UNILATERAL OPHTHALMOPATHY AFTER RADIOIODINE ABLATION IN A PATIENT WITH WELL-DIFFERENTIATED PAPILLARY THYROID CARCINOMA COEXISTENT WITH HASHIMOTO'S THYROIDITIS: A CASE REPORT.

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Thyroid-associated ophthalmopathy (TAO) is an inflammatory orbital disease of autoimmune origin. The most common cause of TAO is Graves' disease, but it may also arise in other conditions, eg. Hashimoto's thyroiditis or thyroid carcinoma. We present a case of the patient with well-differentiated papillary thyroid carcinoma coexisting with Hashimoto's thyroiditis who developed left eye proptosis and left eyelid retraction 2 months after post-operative radioiodine ablation. Laboratory findings showed a high serum thyroglobulin antibody titer and elevated FT4 from thyroxine suppressive therapy. No iodine uptake at the orbital region was detected. After reduction of the thyroxine dose and a short course of oral corticosteroid, the patient's eye problems improved and the thyroglobulin antibody titer also decreased. An association between the therapy given in this case and ophthalmopathy on pre-disposing Hashimoto's thyroiditis cannot be excluded.

Key words; thyroid carcinoma, ophthalmopathy, Hashimoto's thyroiditis, radioiodine ablation, I-131

INTRODUCTION

Thyroid-associated ophthalmopathy (TAO) is an inflammatory orbital disease of autoimmune origin with the potential to cause severe functional and psychosocial effects. Pathogenesis of the disease is not yet fully understood. TAO has a variable clinical presentation; it may cause severe damage to vision and orbital architecture.[1] The most common associated cause of TAO is Graves' disease, which is far more commonly associated with TAO than other diseases, including Hashimoto's thyroiditis[2,3] or thyroid carcinoma.[4] Correlation between Hashimoto's thyroiditis and well -differentiated thyroid carcinoma has been reported, in approximately 23.8% -26.7% of cases.[5,6]

In the present report, we describe a case of the woman with well-differentiated papillary thyroid carcinoma coexisting with Hashimoto's thyroiditis who developed thyroid-associated ophthalmopathy after a single low dose of radioiodine ablation. To our knowledge, there is only one report in the literature on TAO after radioiodine treatment in a patient with disseminated thyroid carcinoma[7] but there is no report on TAO in patient with differentiated thyroid carcinoma coexistent with Hashimoto's thyroiditis.

CASE REPORT

A 40-years-old Thai woman had a asymptomatic neck mass of 3 cm. for 4 months. FNA of the nodule was suspicious for malignancy and her blood

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test showed normal thyroid hormones level. She underwent a near total thyroidectomy. The histopathology reported a 2 cm papillary carcinoma on the left lobe and another of 3 mm on the right lobe. Hashimoto's thyroiditis was also detected in the rest of both lobes. She was referred to our division 1 month after the operation. The physical examination, including the eyes, revealed no abnormalities. A chest radiograph was normal. The results of the screening tests are shown in Table 1, showing elevated titer of antibody against thyroglobulin in serum (ATg ; Serodia ®-ATG, Fujirebio inc., Chuo-ku, Tokyo, Japan; positive control 1:1,600). Thyroid ablation was done with radioiodine (I-131 30 mCi). A whole body scan 1 week later showed uptake at the thyroid bed only. Thyroxine 200 μg. daily was given (body weight of 52 kg).

Approximately 2.5 months later, she experienced discomfort in her left eye. An eye examination revealed left eye proptosis, left upper eyelid retraction and periorbital swelling. There was full movement of the extraocular muscles. She had no complaint of any abnormal vision. A thyroid function test approximately 3 hours after taking thyroxine showed slightly elevated FT4 and suppressed TSH (FT4 = 1.88 ng/dl, TSH = 0.02 mIU/mL). A CT scan of the orbit was refused. The thyroxine dose was reduced to 200 μg/day, six days per week for a short period, and oral prednisolone was started at 60 mg/day, tapered off over 6 weeks. Three months later, her left ophthalmopathy had partially improved and the serum thyroglobulin antibody titer had also decreased to 1:320. At the present date (June 2006), her I-131 whole body scan study and serum thyroglobulin level are all negative. The serum thyroglobulin antibody are stable at 1:320 during 1 year follow up. Her ophthalmopathy has further improved after we increased thyroxine back to the previous dose. (Figures 1-4)

Table 1 Serial laboratory findings on serum in a patient with Hashimoto's thyroiditis coexistent with differentiated papillary thyroid carcinoma

Month/Year	**Tg, ng/ml** (2.7-21)	**Anti-Tg**	**TSH, mIU/mL** (0.25-4)	**FT4, ng/dl** (0.7-1.75)	**Remarks**
10/2004	0.24	1:1,280	42.45	-	1st ablation
1/2005	-	-	0.02	1.88	Ophthalmopathy
4/2005	-	1:320	>100	-	WBS post 1st ablation Partially improved ophthalmopathy
4/2006	<0.1	1:320	>100	-	WBS post 2nd ablation Stable eye symptoms
6/2006	-	-	0.299	2.06	Obviously improved ophthalmopathy

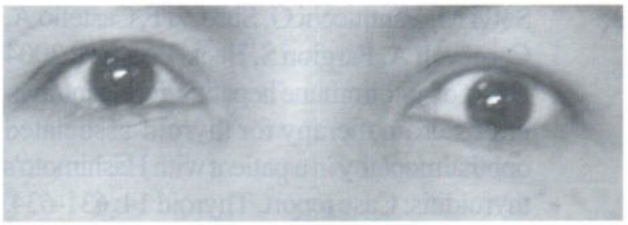

Fig.1

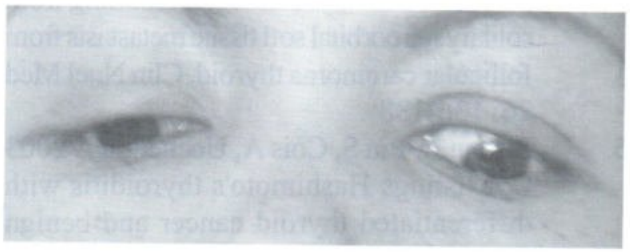

Fig.2

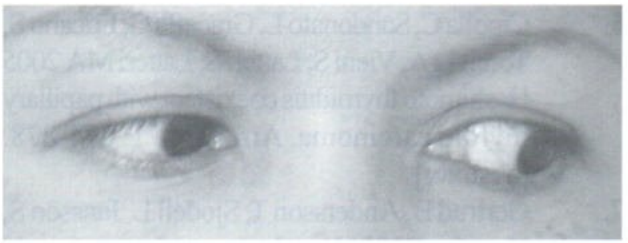

Fig.3

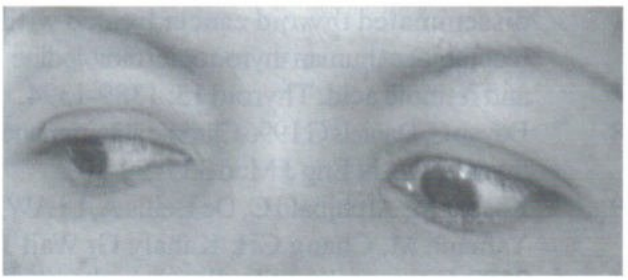

Fig.4

Fig.1-4 (see attached files) Photos of the same patient in April 2006 (1 year 2 months after oral prednisolone treatment) showing upper eyelid retraction, mild periorbital swelling and mild proptosis on the left eye. The motility of the eye muscles and vision are normal.

DISCUSSION

Thyroid-associated ophthalmopathy (TAO) is an autoimmune ophthalmopathy, closely related to autoimmune thyroid disorder, in which the ocular muscles and the retro-ocular fat and connective tissue are the putative targets of immune reactions.[3] It is the most frequent cause of unilateral or bilateral proptosis in adults.[1] Most cases of TAO are associated with Graves' ophthalmopathy. It may also arise from other causes including Hashimoto's thyroiditis[2,3] and thyroid carcinoma,[4] but these are extremely rare. Other non-thyroidal diseases which can cause proptosis, eg. neoplasm proptosis, orbital pseudotumor or abscess, have also been reported.

Hashimoto's thyroiditis and Graves' disease are autoimmune thyroid diseases (AIDs) that are generally thought to be discrete clinical entities with different outcomes. It has been suggested that they may share the same pathogenic mechanism.[8] The finding of ophthalmopathy in patients who appear to have Hashimoto's hypothyroidism support this concept.[2,3]

Although TAO can occur in patients with Hashimoto's thyroiditis, such an occurrence is far less common than in patients with Graves disease. Kaspar et al.[9] studied prevalences of serum antibodies against eye muscle antigens in patients with TAO, Graves' hyperthyroidism and Hashimoto's thyroiditis. He found these patients had significant levels of anti-G2 antibodies compared to normal subjects and multinodular goiter patients ($p<0.05$). This may explain in part the occurrence of TAO in patients with Graves' disease and Hashimoto's thyroiditis.

A previous report by Basu et al. in 2001[4] described a case who presented with unilateral proptosis with thyrotoxicosis resulting from solitary orbital soft tissue metastasis from follicular thyroid carcinoma. The diagnosis was made by CT scan and radioiodine uptake in the orbital area. In our patient, there was no evidence supporting such metastasis, although the patient did not wish a CT scan which could have confirmed this.

To our knowledge, there is only one report describing ophthalmopathy after radioiodine treatment of a thyrodectomized patient with thyroid cancer.[7]

Radioiodine treatment has previously been shown to be associated with development of TAO in various thyroid disorders including Graves' disease and toxic multinodular goiter.[10] This effect of radiation may be related to an effect on T-cell populations, as activated T-cells have been shown to appear in the circulation after radioiodine treatment. This activation and enhanced contrasuppressor activity may in part be responsible for the rise in autoantibodies after radioiodine, which may also contribute to the worsening of ophthalmopathy.[11]

Coexisting Hashimoto's thyroiditis with differentiated thyroid carcinoma can be found in up to 26.7% of the thyroid carcinoma patients.[6] To the best of our knowledge, there has been no report prior to this one describing the development of ophthalmopathy following radioiodine treatment in patients who have both coexisting conditions. This case appears unique in that context. However, the appearance of ophthalmopathy only a few months after treatment is a remarkable finding, which may not be coincidental. Radioiodine itself can aggravate ophthalmopathy in underlying thyroid disorders, especially in patients such as this one with a tendency to some autoimmune activity. Early detection and treatment can be aided by an earlier follow up period after the radioiodine treatment. We hope that this case will be useful for other clinicians treating thyroid carcinoma patients.

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