Pediatr Radiol (2003) 33: 485–488
DOI 10.1007/s00247-003-0929-2

CASE REPORT

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Fibrosing mediastinitis with superior vena cava obstruction as the initial presentation of Langerhans' cell histiocytosis in a young child

Received: 28 February 2003
Accepted: 25 March 2003
Published online: 24 April 2003

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Abstract We present a 2-year-old girl with an unusual presentation of Langerhans' cell histiocytosis (LCH). Five months prior to admission to our hospital, she received IV steroids for bronchial obstruction. On admission, clinical signs of SVC obstruction were evident and a mediastinal mass was evident on the chest radiograph and MRI. Biopsy revealed fibrosing mediastinitis. Five months later, osteolysis was present on a skull radiograph. Surgical biopsy of the skull lesion revealed LCH. This case is unique because it demonstrates a rare initial manifestation of LCH that has not been previously reported. Furthermore, the primary, solitary mediastinal manifestation without calcifications was histologically interpreted as fibrosing mediastinitis, and the final diagnosis of LCH was only made after identifying the skull lesion.

Keywords Thorax · Mediastinum · Head · Skull · Langerhans' cell histiocytosis · Fibrosing mediastinitis · Superior vena cava obstruction

Introduction

The list of mediastinal masses in the paediatric age group includes a number of malignant and benign entities [1]. A very rare cause for a mediastinal mass is sclerosing mediastinitis. This condition results in fibrosis and sclerosis of the mediastinum, often leading to obstruction of intrathoracic organs. Only single paediatric cases of sclerosing mediastinitis have been reported in the medical literature to date [2].

Langerhans' cell histiocytosis (LCH) is a reactive disorder characterised by infiltration of either single or multiple organ systems with proliferating cells of epidermal Langerhans' cells [3]. According to one study, mediastinal mass as a manifestation of multisystem LCH is relatively rare (1 of 42 children), while pulmonary involvement without mediastinal mass is more frequent (8 of 42 children) [4].

We report the unusual course of a 2-year-old girl with LCH who initially presented with a solitary anterior mediastinal mass with SVC obstruction without calcification or pulmonary involvement. The radiological and histological findings are described.

Case report

A 2-year-old girl was admitted to our hospital with progressive signs of upper mediastinal vessel obstruction. Her growth and development were normal. The medical history disclosed an episode of cough and dyspnoea 6 months previously. In another

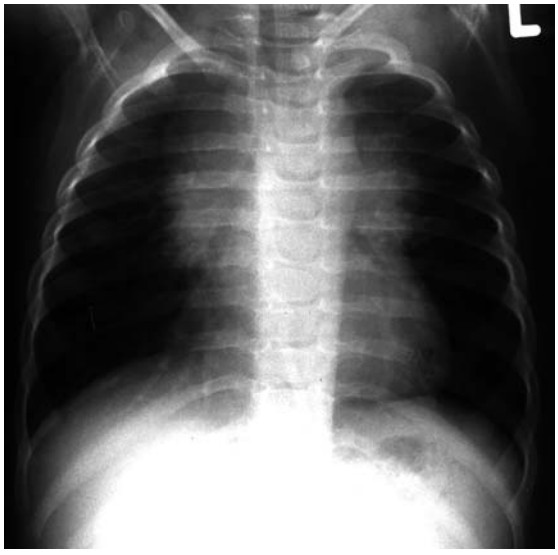

Fig. 1 Chest radiograph at first presentation shows mediastinal mass without pulmonary infiltration

hospital, IV prednisone had been given to treat presumed bronchial obstruction. Mediastinal enlargement on a chest radiograph at that time was interpreted as simple thymic hyperplasia (Fig. 1). Physical examination revealed oedema of head and neck as well as dilated neck veins. All laboratory results were unremarkable. The current chest radiograph and US demonstrated a large anterior mediastinal mass (Fig. 2). MRI of the chest (1.5-T Siemens Vision, Erlangen, Germany) showed a large, well-defined tumour occupying the upper anterior mediastinum. All portions of the tumour demonstrated medium signal intensity, slightly higher than muscle on T1-weighted images (Fig. 3a). After IV administration of contrast medium (0.1 mmol/kg Gd-DTPA) heterogeneous enhancement was observed (Fig. 3b). SVC compression was confirmed (Fig. 3c). Chest CT did not reveal any calcification. A CT-guided core biopsy was obtained.

Immunohistochemistry revealed vimentin and focal actin expression in the spindle cells of the processes, suggesting fibroblastic and myofibroblastic differentiation. A few CD68-positive histiocytes were detectable, but Langerhans' cells were not identified by anti-CD1a and S100 antibodies. In addition, extensive electron-microscopic studies did not reveal Birbeck granules in the cytoplasm of histiocytes of the mediastinal process. There was no suggestion of lymphoma or carcinoma by CD3, CD20, CD30, kappa, and lambda immunohistochemistry. The number of plasma cells was low and the proliferative activity of the spindle cells and the few lymphoid cells was minimal (Ki67 index $< 5\%$). Histoplasmosis and other fungi were undetectable by PAS and Grocott stains. In conclusion, a descriptive diagnosis of 'sclerosing mediastinitis' was made.

In another hospital a Palmaz stent was implanted in the SVC. The child was then referred for open biopsy of the mass to substantiate this unusual histological finding. Again, histology compatible with fibrosing mediastinitis was obtained, which was confirmed by three further pathology reference centres (Fig. 4).

Two months later, a skull radiograph, performed to investigate macrocephaly, revealed osteolysis in the left parietal bone. Excision biopsy of the skull was fixed in buffered paraformaldehyde (4%) for 24 h. The material was decalcified in an EDTA-based buffer for 48 h. Paraffin-embedded material was cut and processed for H&E, periodic acid-Schiff (PAS), Grocott, Giemsa and reticulin (Gomori) stains. Primary antibodies comprised reagents to CD1a, S100, vimentin, actin, desmin, AE1/3 (pancytokeratin) and cytokeratin 19, CD3, CD20, CD30, CD31, CD34, CD68, kappa and lambda light chains and Ki67 (MIB1). The avidin-biotin peroxidase technique was applied, as previously described [5]. Positive and negative controls were carried out on tissues known to contain each of the antigens under study. In negative control experiments the specific primary antigens were replaced by phosphate-buffered saline (PBS). In conclusion, the biopsy of the skull showed minimal infiltration by Langerhans' cells with considerable fibrosis. Comparison of the mediastinal and skull specimens revealed similarity of the fibrous reaction in the skull and the mediastinum. This reaffirmed the probability that the mediastinal mass was also caused by LCH. With the diagnosis of LCH with multisystem involvement, chemotherapy (prednisone and vinblastine) was instituted according to the European LCH-3 protocol. Follow-up examinations (currently now 22 months) do not reveal any further manifestation of LCH. The mediastinal mass is slowly regressing.

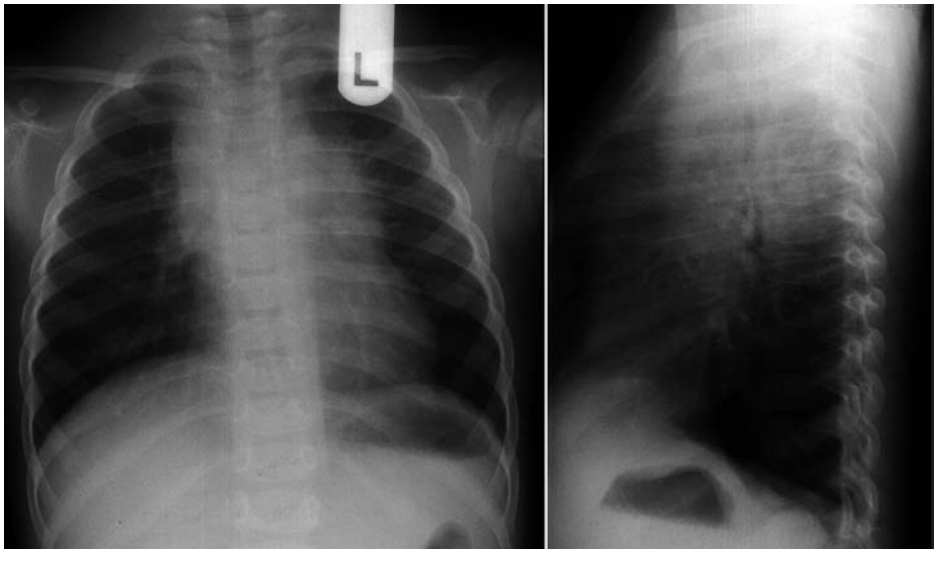

Fig. 2 Chest radiograph 7 months later shows regression of the mediastinal mass

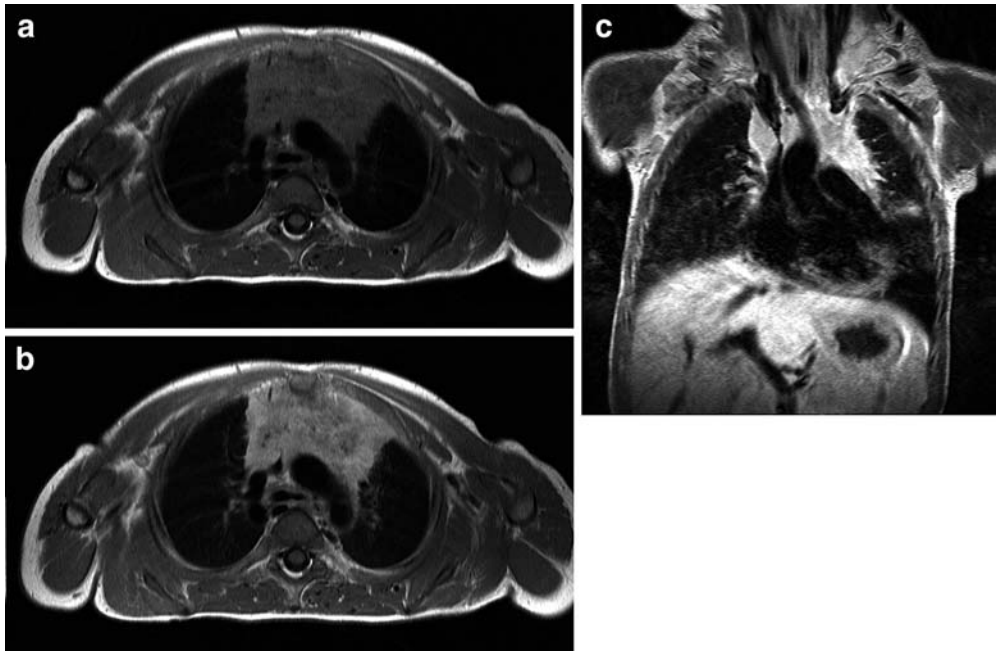

Fig. 3a–c MRI of the thorax. **a** Axial, T1-weighted TSE sequence (TR/TE, 703/10) confirms the mediastinal mass. **b** Axial, contrast-enhanced TSE sequence (TR/TE, 703/10) demonstrates inhomogeneous contrast enhancement. **c** Compression of the SVC is seen on the coronal T1-weighted sequence

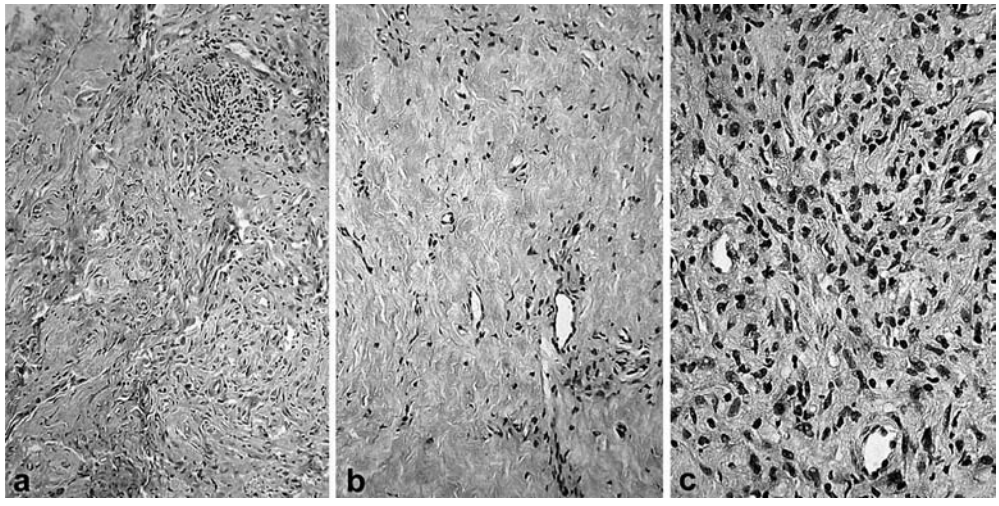

Fig. 4a–c Histology of the mediastinal specimen. **a** Low-power view of the sclerosing process as revealed in a mediastinal core biopsy specimen. Predominance of scar-like regions rich in collagen bundles around a minor population of bland-looking, fibroblastic spindle cells and a small focus of mononuclear inflammatory cells (*left upper corner*), (H&E ×40). **b** High-power view of the scar-like region (H&E ×400). **c** Minor region with focal increase in plump fibroblasts somewhat reminiscent of fibromatosis. (H&E **x**400)

Discussion

Mediastinal masses causing SVC syndrome are rare in childhood and comprise mostly malignant tumours such as lymphomas. In our case, a malignant tumour was not very likely because of the normal laboratory results and slight regression of the mediastinal mass on the chest radiograph over a period of 6 months prior to treatment. Moreover, thymic hyperplasia was unlikely to cause venous obstruction. No infectious causes could be identified.

Both the CT-guided and open biopsies yielded histology of fibrosing mediastinitis, which in itself is a non-specific diagnosis never previously made in a 2-year-old child. The youngest patient with fibrosing mediastinitis reported in the literature was a girl aged 9 years [6]. In our case, the development of a skull lesion eventually led to the diagnosis of LCH. The prior IV administration of steroids in our patient could have triggered the regression and fibrosing process in the mediastinal mass. In the context of the histology of the skull lesion, the mediastinal mass was the original focus of involvement by LCH. Reports of SVC obstruction due to mediastinal fibrosis and LCH can be found in the literature [2, 7, 8]. Mediastinal masses owing to LCH most often occur in disseminated disease. However, as in our case, Nakata

et al. [9] reported an isolated mediastinal mass as the initial manifestation as a result of LCH. We did not find cavitations as described by Abramson et al. [10] Punctate calcification of mediastinal masses in LCH has been described, unlike the appearance in our case [11, 12].

In conclusion, mediastinal masses with histology of fibrosing mediastinitis can be caused by LCH. Further evaluation of obscure mediastinal lesions should include LCH in the potential differential diagnosis. Mediastinal mass as a primary site of manifestation of LCH is rare, particularly in combination with SVC obstruction.

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