Case report

Flushing out the diagnosis

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Learning Point for Clinicians

Always consider the non-infectious differential of the SIRS. Measuring serum tryptase may be useful in the setting of shock, particularly when the presentation may be due to an anaphylactoid reaction.

Case presentation

A 30-year-old man presented with a 4-h history of severe headache, vomiting, diarrhoea and epigastric pain. 1 week previously, he had undergone a left hip arthroscopy in another hospital. He had no other medical history and his only medication was naproxen for post-operative pain. His blood pressure was 70 mmHg systolic, pulse rate 130 bpm, respiratory rate 24 bpm and temperature was 38.3°C. Physical examination was notable for a diffuse erythematous, blanching rash involving his face and trunk, conjunctival suffusion and mild abdominal tenderness. Laboratory studies were normal apart from a leucocytosis (18.1 × 10⁹/l) and a creatinine of 149 μmol/l. The provisional diagnosis was of toxic shock syndrome (TSS) secondary to peri-operative staphylococcal infection of the hip joint. He stabilized initially with fluid resuscitation and intravenous hydrocortisone for worsening vasodilatory shock. Orthopaedic surgery explored his left hip joint and it appeared clean. Synovial fluid gram stain was negative. He rapidly improved in the intensive care unit, was extubated, weaned from vasopressors and was subsequently discharged 1 week later. The rash resolved entirely during the admission. There was concern over the diagnosis of TSS as no staphylococcal or other micro-organisms were identified in blood or synovial fluid cultures and he did not fulfil the clinical criteria for diagnosis of TSS. Although the rash did not recur, he returned some months later complaining of episodic facial flushing, diarrhoea and headache prompting further investigations. Urinary catecholamines, metanephrines and 5-indolacetic acid were normal as were thyroid function tests, synacthen test and calcitonin levels. Serum tryptase was elevated at 23.7 μg/l (normal: 2–14). This indicated increased mast cell burden or activation. A bone marrow biopsy confirmed a diagnosis of systemic mastocytosis (SM), demonstrating characteristic overpopulation of morphologically abnormal mast cells with the gain of function KIT D816V mutation (Figure 1).

Discussion

SM occurs due to mast cell proliferation with accumulation in one or more tissues. This is usually caused by an activating mutation in the KIT gene, which encodes c-kit (CD117). C-kit is the receptor which binds stem cell factor, a major mast cell
growth factor. The WHO diagnostic criteria are based on combinations of the following: an increased burden of KIT mutation positive mast cells in the marrow; abnormal mast cell surface antigen expression of CD2 and CD25 and increased serum levels of mast cell mediators, including tryptase. The clinical features of the disease depend on the organs involved, the degree of infiltration or organ dysfunction and the extent of mast cell proliferation. By consensus, disease manifests as a spectrum from limited cutaneous to systemic disease. Several factors including drugs (e.g. NSAIDs), surgery, stress and allergens are known to exacerbate symptoms, which result mainly from release of mast cell mediators such as histamine. Typically, these include flushing, hypotension, headache, gastrointestinal irritation and respiratory compromise.

This case highlights the need to consider non-infectious differential diagnoses, in particular anaphylactoid reactions, in patients with systemic inflammatory response syndrome (SIRS). In our patient, systemic mast cell degranulation was probably triggered by post-operative stress and the use of NSAIDs. Vancomycin and intravenous contrast may have exacerbated the problem as both are known to cause mast cell activation. The diagnosis of SM should be considered in cases of dry episodic flushing or unexplained macular rash. Treatment of acute mast cell degranulation is as recommended for anaphylaxis of any cause. Ongoing symptoms should be treated by trigger avoidance, antihistamines, cromoglicate or leucotriene antagonists. Osteoporosis is another important complication that can occur, possibly secondary to the effects of mast cell mediators such as histamine and interleukin-6 on osteoclast activation and is treated with calcium, vitamin D and bisphosphonates. Various kinase inhibitors are currently the subject of investigation in aggressive SM.

Acknowledgements

All authors were involved in drafting the article and revising it critically for important intellectual content and have read and approved the final version of the manuscript. Permission was obtained from the patient for submission of this case report for potential publication.

Conflict of interest: None declared.

References


Figure 1. CD117 stain of bone marrow biopsy showing focal aggregates of abnormal spindle-shaped mast cells.