

Short reports

An unusual presentation of systemic mastocytosis

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Abstract

A 47 year old man presented with mastocytosis, a disease process characterised by proliferation of mast cells. The clinical features and outcome are discussed.

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Case report

A 47 year old white male was referred to the surgical outpatient department of our hospital with a three month history of lethargy, night sweats, intermittent abdominal pain, diarrhoea, and a weight loss of around 12.5 kg. He had attended a dermatologist two years previously complaining of pruritus but otherwise had no significant past history.

On examination he looked pale and cachectic, but initially there were no other positive findings. Initial routine blood and radiological investigations were normal except for a mildly raised alkaline phosphatase and a minimal coagulation disturbance. Further investigation of the gastrointestinal tract revealed no mucosal abnormality, and ultrasound examination of the abdomen initially showed only a slightly enlarged spleen. Computed tomography (CT) of the chest and abdomen showed several groups of mildly enlarged lymph nodes above and below the diaphragm and ill defined areas of low attenuation in the right lobe of the liver (fig 1), apparently confirming the clinical suspicion of either lymphoma or metastatic disease, or possibly a systemic infective process with hepatic involvement. Many further blood tests were performed to search for an infective or immunological cause, all of which were unhelpful. Faecal fat studies suggested mild malabsorption. Biopsies from the right lobe of the liver, first under ultrasound then under CT guidance, failed to show any specific abnormality. Excision of a moderately enlarged cervical lymph node also failed to produce a diagnosis. However, evaluation of the alkaline phosphatase isoenzymes suggested a bone abnormality and subsequent bone marrow biopsy showed generalised hyperplasia with dysplastic features and a marked increase in mast cells (fig 2).

During the period of inpatient and outpatient investigation, the patient had continued to lose weight and suffer from severe night sweats along with abdominal pain and pruritus. Immediately on confirming the diagnosis he was started on astemizole, ranitidine, prednisolone, and hydroxyurea. These produced marked symptomatic improvement within 48 hours and the patient was discharged a few days later. He has since been started on α -2b interferon and continues to improve clinically. This disease has been associated with trisomy of chromosome 8 or 9,¹ but no such abnormalities were detected in this case.



Figure 1 Computed tomography showing ill defined areas of low attenuation in the right lobe of the liver.

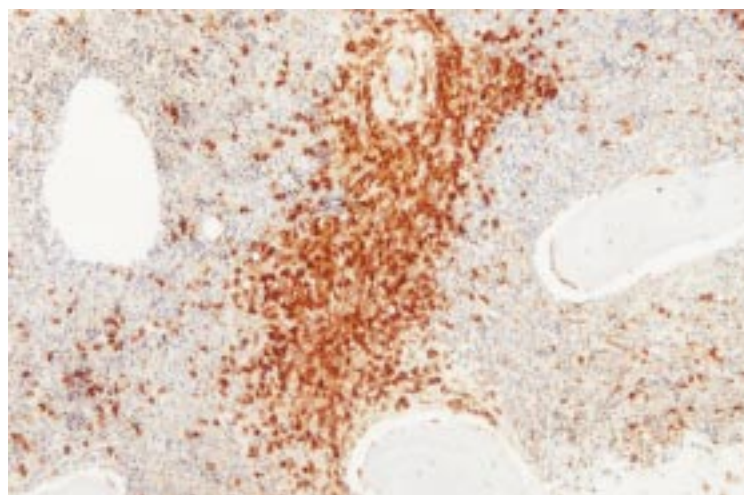


Figure 2 Immunoperoxidase stain of bone marrow trephine using mast cell tryptase marker. This shows paratrabecular infiltration by tumour composed of masses of small uniform cells with round/ovoid nuclei, moderately clear cytoplasm and ill defined borders.

Discussion

Systemic macrocytosis is a rare disease with a reported annual incidence of 0.3 new cases per 100 000 of the population. It affects both sexes and occurs in all races but is more common in whites. Several different clinical presentations have been described.² Mast cells contain a wide variety of chemically active substances which, when released, produce many of the symptoms associated with the disease, including the coagulation disorder which proved troublesome at liver biopsy. Histamine when released from its secretory granules accounts for flushing, pruritus, and gastric manifestations. Mast cells also release membrane derived lipid mediators such as leukotrienes, prostaglandins, and platelet activating factor, along with cytokines intrinsically linked to the body's inflammatory response. These include tumour necrosis factor, interleukins 1, 3, 4, 5, and 6, and interferon. Other symptoms of the disease are caused by the increased bulk of mast cells in the tissues. Commonly patients present with a reddish macular rash—urticaria pigmentosa—owing to increased collections of cells in the skin. Proliferation in bone produces pain, and several cases of mastocytosis-induced osteoporosis have been described. Malabsorption may occur, as in this case, owing to increased mast cell load in the bowel wall.

The skin is the most commonly affected organ in mastocytosis, urticaria pigmentosa being the most common cutaneous manifestation. Several other rashes have been described. In these cases skin biopsy is the investigation of choice. Systemic disease without cutaneous signs, as in our patient, is said to occur in about 1% of cases.³ This is probably an underestimate because the diagnosis is often missed or delayed. The diagnosis in these cases is based on clinical suspicion. Recently it has been found that in adults there is an increase in urinary histamine or metabolites of histamine or prostaglandin D₂. When combined with the clinical picture these measurements are both sensitive and specific indicators of systemic mastocytosis. Bone marrow infiltration with mast cells, seen on bone marrow biopsy, occurs in nearly all affected patients. Further investigations depend on the individuals specific complaints.

Treatment is symptomatic⁴ and is based on the use of antihistamines. H₁ antagonists such as astemizole or hydroxyzine relieve pruritus and flushing; H₂ antagonists are often beneficial in improving gastrointestinal symptoms. Stabilisation of mast cell membranes using sodium cromoglycate may reduce headaches, bone pain, diarrhoea, and abdominal pain. Non-steroidal anti-inflammatory agents arrest severe flushing and have been used to prevent episodes of vascular collapse by preventing synthesis of prostaglandin D₂ within mast cells. The proliferation of mast cells can be slowed by hydroxyurea. Treatment with inhibitors of bone resorption such as biphosphonates have been shown to be useful in the treatment of mastocytosis-induced osteoporosis.

In 1992, Kluin-Nelemans *et al* described the use of interferon α -2b in a patient with systemic mastocytosis.⁵ After two months of treatment there was a large increase in haematopoietic cells in the bone marrow and a decrease in infiltration by mast cells. This was sustained for one year. Several subsequent reports confirm the benefits of this treatment. More recently interferon and radiotherapy have been shown to have short term benefits in the treatment of systemic mastocytosis.

This case highlights the difficulty in diagnosing mastocytosis in the absence of a recognised cutaneous lesion. Clinical suspicion should be followed by assessment of the urinary metabolites of histamine and prostaglandin D₂ and then bone marrow biopsy. Treatment is symptomatic but improves life expectancy by a few years in the aggressive form of the disease and significantly improves the patient's quality of life.

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