CASE REPORT

Orbital involvement in Erdheim-Chester disease

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Erdheim-Chester disease is a rare, idiopathic, non-Langerhans' cell, histiocytic disorder. To our knowledge this is only the second case of Erdheim-Chester disease reported in the Chinese population. We describe a 45-year-old woman presenting with unilateral proptosis and periorbital xanthelasma. Histopathological examination revealed a xanthogranulomatous lesion expressing CD68, but negative for S100 protein, CD1a, CD3, or CD20. Systemic involvement was evident on bone scanning, and involvement of the thorax and abdominal aorta was seen on computed tomography. Despite treatment with systemic steroids, immunosuppressants, chemotherapy and interferon, progressive deterioration occurred. Our patient's clinical course was consistent with reports in the literature. Unfortunately, our patient developed neutropenic fever and died from septicaemic shock. Although Erdheim-Chester disease is a rare entity, especially in the Chinese population, an unusual presentation with orbital masses and bilateral xanthelasma, associated with systemic features, should raise the suspicion of this serious and potentially fatal disease.

Introduction

Erdheim-Chester disease is a rare, idiopathic type of non-Langerhans' cell, histiocytic disorder, characterised by xanthogranulomatous infiltrations in both the orbit and systemically. We report the orbital and systemic clinical course and histological findings of a patient with Erdheim-Chester disease.

Case report

A 45-year-old woman presented to the Department of Ophthalmology of Pamela Youde Nethersole Eastern Hospital in December 2003 with proptosis of the right eye and headaches for 1 month. A physical examination showed bilateral periorbital xanthelasma, and a visual acuity of 6/6 in the right eye, and 6/9 in the left eye. Her right eye had full extra-ocular movement, normal intra-ocular pressure, and normal colour vision. Using Hertel's exophthalmometer the right eye measured 21 mm and the left eye 19 mm. Routine blood tests and a chest X-ray were unremarkable. Computed tomography (CT) of the brain and orbits with contrast showed bilateral infiltrative intraconal masses (Fig 1). Three months after her initial presentation, the visual acuity in her right eye suddenly deteriorated to only detecting hand movements, secondary to optic nerve compression. She was admitted for a course of intravenous corticosteroids and her visual acuity improved transiently to 3/6. Unfortunately, despite continued treatment with systemic steroids, the visual acuity in her right eye later dropped to 2/60 within 10 days then worsened further to only light perception.

We performed an orbitotomy and biopsy of the intraconal mass, which showed a xanthogranulomatous lesion (Fig 2). Immunohistochemical studies showed that the foamy histiocytes expressed CD68 (a marker for histiocytic differentiation), but did not express S100 protein, CD1a, CD3, or CD20. There was no evidence of lymphoma or carcinoma.

Postoperatively, as the lesion was not resectable, she was given a course of radiotherapy by the oncologists. Unfortunately, physical examination revealed a pale right disc, and her right visual acuity remained at no light perception, despite treatment.

Systemically, our patient complained of generalised joint pain over her wrists, elbows, hips, knees, and ankles. X-rays of both hands showed mild periarticular osteopaenia. A chest X-ray showed streaky densities over the right lower zone, suggestive of mild fibrosis, and magnetic resonance imaging (MRI) of the thorax and abdomen showed circumferential wall thickening of the abdominal aorta. After consultation with a haematologist, cyclophosphamide was also initiated.

Fourteen months after her initial presentation, our patient's other (left) eye developed disc swelling. No proptosis was noted, and extra-ocular movement was not impaired at this juncture, so systemic steroids were prescribed. Nonetheless, within 1 week, her left visual acuity

Key words
Eyelid diseases; Histiocytosis, non-Langerhans' cell; Orbital diseases; Xanthomatosis

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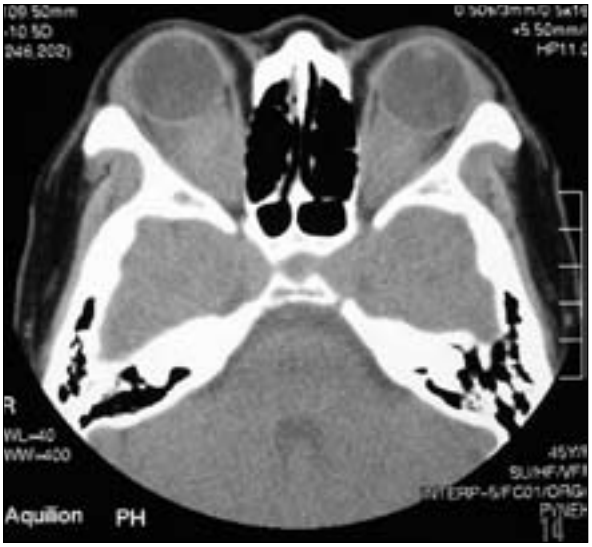

FIG 1. Computed tomography of the brain and orbits with contrast showing bilateral infiltrative intraconal masses

眼眶受埃德海姆—切斯特病侵入

埃德海姆—切斯特病是一種特發性非朗格漢斯細胞的組織細胞疾病，這種病非常罕見，據我們所知，本文所報告的病例是華裔病例的第二宗。患者是一名45歲的女性，有單眼眼球突出和眶周黃斑瘤的徵狀。組織病理學檢查發現一處黃色肉芽腫性病變，CD68呈陽性，S100蛋白質、CD1a、CD3以及CD20則呈陰性。骨掃描顯示有系統損害，而電腦斷層掃描發現胸部及腹主動脈亦受到侵入。儘管施以全身性類固醇、免疫抑制劑、化療和干擾素，但患者病情仍然惡化，臨床發展過程與文獻所描述一樣。患者不幸染上嗜中性粒細缺乏性發熱，後因敗血性休克而死亡。雖然埃德海姆—切斯特病並不常見，特別在華裔人口中更為罕有，但假如眼眶腫物和雙眼眶黃斑瘤不尋常地同時出現，就應當檢視病人是否患上這種嚴重可致命的疾病。

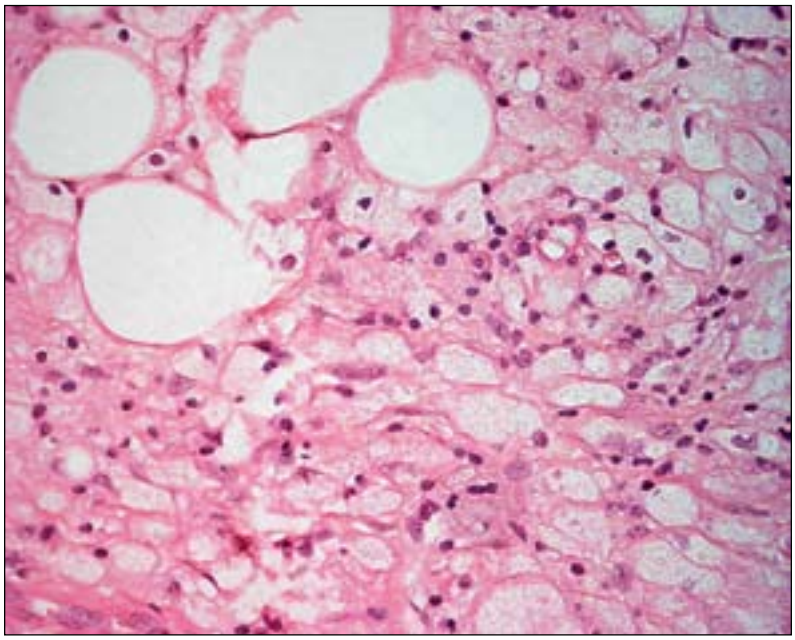

FIG 2. Biopsy of the intraconal mass showing lack of epithelioid histiocytes (H&E, x40)

decreased from 6/9 to finger count, and MRI showed an increase in the extent of the xanthogranulomatous lesions. Urgent orbital decompression was performed. Postoperatively, her left visual acuity improved to 6/9, and the disc swelling subsequently decreased. Four months after orbital decompression, she developed a left lower lid entropion, which was corrected surgically.

Further systemic investigations were performed. Her blood tests remained normal and an echocardiogram showed normal systolic and diastolic function. A chest X-ray showed fibrosis over the right lower lung fields, and CT of the thorax showed inflammatory changes and calcified nodules in the right paratracheal region and right hilum, compatible with lymphadenopathy. Computed tomography of the abdomen showed bilateral adrenal gland swelling and thickening of the aorta, suggestive of abdominal aortitis. A bone scan showed symmetrical uptake in the long tubular bones of the extremities and calcanei, along with abnormal uptake in the skull, mandible, and ribs, compatible with Erdheim-Chester disease. Alpha-interferon and vinblastine were offered, but our patient showed a poor response. Unfortunately, 24 months after her initial presentation, she suffered from neutropaenic fever, developed pneumonia after repeated courses of chemotherapy, and then died from septicaemic shock.

Discussion

Orbital xanthogranuloma is a rare, non-Langerhans' cell, histiocytic disease. Jacob Erdheim and William Chester first described this rare entity in 1930. Ophthalmological manifestations were first reported in 1983 by Alper et al,[1] and are uncommon. Furthermore, Erdheim-Chester disease was first reported in a Chinese patient in 2001[2]; and no other reports have described Chinese patients. Three cases of orbital xanthogranuloma in Chinese patients were reported in 2003, but the authors suggested that Erdheim-Chester disease was unlikely.[3]

The classical ophthalmological manifestations of Erdheim-Chester disease are bilateral xanthelasma and proptosis.[4] It usually affects middle-aged and elderly patients, rarely children. This disease may also present with diffuse orbital masses, afferent pupillary defects, optic atrophy, and ophthalmoplegia, which may be bilateral. Systemically, there may be non-specific neurological deficits, diabetes insipidus, along with infiltration of the heart, lungs, kidneys, and bone. The

long bones are usually affected, and involvement is typically symmetrical.[5] Sclerosis of the metadiaphyseal segments are characteristic.[6]

There are three major types of non-Langerhans' cell xanthogranuloma, namely Erdheim-Chester disease, orbital xanthogranuloma (without systemic involvement), and necrobiotic xanthogranuloma. The pathological features of Erdheim-Chester disease include tissue infiltration by lipid-laden macrophages, inflammatory cells, including lymphocytes and macrophages, and multinucleated giant cells of the Touton type. The characteristic Langerhans' cell features, Birbeck granules seen on electron microscopy and positive staining for S-100 protein, are absent in the non-Langerhans' histiocytes of Erdheim-Chester disease.[7] Differential diagnoses for this histopathology include juvenile xanthogranuloma (typically affecting children), necrobiotic xanthogranuloma, and idiopathic inflammatory pseudotumour. Other orbital histiocytic disorders include Rosai-Dorfman syndrome (sinus histiocytosis with massive lymphadenopathy) and Langerhans' cell histiocytosis (histiocytosis X). Furthermore, it is possible for dysthyroid orbitopathy and lymphoma to simulate the initial presentation of our patient.

On reviewing the literature, we found that a large range of treatment modalities have been used to manage patients with Erdheim-Chester disease. These have ranged from observation, to systemic steroids, to radiation therapy, and chemotherapy, including cyclophosphamide, doxorubicin, and vincristine. Cladribine has also been tried, with a recent report of a good response and clinical improvement.[8] Alpha-interferon has also been reported to produce reduction in exophthalmos and control of the systemic manifestations in a few cases.[9] In our patient, local radiotherapy was attempted, but with a poor response. This is consistent with findings from a study showing that retro-orbital irradiation was not effective.[10] The first case report of Erdheim-Chester disease in a Chinese patient, by Wu et al,[2] described a good response to treatment, with systemic control of the disease. Nevertheless, our review of the western literature and our experience of the course of our patient's illness, suggests that Erdheim-Chester disease often follows an aggressive course despite treatment. The median survival of patients with Erdheim-Chester disease is only 32 months, with a survival rate of 41% at 5 years.[10]

Conclusion

We have reported a case of Erdheim-Chester disease in a Chinese patient. Although Erdheim-Chester disease is rarely encountered in daily clinical practice, we would like to suggest that when a diagnosis of orbital xanthogranuloma has been confirmed histologically, even in a systemically asymptomatic patient, the possibility of Erdheim-Chester disease must be investigated, in order to facilitate the early diagnosis and management of this potentially fatal condition.

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