis the mast cell accumulation is a result of a proliferative disorder of the haematopoietic mast cell progenitor (4). Thus, mast cells may display an atypical morphology and appear spindle-shaped (2). Indolent SM poses a small risk of transforming into malignant haematological disease associated haematologic non-mast cell lineage disease, (ASM and mast cell leukaemia (3% and < 1%, respectively)) with a more aggressive clinical course (2). The result of a high mast cell burden, may also cause severe side-effects, such as collapse of vertebral bodies (9).

As illustrated, it is worth considering SM in patients with recurrent unexplained anaphylaxis, and a diagnostic programme has to involve a thorough skin examination, a serum-tryptase analysis and a bone marrow biopsy. SM is a multidisciplinary disease and requires involvement of both dermatological, allergological, and haematological expertise.

Omalizumab, approved for the treatment of allergic asthma, is a monoclonal antibody, which selectively binds human IgE, and also reduces the expression of FcεRI on circulating basophils and mast cells (10, 11). Thus, omalizumab seems to lower the activity potentials of basophils and mast cells, thereby reducing profound histamine release (10). Consequently, omalizumab has also found favour in the World Allergy Organization treatment guidelines of chronic urticaria (12).

Searching the literature there is only sparse material on treatment with omalizumab in patients with SM and idiopathic anaphylaxis. A case report from 2007 documented full remission of unprovoked anaphylactic episodes after onset of omalizumab treatment in two patients suffering from SM (13). A few single case reports also demonstrate this tendency (14, 15).

In conclusion, this case suggests that omalizumab may be a rapid, efficient, and well-tolerated treatment for patients with SM and recurrent idiopathic anaphylaxis, resistant to other medications. The use of omalizumab in this patient category is still somewhat experimental, and needs further investigation on larger patient material to become fully integrated in clinical use.

The authors declare no conflicts of interest.