Severe exophthalmos secondary to orbital myopathy not due to Graves's disease

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SUMMARY An 18-month-old white female child presented with severe bilateral exophthalmos. She was thought to have Graves's disease because her orbital CT scan showed massively enlarged extraocular muscles. She was subsequently found to have myelomonocytic leukaemia. This was treated with radiation, with rapid resolution of her exophthalmos and exposure keratitis.

Pathologically enlarged extraocular muscles are most commonly found in patients with Graves's disease, for which this is virtually pathognomonic. B-scan ultrasonography has been the best means of making the diagnosis of enlarged extraocular muscles until recently, when high-resolution orbital computerised axial tomographic (CT) scanning has been used to verify their enlargement. We recently treated a young child with bilateral proptosis presumed secondary to Graves's disease. Both B-scan ultrasonography and an orbital CT scan revealed multiple enlarged extraocular muscles consistent with the diagnosis of Graves's disease. On further investigation she was found to have an acute leukaemia. The finding by orbital CT scan of enlarged extraocular muscles in acute leukaemia is unique and forms the basis of the following case report.

Case report

This 18-month-old white female developed bilateral conjunctival hyperaemia on 5 November 1980 and was initially treated by the referring physician with topical and oral antibiotics for presumed conjunctivitis. The redness continued, and bilateral proptosis developed. She was admitted to his hospital on 19 December 1980 for examination. A CT scan showed bilateral soft tissue thickening with involvement of both superior and lateral rectus muscles. The examination included skeletal x-rays, analysis of blood and urine electrolytes, proteins, and enzymes by Sequential Multiplying Analyzing Computer, and blood cultures. Thyroid functions, including L-thyroxine (T4), tri-iodothyronine (T3),

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free thyroxine index (FTI), and thyrotropin (TSH) were normal. A trial of intravenous antibiotics and systemic steroids was unsuccessful. The proptosis increased and she was unable to close her lids over her eyes (Fig. 1).

She was then referred to the Shands Teaching Hospital for possible decompressive surgery. At the time of admission she was on prednisone, 10 mg by mouth twice a day (maximal dose for body weight) for 5 days. She was unable to fix or follow OU. There was marked proptosis, greater on the right than left side (Hertel measurements were 29/27 mm) (Fig. 1). Firm tissue was noted between the lids and minimal retropulsion. Motility was markedly decreased in all directions. Pupils were 4 mm OU with 4+ light reaction and no evidence of Marcus Gunn pupil. External examination revealed an epithelial defect of OD with clear corneas and no infiltrates. Fundus

Fig. 1 Patient on admission (Hertel exophthalmometer readings of 29 and 27 mm).

Fig. 2 B-scan echography demonstrating marked enlargement of extraocular muscle (horizontal section of left orbit; arrows indicate markedly increased thickness of lateral rectus muscle).

examination showed normal disc and vessels OU. B-scan echography showed enlarged extraocular muscles (Fig. 2). The rest of the examination was normal except for a left peripheral seventh nerve palsy.

The patient was begun on ocular lubricants every 1

Fig. 3 CT scan showing marked and symmetrical enlargement of lateral rectus muscles.

Fig. 4 CT scan showing marked and symmetrical enlargement of superior rectus muscles.

hour OU. The next morning a CT scan (Figs. 3, 4) showed massive enlargement of superior and lateral recti, bilaterally, with no evidence of a retro-orbital mass. A T3 radioimmunoassay was normal, and tests for thyroid antibody, thyroidal globulin antibody, and microsomal antibodies were negative. The haemoglobin was 11.5 g/dl and the leucocytes were $4.8 \times 10^9/l$, with 98% lymphocytes. A microscopic examination showed smudge cells and atypical lymphocytes more than 50%. A bone marrow biopsy was performed (Figs. 5, 6), and a diagnosis of acute myelomonocytic leukaemia was made.

The patient had whole brain and orbit irradiation, and within 48 hours a marked decrease in proptosis was noted. By the fifth day she could close both her eyes with a marked decrease in proptosis (shown in Fig. 7). The patient was begun on systemic chemotherapy, consisting of vincristine and cyclophosphamide. She was doing well at the time of discharge.

Discussion

Orbital involvement may be the presenting sign in acute leukaemia.¹ In our case the diagnosis of leukaemia was obscured by CT scans demonstrating multiple enlarged extraocular muscles. This finding was most consistent with dysthyroid ophthalmopathy. Graves's disease occurs not infrequently in children comparable in age to our case, with a propensity to

Fig. 5 Bone marrow showing marked cellularity. (Haematoxylin and eosin, $\times 0.6$).

affect females.^{2,3} 95% of young patients with dysthyroid ophthalmopathy in one recent series had proptosis.² Frequently patients with endocrine exophthalmos have normal thyroid function tests and no circulating antithyroid antibodies.⁴ And 'Graves' ophthalmology is the most common cause of proptosis in children. . . .²

Other disease processes considered in the differential diagnosis included neuroblastoma, which may present initially with bilateral proptosis⁵ and enlarged extraocular muscles on CT scan.⁶ However, there was no abdominal mass. Other less likely causes, such as bilateral orbital cellulitis and cavernous sinus thrombosis, were ruled out owing to lack of toxic manifestations or foci of infection in our

patient. Pseudotumor was thought unlikely because of its usual unilateral presentation and our patient's unresponsiveness of high dose steroids.

In acute lymphoblastic/lymphocytic leukaemia diffuse conjunctival and orbital infiltrations have been reported.^{7,8} Reticulum cell sarcoma caused bilateral orbital masses in several cases with acute monocytic leukaemia.^{9,10} Acute myelocytic leukaemia is associated with a peculiar greenish tumour called chloroma that has caused bilateral orbital masses and exophthalmos.^{9,11} All the aforementioned cases were reported before the CT scan era, and thus it is not known if they also had involvement and enlargement of the extraocular muscles. Histopathological study of orbital tissue obtained at biopsy in these cases did not, however, show involvement of the extraocular muscles. In our case biopsy was considered but obviated when the diagnosis of leukaemia was made.

Further histochemical studies confirmed that our child was afflicted with myelomonocytic (previously designated monocytic) leukaemia. There is a relationship between reticulum cell sarcoma and monocytic leukaemia. However, only a few cases of reticulum cell sarcoma have been reported to occur in patients with acute myelomonocytic leukaemia.^{9,10} Most cases of reticulum cell sarcoma occur as a systemic disease.¹² It is most unlikely that our patient has this association. All evidence suggests that the orbital deposits causing the proptosis in our case are due to leukaemic cell infiltration in the extraocular muscles. Straatsma and Allen¹³ have shown histopathologically that extraocular muscles can be

Fig. 6 Bone marrow showing monocytic myeloblasts. (Haematoxylin and eosin, $\times 450$).

Fig. 7 Patient after 5 days of radiotherapy.

infiltrated by leukaemic cells, as presumed in our case.

Enlarged extraocular muscles, especially when multiple and bilaterally symmetrically affected, are nearly always due to Graves's exophthalmopathy.¹⁴ Although the most commonly affected muscles in Graves's disease are the inferior and medial rectus muscles, isolated involvement of the lateral and superior rectus muscles has been reported.^{6,14} Other associated diseases with enlarged extraocular muscles by CT scan are pseudotumour, which affected only one muscle in all 7 cases reported; carotid cavernous fistula, with the distinguishing feature of enlarged superior ophthalmic vein in addition to the enlarged muscles; and various malignancies, none of which was a leukaemia.⁶

Neoplasms associated with enlarged extraocular muscles on CT scan cause the enlargement by direct infiltration or compression of the muscle with venous congestion.⁶ In these reported cases⁶ a separate mass

causing muscle compression or infiltration could be verified by CT scan, as opposed to our case in which a separate mass was not associated with enlarged extraocular muscles.

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References

- 1 Zimmerman LE. Lymphoid tumours. In: Boniuk M, ed. *Ocular and Adnexal Tumours*. St Louis: Mosby, 1964: 430.
- 2 Uretsky SH, Kennerdell JS, Gutai JP. Graves' ophthalmopathy in childhood and adolescence. *Arch Ophthalmol* 1980; **98**: 1963-4.
- 3 Baum I. Exophthalmic goiter in children. *Arch Pediatr* 1937; **54**: 419-24.
- 4 Young L. Dystrhyroid ophthalmopathy in children. *J Pediatr Ophthalmol* 1979; **16**: 105-7.
- 5 Iliff CE, Ossosky HJ. *Tumors of the Eye and Adnexa in Infancy and Childhood*. Springfield: Thomas, 1962: 123.
- 6 Trokel SL, Sadek HK. Recognition and differential diagnosis of enlarged extraocular muscles in computed tomography. *Am J Ophthalmol* 1979; **87**: 503-12.
- 7 Mortada A. Bilateral exophthalmos and lymphoblastic aleukaemic leukaemia. *Br J Ophthalmol* 1968; **52**: 68-9.
- 8 O'Rourke JF, O'Connor GR. Unusual ocular involvement in acute lymphatic leukemia. *Arch Ophthalmol* 1957; **57**: 585-9.
- 9 Mortada A. Orbital lymphoblastoma and acute leukemia in children. *Am J Ophthalmol* 1963; **55**: 327-31.
- 10 Mortada A. Orbital reticulum cell sarcoma with monocytic leukemia. *Arch Ophthalmol* 1962; **67**: 572-7.
- 11 Consul BN, Kulshrestha OP, Mehrota AS. Bilateral proptosis in acute myeloid leukaemia. *Br J Ophthalmol* 1967; **51**: 65-7.
- 12 Jakobiec SA, Jones IS. Lymphomatous plasmacytic, histiocytic and hematopoietic tumors. In: Duane TD, ed. *Clinical Ophthalmology*. Hagerstown: Harper and Row, 1980: 2: Chap 39: 9.
- 13 Straatsma BR, Allen RA. Ocular involvement in leukemia and allied disorders. *Arch Ophthalmol* 1961; **66**: 490-508.
- 14 Enzmann D, Marshall WH, Rosenthal AR, Kriss JP. Computed tomography in Graves' disease. *Radiology* 1976; **118**: 615-20.