Neonatal Graves’ disease

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SUMMARY A newborn boy was noted by his mother to have a prominent left eye at birth, but an eye examination was delayed until age 7 months, at which time his ophthalmologist diagnosed exophthalmos. Computed tomography was interpreted as showing mild, diffuse, optic nerve thickening bilaterally suggestive of optic nerve gliomas. Subsequent examination in our clinic revealed pseudoproptosis secondary to retraction of the left upper eyelid. Magnetic resonance imaging demonstrated normal orbital structures. The mother was noted to be clinically hyperthyroid, and abnormal thyroid function tests confirmed the diagnosis. Although the infant was euthyroid, neonatal Graves’ ophthalmopathy was diagnosed. He was managed by close observation while his mother was treated for her hyperthyroidism.

Neonatal or congenital Graves’ disease has been described as a rare disorder of infants born to mothers who have been hyperthyroid during pregnancy. The clinical features of this disease in the newborn range from transient subtle signs of hyperthyroidism lasting four to six months to a severe protracted disorder that significantly affects growth, development, and intellectual and emotional maturation. The pathogenesis of congenital Graves’ disease is unknown, but it is postulated that it is secondary to transplacental transmission of an antithyroid antibody in a genetically preselected population.

Ophthalmologically the affected newborn baby may present with exophthalmos and/or lid retraction. If congenital Graves’ disease is suspected, thyroid function tests in both the patient and mother are indicated, and appropriate systemic treatment should be promptly instituted for this potentially serious disease.

Case report

A newborn boy was noted by his mother to have a prominent left eye at birth (Fig. 1). The appearance of the left eye did not change over the ensuing months, and the child was finally examined by an ophthalmologist at another institution at age 7 months. Clinical findings at that time included proptosis and questionable amblyopia of the left eye (OS). Computed tomography of the orbits was interpreted as showing diffusely thickened optic nerves bilaterally, suggestive of optic nerve gliomas.

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Fig. 1 The patient at birth with left upper lid retraction.
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At age 9 months there is still no apparent change in clinical features.

We examined the child at 9 months of age, at which time he could fixate and follow small objects with each eye, and the pupils were equal and found without an afferent defect. There was 2 mm retraction of the left upper eyelid (Fig. 2), which remained in an elevated position on downgaze. There was no exophthalmos or contralateral blepharoptosis. The extraocular movements showed slightly deficient upgaze OS but were otherwise normal.

The cycloplegic refraction revealed a +2.00 sphere in both eyes, and the fundi and optic discs were normal, with no evidence of disc oedema, optic atrophy, or opticociliary shunt vessels. General physical examination was completely normal. The patient was the product of a normal pregnancy, labour, and delivery. The family history was remarkable for diabetes mellitus and thyroid disease in the mother and several relatives. The patient's mother had recently been diagnosed as having hyperthyroidism characterised by a diffusely enlarged goitre, resting tremor, resting pulse of 130, and widened pulse pressure of 145/70 mmHg.

Laboratory evaluation (Table 1) revealed entirely normal thyroid studies in the 9-month-old patient. Thyroid studies of the patient's mother disclosed significantly raised levels of triiodothyronine (T3), increased T3 uptake, and increased thyroid stimulating immunoglobulins (TSI). The antithyroid antibodies were likewise raised at 1:40.

The results of computed tomography of the orbit, which were interpreted at another institution as showing bilateral diffuse optic nerve gliomas, were subsequently interpreted by several neuroradiologists at our institution as being within normal limits (Fig. 3). A magnetic resonance imaging (MRI) scan of the orbits was performed on the patient and the findings were within normal limits, with no evidence of optic nerve glioma.

From the clinical and laboratory findings the diagnosis of neonatal Graves' ophthalmopathy was made. The young child was managed by observation alone and has remained without changes in his appearance at 10 months follow-up. The patient's mother has undergone appropriate treatment for hyperthyroidism.

Discussion

Hyperthyroidism is uncommon during childhood and adolescence, with an incidence of 3.8 cases per

Table 1  Thyroid studies of the child and his mother

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Child</td>
</tr>
<tr>
<td>T3 RIA</td>
<td>170</td>
</tr>
<tr>
<td>T3 uptake</td>
<td>38</td>
</tr>
<tr>
<td>T4</td>
<td>9-4</td>
</tr>
<tr>
<td>Thyroid stimulating immunoglobulin (TSI)</td>
<td>&lt;2-0</td>
</tr>
<tr>
<td>Antithyroid antibody</td>
<td>*</td>
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</tbody>
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*Test not performed.

mg/dl=Milligrams/decilitre. mcg/dl=Micrograms/decilitre. mlU eq/ml=Microinternational units equivalent/millilitre.
100,000 population per year. The causes of childhood hyperthyroidism are most commonly acquired Graves' disease and much less commonly neonatal or congenital Graves' disease, thyroid adenomas and carcinomas, lymphocytic thyroiditis, and polyostotic fibrous dysplasia (McCune-Albright syndrome).

Neonatal Graves' disease was first described by Ochsner and Thompson in 1910. They reported an exophthalmic baby born to a mother who had exophthalmos and a goitre. Since this initial report several cases have been reported, primarily in the endocrinology literature.

Holingsworth and coworkers suggested that two types of congenital Graves' disease exist. The first and more common type occurs in infants born to mothers with active or recently active Graves' disease. The disease in the newborn baby tends to be mild, transient, and resolves at about 3 to 6 months of age without sequelae or recurrence. The second and less common type of congenital Graves' disease usually has its onset in early infancy, though it may be present at birth. There is usually a family history of Graves' disease, but the mother may or may not have Graves' disease. This type tends to persist with late sequelae of premature fusion of the cranial sutures, microcephaly, short stature, and mental and emotional retardation.

Early clinical features of both types are similar. The patients may be premature and of low birth weight. Periorbital oedema, lid retraction, exophthalmos, and goitre are almost always present, and other manifestations include tachycardia, irritability, and polyphagia.

There is significant variation in the severity of congenital Graves' disease. Some patients may have eye signs only without other signs of thyrotoxicosis, while others may have the spectrum of systemic findings of thyrotoxicosis. Hollingsworth and Mabry reported a series of 74 neonates with congenital Graves' disease and noted that a surprisingly high percentage (16%) of these patients died either from prematurity, respiratory distress, or thyrotoxicosis. They emphasised the possible seriousness of this entity and pointed out that many of the fetuses die in utero.

Several theories exist as to the pathogenesis of neonatal Graves' disease. The most widely accepted postulate is that it develops in an infant with a genetic predilection who has acquired one or several immunoglobulins from the mother via transplacental transmission. It is believed that these immunoglobulins may be antithyroid antibodies with enhancer and blocking agents that either stimulate or inhibit the activity of the antibody.

The patient we report on seems to resemble the milder form of congenital Graves' disease with eye findings only, but his upper eyelid retraction has persisted longer than the typical three to six months. Others have reported persistence of eye signs for more than one year.

It is sometimes difficult to distinguish eyelid retraction from exophthalmos, especially in restless children. Close attention to the movement of the eyelids, especially during duction movements, and careful exophthalmometry readings will usually differentiate between these two conditions. Bilateral and unilateral lid retraction can be seen in a variety of diseases (Table 2). A complete history and examination of the neonate for each of these entities should be performed. In cases of suspected thyroid disease or myasthenia gravis the mother should also be examined. In our patient's mother the thyroid function tests were grossly abnormal, though the child's studies were within normal limits. This may be explained by the fact that the child presented at age 9 months, and most maternal antibodies are not present in the neonate after 3 to 5 months. We postulate that in the first few months of life our patient may have raised thyroid hormones.

Treatment of neonatal Graves' disease includes a combination of antithyroid drugs, preferably propylthiouracil and iodine, and β-adrenergic blockers when needed. Rarely thyroidectomy has been needed after medicinal failure. Our patient had no evidence of thyrotoxicosis at the time when he presented to us, so therapy consisted of observation only.

The ophthalmologist should be aware of this unusual cause of eyelid retraction in the newborn and
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recognise the need for prompt paediatric and endocrinological care of the patient and mother.

This work was supported by a grant from Fight for Sight, Inc. New York to the Fight for Sight Children's Eye Center of Wills Eye Hospital, Philadelphia, Pennsylvania.

References


Accepted for publication 23 April 1987.