Case Report

Ocular Myasthenia Gravis and Auto-Immune Thyroiditis in Children

Kitthisak Kitthaweesin MD*,
Narong Auvichayapat MD**, Ouyporn Panamonta MD**

** Department of Ophthalmology, Faculty of Medicine, Khon Kaen University, Khon Kaen*
*** Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen*

A 7-year-old girl presented at a university hospital with ptosis of the left eye. This resolved spontaneously within 4 weeks but then the right eye became similarly affected but responded to prostigmine. Left hypertropia with restriction of the right inferior rectus, mild exophthalmos, non-tender diffuse enlargement of the thyroid, normal thyroid function tests, anti-thyroglobulin, and anti-microsomal antibodies indicated an association of autoimmune thyroiditis and ocular myasthenia. The ptosis was remedied with pyridostigmine and short-course oral prednisolone, but the hypertropia persisted.

Keywords: *Pediatric myasthenia gravis, Autoimmune, Thyroiditis, Prostigmine*

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Myasthenia gravis in children, as in adults, is caused from an idiopathic production of acetylcholine receptor antibodies[1]. Eyelid abnormalities, including ptosis, fatigability and weakness of eyelid closure, are the most prominent neuro-ophthalmic signs. Pupil-sparing, ophthalmoparesis in any pattern, may also occur[2]. An association of myasthenia gravis and autoimmune thyroiditis has been reported in adults[3-10], but rarely in children[11].

Case Report

A 7-year-old girl presented to a university hospital with a 4-month history of drooping left upper eyelid. She denied having any diplopia. Her parents noted her ptosis usually worsened by the afternoon. The child was normal during the prenatal period and developed normally after birth. When the authors first saw her, she was 124 cm tall and weighed 37.7 kg. The ocular examination revealed left upper lid ptosis with impaired function of left levator superioris muscle, 1-mm margin-reflex distance (4-mm on the right eye), good Bell's phenomenon, and left hypertropia. Her ocular motility was normal, except elevation of the right eye, during the duction and version tests. Except for the mild exophthalmos of the right eye, magnetic resonance imaging of the orbits was normal.

Four weeks hence, the left upper lid ptosis improved spontaneously, but the child developed ptosis on the right side. Vertical diplopia in primary gaze was noted and she tried to turn her head to the left to compensate. Her parents complained that she was gaining too much weight and of a neck mass. At this point, she was 125 cm tall and weighed 41.2 kg. A physical examination revealed normal vital signs, non-tender diffuse enlargement of the thyroid, right upper eyelid ptosis, with impaired function of the right levator superioris muscle, 1-mm margin-reflex distance (4-mm on the left eye), and good Bell's phenomenon. The child had left hypertropia, which was pronounced on the left gaze and leftward head tilt. Ocular motility was again normal, except for elevation of the right eye, during the duction and version tests. Restriction of the right inferior rectus was detected with the forced duction test. Mild exophthalmos of the right eye was noted. Anterior and posterior segments of both eyes were normal. No other neurological deficits were detected. The ptosis improved but an abnormal ocular motility persisted after the prostigmine test.

Correspondence to: Kitthaweesin K, Department of Ophthalmology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand. Phone: 0-4334-8383, Fax: 0-4334-8383, E-mail: Kitthisak@hotmail.com

Thyroid function tests were normal but 1:1,600 serum titers of anti-thyroglobulin, and anti-microsomal antibodies were detected.

This patient was initially treated with oral pyridostigmine 60 mg tid. Since a residual ptosis persisted, the authors prescribed 60 mg pyridostigmine tid and 1 mg of prednisolone/kg/day. The ptosis resolved without any adverse reaction and the prednisolone was tapered off within 2 weeks. At the 12-month follow-up, the child was still on 60 mg of pyridostigmine tid without recurrence. The abnormal head position to compensate for the vertical diplopia caused by the restricted right inferior rectus persisted. Orthophoria and good binocular vision were achieved with this head position and the parents declined strabismus surgery.

Discussion

The presented patient had ptosis, which fluctuated with time and improved after the prostigmine test, signifying ocular myasthenia gravis. However, the incomitant hypertropia did not improve with the test and showed restriction during the forced duction test. The patient had mild exophthalmos and non-tender diffuse enlargement of the thyroid. The thyroid function tests were normal, though positive for anti-thyroglobulin and anti-microsomal antibodies, suggesting an association with autoimmune thyroiditis.

Myasthenia gravis has been associated with other autoimmune disorders such as: scleroderma[3], primary biliary cirrhosis[4], pernicious anemia[7,9], insulin dependent diabetes mellitus[9], polymyositis[11], Graves' disease[10], and autoimmune or Hashimoto's thyroiditis[3-11]. A common cell-mediated immune disorder has been postulated[4].

Autoimmune thyroiditis, the most common cause of thyroid disease in children and adolescents, is diagnosed by diffuse thyroid enlargement and the presence of anti-thyroglobulin and anti-microsomal antibodies[7]. This disorder is more common in girls, particularly after 6 years of age. The most common clinical manifestations are growth retardation and non-tender diffusely enlarged goiter with attendant hypothyroidism. Most affected children are clinically euthyroid and asymptomatic, but a small number may show hyperthyroidism. Some of the clinically euthyroid children may have laboratory evidence of hypothyroidism. A long-term follow-up of the thyroid function test was necessary for the presented patient, even though she was clinically and laboratory euthyroid.

Autoimmune thyroiditis and myasthenia gravis can be considered pathogenetically related because both cause abnormal T-lymphocyte function, so the autoimmune response is directed against cell membrane receptors[10]. Cross-reactivity seems to be a property of pathological autoantibodies[12]. Occasionally, auto-immune thyroiditis may coexist with Graves' disease[13-14]: however, ophthalmopathy may occur without evidence of Graves'.

Diplopia without obvious exophthalmos, caused by infiltrative endocrine ophthalmopathy, has been reported in patients with clinically and laboratory confirmed autoimmune thyroid disease. Vertical diplopia is the most common manifestation of the disorder: this is caused by hypotropia secondary to restrictive tightening of the inferior rectus muscle[15]. The presented patient stared with the right eye, and this secondary deviation made the left hypertropia more prominent.

The association of ocular myasthenia gravis and autoimmune thyroiditis in children was reported by Tsao et al[11]. They reported that their pediatric patient, like an adult, developed generalized myasthenia gravis within two years. The authors, therefore, intend to follow-up the patient for two years.

Pyridostigmine is the first-line therapy in pediatric ocular myasthenia, but just as in adults, the results are often unsatisfactory. Oral corticosteroids have been suggested as an additional control, but the long-term effects of corticosteroids on bone growth must be kept in mind.

The presented patient represented a good candidate for various associated autoimmune diseases, including autoimmune thyroiditis in children with myasthenia gravis. The forced duction test was the best tool to differentiate between a restrictive vs. a paralytic cause of the incomitant strabismus.

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References

1. Fenichel GM. Myasthenia gravis. Pediatr Ann 1989; 18: 432-8.
2. Schmidt D. Signs in ocular myasthenia and pseudomyasthenia. Differential diagnostic criteria. A clinical review. Neuro-ophthalmology 1995; 15: 21-58.
3. Werneck AL, Checcacci-Balod T, Tuma G. Scleroderma, thyroiditis, and myasthenia gravis: study of a case. Arq Neuropsiquiatr 1993; 51: 549-53

4. Rajaraman S, Deodhar SD, Carey WD, Salanga VD. Hashimoto's thyroiditis, primary biliary cirrhosis, and myasthenia gravis. Am J Clin Pathol 1980; 74: 831-4.
5. Osher RH, Smith JL. Ocular myasthenia gravis and Hashimoto's thyroiditis. Am J Ophthalmol 1975; 79: 1038-43.
6. Nishida H, Tanaka Y, Nakao N, Ibi T, Sahashi K. A case of myasthenia gravis following sarcoidosis and Hashimoto's thyroiditis. Rinsho Shinkeigaku 2000; 40: 797-800.
7. Krol TC. Myasthenia gravis, pernicious anemia, and Hashimoto's thyroiditis. Arch Neurol 1979; 36: 594-5.
8. Hashimoto A, Hanada M, Okada S, Aoki N. A case report of myasthenia gravis associated with Hashimoto's thyroiditis. Folia Psychiatr Neurol Jpn 1981; 35: 521-5.
9. Green ST, Ng JP, Chan-Lam D. Insulin-dependent diabetes mellitus, myasthenia gravis, pernicious anaemia, autoimmune thyroiditis and autoimmune adrenalitis in a single patient. Scott Med J 1988; 33: 213-4.
10. Czernobilsky H, Ziegler R. Graves' ophthalmopathy, ocular myasthenia gravis and Hashimoto's thyroiditis. Isr J Med Sci 1985; 21: 377-80.
11. Tsao CY, Mendell JR, Lo WD, Luquette M, Rennebohm R. Myasthenia gravis and associated autoimmune diseases in children. J Child Neuro 2000; 15: 767-9.
12. Mappouras DG, Philippou G, Haralambous S, Tzartos SJ, Balafas A, Souvatzoglou A, et al. Antibodies to acetylcholinesterase cross-reacting with thyroglobulin in myasthenia gravis and Graves' disease. Clin Exp Immunol 1995; 100: 336-43.
13. Leovey A, Bako G, Sztojka I, Bordan L, Szabo T, Kalman K, et al. The pathogenetic connection between Graves' disease and chronic lymphocytic thyroiditis. (The role and incidence of thyroid stimulating antibodies). Acta Med Acad Sci Hung 1982; 39: 1-6.
14. Bartley GB. The epidemiologic characteristics and clinical course of ophthalmopathy associated with autoimmune thyroid disease in Olmsted County, Minnesota. Trans Am Ophthalmol Soc 1994; 92: 477-588.
15. Appen RE, Wendelborn D, Nolten WE. Diplopia in autoimmune thyroid disease. Arch Intern Med 1982; 142: 898-901.

โรค myasthenia ทางตาและโรคต่อมไทรอยด์อักเสบชนิด autoimmune ในเด็ก: รายงานผู้ป่วย

กิตติศักดิ์ กิจทวีสิน, ณรงค์ เอื้อวิชญาแพทย์, อวยพร ปะณะมณฑา

ผู้ป่วยเด็กหญิงไทยมาด้วยอาการหนังตาซ้ายตกและเปลี่ยนเป็นหนังตาขวาตกภายใน 4 สัปดาห์ ตรวจพบตาซ้ายลอยขึ้นและมีพังผืดของกล้ามเนื้อ inferior rectus ของตาขวา อาการหนังตาตกตอบสนองต่อยา prostigmine ตาขวาโปนเล็กน้อย ต่อมไทรอยด์มีขนาดโตขึ้นเล็กน้อย โดยการทำงานอยู่ในเกณฑ์ปกติ แต่ตรวจพบ anti-thyroglobulin และ anti-microsomal antibodies บ่งชี้การเกิดร่วมระหว่างโรคไทรอยด์อักเสบชนิด autoimmune และโรค myasthenia ทางตา อาการหนังตาตกดีขึ้นด้วยยา pyridostigmine และยา prednisolone ระยะสั้น แต่อาการตาเขยังคงอยู่