Hyperthyroidism after Hypothyroidism

The Broad Spectrum of Autoimmune Thyroid Disease

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Graves' disease, primary hypothyroidism, and Hashimoto's thyroiditis are all relatively prevalent clinical syndromes. It is proper to consider these three disorders as closely related autoimmune diseases.[1] Pathological coincidence of Graves' disease and Hashimoto's thyroiditis has been reported,[2] and thyroid-stimulating hormone (TSH) receptor antibodies and antimicrosomal and antithyroglobulin antibodies can occur in both.[3] Clinical presentations of Graves' disease and Hashimoto's thyroiditis can be quite similar, as can Hashimoto's thyroiditis and primary hypothyroidism. Graves' disease presenting as hypothyroidism has also been described, although more rarely.[4]

Described here is a case of Graves' disease that presented as primary hypothyroidism.

CASE REPORT

A 58-year old woman was seen in August 1987, complaining of puffiness of her eyes, 15-lb weight gain, mild fatigue, and some brittleness of her fingernails. There was no history of thyroid disease, neck irradiation, iodine exposure, change in diet, or family history of thyroid disease. Mild periorbital edema was present with no exophthalmous, pretibial myxedema, or goiter. Thyroxine (T_4) was 32.17 nmol/L (2.5 μg/dL, normal 5 to 11.5 μg/dL), triiodothyronine resin uptake (T_3U) was 0.216 (21.6%, normal 25% to 35%), and TSH was 18.6 mU/L (18.6 μIU/L, normal 0.5 to 5 μU/mL). Antithyroglobulin antibodies were absent (Table 1).

The patient was started on L-thyroxin 0.2 mg daily and seen 6 weeks later. At that time she continued to feel fatigued but was less puffy. Her T_4 level was 271.56 nmol/L (21.1 μg/dL), T_3U was 0.436 (43.6%), and TSH was 0.1 mU/L (0.1 μU/mL) (Table 1). She was advised to decrease her L-thyroxin dose from 0.2 mg to 0.15 mg/d.

Because of her continuing concern about eye puffiness, the patient saw an ophthalmologist in November. Ultrasonography demonstrated moderate, generalized enlargement of the extraocular muscles in both orbits with normal exophthalmometry. These findings were felt to be compatible with Graves' disease.

In January 1988 she complained of proximal muscle weakness, tremor, poor hair growth, mild diarrhea, and feeling warm much of the time. On examination, a small goiter without nodules was palpated. Her pulse was 96/min and bounding. Her skin was very moist and warm, and a fine tremor at rest was present. She could not do one deep knee bend. No pretibial changes and no exophthalmous was present. T_4 was 213.64 nmol/L (16.6 μg/dL), T_3U was 0.39 (39%), TSH was 0.3 mU/L (0.3 μU/mL), T_3 by radioimmunoassay (RIA) was 5.47 nmol/L (356 ng/dL, normal 70 to 190 ng/dL) antithyroglobulin and antithyroid microsomal antibodies were slightly increased (1:80 and 1:100 respectively). L-thyroxin was stopped, and 1 month later T_4 was 205.92 nmol/L (16 μg/dL), T_3U was 0.407 (40.7%), T_3 by RIA was 5.47 nmol/L (356 ng/dL), and TSH was 0.3 mU/L (0.3 μU/mL). TSH receptor antibodies were elevated (53% inhibited, normal 0% to 10%). Thyroid uptake showed a 24-hour value of 87% (normal 5% to 30%), homogeneous in nature, consistent with Graves' disease (Table 1).

The patient was begun on propylthiouracil and propranolol (discontinued after 5 weeks). Over a 2-month period she became clinically euthyroid. Her strength improved, tremor and diarrhea decreased, pulse normalized, and goiter decreased in size. T_4 was 41.18 nmol/L (3.2 μg/dL) and T_3U was 0.34 (34%) (Table 1). Her dosage of propylthiouracil was lowered; she continues to be followed.

DISCUSSION

Thyrotoxicosis following hypothyroidism is a rare clinical event. McDermott et al[3] in 1986 found 21 cases in which

Submitted, revised, October 3, 1989.

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TABLE 1. LABORATORY VALUES FROM AUGUST 1987 TO APRIL 1988

Test	1987		1988		
	August	October	January	February	April
Thyroxine (T_4) (nmol/L)	32.17	271.56	213.64	205.92	41.18
Triiodothyronine resin uptake (T_3U)	0.216	0.436	0.39	0.407	0.34
Thyroid-stimulating hormone (TSH) (mU/L)	18.6	0.1	0.3	0.3	
Antithyroglobulin antibodies (ATA)	Absent		1:100		

primary autoimmune or idiopathic hypothyroidism was followed by the development of hyperthyroidism. Japanese workers[4] found 27 cases. The average interval from the diagnosis of hypothyroidism to the onset of hyperthyroidism was 3.4 years in the McDermott et al series with a range of 2 months to 11 years. Infiltrative ophthalmopathy during the hypothyroid stage was seen in seven patients. Histologic findings during the hypothyroid phase have been poorly documented.[5]

Speculation regarding the pathogenesis of this sequence of events centers around the nature of TSH receptor antibody(ies). This set of immunoglobulins is directed at varying sites within the thyroid cell membrane.[6] Some are capable of stimulating adenylate cyclase, resulting in cyclic adenosine monophosphate (cAMP) generation and autonomous thyroid hormone production.[3] Others seem to displace TSH and block the TSH receptor, but are themselves incapable of stimulating cAMP production.[3] Still other antibodies appear to cause only thyroid growth and goiter formation.[3] Clinical presentation may vary, depending upon the status of a patient's immune function at any given point. The development of hypothyroidism spontaneously in or after treatment of Graves' disease[7] and the recurrence of hyperthyroidism after hypothyroidism has been produced by partial thyroidectomy or radioactive iodine treatment of Graves' disease[8–10] support this idea. Kasagi et al[4] reported a case similar to the one presented here, in which they assessed sequential changes in TSH receptor antibody function between the hypothyroid and hyperthyroid phases. They postulated initial glandular hypofunction to be due to autoimmune damage and also documented lymphocytic infiltration on needle biopsy. Later emergence of hyperthyroidism was attributed to either change in antibody type or altered intrathyroidal responsiveness.

Interestingly, the present case also illustrates a possible continuum between Graves' disease and Hashimoto's disease. Either disease can present as hyperthyroidism, euthyroid goiter, or primary hypothyroidism.[3] Ophthalmopathy, acropachy, and pretibial myxedema, although typically seen in Graves' disease, may occur in Hashimoto's thyroiditis as well.[3] There are reports of monozygotic twins in which one disease developed in one twin concomitant with the other disease in the other.[3] Although the present case appears more likely to be Graves' disease, with positive TSH receptor antibody, increased thyroid uptake, and ophthalmopathic findings, the development of thyroid antimicrosomal and antithyroglobulin antibodies (usually associated with Hashimoto's) gives credence to the idea that Hashimoto's thyroiditis and Graves' disease may be representatives of the spectrum of one disease process.[3]

This case serves to illustrate that autoimmune thyroid disease may cross classical disease boundaries and present atypically.

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