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Unusual findings in two cases of Langerhans' cell histiocytosis

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Abstract We report unusual findings in two patients with Langerhans' cell histiocytosis (LCH), namely a cervical mass lesion with extensive destruction of the posterior elements of a cervical vertebra and gastrointestinal lesions as part of multisystem involvement. The aim of our report is threefold. Firstly, LCH can be responsible for osteolysis of the vertebral posterior arches, with or without involvement of the vertebral body, and should be included in the differential diagnoses of cervical mass lesions. Secondly, in a patient with confirmed LCH and additional protein-losing enteropathy, gastrointestinal involvement should be considered as a possibility since it is an important factor for establishing prognosis. Thirdly, LCH lesions can be very extensive and yet have a good response to therapy, whereas less spectacular lesions may not respond or respond only partially to therapy. Thus, an important factor in establishing prognosis is the presence of multisystem involvement at diagnosis, regardless of the extent of a lesion at a particular site.

Introduction

In Langerhans' cell histiocytosis (LCH), spinal bone lesions typically involve a vertebral body, the posterior elements of which are generally spared. Among extraskeletal sites of LCH, involvement of the gastrointestinal tract is unusual and is generally associated with multisystem disease. Only a few reports in the literature describe such lesions [1–5]. In addition to the description of two cases, we draw attention to the bizarre behaviour of LCH and also stress the importance of including LCH in the differential diagnosis of focal mass lesions or multi-organ diseases.

Case reports

Patient 1

A 21-month-old boy was admitted to our institution because of torticollis, neck tenderness, anorexia and transient episodes of imbalance. Clinical examination revealed scaly patches on the scalp, with small erosions. Blood tests showed elevated erythrocyte sedimentation rate (76 mm/h). Skeletal isotope scanning using ^{99m}Tc-pyrophosphate showed heterogeneous uptake in the lower cervical region. Radiographs showed extensive bone lesions of the 5th and 6th cervical vertebrae, involving mainly the posterior arches with normal disk spaces (Fig 1 a). CT demonstrated a markedly enhancing, tumour-like cervical mass with destruction of the posterior elements of the 5th and 6th cervical vertebrae and extension of the lesion into the cervical canal (Fig. 1 b). CT differential diagnoses were infectious disease, osteoblastoma and aneurysmal bone cyst as benign possibilities and rhabdomyosarcoma, leukaemia, lymphoma, metastatic neuroblastoma and LCH as possible more aggressive lesions. MRI better delineated epidural extension with encasement of the right vertebral artery and involvement of the paraspinal soft tissues (Fig. 1 c). The diagnosis of LCH was made after biopsy of the cervical mass.

Therapy was started with prednisolone and vinblastine and completed with 6-mercaptopurine and methotrexate for 1 year. There was no haematological, hepatic or pulmonary involvement and prognosis was good. He has been regularly followed up in our out-patient clinic for 4 years; clinical examination is satisfactory and cervical radiographs and MRI have shown spectacular improvement (Fig. 1 d).

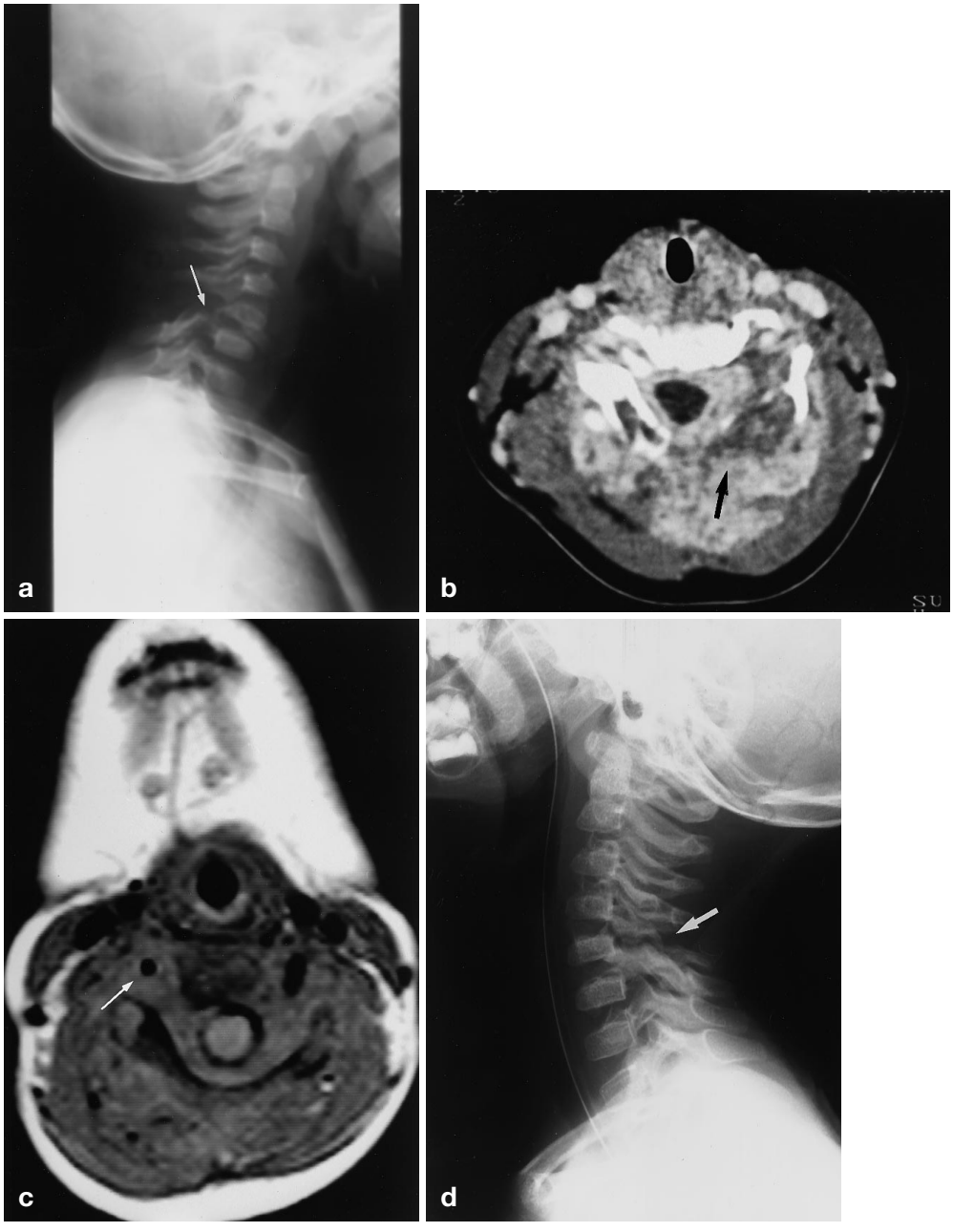

Fig. 1 a–d Patient 1. **a** Extensive destruction of the posterior elements of C5 and C6 (*arrow*). **b** Transverse CT demonstrating an enhancing soft tissue mass with bone destruction and extension into the cervical canal (*arrow*). **c** Transverse MRI showing abnormal tissue in the cervical canal and encasement of the right vertebral artery (*arrow*). **d** Post-therapy radiograph shows bony reconstitution at C5 and C6 without vertebra plana (*arrow*)

Patient 2

A 9-month-old female infant was admitted with diarrhoea, failure to thrive and skin rash. Clinical examination revealed erythematosquamous patches over the scalp, and liver and spleen enlargement. Blood tests showed anaemia, thrombocytopaenia and hypoalbuminaemia. Bone marrow aspirate and histopathological examination revealed haemophagocytosis. Skeletal survey demonstrated osteolysis of the right occipital bone, which was further investigated CT (Fig. 2 a). A barium meal and follow through showed an abnormal pattern of the jejunal mucosa, together with luminal narrowing of the proximal segment of the jejunum (Fig. 2 b). This could explain the diarrhoea and loss of protein via the intestinal tract. MRI of the brain and chest radiographs were normal.

The diagnosis of LCH was confirmed after biopsy of the scalp lesions. This patient had a poor prognosis since multisystem involvement was obvious and, in particular, there was dysfunction of the haematological and digestive systems. Steroids and chemotherapy were started and, after two courses, partial remission was obtained. Therapy was then stopped and follow-up over a period of 2 months has been satisfactory. Diarrhoea has stopped and serum protein level has returned to normal. The patient is free from gastrointestinal symptoms and signs.

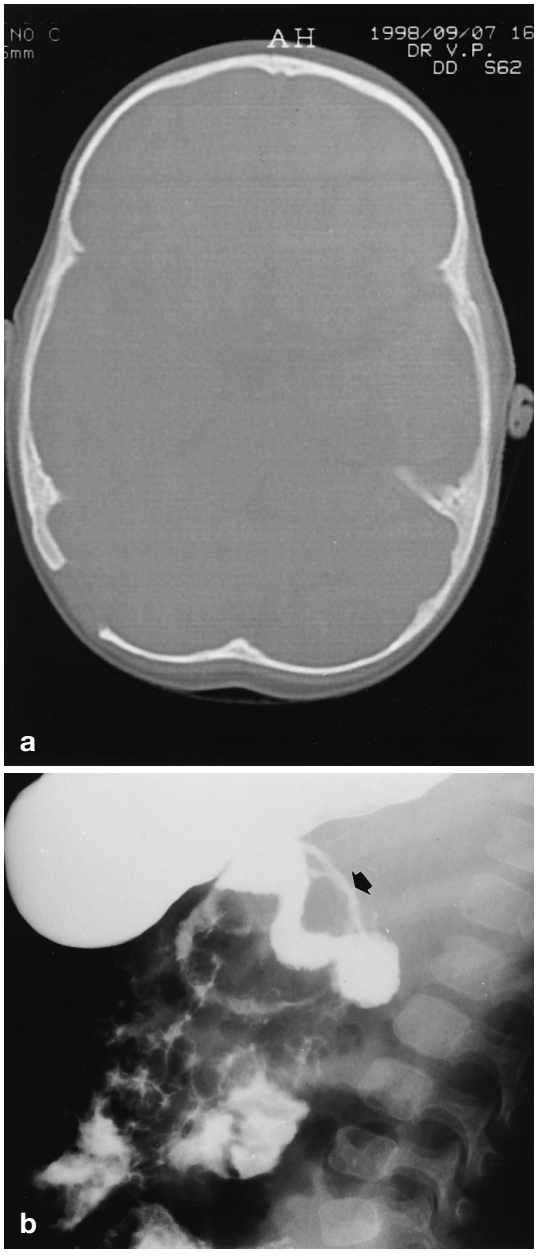

Fig. 2 a, b Patient 2. **a** Transverse CT shows osteolysis of the right occipital bone. **b** Barium opacification of the small bowel. Lateral view shows abnormal jejunal mucosa with segments of luminal narrowing (*arrowhead*)

Discussion

LCH remains an enigmatic disease. It may be self-limiting in some patients, whereas in others even intensive treatment is unsuccessful. The outcome depends on whether vital organ function is compromised at diagnosis, in which case the prognosis is poor.

Cutaneous LCH is very common (50 % of all cases) and may be the first manifestation of the disease [6–8]. It is not necessarily a benign feature as many patients progress to multisystem disease. Both our patients presented skin lesions and in one, skin biopsy provided the diagnosis of LCH.

Bone lesions are the most common radiological manifestations of LCH [1, 9–11]. Lesions of the calvarium are the most frequently observed [12, 13]. On radiographs they appear as lucencies that are typically round or ovoid with well-defined sclerotic margins. If isolated, lesions of the skull generally heal spontaneously. One of our patients had an occipital lesion, but since there was involvement of other systems (liver, spleen, bone marrow and gut), therapy was required. Spinal lesions usually affect the vertebral body. The intervertebral disk spaces are spared and involvement of the posterior elements is rare [1, 14, 15]. Destruction of these elements, as described in our first patient, is an unusual finding. Differential diagnoses included infectious diseases, benign tumours such as osteoblastoma and aneurysmal bone cyst, and more aggressive lesions such as rhabdomyosarcoma, leukaemia, lymphoma, metastatic neuroblastoma and LCH. Pyogenic and non-pyogenic spondylitis were easily ruled out by the presence of normal disk spaces. Osteoblastoma and aneurysmal bone cyst are benign bone tumours that frequently involve the neural arch in young adults [15, 16]. In our first patient, these two diseases were a definite possibility. Even though destruction of the posterior elements was accompanied by extensive soft-tissue infiltration, including the epidural spaces, these benign tumours could not be totally ruled out. Nevertheless, a more aggressive lesion had to be considered. Lesions of the vertebral posterior arches are rare in LCH, unlike in lymphoma and metastatic disease. Biopsy had to be performed to establish a definite diagnosis and pathological study confirmed LCH.

Pancytopaenia as a result of medullary involvement is quite common in infants with disseminated LCH. Hepatic enlargement is very common in disseminated LCH, but the cause is still unclear. An enlarged spleen is found in about 5 % of patients at presentation and, in refractory disease, it may contribute to cytopaenia. Medullary involvement is considered as a factor of poor prognosis and this seems to be the case for our second patient.

The gastrointestinal tract is an unusual site of involvement in childhood LCH. In the event of LCH with multisystem disease, the presence of diarrhoea and protein-losing enteropathy should suggest the possibility of gastrointestinal disease, and radiological studies provide elements that are compatible with this type of rare complication. This was the case in our second patient who presented symptoms and signs of intestinal involvement by LCH. Biopsy of the intestinal tract was

not performed and even though intestinal involvement was based on clinical signs and radiological findings, it seems most probable since multisystem disease was obvious at diagnosis and specific treatment resulted in cessation of diarrhoea and normalisation of serum protein level. Histopathologically, LCH lesions characteristically occupy the lamina propria and submucosa, and there is glandular and mucosal atrophy and possibly erosions [5].

Conclusions

LCH usually remains limited to the skin with or without skull involvement. Lesions of the spine tend to affect the vertebral body, leading to vertebra plana. Destruction of the posterior elements of a vertebra without vertebra plana does not rule out LCH, and it should be considered as a possible differential diagnosis. In the event of multisystem disease associated with LCH, the presence of diarrhoea and a protein-losing enteropathy are highly suggestive of gastrointestinal involvement and should be recognised. Its recognition is generally useful in establishing prognosis of the disease. Lesions limited to bone, without other system disease, show good prognosis. This was the case with our first patient. On the other hand, haematological and gastrointestinal lesions are factors for poor prognosis, as in our second patient.

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