Ophthalmopathy in childhood Graves’ disease

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Aims: To study the ocular manifestations and their severity in children with Graves’ disease.

Methods: All patients with Graves’ disease having regular follow up in a paediatric endocrine clinic were recruited for the study. A comprehensive ophthalmic assessment including ocular motility, exophthalmometry, intraocular pressure (IOP), slit lamp, and fundus examinations was performed.

Results: 83 patients (72 female, 11 male) aged 16 years or below were examined. All are Chinese. Ocular symptoms occurred in 12 patients. Ocular signs of ophthalmopathy were documented in 52 patients (62.7%). Most of them presented with eyelid abnormalities such as lid oedema, lid lag, and lagophthalmos, whereas lower lid retraction was the commonest clinical sign noted (38.6%). Diffuse conjunctival injection was found in four patients (4.8%). 10 patients (12.0%) had mild proptosis of less than 3 mm. Only one patient (1.2%) had limited extraocular motility in extreme gaze. Punctate epithelial corneal erosions were reported in 11 patients (13.3%).

Conclusions: This is the largest series on the ocular complications of childhood Graves’ disease in the literature. Although 52 patients (62.7%) were identified with positive ocular changes, none of them had visual threatening complications or debilitating myopathy.

RESULTS

A total of 83 paediatric patients with the systemic Graves’ disease were studied. There were 72 females and 11 males. The median age of onset of Graves’ disease was 11 years (mean 9.5 (SD 4.8) years). At the time of their ocular examinations, the subjects had been followed up at the paediatric endocrine clinic for a median duration of 45 months (mean 51.3 (29) months). Although 15 patients (18.1%) had more than one relapse, most of them (68 patients, 81.9%) were either in remission or receiving their first course of oral treatment at the time of assessment. Both active and chronic disease states were present in the group. Fifty four patients (65.1%) were still taking medical treatment while 29 (34.9%) were in remission. Among the subjects, family history (mother, father, or siblings) of thyrotoxicosis was positive in 16 (19.3%) subjects. 79 patients (95.2%) were non-smokers, three patients (3.6%) were smokers, and one patient (1.2%) was an ex-smoker. On the other hand, 41 patients (49.4%) had household members who smoked currently. None of the

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patients had associated systemic disease, such as thyroid dermopathy, acropachy, myasthenia gravis, or diabetes mellitus.

All patients were treated with oral antithyroid medication only and none received radioactive iodine treatment.

Among the 83 patients, 12 (14.5%) reported ocular symptoms. These included pain, foreign body sensation, photosensitivity, epiphora, and diplopia. Most of the patients had eyelid signs, four patients (4.8%) had upper lid retraction, 32 (38.6%) had lower lid retraction, five (6.0%) had lid oedema, and five (6.0%) had lid lag. Lagophthalmos was found in eight patients (9.6%) while diffuse conjunctival injection was present in four patients (4.8%). Ten patients (12.0%) were detected to have mild proptosis. When comparing the IOP measured in upgaze and primary gaze, six patients (7.2%) had higher measurement in upgaze position by 3 mm Hg or more. Only one patient (1.2%) had limited extraocular motility in extreme gaze. On the other hand, 11 patients (13.3%) stained positive with fluorescein in their corneas. Clinically, all of them had punctate epithelial erosions; no superior limbal keratitis or corneal ulceration was detected. None of the patients was found to have visual impairment or optic nerve dysfunction.

In categorising the oculomotor manifestations of Graves’ diseases with an abridged NOSPEC classification into classes 0 to 6, 31 patients (37.3%) would be in class 0, 21 (25.3%) in class 1, 12 (14.5%) in class 2, seven (8.4%) in class 3, one (1.2%) in class 4, 11 (13.3%) in class 5, and 0 in class 6 (Fig 1)."
The proportion of patients with positive ocular manifestations was the highest in this cohort (62.7% in the current study). Eyelid signs were the predominant complication in all studies. Symptomatic conditions and soft tissue involvement occurred in about 10–15% of all patients. Exophthalmos did present in this age group but was uncommon. In Liu’s series,11 all the children had prominent proptosis and were associated with a hyperthyroid state. In contrast, some of our patients were found to have mild proptosis despite being euthyroid. More importantly, 11 patients were found to have corneal complications in the current study but none in the other studies. Nevertheless, all of them only had mild punctate epithelial erosions rather than any vision threatening corneal condition. This might be related to the high incidence of lower lid retraction and lagophthalmos as the lesions were located at the inferior periphery of the cornea. The punctate epithelial erosions in the cornea can be managed with lubricating eye drops; however, the treatment may need to be continued even if the Graves’ disease is in remission.

Graves’ disease clusters in families but the importance of heredity in the pathogenesis of the associated ophthalmopathy is unclear. In the present study, 16 patients (19.3%) had a positive family history of Graves’ disease. We did not examine the family members of patients to document the family history of Graves’ ophthalmopathy for further correlation. From the literature, Villanueva35 had studied the family history of 114 consecutive, ethnically mixed patients with severe Graves’ ophthalmopathy. Only three of the 114 patients had a family history of severe Graves’ ophthalmopathy, which were all in second degree relatives. His data did not support a major role for familial factors in the development of severe Graves’ ophthalmopathy.

Various studies11–28 suggested that other factors, rather than major genes, were likely to predispose certain individuals to severe Graves’ ophthalmopathy. Smoking and radioactive iodine treatment have been implicated in the manifestations of thyroid ophthalmopathy.29 Mann29 reported a sevenfold increase in risk of thyroid associated orbitopathy, and the number of cigarettes smoked per day appeared to be a significant independent determinant for the incidence of proptosis and diplopia. We also included the patients’ smoking history and environment with cigarette smoking in our study. Both the number with proptosis and smokers in the current study were small such that a definitive conclusion regarding the relation of active or passive smoking and childhood thyroid eye disease cannot be made from this study. Radioidine treatment was not a factor contributing to the development of ophthalmopathy in our subjects as none received such treatment.

In conclusion, ocular manifestations are common in paediatric Graves’ disease. However, they are much milder than in adult Graves’ ophthalmopathy. Among the 52 patients (62.7%) with positive ocular changes, none of them had visual threatening complications or debilitating myopia. Most of the patients only required treatment with lubricating eye drops.

ACKNOWLEDGEMENTS

Financial support: Supported in part by the Action for Vision Eye Foundation, Hong Kong. Proprietary interest: Nil.

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doi: 10.1136/bjo.86.7.740

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