

# Surgery for Hyperthyroidism in Down Syndrome:

## Case Report

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### Abstract

Thyroid disorders are common in patients with Down syndrome (DS). In these patients, hyperthyroidism occurs much less frequently than hypothyroidism, but it is likely to be underestimated. We report a case of an adult man with DS and hyperthyroidism. After 2 years of antithyroid therapy in a special facility, he was referred to our center with recurrence of hyperthyroidism with leukopenia and elevations of liver enzymes 14 months after remission. The patient underwent subtotal thyroidectomy, with rapid preparation with inorganic iodine and prednisone. After thyroidectomy the patient was found to have hypothyroidism and was given thyroid replacement therapy. We also review the literature on the treatment options for hyperthyroidism with DS. We conclude that the role of surgery in the treatment of hyperthyroid patients with DS has yet to be defined.

**Key Words:** Hyperthyroidism, Down syndrome, surgery.

### Introduction

THYROID DISORDERS OCCUR with increased frequency in patients with Down syndrome (DS). The overall incidence of thyroid dysfunction ranges from 7% (1) to more than 50% (2), depending on the sample size, the selected population, and the criteria for diagnosis. The etiology of most acquired thyroid disorders in DS is believed to be an autoimmune disturbance.

Hyperthyroidism occurs much less frequently than does hypothyroidism among individuals with DS (3). A community-based study of 138 individuals with DS found 28 to be hypothyroid and 2 to be hyperthyroid (4). Hyperthyroidism associated with DS usually occurs as a result of diffuse enlargement of the thyroid gland (Graves' disease).

All guidelines recommend yearly screening for thyroid disease, since the frequency increases with age and is reported to be greater than 15% in individuals with DS (5).

Graves' disease definitely requires treatment. Treatment options for hyperthyroidism are surgery, medical treatment, and radioactive iodine therapy.

### Case Report

The patient was a 43-year-old Turkish man. Developmental retardation had been noted at the age of 6 months, and the diagnosis of DS was made. Chromosomal analysis revealed a regular trisomy-21-karyotype (47,XY,+21). He has been followed by personnel at a special rehabilitation center since the age of 13 years.

The case history begins in November 2001, when a physician in a specialized medical facility noted that the patient had a diffuse vascular goiter. Physical examination revealed sinus tachycardia, excessive sweating, and warm hands with fine tremors, but there was no evidence of Graves' ophthalmopathy. Thyroid studies were consistent with hyperthyroidism. A thyroid scan showed enlargement of both lobes. There were no available data for TSH receptor antibody and thyroid <sup>131</sup>I uptake. Antithyroglobulin antibody was increased; antithyroid peroxidase antibody was normal. The physician started antithyroid medication and followed the patient with tests for periodic liver enzymes and whole blood count. In March 2003, re-

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Accepted for publication July 2005.

mission was achieved. In May 2003, recurrence of hyperthyroidism was diagnosed, and after a short time during which there was an elevation of liver enzymes and leukopenia was diagnosed, Propylcil® (propylthiouracil) was started again. (This is not advisable, since further exposure to the drug may cause hepatitis and further decrease of the low neutrophil count.) The patient also had a history of diabetes mellitus, which for 5 years had been controlled by diet and oral antidiabetics.

The patient was referred to our clinic in November 2003. He had a fever (38.3°C) and his thyroid gland was large, diffuse, and palpable. Splenomegaly and corneal opacities were observed during physical examination. His blood pressure was 110/70 mm Hg, and his pulse rate was 76 beats per minute. His weight was 86 kg and his height was 179 cm. Sedimentation rate and C-reactive protein were within the normal range. Results of thyroid function tests were total T<sub>4</sub>: 29.2 µg/dL; total T<sub>3</sub>: 5.3 ng/mL; and sTSH: 0.01 IU/mL.

Laboratory analyses revealed the following levels: alanine aminotransferase, 112 U/L; aspartate aminotransferase, 64 U/L; glutamyl transpeptidase, 67 U/L; alkaline phosphatase, 310 U/L; white blood cell count, 2,000/mm<sup>3</sup> (normal: 4,500–11,000/mm<sup>3</sup>); neutrophil count, 1,200/mm<sup>3</sup> (2,000–7,800/mm<sup>3</sup>); thrombocyte count, 41,000/mm<sup>3</sup> (150,000–400,000/mm<sup>3</sup>); zinc, 81 µg/dL (range, 70–150 µg/dL); folic acid, 11.3 ng/mL (range, 3–17 ng/mL); and vitamin B12, 199 pg/mL (157–1059 pg/mL). (Patient was on vitamin B12 replacement therapy.) In addition, his hepatitis B antigen was positive. Patient's low neutrophil and thrombocyte count may have been related to his liver disease, antithyroid drug therapy, and thyrotoxic status.

A thyroid ultrasound revealed no nodularity. Blood and urinary cultures were negative. The thyroid <sup>131</sup>I uptake was 19.9% (normal: 6–18%) after 4 hours and 67% (normal: 10–30%) after 24 hours. TSH receptor antibody, antithyroid peroxidase, and antithyroglobulin levels were within normal limits.

A bone marrow biopsy revealed normocellular bone marrow, a liver biopsy revealed chronic hepatitis B (precirrhotic liver), and an endoscopic biopsy revealed chronic atrophic gastritis. Tests for anti-islet and anti-GAD antibodies were negative.

Due to the late effect of radioactive iodine (RAI) therapy, we did not consider this modality as a first-line measure. The patient was prepared for surgery in 10 days, with a regimen of prednisone (30 mg/day) and inorganic iodine (3 times a day) (6). In addition, propranolol was given in a dose of 120 mg daily to relieve associated symptoms such

as palpitation. Because of the patient's severe degree of mental retardation (IQ 35), his brother signed the consent form for the treatment. The patient underwent a subtotal thyroidectomy 1 week later, with no adverse events. A diffuse enlarged gland and hyperplasia were found on histopathology.

When thyroid function was assessed 1 month postoperatively, a profile of definite hypothyroidism was noted. It was decided that the patient needed thyroid replacement therapy with L-thyroxine, and this was started. The dose of L-thyroxine was then adjusted according to the thyroid function, until a replacement daily level was reached. Thyroid function was checked every 6 months thereafter, and the patient continued to require thyroxine replacement (100 µg/day). The patient's liver enzymes and white blood cell count have returned to normal values during follow-up (after 2 months).

## Discussion

Hyperthyroidism in patients with DS is an uncommon condition (1, 3–5). The symptoms of hyperthyroidism may be missed in patients with mental retardation. Because of this, routine thyroid function testing must be done for patients with DS.

Once the diagnosis of Graves' disease has been made, an appropriate treatment modality must be selected, depending on the presence of associated medical conditions.

There is a lack of consensus on the role of thyroidectomy in the treatment of Graves' disease. Surgical intervention involves partial thyroidectomy, but this is rarely undertaken in patients with DS. Also, no real data are available about thyroid surgery for patients with DS and Graves' disease. Aberrant craniofacial features frequently seen in individuals with DS include short neck, prominent (macroglossia) furrowed tongue, midfacial and mild mandibular hypoplasia, and general muscle hypotonia (7). These craniofacial anomalies of patients with DS lead to a higher incidence of obstructive airway problems, such as difficulties during anesthetic induction and emergence. The three most frequent anesthesia-related complications among patients with DS are bradycardia, natural airway obstruction, and postintubation stridor (7). Also, these patients, because of their short necks, may present a surgical risk for thyroidectomy. A smaller diameter endotracheal tube for intubation was used in our patient.

For our patient, surgery was the therapy of choice for recurrence of hyperthyroidism, because of concomitant leukopenia and liver enzyme elevation. It is not advisable to give Propylcil again

after leukopenia and liver enzyme elevation. RAI was not a choice because of the late effect of this therapy modality. Successful surgery tends to terminate the thyrotoxic state within a few days, and the prompt effect of surgery may indeed be particularly desirable for these patients (8).

Hyperthyroidism in DS is generally treated with carbimazole, propylthiouracil or radioactive iodine (9, 10). Most of the cases in the literature treated with RAI achieved remission (11,12). However, there may be contraindications for the use of antithyroid medication. For patients in whom its use is contraindicated, surgery with rapid preparation may be considered. The practice of surgery for hyperthyroid children with DS is debatable.

### Conclusions

Hyperthyroidism is an uncommon condition in patients with DS, but one that is likely to be underdiagnosed and underreported. There is no consensus in the DS literature on the role of surgery. However, for some patients with hyperthyroidism and DS, surgery may be the preferred treatment modality.

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