

Long Term Follow up of Eosinophilic Granuloma of the Rib

Dlouhodobé sledování pacienta s eozinofilním granulomem žebra

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Summary

Backgrounds: Eosinophilic granuloma is one of the rarest causes of bone tumors, especially in adults. Eosinophilic granuloma is the commonest form of Langerhans cell histiocytosis and represents the unifocal osseous form of the disease which usually affects the skull and long bones. Eosinophilic granuloma, is a benign disease in which diagnosis and differential diagnosis presents more difficulties than treatment. **Observation:** We present a case of eosinophilic granuloma of the rib with long term follow-up of 14 years which was treated with a combination of surgery and chemotherapy. **Conclusion:** Prognosis of adult eosinophilic granuloma is excellent and the recurrence rate is limited. All available treatment options, including surgery, chemotherapy, corticosteroids, radiation, and even palliative treatment have very good results and in many cases the disease seems to heal spontaneously. However the disease, due to its rarity and unknown pathogenesis still remains an enigma for the clinical doctor.

Key words

adulthood – eosinophilic granuloma – histiocytosis X – Langerhans cell histiocytosis – unifocal osseous form

Souhrn

Východiska: Eozinofilní granulom je, obzvláště u dospělých, jedním z nejméně častých kostních nádorů. Eozinofilní granulom je nejčastější formou histiocytózy z Langerhansových buněk a je charakterizován výskytem solitární kostní léze, obvykle v lebce či dlouhých kostech. Eozinofilní granulom je benigní onemocnění, jehož diagnóza a diferenciální diagnóza představují větší problém než jeho léčba. **Sledování:** Prezентujeme kazuistiku pacienta s eozinofilním granulomem žebra, sledovaného po dobu 14 let a léčeného kombinací chirurgické léčby a chemoterapie. **Závěr:** Prognóza dospělého pacienta s eozinofilním granulomem je skvělá a relaps onemocnění zřídka. Všechny léčebné přístupy, včetně chirurgické léčby, chemoterapie, kortikosteroidů, ozáření a paliativní péče mají velmi dobré výsledky a zdá se, že onemocnění v mnoha případech samo odezní. Vzhledem ke svému vzácnému výskytu a neznámé patogenetice zůstává toto onemocnění zahalené jistým tajemstvím.

Klíčová slova

dospělost – eozinofilní granulom – histiocytóza X – histiocytóza z Langerhansových buněk – solitární kostní léze

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Introduction

The term Langerhans cell histiocytosis (formerly known as histiocytosis X) [1] is used to describe a group of diseases characterized by proliferation or accumulation of a clonal population of cells bearing the Langerhans cell phenotype that is functionally deficient and has been arrested at an early stage of activation [2]. Multiple different organs can be affected by Langerhans cell histiocytosis including bones, lungs, skin, lymph nodes, ears, endocrine glands (except adrenals and gonads), pituitary, thymus, central nervous system, gastrointestinal tract, liver, spleen, bone marrow and blood [1,2]. Langerhans cell histiocytosis encompasses three clinical syndromes which are so different in presentation, degree of disability and survival, but with indistinguishable histopathological findings [3,4]. These three main types of Langerhans cell histiocytosis are:

1. eosinophilic granuloma, solitary or multifocal, which is localized, the best-differentiated form and with very good prognosis [3–5];
2. Hand-Schüller-Christian disease which has variable prognosis and is the chronic form presenting with skeletal lesions, exophthalmos and diabetes insipidus [3–5] and
3. Letterer-Siwe disease which is the most aggressive, disseminated form affecting multiple visceral organs and is usually fatal [3–5].

While, Langerhans cell histiocytosis can occur at any age, most cases present at patients younger than 15 years [1,4] with an incidence 2 to 5 cases per million per year [1], whereas the disease is much rarer in adults with an incidence 1 to 2 cases per million per year [6]. We present a case of eosinophilic granuloma of the rib treated with combination of surgery and chemotherapy with a follow up of 14 years.

Case Report

A 31-year-old male presented to our department complaining about chest pain of the right lateral thoracic wall for 3 weeks that worsened during night. The patient didn't have any prior medical history. Physical examination revealed

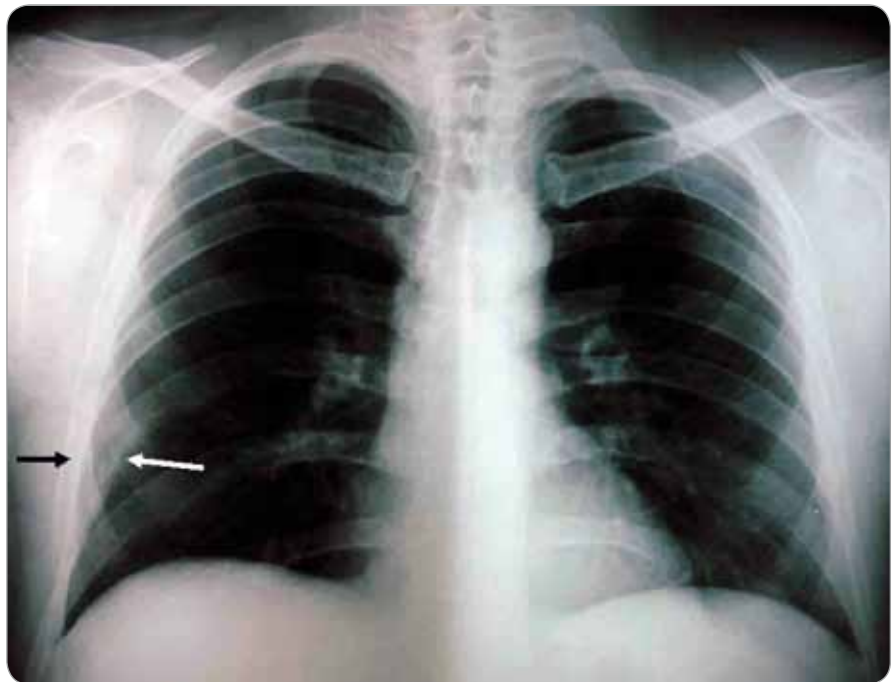


Fig. 1. Chest X-ray showing an osteolytic lesion of the right 8th rib.

a sensitivity of the 8th rib while the remainder was normal. The plain chest X-ray demonstrated an osteolytic lesion 2 cm in diameter of the 8th rib with limited periosteal reaction and pathologic fracture (Fig. 1). Differential diagnosis included osteolytic metastasis, eosinophi-

lic granuloma, myeloma, chondroma, osteomyelitis and fibrous dysplasia. Laboratory examination was within the normal limits except from a slightly elevated erythrocyte sedimentation rate (42 mm/hour). A CT scan with simultaneous guided biopsy was performed.

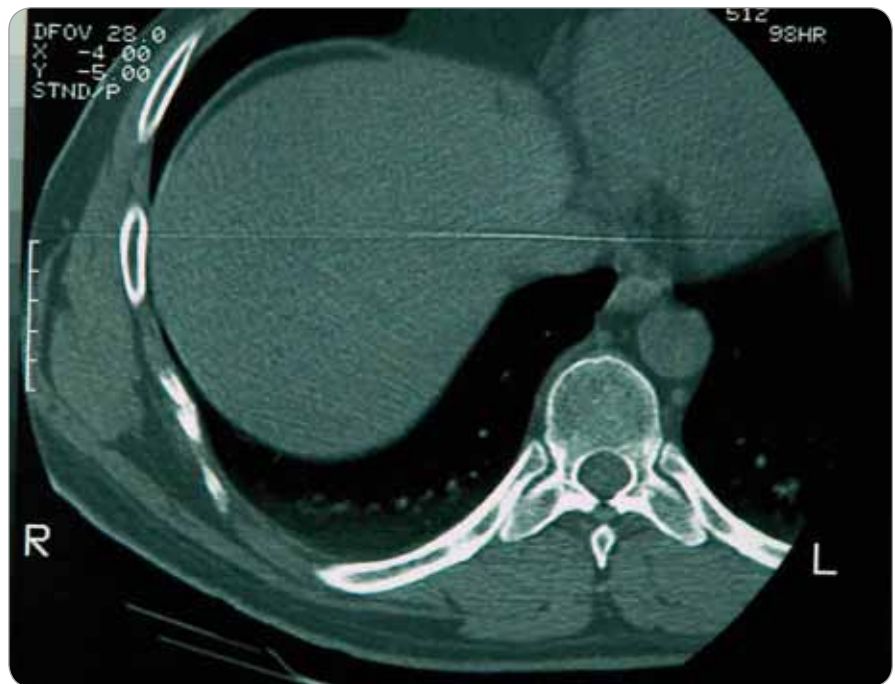


Fig. 2. Thoracic CT scan demonstrating osteolytic lesions and pathologic fracture of the 8th rib and thickening of the adjacent soft tissue.

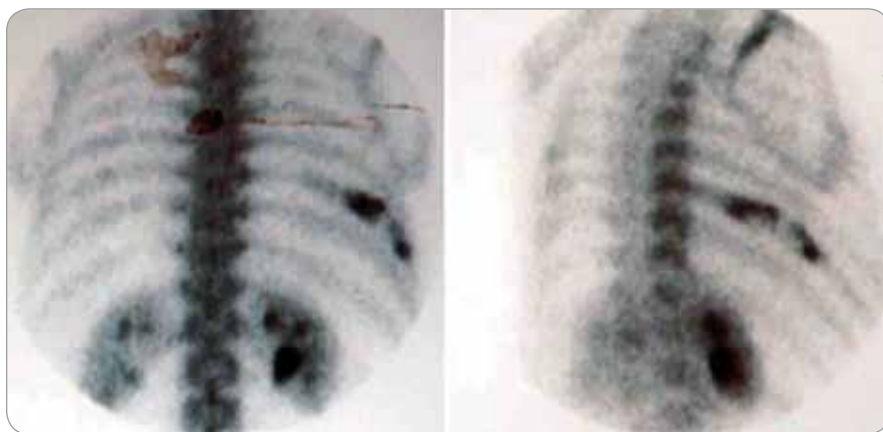


Fig. 3. Bone scan revealing pathologic enhancement of the 8th rib.

The CT scan showed the osteolytic lesion and the pathologic fracture of the 8th rib, local thickening of the surrounding soft tissue and a small pleural effusion (Fig. 2). Histopathologic examination of the received specimens was not diagnostic. Following, a bone scan was performed which demonstrated a slightly increased enhancement of the radioisotope to the 8th rib but no other lesion (Fig. 3). Also the bone marrow aspiration and abdominal CT scan were normal. Because of the difficulty in diagnosis, an open biopsy under local anes-

thesia was performed. Macroscopically the lesion had a fragile and granulomatous texture and microscopic examination revealed infiltration by lymphocytes, macrophages, eosinophils and also typical Langerhans cells and so the diagnosis of eosinophilic granuloma was established (Fig. 4). The neoplastic cells showed strong positivity for CD1a and S100 while the Ki67 index was 30%.

After consulting with the Hematology department of our hospital the patient was started on chemotherapy and surgical resection of the lesion was planned

for after 6 months. Specifically, the patient received prednisone (beginning at 80 mg per week and gradually reducing it to 40 mg) and viblastine (10 mg per week). One month after the treatment initiation the patient presented tetany due to hypomagnesemia and the second month the patient presented with a periodontal abscess of the left superior canine which where both treated conservatively and subsided. Four months after treatment, pain has fully disappeared and the radiographic findings have improved, both in the plain X-ray as well as in the CT scan. Pharmaceutical treatment with prednisone at 10 mg per week continued and at six months after diagnosis segmental resection of the 8th rib was performed. The resection was complicated postoperatively by a small pneumothorax which was conservatively treated and the patient was discharged at the 6th day. Histopathologic examination showed a slightly elevated nodule of the middle of the rib measuring 1 cm in diameter and reactive lesions with a few eosinophils but no Langerhans cells.

Three months after surgery the patient was submitted to a thoracic CT which revealed a small pleural effusion and enlarged subclavian and mediastinal lymphnodes and the treatment was continued. Six months later the new CT was normal and the treatment was discontinued (Fig. 5). The patient's follow up included physical examination and chest X-ray and orthopantomogram every 3 months for 2 years and thoracic CT scan every 6 months and then plain X-rays every 6 months. Six years after presentation the skull X-ray demonstrated confluent diluent lesions of the sin-cipital bones possibly caused by deossification. The patient was submitted to a pituitary MRI that was normal. Fourteen years after the initial diagnosis no recurrence has presented either locally or at any other site. However, the patient has presented some facial cutaneous lesion which histopathology revealed to be cutaneous lupus erythematosus.

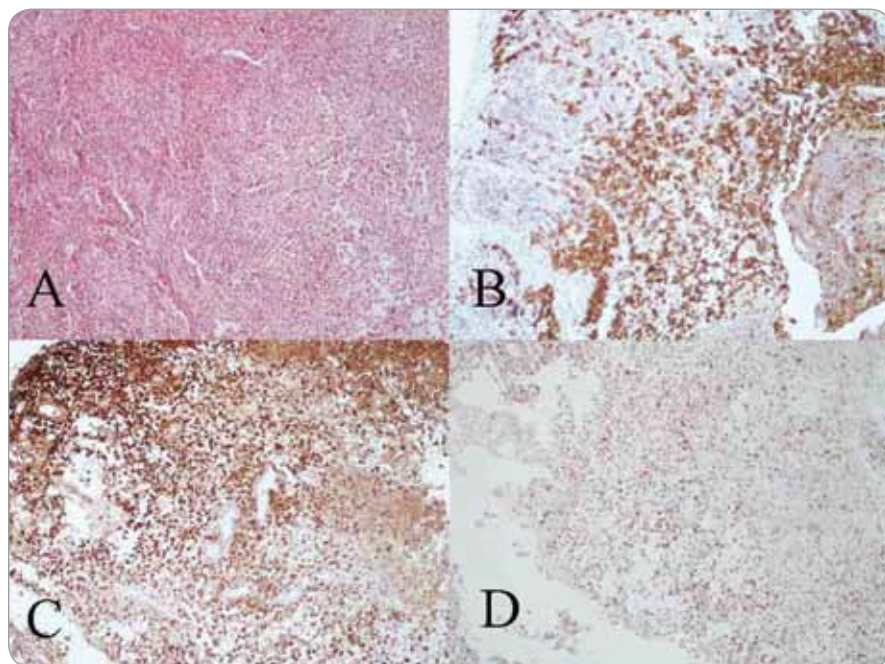


Fig. 4. Hematoxylin and eosin stain showing infiltration by lymphocytes, macrophages, eosinophils and typical Langerhans cells (A X100) while immunohistochemistry revealed strong positivity for CD1a (B X100) and S100 (C X100). The Ki67 index was 30% (D X100).

Discussion

Langerhans cell histiocytosis generally represents a childhood disease

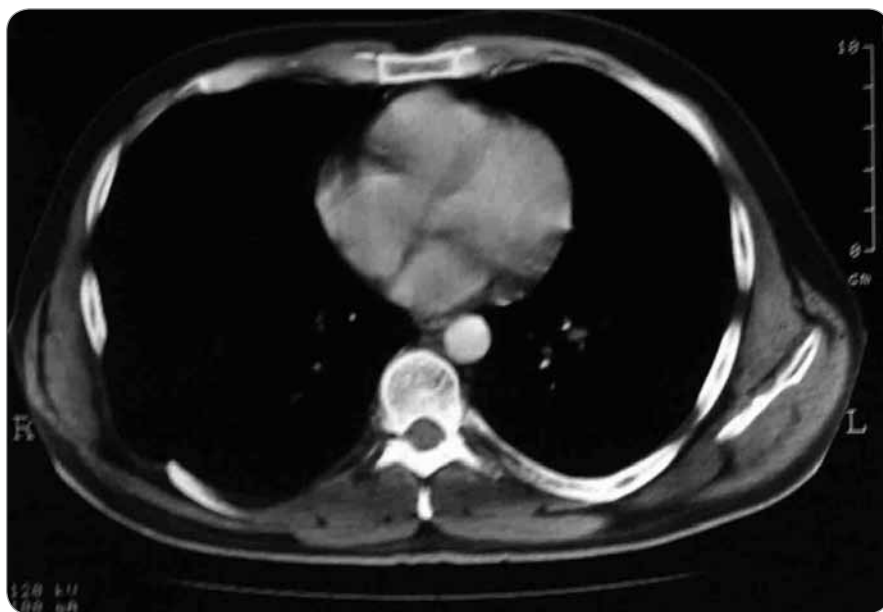


Fig. 5. Postoperative CT scan with normal findings. Also the CT demonstrates the segmental resection of the 8th rib.

and the two multisystem forms of the disease, formerly called Hand-Schüller-Christian and Letterer-Siwe disease, appear almost exclusively in children between 1 to 5 years old and younger than 2 years respectively [7], while eosinophilic granuloma is usually seen in children 5 to 15 years old [7] and seldom in adults. The etiology and pathogenesis of the disease still remains unknown. Langerhans cell histiocytosis has been considered to have a viral or other infectious cause, to be of neoplastic etiology or to represent a disorder of the immune system [3,4]. All the forms of Langerhans cell histiocytosis are characterized by clonal proliferation of CD1+ histiocytes [1,4,8,9] and have been reclassified as single organ system disease, unifocal or multifocal, and multisystem disease, complicated or not by organ dysfunction [10]. The monosystemic osseous form of the disease is known as eosinophilic granuloma. Adult Langerhans cell histiocytosis has a much lower incidence than in children [6] with a male predilection (male to female ratio is 2 : 1) but no race predilection [1] and a mean age of presentation of 35 ± 14 years. Clinically, patients complain about local pain, due to bone involvement, swelling, pathologic fractures, soft tissue mass, weight loss

and fever [1,4,6]. Systematic manifestations including cutaneous, hematologic, pulmonary and endocrine manifestations are uncommon in adults [1]. Eosinophilic granuloma in the adults usually affects the skull (51%), followed in frequency by tubular bones (17%), vertebrae (13%), pelvis (13%) and ribs (6%) [6]. Initial diagnostic investigation of Langerhans cell histiocytosis includes routine laboratory test (full blood count, liver function tests, coagulation studies), skeletal X-ray survey (which typically show osteolytic, modestly destructive lesions with marked periosteal reaction), radionuclide bone scan, chest X-ray and abdominal ultrasound [1,2,3,6,10]. Other diagnostic procedures are indicated depending on the organ involved but in the case of eosinophilic granuloma computed tomography and magnetic resonance imaging are helpful in order to determine the soft tissue involvement [3,6].

The definite diagnosis is established by biopsy of organ lesions, percutaneous, with an 11% rate of misdiagnosis, or open [11]. Gross examination shows a yellow-brown granulomatous lesion. Conventional histologic examination demonstrates histiocyte-like, mononuclear, non-pigmentary, dendritic cell with monocytic elements but indented

vesicular nuclei and vacuolated cytoplasm. The cells are positive for CD1a, S100 and electron microscopy reveals the pathognomonic Birbeck granules, which are tiny linear-rod-shaped inclusions in the cytoplasm thought to originate as invaginations of the cell membrane [1,3,6]. Langerhans cells may also be positive for CD31, CD68, CD40, CD52, CD154, CD11, PNA, PLAP and MIB-1 [1,3,6]. A concomitant inflammatory infiltrate of eosinophils, lymphocytes, neutrophils and multinucleated giant cells are also present [1,6,8]. Differential diagnosis includes lymphoma, leukemia, Ewing sarcoma, metastasis, myeloma, fibrous dysplasia and osteomyelitis [4,9].

Regarding the treatment options for eosinophilic granuloma there isn't any unanimity as the disease is quiet rare but also may commonly show spontaneous remission, especially in adults, so all treatment modalities are considered successful [1,9,12]. Successful treatment regardless the therapeutic option has been reported to be as high as 95% [13]. Possible treatments include watchful waiting, surgical resection, systemic steroids, chemotherapy (vinblastine, etoposide, prednisone, methotrexate, and 6-mercaptopurine), intralesional steroids, bisphosphonates and radiation in non accessible surgically or multiple lesions [1,6,14]. In general, the meticulous follow up of the patients is significant and the optimal treatment still remains to be defined. Prognosis is related to the age at diagnosis, the presence of organs involved and the presence of organ dysfunction [1,2]. Prognosis of eosinophilic granuloma is very good and recurrence is rare [3].

Eosinophilic granuloma, the single system osseous form of Langerhans cell histiocytosis, is a benign disease in which diagnosis and differential diagnosis presents more difficulties than treatment. All available treatment options, including surgery, chemotherapy, local infiltration with corticosteroids, radiation, and even palliative treatment have very good results and in many cases the disease seems to heal spontaneously. However the disease, due to its rarity and unknown pathogenesis still remains an enigma for the clinical doctor.

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