Eosinophilic granuloma of the spine involving C1 and pulmonary infiltration in young children – Presentation of two cases with a follow-up over 10 years including review of the literature

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ABSTRACT

Objectives: The incidence of spinal eosinophilic granuloma in children is low.

Methods: Clinical case presentation of two children (♀ 18 months old, ♂ 16 months old) complaining of acute torticollis. Follow-up period was 11 years in the female patient and 13 years in the male patient.

Results: The diagnostics certified a spinal eosinophilic granuloma: the girl had a multilevel spinal disease including the atlas, the boy a thoracic and pulmonary manifestation. Both were treated with chemotherapy with good clinical results.

Conclusions: Overall, the above described is a very rare clinical entity. However, persisting torticollis in children should be clearly diagnosed.

1. Introduction

The eosinophilic granuloma is a rare tumor, the incidence is approximately 1:1.500.000 people.¹ It is one of the three described manifestations of the Langerhans cell histiocytosis (LCH). The two other forms are the Letterer-Siwe disease and the Hand-Schüller-Christian disease. These three disease manifestations show the same disorder process – a clonal proliferation of Langerhans cells.^{2,3} Langerhans histiocytes are dendritic cells which present antigens. They are usually found isolated in the epidermis and in a small number throughout the whole body. Letterer-Siwe disease is the most malignant form: Disseminated clusters of Langerhans cells are found throughout the body. Hand-Christian-Schüller disease classically presents with the clinical triad of skull lesion, exophthalmus and diabetes insipidus. The eosinophilic granuloma is a benign proliferation of Langerhans cells occurring in a multifocal manner that commonly affects the skeleton.⁴ The most typical manifestations are the skull, femur, ribs, pelvis and the spine. At the spine, the thoracic level is most commonly affected, followed by the lumbar and cervical spine.^{2,5} 90% of the patients are between 5 and 15 years old.⁴ In 79% of eosinophilic granulomas, the disease is solitary, in about 7% a multifocal manifestation are described, and 14% belong to other forms of the disease.⁶ The clinical course of children with a cervical manifestation of eosinophilic granuloma is quite variable. Affected

children normally present with an acute onset of neck pain, a reactive torticollis and stiffness without history of trauma.^{7–10} Denaro et al.⁸ reported an incidence of torticollis in 71% of their 7 pediatric patients with an eosinophilic granuloma of the cervical spine.

2. Patients and methods

In August 2004, one girl (18 months old) and one boy (16 months old) were referred to our outpatient clinic. The girl complained of torticollis since 10 days after a slight trauma and an upper air way infection. The boy had a history of spontaneous neck pain and torticollis of about 2 weeks. No trauma or infection in the previous history could be detected.

The physical evaluation showed in both patients no neurological deficits, body temperature was normal. Both patients showed tenderness of the upper cervical spine and a right lateral tilt of their head with a minimal rotation to the left.

In both children, white blood cell account was normal and further laboratory investigation showed a slightly elevated CRP and cell sedimentation rate.

Plain radiographs showed a mild head and neck tilt. Further diagnostic work-up was started in both children in mild sedation.

In the female patient, computed tomography (CT) (Fig. 1) and

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Fig. 1. a, b, c. CT scans of the cervical spine of the female patient: Lytic lesions of the left lateral mass of the atlas (C1) and the sixth cervical vertebra (C6).

magnetic resonance tomography (MRI) (Fig. 2) showed a lytic lesion in the left lateral mass of the atlas (C1), the sixth cervical vertebra (C6) and the seventh thoracic vertebra (T7). No additional soft tissue was involved. No unstable fracture but a characteristic vertebra plana could be diagnosed at the level of T7. CT and MRI did not show skeletal lesions of the skull, ribs and the lumbar spine. A visceral co-affection could also be excluded via CT.

In the male patient, CT of the cervical and thoracic spine and the thorax revealed a lysis of left portion of the third thoracic vertebra (T3) and a pulmonary infiltration of the right second segment (Fig. 3). MRI of the complete spine and skull showed a classical vertebra plana at the level of T3 leading to a hyperkyphosis and left-lateral scoliosis of the upper spine (Fig. 4).

No additional bony lesions could be observed. At the level of T3 the intervertebral discs were not affected. Paravertebral, the adjacent soft

Fig. 2. a. MRI of the atlas (C1) of the female patient showed a lytic lesion of the left lateral mass. b. MRI of the female patient showed fluid between the dens axis (C2) and the anterior arch of the atlas (C1). The seventh thoracic vertebra (T7) is shown as a classical vertebra plana.

tissues were not sharply defined and the anterior ligament was elevated. The myelon was not compromised or infiltrated.

3. Results

To verify the diagnosis of eosinophilic granulomas and to exclude other diagnosis like Ewing sarcoma, osteosarcoma or infection, biopsy was performed in both patients. The female patient was biopsied at the first and sixth cervical vertebrae, the male patient at the third thoracic vertebra. In both cases the histological investigation showed proliferated cells with eccentrically located round or oval nuclei and eosinophilic cytoplasm, corresponding to clons of Langerhans cells in a granulomatous tissue. The diagnosis of eosinophilic granuloma could be clarified and both children were treated with chemotherapy.

After referring the children back to the pediatric department, both were treated following the LCH III International Study Protocol for patients with Langerhans Cell Histiocytosis and “Multifocal Bone

Fig. 3. CT of the male patient showing a lytic destruction of the third thoracic vertebra (T3) with involvement of the adjacent soft tissue and osteolysis of the left pedicle. In the scans the pulmonary infiltration in right second segment can also be observed.

Fig. 4. MRI of the complete spine of the boy with a vertebra plana at the level of the third thoracic vertebra (T3).

Diseases and Special Site Involvement".¹¹ The treatment protocol includes vinblastin (6 mg/m^2) as intravenous bolus at day 1 of the week for 6 weeks and oral prednisone ($40 \text{ mg/m}^2/\text{day}$) continuously for 28 days and then stepwise reduction over 2 weeks. Both children got the

Fig. 5. MRI of the cervical and thoracic spine of the girl with stable situation due to T7. The atlas (C1) and C6 come regularly to the presentation. New, but healed fracture of C3.

following therapy circle for the next 25 weeks with intravenous application of vinblastin 6 mg/m^2 once a week and oral prednisone $40 \text{ mg/m}^2/\text{day}$ on days 1–5/week.

In both children symptoms decreased, and they were free of pain and of neurological deficits. Both patients remained under care in the pediatric department for several years.

In the female patient, last MRI of the spine was performed after 11 years (Fig. 5). There were no pathological findings referring formerly affected vertebrae C1 and C6. In addition, stable bony structures were found in T7. However, diagnosed was an old fracture of C3.

Within the clinical examination, the girl was painless and normal neurological status was ascertained.

In the male patient, last MRI of the spine was done after 13 years (Fig. 6). By that time, the former affected vertebra T3 showed almost complete restoration. There was no more pulmonary manifestation.

The patient was also free of pain and of neurological disturbances.

4. Discussion

The eosinophilic granuloma is a tumor of the child or young adolescent. 80% of the patients are younger than 10 years old.¹² The gender distribution (female to male) in children is 1:1.7.⁷ The typical

Fig. 6. MRI of the cervical and thoracic spine of the boy with almost complete restoration of the previous concerned T3 vertebra. Pulmonary affection was excluded.

clinical picture of the affected cervical spine is an acute torticollis combined with a restricted range of motion or neck pain.

In a review, Bertram et al. reported these symptoms in 76% and neurological symptoms in 33%.⁷ In comparison, Denaro et al.⁸ described pain in 100%, torticollis in 71%, and neurological deficits in 29% of their 7 pediatric patients.

The manifestation of an eosinophilic granuloma at the cervical spine is rare. In a meta-analysis, Bertram et al. reported in 2002 only 53 cases worldwide, 10 involving adults, 43 children.⁷ In 2004, Garg et al.³ added 11 cases and Tan et al.¹³ 4 additional cases in children.

Simanski et al.¹⁴ and Ngu et al.² reported also in 2004 a cervical involvement in two case reports about one adult¹⁴ and one child.² In 2008, Denaro et al.⁸ described 7 cases of pediatric cervical spine affection. In the following years, less articles about eosinophilic granuloma of the pediatric cervical spine with one,⁹ two⁵ and 4¹⁰ patients were published.

A multilevel spinal manifestation is described in about 11%,⁷ an additional extraskeletal manifestation in about 8%.³ According to Bertram et al., C3–5 are involved in 60%.⁷ Until now, there have been only less than 10 cases published, describing an eosinophilic granuloma of the first vertebra in children and furthermore with a follow-up over 10 years.^{2,3,15–18} The spinal eosinophilic granuloma commonly affects

the vertebral bodies, but it usually spares the posterior elements.

Since eosinophilic granulomas show a variety of clinical presentations, there are several treatment options leading to a good outcome.⁷ These options include observation, prolonged immobilisation,^{8,10} chemotherapy,⁷ curettage with or without bone grafting and/or stabilization,^{2,4,5,8–10} corticosteroid injection,^{13,19} and low dose radiation therapy.^{4,10} With regard to the different treatment options, a biopsy should confirm the diagnosis.^{2,4,8,10,13,19,20} Due to small case numbers, there are no randomized, prospective studies evaluating the efficiency of different treatment methods.

Nevertheless, several treatment suggestions have been made. Surgical treatment is recommended in spinal instability or neurological deficits.^{2,4,5,8,20} Symptomatic lesions that have not compromised the spinal cord could be treated by excessive curettage with or without bone grafting and/or stabilization.^{2,4,8,9} Capanna et al.¹⁹ and Tan et al.¹³ reported the intra-lesional injection of corticosteroids. Finally, the use of systemic chemotherapy is recommended in eosinophilic granulomas with multilevel spinal involvement and/or additional visceral manifestation.^{2,10,11}

Therefore, our patients were treated with systemic chemotherapy using vinblastin and prednisone¹¹ and have shown a good response.

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