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CASE REPORT

Primary solitary eosinophilic granuloma of the brain and postoperative radiotherapy: A clinical case

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Summary

A case of solitary eosinophilic granuloma (EG) of the brain in a 53-year-old woman is presented. The tumor developed in the anterior cranial fossa causing destruction of the skull basis and the retrobulbar space, accompanied by vision impairment. The tumor was partially excised and the patient was irradiated postoperatively with 40 Gy 6 MV x-rays, followed by 10 cycles of chemotherapy. Follow-up computed tomography (CT) showed no response at 30 Gy and no progression during chemotherapy. Attention is drawn to cases of EG indolent in growth but resistant to radiation and chemotherapy.

Key words: central nervous system, chemotherapy, eosinophilic granuloma, radiation therapy

Introduction

Langerhans' cell histiocytosis (LCH) is a rare disease that includes 3 clinical forms - acute disseminated (Letterer-Siwe syndrome), multifocal form (Hand-Schüller-Christian syndrome) and the unifocal form EG [1]. The name LCH was adopted by the Histiocytosis Society in 1987 and the diagnostic criteria were defined [2]. The frequency of the disease is quite low - about 1/200,000 children and even lower in adults [2]. In 70% of the cases LCH develops before the age of 17, the peak incidence is in children aged between the 1st and the 3rd year and the multifocal form is the most frequent.

The most prominent morphologic sign of the disease is the abnormal accumulation of Langerhans' cells (LC) [3]. Normal LCs are derived from CD34-positive stem cells in the bone marrow and their dendrites cover about 25% of the skin surface. Under the influence of different cytokines [1] they differentiate into two types of cells: a) antigen-processing macrophages and b) antigen-presenting dendritic cells. The CD-1a antigen and Birbeck granules on electron microscopy are specific cellular markers LCs and S-100 protein is a marker of high probability. Normal LCs migrate to the epidermis, oral mucosa, lungs and other sites. After the capture of the antigen LCs migrate to the paracortical zone of the lymph nodes to accomplish their main role - presenting antigens to T-lymphocytes.

Pathologic LCs in LCH differ from normal LC cells in that they lack dendritic morphology but they still express CD1a, S-100 and Birbeck granules. In contrast to normal LCs, pathologic LCs can infiltrate all organs [1,2] and accumulate in great numbers. Eosinophilic cells, which give the name of the unifocal form EG, lymphocytes and macrophages are the other most widely cells present in the lesions. Abnormal LCs in LCH show an impaired antigen-presenting capacity. They also produce a variety of cytokines (interleukin-1, tumor-necrosis factor-α and granulocyte/macrophage-colony-stimulating factor), which can explain some systemic signs of the disease like fever and cachexia [2]. Interleukin-1 is the major factor of osteoclast activation and a potent osteosynthesis

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inhibitor and this might explain the frequent bone involvement [1].

The etiology of LCH is still unknown. Different theories suggest a role for environmental, viral (herpesvirus 6, cytomegalovirus, Epstein-Barr virus and HIV), immunologic and genetic causes or a neoplastic nature of the disease, but without direct evidence as yet [1].

The organs most frequently involved in LCH are bones, skin, lungs, lymph nodes and central nervous system (CNS; predominantly hypothalamo-pituitary axis and the cerebellum). EG most often involves the bones (80%), lymph nodes and lungs, while CNS involvement, besides the hypothalamo-pituitary axis, is very rare (about 4% of the cases) [2]. Hematopoietically active bone marrow as a residence of LC precursor cells is a natural site of predilection for LCH. The typical orbital involvement in a large number of patients can be explained by the fact that the frontal bone retains active bone marrow function into adulthood [1]. In some of the patients the symptoms subside spontaneously or after minimal treatment (mainly in the unifocal form), but in multisystem involvement and treatment-resistant forms the outcome is fatal [2].

Case presentation

At the beginning of 2004 a 53-year-old lady developed gradual vision impairment of both eyes and headache. The patient presented at the Neurosurgery department with complete loss of vision of the left eye and eyelid ptosis, no pupil reaction, deficiency of left eye movements in cranial and lateral direction and decrease of right eye vision to 30-40%. CT of the brain revealed a tumor mass in the anterior cranial fossa with destruction of the skull base and retrobulbar space bilaterally (Figure 1). The patient underwent partial excision of the tumor which was interpreted as solitary myeloma. After a second examination and immunohistochemistry tests (S-positive test) of the specimen at the National Center of Transfusion Hematology in Sofia the lesion was defined as eosinophilic granuloma. X-ray examination of the skull, spine and pelvis showed no bone involvement.

After one course with dexamethasone and cyclophosphamide at the Hematology department the patient was sent for radiation therapy. The clinical tumor volume (CTV) encompassed the tumor with minimal safety margins (Figure 2). Radiotherapy was performed with 6 MV x-rays on a linear accelerator MEVATRON Primus with two opposed lateral fields and one anterior field (isocentric technique). A ther-



Figure 1. CT scan before radiotherapy showing the tumor mass (arrow).

moplastic head mask was used for immobilization and standard cerobent blocks were used for the right and the anterior fields to protect the right eye (Figure 3). A total dose of 40 Gy (200 cGy daily dose) was delivered to the CTV. A control CT scan at 30 Gy showed no change of the tumor mass.

After completion of the radiation therapy the patient had 10 more chemotherapy cycles (dexamethasone, cyclophosphamide, vincristine, CCNU; and IMVP (ifosfamide, methotrexate, etoposide)) and the effect was periodically checked on CT scans. After the 5th course a contrast-enhanced CT of the brain revealed mild disease progression - presence of osteolytic lesions of the frontal bones. The contrast-enhanced CT scan made in March 2006 showed no further progression and chemotherapy was discontinued. The latest CT in October 2006 confirmed the lack of disease progression (Figure 4).

Discussion

The treatment of LCH depends on the type of the disease and its extent. In cases of unifocal form (EG) biopsy and/or operative treatment and corticosteroids (with or without chemotherapy) is usually sufficient. Radiotherapy is recommended in cases with bone involvement [4], inadequate surgery or recurrence [5] and it is highly effective in vertebral lesions and lesions of the femoral neck with a risk of fracture [4]. In multisystem forms corticosteroids and chemotherapy with vinca alkaloids and antimetabolites [1] are the treatment of choice. Solitary involvement of CNS by

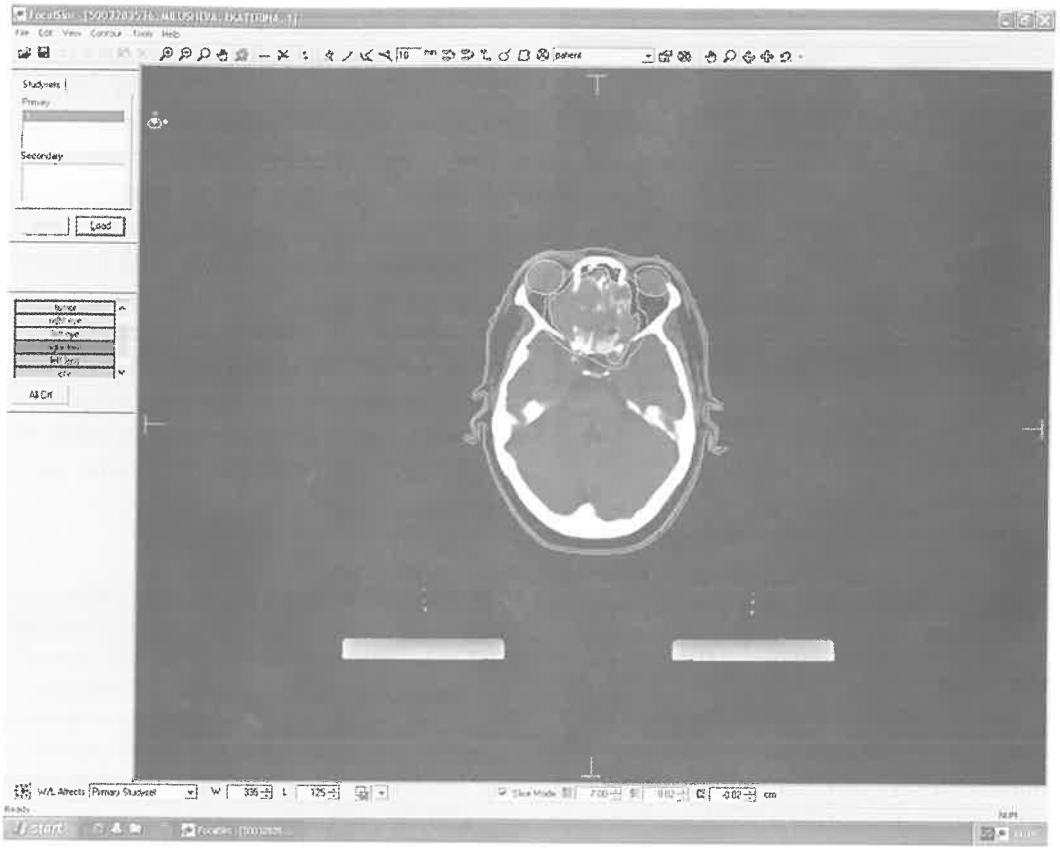


Figure 2. Clinical tumor volume with safety margins.

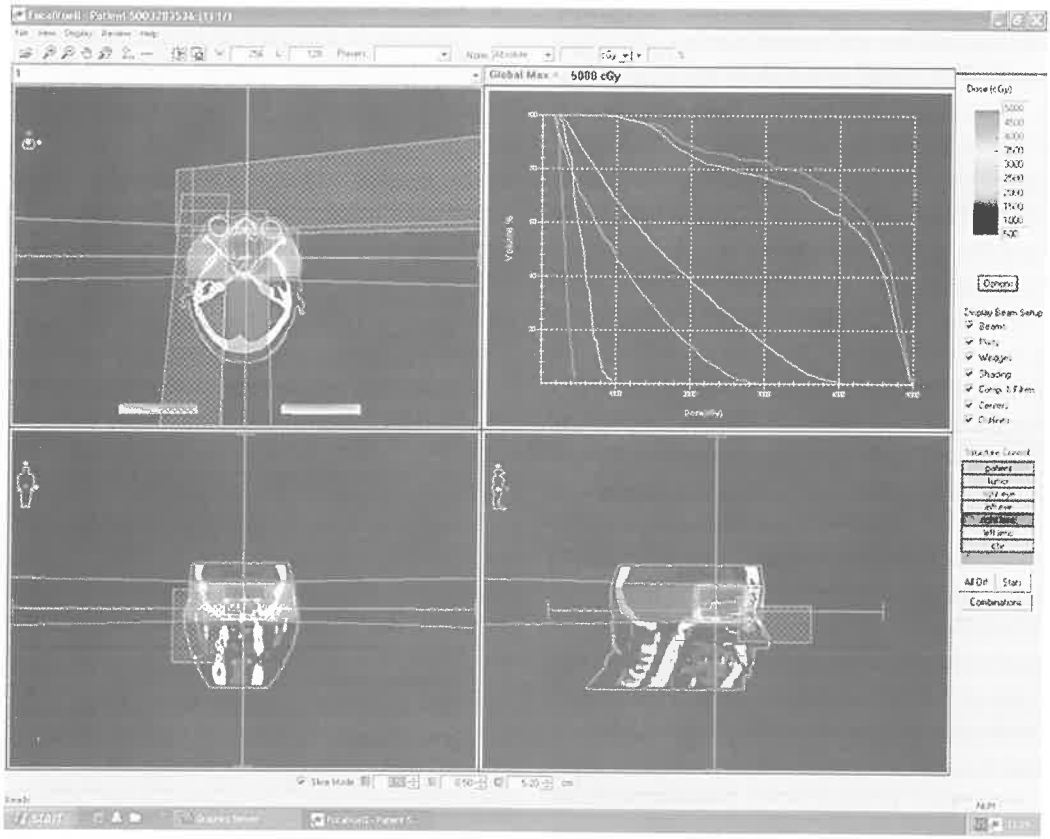


Figure 3. Field arrangement and dose-volume histograms.

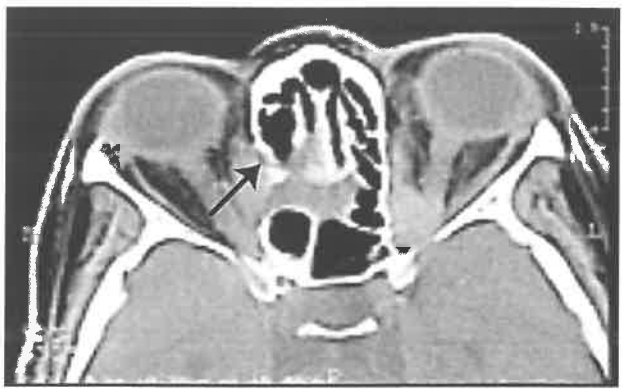


Figure 4. CT scan 18 months after radiotherapy (arrow shows the tumor area).

EG, besides the hypothalamo-pituitary axis, which is accompanied by diabetes insipidus, is very rare – only 4% [6].

There is no consent about the therapeutic approach to EG, and the low incidence of that form is one reason for that. In some patients the disease symptoms disappear spontaneously or after minimal treatment, but there are reports about cases with a lethal outcome [7]. In most of the cases, depending on the site of involvement, treatment usually includes minimal surgery and systemic corticosteroid treatment with or without chemotherapy, and the role of radiotherapy and the doses applied are still controversial. Minehan et al. [8] reported 28 cases of LCH of the hypothalamo-pituitary axis controlled by low-dose irradiation; a response was achieved in 60% of the cases treated with doses above 15 Gy, and in 30% of the cases with doses less than 15 Gy. In a case of EG of the clivus in a 4.5-year-old boy [5] and the orbit in a 15-year-old boy [9], the disease was controlled with minimal operation, systemic steroid treatment and low-dose stereotactic radiation therapy (the exact dose was not mentioned). However, there are cases of recurrent EG of the temporal bone after doses of 20 - 30 Gy [10], as well as a recurrent case after 16 Gy with fatal outcome 4 months after the diagnosis. On the experience of 2 own cases of EG of the clivus and the review of 87 cases of EG of the temporal bone Brisman et al. [5] recommended stereotactic radiotherapy if there was incomplete resolution of symptoms or recurrence. Similar conclusions were reported by Greenwood et al. [11]. In case of LCH in children one should always bear in mind the possibility of developing a radiation-induced cancer [1,2].

The follow-up CT of our case of solitary EG of the brain during radiation therapy at 30 Gy, 2 months after its completion at 40 Gy, and during systemic treatment (18 months after diagnosis; Figure 4) confirms the existence of cases of EG resistant to radiotherapy.

Our review of the literature on LCH supports the opinion that it is a disease with a variety of clinical symptoms and often with an unpredictable course and outcome [2], and should no longer be considered neither so rare nor with a so good prognosis, and the follow-up period should be long enough [7]. That is why we want to draw attention to cases of EG with an idle course but resistant to systemic treatment and radiotherapy.

References

1. Harris GJ. Eosinophilic granuloma of the orbit: a paradox of aggressive destruction responsive to minimal intervention. Trans Am Ophthalmol Soc 2003; 101: 93-105.
2. Donadieu J. Langerhans' cell histiocytosis. Orphanet Encyclop May 2003; 1-8.
3. Lieberman PH, Jones CR, Steinman RM et al. Langerhans' cell (eosinophilic) granulomatosis: A clinicopathological study encompassing 50 years. Am J Surg Pathol 1996; 20: 519-552.
4. Polyzois M, Papadogias D, Samara C et al. Langerhans' cell histiocytosis in an adult patient manifested as recurrent skull lesion and diabetes insipidus. Hormones 2004; 3: 59-64.
5. Brisman JL, Feldstein NA, Tarbell NJ et al. Eosinophilic granuloma of the clivus: case report, follow-up of two previously reported cases, and review of the literature on cranial base eosinophilic granuloma. Neurosurgery 1997; 41: 273-278.
6. Glotzbecker MP, Carpentieri DF, Dormans JP. Langerhans' cell histiocytosis: clinical presentation, pathogenesis, and treatment. Univ Pennsylv Orthopaed J 2002; 15: 67-73.
7. Al-Anazi AH, Ammar A, Sheikh B, Barayan SS, Mulhim FA. Primary Langerhans' cell histiocytosis of the brain – case report and literature review. Pan Arab J Neurosurg 2001; 5.
8. Minehan KJ, Chen MG, Zimmerman D, Su JQ, Colby TV, Shaw EG. Radiation therapy for diabetes insipidus caused by Langerhans' cell histiocytosis. Int J Radiat Oncol Biol Phys 1992; 23: 675-676.
9. Harris NL, McNelly WF, Shepard JO, Ebeling SH, Ellender SM, Peters C. Case 5-2002. Case Records, Massachusetts General Hospital. N Engl J Med 2002; 346: 513-520.
10. Levy R, Sarfaty SM, Schindel J. Eosinophilic granuloma of the temporal bone: two cases with bilateral involvement. Strahlentherapie 1980; 156: 611-615.
11. Greenwood SM, Martin JS, Towfighi J. Unifocal eosinophilic granuloma of the temporal lobe. Surg Neurol 1982; 17: 441-444.