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HISTIOCYTOSIS X – A TIME-OVERLAPPING SKELETAL DISEASE. REPORT ON A RECENT CASE OF POLYOSTOTIC MANIFESTATION.*

ABSTRACT: With regard to the literature on the paleopathological findings, a report on an actual clinical case of slowly progredient histiocytosis X in a 16-year-old male individual is given. In 1978 the first site (left femur) was treated surgically, in 1983 a further one in the dorsoparietal region. Since then a combined cytostatic therapy and telecobalt radiation were applied. The process nevertheless remained progressive: until 1987 eosinophilic granulomata were seen in 10 resp. 11 different locations.

KEY WORDS: Histiocytosis X – Osteopathology – Eosinophylic granuloma.

Beyond the osteolytic processes with sharply limited, sometimes like punched defects, not seldom in a circular form, the eosinophilic granuloma earns special attention. Not only radiographically but also in paleopathological view it is the classical differential diagnosis of all destructive bone processes (e.g. multiple myeloma, bone sarcoma, Burkitt-tumor, metastases, osteomyelitis, syphilis etc.). The eosinophilic granuloma is classified as a nonneoplastic osteomyelitic process of the reticular bone-marrow cells. It generally occurs as a benign disease of unknown etiology.

The first definite description of eosinophilic granuloma was given by T. Smith in 1865 (quoted from Slater and Swarm 1980). The term „eosinophilic granuloma" is connected with Lichtenstein and Jaffé (1940); independently the disease was described by Ottani and Ehrlich (1940).

After the attention has been drawn to this entity, numerous casuistic reports followed. The diversity of information allowed a synopsis of primarily separately described syndroms of Abt-Letterer-Siwe and Hand-Schüller-Christian type, which together with the eosinophilic bone-granuloma were taken into the superior entity of histiocytosis X in one nosologic conception (Lichtenstein 1953).

Possibly the proposed different types represent different sequels of the disease: while the eosinophilic granuloma of the bone represents the easier running, limited form, the Letter-Siwe type means an acute severe form and the Schüller-Christian type a chronically disseminated form of great clinical variability (Jaffé 1972).

In the survey of literature published in 1980 by Slater and Swarm 686 cases were recorded between 1940 – 1974, world-wide yearly about 20 cases. In solitary location the diagnosis is evidently more complicated than in multiple appearance, which is the case in about 50% (Heitner and Bartolomaeus 1981).

* Dedicated to Prof. Dr. mult. W. Bernhard, director of the Institute of Anthropology and Human Genetics, on the occasion of his 60th birthday.

The development of the disease can run over years, or in pushwise repetitions, or quickly progredient up to fulminant. Transition to neoplastic growth of the Langerhans-cells in foudroyant processes are discussed, especially since long-term observation seems to prove a tendency towards malignancy (Lipton 1983). A reactive proliferation on the basis of a disturbed immunoregulation is discussed. Defects in surpressor-T-cells may give a hint in this direction (Groopmann and Golde 1981, Osband et al. 1981). Generally multifactorial pathomechanisms are considered, including genetic disposition, viral factors and autoimmune processes (Lipton 1983, Görg et al. 1985). HLA-specifities (BW 61 and CW 7) could be associated statistically significantly with histiocytosis X (Tomooka et al. 1986).

The preferred localisation of eosinophilic granuloma is the calvarium („Lückenschädel" = gapskull, Heitner and Bartholomaeus 1981), occurring in about 1/2 – 2/3 of all cases (Burkhardt 1970, Bartholdy and Thommesen 1983), the tabula externa being involved more extendedly than the tabula interna, with funnel-shaped pictures resulting (Dominok and Knoch 1977). The ossa frontalia and parietalia are the most preferred sites in the calvarium. One of the main foci of localization is also the vertebral column. Calvé's flat-vertebra (*vertebra plana Calvé*), formerly described as a separate symptom, today is classified as histiocytosis X (Dihlmann 1982). Basically any bone of the body can be affected – solitary or multiple – hands and feet are however an exception. The main age of affection is the 1st and 2nd decennium, 80% occur in this period (Ferguson and Shapiro 1979), the masculine sex prevails.

The histological cell picture is a granulomatous, tissue destructing growth of histiocytic cells in locations of the reticuloendothelic system (Freyschmidt 1988).

Radiologically the process of granuloma restoration is a complete one; in a pathologic-anatomic view the bone structure, however, is only incompletely restored. Spontaneous reparation of vertebral lesions with wafer-like bone destruction is frequently seen, with complete consolidation (Brocher 1966, Green et al. 1980, Seimon 1981). Beside osseous manifestation organic manifestations of eosinophilic granuloma may occur – of course not belonging to the term „eosinophilic granuloma of the bone" (e. g. skin, mucous membranes, eyes, dura, brain, lung, liver, vulva, vagina, gingiva etc.). A clear definition is complicated anyhow, insofar definite extraosseous manifestations cannot be filed in this frame, but combinations of osseous and soft tissue forms due to infiltration may occur, which then – sensu latiori – are to be considered.

Neither the radiographic nor the scintigraphic representation can give a prognosic statement relative to the speed of the process (Benz-Bohm and Georgi 1981, Sugiyama 1981).

Between the therapeutic concept of the radiation therapy, chemotherapy or no therapy at all no

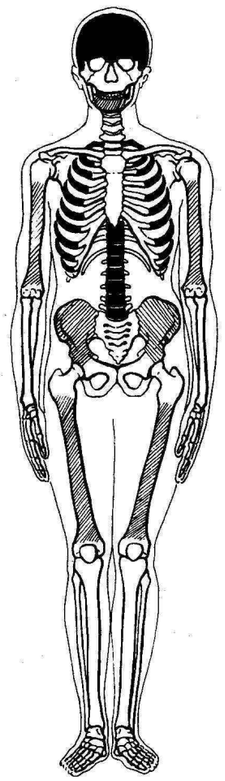

FIGURE 1. *Possible skeletal distribution of histiocytosis X (From: Steinbock 1976).*

statistically significant differences are noticeable, especially since spontaneous remissions are not uncommon (Sartoris and Parker 1984). The remissionrate is given with 95% (Slater and Swarm 1980), referring to 686 cases from literature. In about 5% follows direct transition to the Schüller-Christianform (Uehlinger 1981).

During surgical therapy new sites may develop („Herdjagen" = site-rush), out of this reason a covering cortisone therapy is usual. Also in paleopathology histiocytosis X is the object of referring examinations and differential diagnostic considerations. Morse 1969 (quoted from Steinbock 1976) describes a possible case of eosinophilic granuloma in a skeletal find of the Mississippian Culture of Illinois (1000 – 1600 AD) in a 2 1/2 years old child. Lytic defects in two vertebrae and the left *os ilium* are to be seen.

Another similar case of histiocytosis X in a 10-year-old child from New York State, dated about 1200 AD, had originally been interpreted as multiple myeloma (Williams 1941, cited in Steinbock 1976), which, however, occurs in higher ages. The multilocular appearance of punched-out lesions seems plausible for the diagnosis of histiocytosis X (Steinbock 1976).

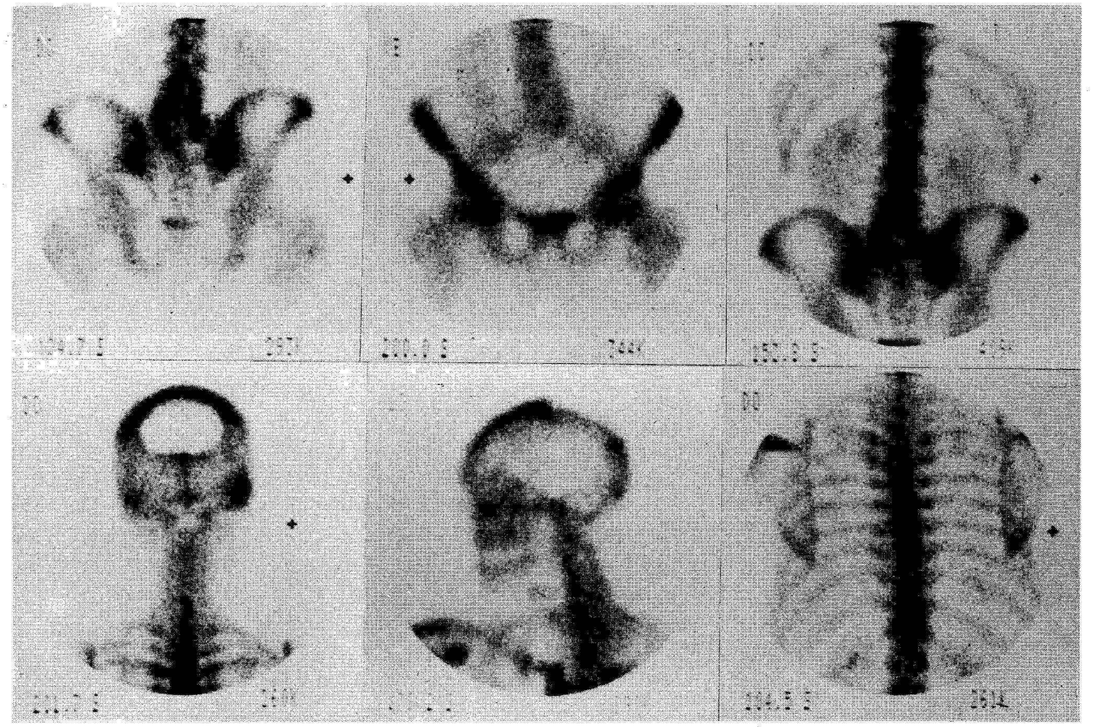

FIGURE 2. *Bone scintigram. Spotty higher concentration in the vertebral bodies of the lower lumbal spine and in both ileosacral joints. Occipital a great osteoclastic defect, after implantation of a calvarian plastic.*

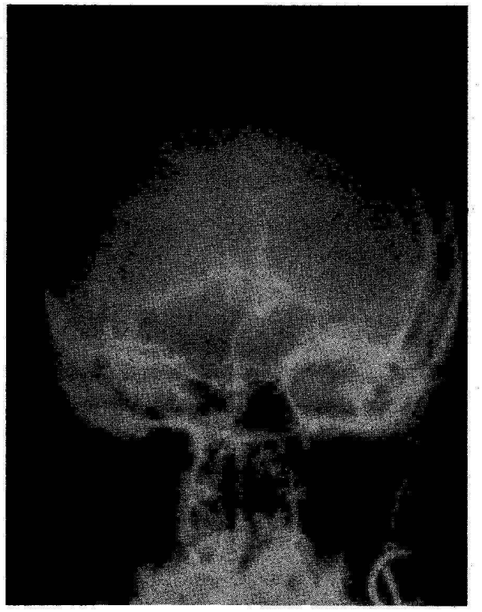

FIGURE 3. *Roentgenograms of the skull in two planes. About 6 cm osteolytic large destruction in the calvarium, partly with brushseamlike hyperostotic border. Distension of the lamina interna and externa.*

Strouhal (1978) described two further pathologic skeletal findings from an excavation in 1901 – 1903 at the Eastern bank of the Nile (Naga-ed-Dêr, Upper Egypt) in a series of 624 graves from the Pyramid age, 5th – 6th dynasty (deposited in the Lowie Museum of Berkeley, California). The first case: feminine, about 12 years of age, the second case: masculine, about 25 years of age – with multiple osseous changes, which – after differential diagnostic revaluation with view to tumorous diseases, infectious or parasitic diseases, were classified as belonging most probably to the chronic form of histiocytosis X (Hand-Schüller-Christian disease).

An analogous finding from Upper Egypt, near Luxor, described in 1907 by Lortet (quoted from Strouhal 1978), feminine, about 20 – 23 years of age, could be as well interpreted as histiocytosis X. The skeletal defects had primarily been interpreted as a syphilitic affection. This supposition is, however, inapplicable insofar as there is no evidence of syphilis in Ancient Egypt (Sandison 1969).

After detailed renewed macroscopic and radiologic examination, and after exclusion of other skeletal affections, Thillaud (1982) classified the masculine skeleton („No.1") from the Abri of Cromagnon (found in 1868) in spite of its characteristic features to the diagnosis of histiocytosis X. In a synoptic review the hitherto existing paleopathological findings, which fit to the diagnosis of histiocytosis X, are subject to critical assessment (Capasso 1985).

With the intention to document the time-overlapping character of histiocytosis X, a contribution with a detailed report concerning an actual clinic case (Eckes), is given, unusual in its multilocular appearance and being also of interest in paleopathologic diagnosis.

CASE REPORT

A young man of 16 complains of pain in his right leg. A juvenile cyst of the bone is proposed, localized in the right upper femur. The material from the surgical exploration and curettage of the osteolytic process[1] shows the histologic picture of an eosinophilic granuloma. A year later complete restoration of this part of the bone is achieved.

During the following years continuous pain in the back. In 1983, 5 years later, the patient notices that his skull feels soft in a certain part. It can be localized as a pulsating rightside parieto-occipital bone lesion, well represented scintigraphically.[2] The following examination of the whole skeleton shows multiple osteoclastic sites in several thoracic and lumbal vertebrae, as well as a lesion in the ventral part of *os sacrum*. The lytic process in the calvarial region is cleared surgically and closed,[3] the histologic diagnosis being again eosinophilic granuloma. During the stay in the hospital another osteolytic process in the skull is detected – in the area of the right mastoid, with peripherial sclerosed parts in the neighbouring *os occipitale* (*Figures 2, 3*).

A combined cytostatic therapy is initiated[4] with Vinblastin 6 mg/m^2 (once per week during 4 weeks) and prednisone (14 mg/m^2), daily, in monthly alternating cyclic therapy and pauses.

There occurred no visible improvement of the multilocular bone affections, the process developed instead noticeably: a compression-fracture of the 5th lumbal vertebra occurred, in the 12th thoracic vertebra a new punched defect could be proved close to the spinal channel, and a further osteoclastic site could be seen in the 9th left rib.

In the beginning of 1984 a telecobalt-radiation-therapy of the spine and the mastoid started. In 1987 a new locality of the eosinophilic granuloma was diagnosed in the backside of the left pelvis bone.

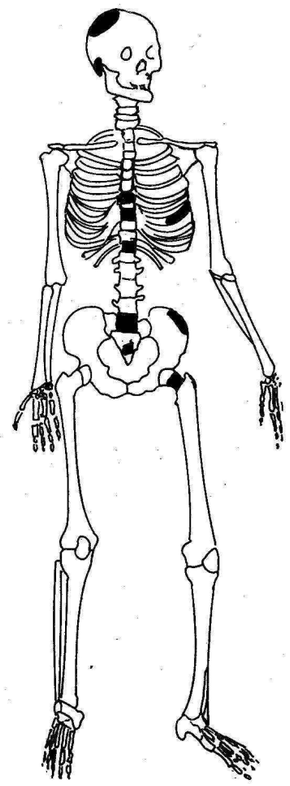

FIGURE 4. *Sketch of the radiographically proved skeletal sites of histiocytosis X in the referred case.*

1. parieto-occipital (right)
2. mastoid (right)
3. 9th rib (left)
4. 5th, 7th, and 12th thoracic vertebrae
5. 5th lumbal vertebra
6. the lowest end of the os sacrum
7. ala ossis pelvis (left)
8. upper parts of the tight (collum femoris) (left)

Other pathologic findings such as recurrent duodenal ulcera, reticular condensation in both upper parts of the lungs and hepatomegaly were not seen in connection to histiocytosis X. Summing up, a male of 16 is presented, in whom during the course of 9 years multiple lesions in the skeleton and skull occurred – in the *ossa plana* as well as in the *ossa longa* – with 10 or even 11 sites (if the double appearance of eosinophilic granuloma in the 12th thoracic vertebra is considered separately).

In correspondence with the hitherto published comparable findings, we can confirm the condition of the juvenile age of the affection, the site pattern of the skeleton, as well as the not time-period-related character of histiocytosis X.

The reported case has occurred singularly until now; a familiar involvement is not given.

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