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Aetiology of childhood proptosis

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Objective: To retrospectively analyse causes of childhood proptosis and their investigations and treatment.
Methodology: The records of children under 15 years of age presenting with proptosis to The Children's Hospital, Camperdown, Sydney, were reviewed for the period 1983–92 inclusive.
Results: Fifty-seven cases of proptosis were found. In order of frequency the causes were: orbital cellulitis 22, thyroid eye disease 8, optic nerve ± optic chiasm glioma 8, orbital rhabdomyosarcoma 7, metastatic neuroblastoma 4, orbital neurofibroma 3, orbital haemangioma 2, metastic Ewing's sarcoma 2 and orbital dermoid cyst 1.

Treatment depended on the cause (antibiotics, antithyroid drugs, chemotherapy, radiotherapy, surgery) and was multidisciplinary.
Conclusions: The most common cause of proptosis in children presenting to The Children's Hospital, Camperdown, Sydney, was infective orbital cellulitis. The most useful initial investigation was an orbital computed tomography scan. Treatment depended on the cause of the proptosis and was multidisciplinary.

Key words: Exophthalmos; orbit; orbital cellulitis; proptosis.

The relative incidence of the different causes of proptosis in children vary considerably amongst different studies because of variations in the source of the material (clinical, histopathological or radiological), the time the study was carried out, as well as the country of the study.

Studies based on biopsies for histopathology are biased towards neoplasms rather than infective processes which are much less likely to be biopsied. The study by Shields,[1] which is entirely based on histopathological cases showed that cystic lesions were the commonest cause of orbital biopsies.
However, studies which include clinically diagnosed cases such as Rootman[2] and Bullock[3] reveal that conditions such as inflammatory/infective processes and vascular and neural tumours become more common causes of orbital disease.

Silva[4] reported, in 1968, 65 cases of orbital tumours in children under 10 years of age. Of these, 20 were due to orbital extension of retinoblastoma, which is very rare today due to early detection and treatment.

Radiologically based studies have revealed that sinus mucocoele was the most common cause of unilateral proptosis.[5]

Finally, geographic variations also play a role. Templeton's study[6] of childhood proptosis in Africa revealed Burkitts lymphoma as the most common neoplastic cause of proptosis.

Despite the variations in these different studies, it can be summarised that about 90% of the space occupying orbital lesions in children under 18 years old are benign and that about half of these are cystic lesions of which most are dermoid cysts. The remaining 10% of space occupying lesions are malignant tumours such as rhabdomyosarcoma, metastatic neuroblastoma, leukaemia/lymphoma and orbital extension of retinoblastoma.[3]

Our study differs from the surveys of Shields,[1] Rootman[2] and Bullock[3] in that it only deals with children under 15 years, compared with those under 18 years. In addition, we have included only orbital lesions that cause proptosis. This excludes most of the dermoid cysts which have a large contribution in the other surveys but rarely cause proptosis. Over the same 10-year period in our study there were 55 dermoid cysts not causing proptosis.

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METHODS

The files of all patients presenting to The Children's Hospital, Camperdown, Sydney, Australia, with all possible causes of proptosis or exophthalmos were retrospectively reviewed using the International Classification of Diseases—9-CM over a 10-year period 1983–92. Cases of pseudo-proptosis such as buphthalmos and orbital bone hypoplasia as well as orbital margin dermoid cysts which did not cause proptosis were excluded.

RESULTS

Table 1 delineates the causes of proptosis in children under 15 years seen at The Children's Hospital, Camperdown, Sydney, over the 10-year period 1983–92.

All 22 cases of infective orbital cellulitis were secondary to sinusitis, particularly of the ethmoid sinuses. Orbital cellulitis only refers to those cases with infection posterior to the orbital septum and thus excludes preseptal cellulitis. Age of onset of the cellulitis varied from 1 month to 14 years. All cases were treated with combined broad-spectrum intravenous antibiotics (varying combinations of ampicillin, penicillin, flucloxacillin, cefotaxime, gentamicin, metronidazole and chloramphenicol). Eighteen of the 22 cases also had surgical intervention with ethmoidectomy and drainage of a subperiosteal abscess. The two most common causative organisms were *Staphylococcus*

Table 1 Number and percent of lesions causing proptosis in children

Lesion	No.	%
Infective orbital cellulitis	22	38.6
Thyroid eye disease	8	14.1
Optic nerve ± optic chiasm glioma	8	14.1
Orbital rhabdomyosarcoma	7	12.3
Metastatic neuroblastoma	4	7.0
Orbital neurofibroma	3	5.2
Orbital haemangioma	2	3.5
Metastatic Ewing's sarcoma	2	3.5
Orbital dermoid cyst	1	1.7
Total	57	100

aureus and *Streptococcus milleri*, as determined from pus drained from the abscess.

Of the 8 cases with thyroid eye disease, 7 were thyrotoxic and 1 was euthyroid. Age of onset was from 5 to 14 years. One case also had myasthenia gravis. The 7 thyrotoxic cases were all originally managed with medical therapy but 4 cases went on to have thyroidectomy because of either non compliance or intolerance of medical therapy. No patients required surgical orbital decompression. The visual outcome was normal in all cases.

Of the 8 optic glioma cases, 6 had gliomas confined to the optic nerve (3 cases had confirmed neurofibromatosis) and 2 had gliomas involving both the optic nerve and optic chiasm (both had neurofibromatosis). The age of presentation with optic nerve glioma was younger in those with neurofibromatosis (3–4 years) than those without neurofibromatosis (7–11 years). Of the 3 cases with neurofibromatosis, 2 went blind and had surgical excision of the tumour for unsightly proptosis and 1 retains 6/6 vision without any treatment. Of the 3 cases without neurofibromatosis all have been observed, with acuities ranging from 6/12 to count fingers. Of the 2 cases with optic nerve and chiasm involvement, 1 had radiotherapy and the other a shunt for hydrocephalus. The acuities on the side of optic nerve involvement varied from 6/36 to hand movements. The acuity in the uninvolved eye in both cases was 6/5 with a temporal hemianopia.

The age of onset of orbital rhabdomyosarcoma varied from 3 to 12 years. One case was Stage 2, four were Stage 3 and two were Stage 4. One case later developed acute lymphoblastic leukaemia. All cases were treated with chemotherapy and radiotherapy, with one case having a bone marrow transplant in addition. The visual outcome of the involved orbit varied from normal to blind, with one case dying.

The age of onset of orbital metastatic neuroblastoma varied from 9 months to 7 years. Treatment included surgery, chemotherapy, radiotherapy and in one case bone marrow transplant. The visual acuities ranged from normal (this case died) to blind.

Of the 3 cases with orbital neurofibroma, one had confirmed neurofibromatosis. Age of presentation varied from birth to 2 years. Two cases had debulking surgery and the third case is awaiting surgery. The visual outcome of the involved eye varied from 6/24 to blind.

The age of presentation of the 2 cases with orbital haemangioma was at birth and at 7 months. There was no record of visual acuity or treatment for the first case. The second case had initial acuities of 6/30 in each eye (as assessed by Teller visual acuity cards) and had systemic interferon with some success in tumour regression at 4 months follow-up after initial failure with steroid therapy.

The 2 cases of Ewing's sarcoma presented at 11 and 13 years. Both had radiotherapy, chemotherapy and surgery. One child died and the other had a visual acuity of 6/60 in the involved eye.

The one case of orbital dermoid cyst presented at 3 years. The child underwent a subtotal surgical excision and at present the visual acuity is normal with no sign of recurrence.

DISCUSSION

The clinical approach to the management of a child with proptosis largely depends on the history of presentation.

By far the most common cause in our series was infective orbital cellulitis. The typical presentation was with pain, eyelid erythema, chemosis and proptosis, with or without fever and malaise. Although all cases were secondary to sinusitis many cases gave no definite preceding history of sinusitis. The differential diagnosis of this inflammatory presentation is delineated in Table 2.

Children with Grave's disease may have other ocular and systemic signs and symptoms of thyrotoxicosis.

Optic nerve gliomas associated with neurofibromatosis (type I) in this group notably had a worse course than those independent of systemic disease. This contrasts with traditional teaching that gliomas associated with neurofibromatosis have a more quiescent course, but may be accounted for by the small numbers of this subgroup within this study.

With rhabdomyosarcoma, additional signs and symptoms may include epistaxis and a palpable subconjunctival or lid mass, whereas ruptured dermoid cysts should have a history of long-standing proptosis.

Neuroblastoma metastasizing to the orbit may present with proptosis and periorbital eccymosis. A small proportion of neuroblastoma (2.8–6.2%)[7,8] present with orbital metastases.

No cases of the following lesions causing proptosis were seen: lymphoma/leukaemia, orbital spread of retinoblastoma, Langerhan's cell histiocytosis, pseudotumour and tumours of adipose, osseous, fibro-osseous and cartilaginous tissues.

The most useful initial investigation of a child presenting with proptosis is a computed tomography (CT) scan of the orbits (fine cuts with axial and coronal views and use of contrast) and brain. This investigation reveals most orbital tumours, subperiosteal abscess, sinusitis, bony abnormalities or enlarged extraocular muscles.

A magnetic resonance imaging (MRI) scan (1.5 tesla magnet with surface coil receptors is best for orbital examinations) is not as cost effective nor as accessible as a CT scan. Nevertheless, it does have some advantages over a CT scan as an additional investigation in the following situations:

Table 2 Differential diagnosis of inflammatory proptosis

Infective orbital cellulitis
Orbital rhabdomyosarcoma
Grave's disease
Ruptured orbital dermoid cyst
Pseudotumour
Retinoblastoma with extraocular spread
Lymphangioma with orbital cellulitis secondary to URTI
Eosinophilic granuloma of orbital wall

1 To distinguish tumours, such as haemangiomas, as being separate from the optic nerve.[9]

2 For optic nerve and chiasm lesions.

3 To date, the duration of a haematoma[10,11]
(the state of and location of the haemoglobin and its breakdown products changes with the duration of an haematoma, with each product having a characteristic T_1 and T_2 signal on MRI scanning).

4 For orbital apex lesions, by eliminating bony artefact.

5 To diagnose pseudotumour[12] (isointense to muscle on T_1 and isointense to muscle and fat on T_2). In this situation, MRI scanning may be useful as an adjunct but is rarely diagnostic.

However, for lesions with bony involvement or calcification (e.g. meningioma) a CT scan is superior. In practice, both the CT and MRI scans are complementary and both may need to be performed to plan management.

Other investigations that need to be considered, depending on the clinical presentation are presented in Table 3.

The principal indication for orbital biopsy is to obtain tissue diagnosis when proptosis is due to a mass lesion, which is likely to be malignant in nature. In our experience, this is most frequently required when a rhabdomyosarcoma is suspected.

It is important to liaise with the pathologist. Frozen sections are useful to ensure that the correct tissue has been biopsied and, in the case of an excision biopsy, that the margins are clear of tumour. Specimens should be provided fresh or in liquid nitrogen for immunohistochemistry, in formalin for light microscopy and in glutaraldehyde for electron microscopy.

Treatment of proptosis in children depends on the cause and is often multidisciplinary. Children with orbital tumours require management with input from a number of paediatric subspecialities, including ophthalmology, oncology, radiotherapy and neurosurgery. More than any other group in our series, they illustrate the need for a multidisciplinary approach to the diagnosis, treatment and total management of a child presenting with proptosis.

Table 3 Investigations of a child with proptosis

Investigation	Indication
CT orbits and brain	Initial investigation
MRI orbits and brain	Optic nerve lesions
	Vascular lesions (+ dating haemorrhage)
	Orbital apex lesions
CT thorax and abdomen	Neuroblastoma
Blood tests:	
FBC, blood culture	Leukaemia,suspected infections
TFTs	Thyroid related orbitopathy
LFTs	Suspected malignancy
Urinary catecholamines	Neuroblastoma
Bone marrow	Leukaemia
	Tumour staging
Lumbar puncture	Tumour staging
Bone scan	Langerhan's cell histiocytosis
	Tumour staging
Liver/spleen scan	Langerhan's cell histiocytosis
Orbital biopsy	To obtain tissue diagnosis

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