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Atypical lymphohistiocytic bone tumour (osseous variant of Rosai-Dorfman Disease?)

Jacques Hamels[1], **Léon Fiasse**[2] **and Jacques Thiery**[3]

[1] Institute of Morphological Pathology, Allée des Templiers 41, B-6280 Gerpinnes (Loverval),
[2] Division of Pediatrics,
[3] and Orthopedic Surgery, Clinique Saint Pierre, B-1340 Ottignies, Belgium

Summary. A single osteolytic bone tumour with a cellular composition similar to that of the extra-nodal localization of Sinus Histiocytosis with Massive Lymphadenopathy although with greater cellular atypicality is described. This histological similarity suggests the possible occurrence of isolated bone involvement of Rosai-Dorfman disease, with atypical cytology but benign evolution, which has not been reported in the literature.

Key words: Bone – Tumour – Haemophagocytosis – Atypical Histiocytosis

Introduction

Since its description by Destombes (1965) and its identification by Rosai and Dorfman (1969), Sinus Histiocytosis with Massive Lymphadenopathy (SHML) has been discussed in numerous publications (Buchino et al. 1982; Lampert and Lennert 1976; Sanchez et al. 1977; Rosai et al. 1972; Ngendahayo et al. 1983). Apart from lymph node involvement, which was first considered essential, non-nodal localizations, whether concomitant or not, have been described (Sanchez et al. 1977; Thawerani et al. 1978; Foucar et al. 1978; Foucar et al. 1979). Among them, bone localization as well as localization in the airways, digestive tract, skin and orbit, are the most frequent, always associated with other ganglionic or visceral, proximal or distal, manifestations (Walker et al. 1981; Ramos 1976; Sauvaget et al. 1982; Wright and Richards 1981; Aoyama et al. 1983).

We will describe here a case of haemophagocytic lymphohistiocytosis localized strictly in one bone and showing a favorable evolution. Its histology was almost identical to that of SHML, with however, cytological atypia of the large histiocytic cells, facts which, to our knowledge, have never been reported before.

Offprint requests to: J. Hamels at the above address

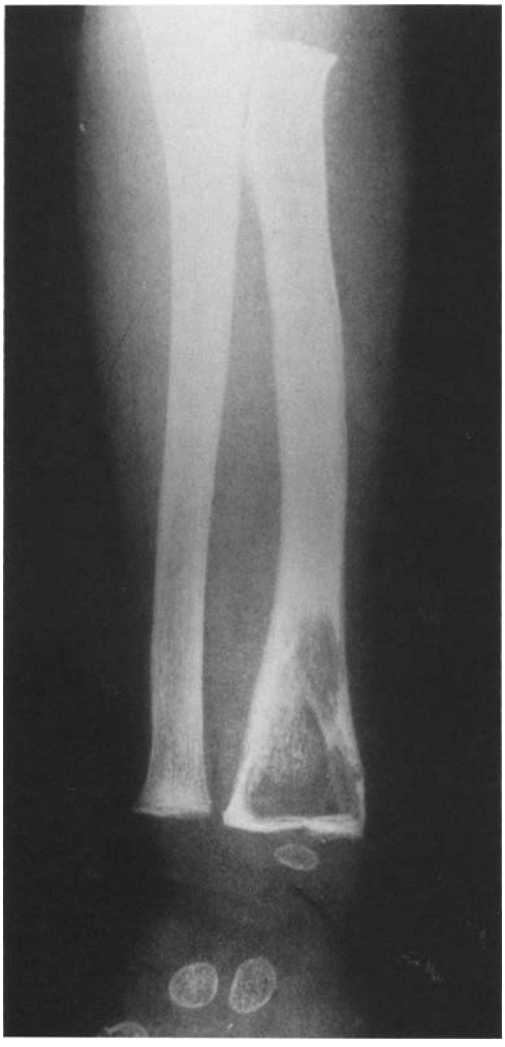

Fig. 1. Large lytic medullary defect with focal periosteal reaction and irregular borders in the epiphysis and metaphysis of the left radius

Clinical history

A young boy ($1^{1/2}$ year) was admitted to the hospital two days after he fell on his left arm. The history only mentioned an episode of otitis one month before the admission. Weight and length developed normally. A considerable swelling, spontaneously painful, showed on the forearm and wrist, and the boy's temperature was 37.8° C.

No adenopathy or hepatosplenomegaly were observed. The radiography (Fig. 1) showed an osteolytic lesion in the distal quarter of the radius with a discrete periosteal reaction of the corresponding cortical area. The following abnormal biological values were found: sedimentation rate 13 mm/h, slight leukocytosis with a relative lymphocytosis of 61%, increased $\alpha 2$ glob-

ulins (600 mg %) and a moderate deficiency of IgA and IgM. A curettage of the lesion was carried out. At the time of complementary postoperative care, tiny lymph nodes could be felt on palpation in all the ganglionic areas, but they were too small to warrant a biopsy. The biological anomalies were regressing. No other bone lesion was seen (Xray and scintigraphy). The thorax Xray was normal. Search for anti-EBV antibodies (Epstein Barr Virus) was negative.

Subsequent Xray checks showed that the bone hiatus was being gradually filled up, and the appearance was normal again after two years. This was confirmed (Xray and general clinical status) at the last control one year later (3 years follow-up).

Materials and methods

The bone curettage yielded numerous soft fungoid fragments of a greyish colour, from which samples were taken and fixed in Bouin's solution and embedded in paraffin. The sections (5 μ) were stained with haemalun-eosin-safran, Masson's trichrome, PAS, with and without diastase digestion, and Wilder's reticulum stain. The imprints were stained with Giemsa and also treated for the demonstration of acid phosphatases. For the immunohistological investigation with immunoperoxidase on deparaffinized sections, antisera (Dako) were used which were coupled to peroxidase and diluted 1/200 for heavy chains (A, G, M) and light ones (K and λ) or demonstrated indirectly (PAP technique) and diluted 1/100 for muramidase and α-1-antichymotrypsin. Protein S 100 marker, provided as kit (MILES), was also revealed by PAP technique.

Results

The medullary spaces were massively occupied in all the fragments by a dense and polymorphic tumor cell population, with extensive lysis of the trabeculae and focal extension in the epiphyseal cartilage.

The tumour was partially composed of mature lymphoid cells (mainly small lymphocytes) with a limited number of plasma cells. These cells were often clumped, alternating with lighter zones occupied by histiocytes of varying size, some of normal size, non-atypical, others being larger and sometimes even giant and multinucleated (Fig. 2). In the cytoplasm of these large histiocytes there were numerous cells, mostly small mature lymphocytes, sometimes arranged as a peripheral crown, but also polynuclear neutrophils (Fig. 3 A). The nuclei of these cells were hyperchromatic and anisokaryotic, with one or two medium-sized nucleoli (Fig. 3 B). There was no mitotic activity. The stroma consisted of a loose reticulin network with a limited number of small vessels.

There were some islets of peritrabecular collagen fibrosis. On the *imprints* lymphoid and histiocytic cells were found in almost equal numbers. The histiocytes contained a considerable amount of diffuse granular acid phosphatase, which was clearly predominant in the smallest cells. The *Immunohistochemical* examination showed plasma cells that were positive for the heavy G or M chains, as well as for the light ones K and λ, depending on the cells. The cytoplasm of the small histiocytes was very positive for muramidase, whereas that of the haemophagocytic cells was negative, being on

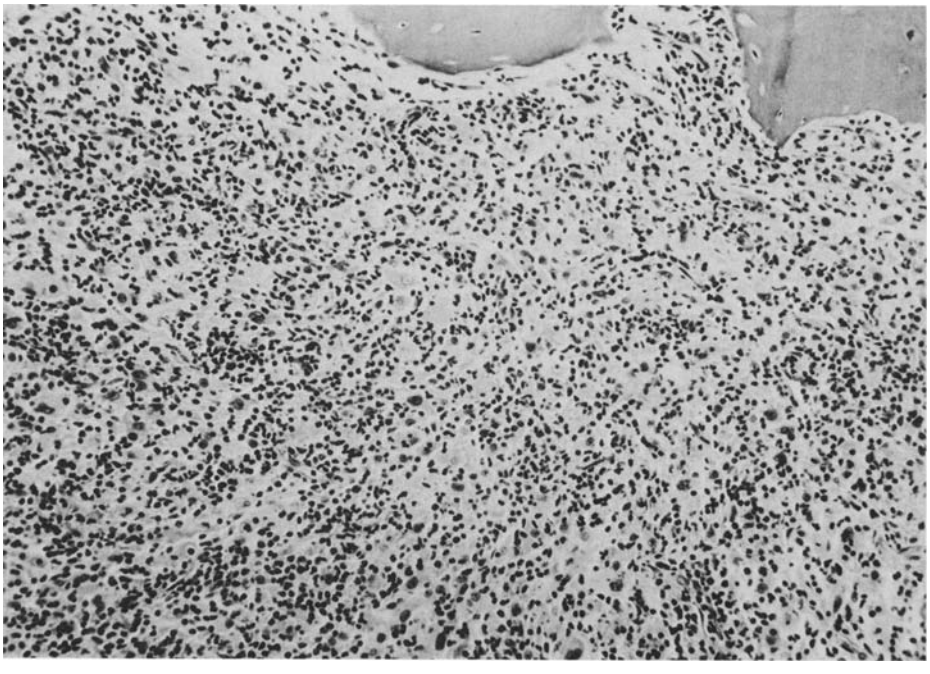

Fig. 2. Osteomedullary tissue, massively infiltrated by a tumour consisting of mature lymphoid cells (mostly small lymphocytes) and of histiocytes, some of them with a large hyperchromatic nucleus. HES, ×125

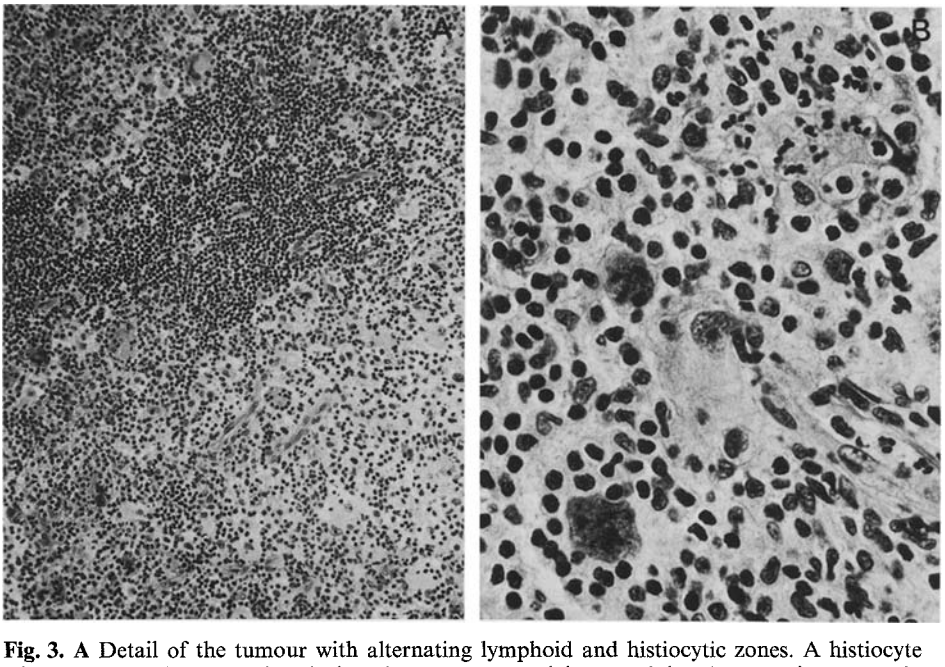

Fig. 3. A Detail of the tumour with alternating lymphoid and histiocytic zones. A histiocyte with numerous intracytoplasmic lymphocytes arranged in a peripheral crown is present in the center of the field. HES, ×125. **B** View of the haemophagocytic histiocytes, one containing lymphocytes, another one polynuclear neutrophils. HES, ×500

the contrary slightly positive for α-1-antichymotrypsin, which was absent in the non-phagocytozing cells.

The large histiocytic cell population showed also a strong positivity for S 100 protein, the smaller ones being only weakly positive.

Discussion

The Xray aspect of this single lytic bone tumour allowed to consider, taking into account the patient's age, a vast diagnostic range including mainly an eosinophilic granuloma, metastatic disease and various forms of essentially osseous tumours (monostotic fibrous dysplasia, solitary xanthoma, solitary osseous xantho-endothelioma, etc).

The absence of any associated pathology allowed us to exclude a number of other diseases: neurofibromatosis, sarcoidosis, metabolic lipidosis, histoplasmosis. Neither histologically nor clinically, did the case fit into the group of children's haemophagocytic reticulosis. This contains familial haemophagocytic reticulosis (Farquhar and Claireaux 1952), the virus-associated haemophagocytic syndrome (Risdall et al. 1979) and familial reticuloendotheliosis with eosinophilia (Omenn 1965). All those diseases present with frequent family history, distinct clinical features and involvement of several organs. Similarly, histiocytic medullary reticulosis (Scott and Robb-Smith 1939) which is rarely described in children can be discarded.

Histological examination may show frothy histiocytes in several of these entities (xanthoma, fibrous histiocytoma, xantho-endothelioma, lipidosis, nonossifying fibroma) but typical of this case was the clearly haemophagocytic nature of the histiocytes, the considerable lymphoid component and the absence of other characteristics that would suggest any of the above mentioned tumours. Conversely, these elements were very similar to those described in SHML with localization in the bone, of which 12 cases have been reported (Lampert et al. 1976; Walker et al. 1981; Sauvaget et al. 1982; Ramos 1976; Wright et al. 1981; Aoyama et al. 1983; Buchino et al. 1982). The age of the patients ranged between 2.5 and 56 years and there is a clear male predominance (10 m, 2 f).

There is no preferential bone localization. In 8 patients the bone lesions were multifocal. In all, one or more extra-osseous tissues, whether lymphoid or not, were also affected. The evolution was slow, (following-up for 6 months to 17 years) mostly characterized as stationary or progressively involutive. However, in 2 cases, the issue was fatal after 10 (Buchino et al. 1982) and 17 (Wright et al. 1981) years.

An overall survey of current literature does not disclose any specific form of treatment other than surgical excision. The favorable course and good local repair, demonstrated in the present case, probably indicates the completeness of bone curettage.

The slight plasma cell involvement and the fibrosis which were observed in this case are characteristics of the extra nodal lesions which have already been reported in bone sites (Walker et al. 1981), and have been interpreted as evidence of spontaneous regression.

The enzymatic contents of the histiocytes included an abundance of

lysosyme in the small cells, whilst the large ones did not contain any or only little α-1-chymotrypsin, is in agreement with similar observations which were made under different circumstances (Burgdorf et al. 1981; Mendelsohn et al. 1980). This might be explained by a considerable consumption and/or dilution of lytic enzymes in larger, actively absorbing cells. Conversely, in a recently reported case (Aoyama et al. 1983), these enzymatic markers were practically absent, the histiocytic cells showing characteristics (Protein S 100 marker positivity and ultrastructural aspects) that were similar to the interdigitated reticular cells of the T-dependent lymphoid territories, as was also observed in Histiocytosis X (Nihei et al. 1984). Protein S 100 positivity was similarly present in this case.

If, as we think, this observation is part of the SHML syndrome, this would imply that this possible diagnosis is to be added to the group of strictly osseous lytic tumours. It is not clear if the cytological atypia of the histiocytes is an incidental abnormality or justifies the isolation of this tumour as a distinct entity.

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