Lessons from practice

Anaphylactic shock in a patient with mastocytosis

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Clinical record

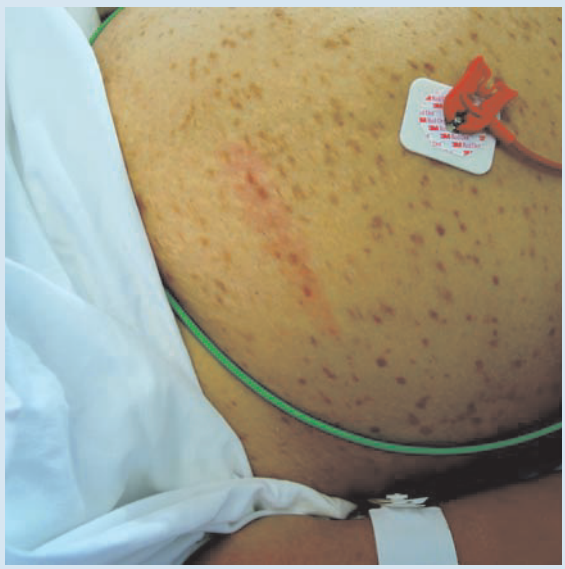
A 40-year-old, previously healthy woman presented with sudden loss of consciousness and collapse. Her work colleagues noted that she had become drowsy and light-headed moments before the collapse. She had reported a suspected spider bite about 10 hours earlier, which had caused her skin to become generally itchy.

Paramedics found the woman to be in a state of pulseless electrical activity 20 minutes after the cardiovascular collapse. They immediately commenced an adrenaline infusion and performed cardiopulmonary resuscitation and intubation before transporting her to the emergency department. The adrenaline infusion was ceased after 3 hours, when she was deemed to be haemodynamically stable. On presentation, there was no apparent urticaria or angio-oedema and no sign of a bite mark. Further examination showed no signs of wheeze, cardiac failure, pulmonary hypertension or deep vein thrombosis. An electrocardiogram showed mild ST depression in leads V_1–V_3. Troponin levels were mildly elevated (0.63 μg/L initially and 0.35 μg/L 6 hours later; reference interval [RI], < 0.1 μg/L), and aspirin 100 mg daily was commenced. A full blood cell count, urea and electrolyte levels and liver function tests were unremarkable. Venous blood gas analysis demonstrated a mixed respiratory and metabolic acidosis. A coagulopathy was noted, with an increased international normalised ratio (1.9; RI, < 1.5) and activated partial thromboplastin time (> 250 s; RI, 22–32 s). Toxicology and venom screens gave negative results. A chest x-ray and a computed tomography scan of the brain were normal.

The patient's Glasgow Coma Scale score remained 3, and she was transferred to the intensive care unit. It was noted that she had multiple brown macules on the trunk and limbs, and a dermatology consultation was sought. The patient's husband reported that these skin lesions had been present for more than 10 years and had gradually increased in number. They were asymptomatic, and she had not sought medical advice about them. Gentle stroking of the macules resulted in localised erythema and swelling (Darier's sign; Figure). There was no significant lymphadenopathy or hepatosplenomegaly. A clinical diagnosis of urticaria pigmentosa was made, and it was considered that an anaphylactic reaction in the setting of mastocytosis was the likely cause of her presentation. A causative entity could not be identified, but as spider bites are not a reported cause of anaphylaxis, the history of a "bite" suggested the possibility of a bee or wasp sting as the precipitant. The aspirin treatment was not thought to have played a role in the patient's progression.

A skin biopsy supported the diagnosis of mastocytosis, with an increased number of dermal mast cells identified on Leder stain. The serum tryptase level (14.8 μg/L; RI, 0–11.4 μg/L) was slightly elevated, and the 24-hour urinary histamine level (0.4 μmol/24 h; RI, 0–0.8 μmol/24 h) was normal. Due to the delay in clinical diagnosis, these samples were not collected until 4–5 days after presentation. The 24-hour urinary 1-methylhistamine level (4.0 μmol/24 h; RI, 0–1.5 μmol/24 h) was noted to be increased. The serum IgE level was mildly elevated (228 kU/L; RI, 0–160 kU/L). A bone marrow biopsy was not performed because of the patient's poor prognosis.

The patient remained in a persistent vegetative state due to hypoxic cortical damage sustained from the cardiac arrest, until her condition subsequently deteriorated and she died. An autopsy was not performed.



Urticating reddish brown macules suggestive of mastocytosis

Mastocytosis refers to a group of disorders of mast cell proliferation, in most cases associated with mutations of the *c-kit* proto-oncogene. The World Health Organization classifies this condition into the categories of cutaneous mastocytosis, systemic mastocytosis, mast cell leukaemia and sarcoma, and extracutaneous mastocytoma.[1] Systemic disease is confirmed by demonstrating an abnormal mast cell infiltrate in an extracutaneous site, most often through a bone marrow biopsy.

Urticaria pigmentosa is the most common presentation of mastocytosis in the skin. It is characterised by multiple red and brown macules, typically on the trunk, which "urticate" (ie, become swollen, itchy and red) when stroked or rubbed — the so-called Darier's sign. Most cases of urticaria pigmentosa occur in early childhood, and these have a favourable prognosis, often involving skin alone. Cases that occur in adulthood, typically developing between the ages of 20 and 40 years, are usually associated with systemic disease. Some studies suggest the frequency

Lessons from practice

- Mastocytosis is a rare cause of potentially fatal anaphylaxis.
- The presence of multiple reddish brown macules that urticate when rubbed should suggest the diagnosis of mastocytosis.
- Hymenoptera (eg, bee and wasp) stings may lead to acute mast cell degranulation in patients with mastocytosis. Aspirin and other non-steroidal anti-inflammatory drugs, opiates and radiocontrast media are also potential triggers.
- An anaphylaxis management plan and adrenaline auto-injector should be considered for all patients with systemic mastocytosis. ◆

of occult bone marrow involvement in affected adults to be as high as 92%.[2] Neither the frequency nor the severity of systemic events seem to correlate with the category of mastocytosis or the burden of neoplastic cells.[3]

The manifestations of systemic mastocytosis may be due to the release of mast cell-derived molecules or the direct infiltration of mast cells into tissue, including the bone marrow, liver, spleen, lymph nodes and gastrointestinal tract. Mast cells are known to release a large array of molecules, including histamine, heparin, tryptase, leukotrienes and prostaglandins. Mastocytosis may be associated with symptoms of pruritus, flushing, headache, palpitations, light-headedness, dyspnoea, wheezing, abdominal pain, nausea, vomiting, diarrhoea and musculoskeletal pain. Anaphylaxis is an uncommon presentation that is generally associated with systemic involvement, although patients with mastocytosis apparently confined to the skin may still be at risk of anaphylaxis.[4]

A biopsy of the distinctive pigmented macules of urticaria pigmentosa will usually demonstrate an elevated number of mast cells in the dermis, although the diagnosis may be missed by pathologists in the absence of clinical guidance. Systemic mastocytosis is suggested by an increased level of mast cell mediators. A serum tryptase level greater than 20 μg/L strongly suggests systemic mastocytosis,[5] although transient elevations may occur after acute mast cell degranulation, and testing should be repeated if levels are initially elevated. Changes in the coagulation profile during acute episodes may be due to the release of heparin from mast cells. Bone marrow biopsy should be considered in all patients with suspected systemic mastocytosis, even in the absence of a raised serum tryptase level.[6]

Treatment of mastocytosis is primarily symptomatic, although cytoreductive therapy is sometimes indicated in aggressive cases or for treatment of an associated clonal haematological non-mast cell lineage disease. Antihistamines (H1 blockers) are often sufficient to control the pruritus and flushing, and phototherapy can also be helpful for the cutaneous manifestations.[7] Combined H1 and H2 blockers, proton pump inhibitors, and mast cell stabilisers such as sodium cromoglycate may help alleviate gastrointestinal symptoms. Short courses of prednisolone may be needed for severe symptoms. Other agents used include leukotriene antagonists and, more recently, omalizumab.[8]

Adrenaline remains the drug of choice for treating acute anaphylaxis, and an adrenaline auto-injector prescription and anaphylaxis management plan should be considered for all patients with systemic mastocytosis, irrespective of the severity of prior reactions. The wearing of emergency identification, such as a MedicAlert bracelet, should be encouraged. Severe systemic allergic reactions are well recognised in response to Hymenoptera (eg, bee and wasp) stings,[9] and care should be taken to avoid stings when engaging in outdoor activities. In cases of known allergy, venom immunotherapy should be strongly considered. Agents that may precipitate mast cell degranulation, such as aspirin, other non-steroidal anti-inflammatory drugs, radiocontrast media and opiates, should be avoided. Rarely, procedures such as endoscopy and general anaesthesia have been reported to trigger cardiovascular collapse in patients with mastocytosis,[10] and prophylactic corticosteroids and antihistamines have been advocated, although they may not necessarily be protective.

Systemic mastocytosis is a rare cause of severe or fatal anaphylaxis, which may be triggered by an insect sting or drug. Most patients with mastocytosis will have a history of pigmented macules on the skin that urticate when rubbed, or display symptoms related to mast cell mediator release. An awareness of this condition, its potential triggers, and both prophylactic and self-administered emergency treatment may help to avoid a life-threatening situation.

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