Retrospective Review of Pediatric Thyroid Eye Disease Cases Referred to Nicklaus Children's Hospital

Abstract

**Purpose:** We evaluate presenting features and treatment options of pediatric thyroid eye disease, and discuss the morbidity of this condition in the pediatric population.

**Methods:** A retrospective chart review of 11 patients referred for evaluation of thyroid eye disease at a pediatric tertiary care facility in Miami, Florida.

**Results:** The average age at presentation was 12.7 years. The most common ocular complaint was mild irritation. The average displacement on Hertel exophthalmometry was 21 mm for the right eye, and 21.45 mm for the left eye. Lower scleral show was the most common eyelid finding. Patients tended to be positive for thyroid stimulating immunoglobulin and thyroid peroxidase antibody.

**Conclusion:** In contrast to thyroid eye disease in adults, the condition tends to present with mild ocular findings in children. Pediatric patients presenting with thyroid eye disease respond very well to medical therapy aimed at enhancing the altered ocular surface.

**Keywords:** thyroid eye disease; proptosis; Graves’ Disease; lower scleral show.

Introduction

Less common in children than in adults, thyroid eye disease (TED) occurs in 0.79 to 6.5 per 100,000 children annually, with greater frequency in females, in those with concurrent autoimmune disorders or with a family history of autoimmune thyroid disease, and in those of Chinese ancestry. As in adults, TED is most often associated with acquired hyperthyroidism, but may occur in hypothyroid and euthyroid states as well. One-third of children with Graves’ disease develop ophthalmopathy, with a median time of one month from diagnosis of Graves’ disease until development of TED, although 82% of children had ocular complaints prior to being diagnosed in a study by Jarusaišiene et al. Two-thirds of children with TED are between the ages of 11 and 18 years, presumably due to an increased prevalence of smoking in this age group. Although postpubertal children seem to experience more serious complications, signs of TED are generally mild and self-resolving, potentially delaying diagnosis. Common manifestations noted in the literature include upper eyelid retraction, proptosis, eyelid lag, pain, foreign body sensation, photosensitivity, tearing, and diplopia, while optic neuropathy and corneal breakdown are infrequent. In addition, myopia may accompany proptosis. In contrast to children, adults with Graves’ ophthalmopathy seem to experience more severe disease manifestations, with higher rates of exophthalmos, restrictive myopathy, and optic nerve dysfunction.

Methods

We performed a retrospective chart review of children with Graves’ ophthalmopathy who had been referred for ophthalmic evaluation at Nicklaus Children’s Hospital, a tertiary care center in Miami, Florida. We selected our patients based on diagnostic ICD-9 codes. Since the aim of the study was to further characterize the manifestations
of TED, patients whose ocular exams did not exhibit findings consistent with TED were excluded. Each patient’s sex, age, systemic symptoms, thyroid autoantibody results, best corrected Motility (BCVA), visual field results, stereoacuity, Ishihara color plate results, motility, Hertel exophthalmometry measurements, external and biomicroscopy findings, ocular symptoms, treatment, and thyroid disorder were documented, and most of the results were averaged.

**Results**

We identified a total of 55 patients with Graves’ disease who had been examined by the endocrinology team in the last decade. Of this cohort, 15 patients had ocular complaints that prompted referral to the pediatric ophthalmology service. Only 11 of these 15 patients exhibited signs of TED, and were included in this case series.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Demographic Information</th>
<th>Systemic Symptoms</th>
<th>Exophthalmometry</th>
<th>Antibodies</th>
<th>Ocular Symptoms</th>
<th>Motility</th>
<th>Stereo-acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP</td>
<td>Female, 8 years of age</td>
<td>not recorded</td>
<td>base 90: 16mm OD and 20mm OS</td>
<td>data unavailable</td>
<td>mild irritation</td>
<td>-1 abduction OD, -1 adduction left eye</td>
<td>40 seconds of arc</td>
</tr>
<tr>
<td>AM</td>
<td>Female, 4 years of age</td>
<td>tremor, tachycardia, diarrhea</td>
<td>base 90: 20mm OU</td>
<td>TSI +</td>
<td>none</td>
<td>E’X 20 - full</td>
<td>40 seconds of arc</td>
</tr>
<tr>
<td>EL</td>
<td>Male, 19 years of age</td>
<td>tremor, tachycardia/palpitations</td>
<td>base 100: 19mm OD, 20mmOS</td>
<td>data unavailable</td>
<td>none</td>
<td>ortho</td>
<td>not recorded</td>
</tr>
<tr>
<td>YB</td>
<td>Female, 19 years of age</td>
<td>tremor</td>
<td>base 95: 25mm OU</td>
<td>data unavailable</td>
<td>none</td>
<td>ortho</td>
<td>40 seconds of arc</td>
</tr>
<tr>
<td>JC</td>
<td>Female, 19 years of age</td>
<td>not recorded</td>
<td>base:90 19mm OU</td>
<td>data unavailable</td>
<td>irritation</td>
<td>ortho</td>
<td>40 seconds of arc</td>
</tr>
<tr>
<td>JO</td>
<td>Female, 14 years of age</td>
<td>suicide attempt, anxiety</td>
<td>base 98: 21mm OU</td>
<td>TSI +</td>
<td>none</td>
<td>ortho</td>
<td>not recorded</td>
</tr>
<tr>
<td>CH</td>
<td>Female, 15 years of age</td>
<td>tachycardia, diarrhea, weight loss</td>
<td>base 100: 22mm OU</td>
<td>Tg Ab +, TPO +</td>
<td>none</td>
<td>ortho</td>
<td>40 seconds of arc</td>
</tr>
<tr>
<td>CS</td>
<td>Female, 14 years of age</td>
<td>tremor</td>
<td>base 95: 22mm OU</td>
<td>TSI +, TPO +, Tg Ab +</td>
<td>none</td>
<td>-1/2 abduction OU</td>
<td>40 seconds of arc</td>
</tr>
<tr>
<td>CS</td>
<td>Female, 11 years of age</td>
<td>weight loss, tremor, anxiety, shortness of breath</td>
<td>base90: 22mm OU</td>
<td>TPO Ab +, TBII +, Tg Ab +</td>
<td>itching/burning/blurry vision</td>
<td>ortho</td>
<td>not recorded</td>
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<tr>
<td>MR</td>
<td>Female, 11 years of age</td>
<td>weight loss, anxiety, polydipsia, polyuria</td>
<td>base 110: 26mm OD 25.5 OS</td>
<td>TSI +, TrAB</td>
<td>mild irritation, burning</td>
<td>ortho</td>
<td>not recorded</td>
</tr>
<tr>
<td>LR</td>
<td>Female, 12 years of age</td>
<td>weight loss, sleepiness, tachycardia</td>
<td>base 110: 19mm OD 19.5 OS</td>
<td>TPO +, Tg Ab +</td>
<td>irritation</td>
<td>ortho</td>
<td>not recorded</td>
</tr>
<tr>
<td></td>
<td>12.7 years on average</td>
<td>45.4% tremor</td>
<td>21 OD - 21.45 OS</td>
<td>36.3%TPO, TSI 36.3%</td>
<td>30% mild irritation</td>
<td>18% presented with motility</td>
<td>40 second of arc on average</td>
</tr>
</tbody>
</table>
The baseline ocular examination findings are displayed in Table 1. The average age of presentation in our series was 12.7 years. Most of the patients were females, constituting 90% of the study group. The most common systemic complaint was a fine tremor. Diarrhea, weight loss, anxiety, and tachycardia were also heavily present throughout the study population. One patient presented with suicidal ideation. The most common ocular complaint was itching and mild irritation, with over 30% of patients expressing these symptoms. The vast majority of patients did not complain of visual disturbances, and 82% had a BCVA of 20/20 in both eyes. Average refractive error by retinoscopy was +0.44 +0.70 x 88.33 OD and +0.41 +0.68 x 107.75 OS.

One child with exposure keratopathy had a BCVA of 20/50, while another child with intermittent exotropia had a BCVA of 20/50 in one eye and a BCVA of 20/20 in the fellow eye. All patients presented with lower scleral show. Superior eyelid retraction was present in 18% of patients, and another 27% presented with eyelid lag on downgaze. The average displacement on Hertel exophthalmometry was 21 mm for the right eye, and 21.45 mm for the left eye. In addition, 18% of patients presented with hyperemia over one of the extraocular muscles. A minority of cases, constituting 18% of the study cohort, presented with slight limitation of abduction. One patient presented with an unrelated intermittent exotropia.

Available laboratory findings are displayed in Table 1. Of the seven patients who had thyroid autoantibody studies available, four (57%) were positive for thyroid peroxidase (TPO). Thyroid stimulating immunoglobulin (TSI) titers were also positive in 57% of patients. It is important to note that there was considerable overlap between antibody titers, with five of the seven patients (71%) being positive for two or more thyroid auto-antibodies. Approximately 90% of patients presented with low TSH.

Treatment plans for nine patients were available Table 1. Of these nine patients, 78% were treated with either methimazole or thiamazole. Three patients (33%) underwent thyroidectomy, while two patients (22%) actually received radioactive iodine. Four patients (44%) were also treated with beta blockers. All patients received topical lubricants since lower scleral show was such a
prevailent finding, and all five patients who presented with complaints of itching and irritation experienced subjective improvement, as well as decreased punctate epithelial erosions after instillation of fluorescein.

Discussion

In Jankauskiene and Jarusaitiene's retrospective study of 18 children with TED secondary to Graves' disease, the clinical activity score (CAS) based on inflammatory ocular symptoms was generally mild. In their study, 72.3% of children had upper eyelid retraction, 66.7% had proptosis, and 44.4% had eyelid lag. Our results exhibited a comparable incidence of proptosis (54%) and eyelid abnormalities (100%), though lower scleral show secondary to proptosis or lower eyelid retraction was our most common adnexal finding. In comparison, Chan et al reported proptosis in only 12.0% of 83 children studied. Similar to our study however, restrictive extraocular myopathy was an uncommon finding, exhibited in only 1.2% of children in their study, and they reported no cases of optic nerve dysfunction. Two children (18%) in our case series displayed mild ocular motility disturbances secondary to TED, and none displayed evidence of optic nerve dysfunction. In contrast to the typically mild findings of Graves' ophthalmopathy in children, proptosis can be found in up to 60.8% in adults, while restrictive myopathy and optic nerve dysfunction have been reported in 42.5% and 5.8% of adults, respectively.

The most common ocular complaints in our study were itching and mild irritation, which we believe to be secondary to increased corneal exposure caused by inferior scleral show and mild proptosis. Mild and moderate ocular surface symptoms respond excellently to topical lubrication, as demonstrated by Goldstein et al in their study of the course of pediatric TED and its most common findings in 26 children. We found therapeutic results similar to those of Goldstein et al with resolution of these symptoms in all children who received topical lubrication.

Positive TSI titers, which have been shown to be associated with development of TED in adults, also correlated with the development of TED in children in a study of 49 patients with Graves' disease by Acuna et al. Fifty-seven percent of our patients presented with positive TPO antibodies, while another 57% presented with positive TSI titers in our study. Shibayama et al found that TSI levels in children with TED were not significantly different from those without TED however, and instead found a strong correlation between TED and higher thyrotropinbinding inhibitory immunoglobulin (TBI) levels in their study of 35 serum samples from children with untreated active Grave's disease. We did not evaluate TBI titers in our cohort.
Diagnosis of pediatric TED is based on ocular manifestations and evidence of thyroid autoimmunity. Even though the orbital fat tends to be more involved in this age group, orbital MRI may be helpful for detection of extraocular muscle inflammation. The typical treatment of Graves’ disease in children is two years of antithyroid therapy, such as with methimazole, followed by re-evaluation and monitoring thereafter. Radioiodine is a treatment option as well, but its use in children less than five years of age can increase risk of thyroid cancer; retrobulbar irradiation is also contraindicated due to risk of malignancy in children. Thyroidectomy can generally improve ocular symptoms. Ocular manifestations typically resolve once a euthyroid state is established. With antithyroid treatment, 46.1-56.6% of Asian children are able to achieve remission, compared to 12-33% of children in other studies. Corticosteroids, somatostatin analogs, and immunomodulatory therapy may be necessary if symptoms do not improve even in the presence of a euthyroid state. The majority of patients in our study were treated with an antithyroid drug, while 33 underwent thyroidectomy, and two patients, ages 8 and 11, were treated with radioactive iodine.

Conclusion

Compared to the adult disease course, pediatric TED demonstrates much more benign manifestations, and restrictive strabismic patterns and optoclonal nerve dysfunction are much less common in pediatric TED than it is in adult TED. The most prevalent findings in our study of 11 children with pediatric TED were lower scleral show, mild to moderate ocular surface disturbances, and a small degree of proptosis. Symptoms of ocular exposure in children are amenable to lubrication and conservative medical measures. Treatment plans of most children in our study included antithyroid therapy. Children’s symptoms tend to regress after an adequate thyroid status is achieved.

References