Development of Graves’ disease after subacute thyroiditis: two unusual cases

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Subacute thyroiditis is generally caused by viral infection (1). Although spontaneous recovery within a few weeks or months is general, the final outcome of subacute thyroiditis is unpredictable in some patients (2). For instance, hyperthyroidism and chronic thyroiditis may develop (1). To date, there have been only four reports of patients with subacute thyroiditis developing hyperthyroidism within one year (3–6). In this report, we describe two unusual cases of subacute thyroiditis from which hyperthyroidism developed seven to eight years after complete recovery from subacute thyroiditis.

Case report

Case 1: A 45-year-old woman was first seen in April 1981 complaining of neck mass with tenderness. The right lobe of the thyroid gland was enlarged and firm with tenderness. The erythrocyte sedimentation rate was 70 mm/h. Her serum T4 and TSH levels were 261.3 nmol/l (normal: 57.9–173.7 nmol/l) and less than 1.5 mU/l (normal: < 5 mU/l), respectively; serum antimicrosomal (Mi-ab) and anti-thyroglobulin antibodies (Tg-ab) were negative. The thyroid radiiodine uptake was 1.3% at 24 h (normal: 10–40%). She was diagnosed to have subacute thyroiditis and was treated with betamethasone. Three weeks after the treatment her symptoms subsided and thyroid hormone levels returned to normal. Her goiter also disappeared two months later. This patient was seen again seven years after the first visit with chief complaints of palpitation and fatigue of three months’ duration. At this time, a diffuse goiter with estimated size of 40 g was palpable; there was no tenderness over the gland. Her serum T4 level was greater than 308.9 nmol/l and the serum TSH level was suppressed to less than 0.05 mU/l (normal: 0.3–4.0 mU/l). Thyroid radiiodine uptake at 24 h was increased to 62.7%. Serum Tg-ab were negative but Mi-ab were strongly positive (23 × 105). The serum TSH-binding inhibitory immunoglobulin (TBI) was 46.7% (normal: < 15%) and thyroid stimulating antibody (TSAb) 1245% (normal: < 140%). HLA typing indicated A24 (9); B35, BW46; CW11; DRW8. A diagnosis of hyperthyroidism was made and she was started on methimazole therapy.

Case 2: A 60-year-old woman was first seen in September 1977 because of pain in the thyroid gland of three weeks’ duration. Both lobes were enlarged with tenderness. Erythrocyte sedimentation rate was 127 mm/h. T3 resin uptake was 57.4% (normal: 23–39%) and serum protein-bound iodine was 80 µg/l (normal: 35–80 µg/l). Thyroid radiiodine uptake at 24 h was 1.2%. Serum Mi-ab and Tg-ab were negative. She was diagnosed as having subacute thyroiditis and treated with betamethasone. Her symptoms subsided rapidly and the thyroid functions returned to normal within one month of treatment. The patient was seen again eight years after the first visit because of a diffusely enlarged goiter. The ultrasound study demonstrated a small cystic lesion in the right upper lobe of her thyroid gland. Her serum T4 and T3 levels were 56.6 nmol/l and 1.51 mU/l, respectively; thyroid radiiodine uptake at 24 h was elevated to 52.3%. She received suppressive therapy with 100 µg L-thyroxine a day for one month and then it was discontinued. Two months later, her serum T4 and T3 levels were increased to 319.2 nmol/l and 10.68 nmol/l (normal: 1.23–2.77 nmol/l), respectively; her
serum TSH was less than 1.5 mU/l with an elevated radiiodine uptake of 83% at 24 h. TBI and TSAb were 71.6% and 1752%, respectively. HLA typing indicated A11, A26; BW54; BW67; CW1, CW7; DRW15 (DR2), DR4, DRW53. She was treated with radioactive iodine.

Discussion
Subacute thyroiditis is considered to be a post-viral inflammatory disorder of the thyroid gland and runs a characteristic clinical course with spontaneous remission within six to nine months in most cases (1). Permanent thyroid dysfunction after subacute thyroiditis is considered very rare (1). Greene (2) could find only two cases of permanent hypothyroidism. However, mild thyroid dysfunction, ultrasonic abnormalities and recurrent episodes have been reported in patients with subacute thyroiditis who are followed for a long time. Tikkanen et al. have reported hypothyroidism in two of their 32 patients with earlier subacute thyroiditis (7). Benker et al. have described three patients with subclinical hypothyroidism and 14 cases with abnormal ultrasonography in their follow-up study of 37 patients (8). Moreover, Yamamoto et al. have reported three patients with recurrent episodes of subacute thyroiditis more than 10 years after the first episode of subacute thyroiditis (9). Recently, Roti et al. (7) described how euthyroid subjects with a previous history of subacute thyroiditis are prone to develop iodine-induced hypothyroidism, suggesting that subtle abnormalities in iodine organization and subsequent thyroid hormone formation persist for years after the episode of subacute thyroiditis.

There have been only nine reported cases in which hyperthyroidism developed after recovery from subacute thyroiditis (3–6). Hyperthyroidism occurred within one year of the onset of subacute thyroiditis in these cases. The unusual feature in our cases is long lag period to develop hyperthyroidism following subacute thyroiditis: approximately 7–8 years. Although the development of hyperthyroidism after subacute thyroiditis can be fortuitous, there is evidence suggesting that the development of hyperthyroidism may be related to the previous episode of subacute thyroiditis. Strakosch et al. have reported the transient appearance of TBI after the onset of subacute thyroiditis (11). Weetman et al. (12) demonstrated the presence of multiple thyroid autoantibodies over a period of up to 39 months after the onset of subacute thyroiditis using an immunoblotting technique. Considering these facts, subacute thyroiditis may cause the production of thyroid stimulating antibodies and hence induce hyperthyroidism. Indeed, our two patients had positive TBII and TSAb after the episode of subacute thyroiditis. It would have been interesting to observe serial changes in thyroid function and thyroid antibodies from the onset of subacute thyroiditis to the development of Graves' disease. However, we were unable to do it. Interestingly, our case 1 had HLA-BW46 and -B35 which are hereditary risk factors for Graves' disease and subacute thyroiditis, respectively (13, 14). Thus, patient 1 had a genetic predisposition to both subacute thyroiditis and hyperthyroid Graves' disease.

In conclusion, although subacute thyroiditis is usually a self-limiting disease, it may trigger to develop hyperthyroidism years after the onset of subacute thyroiditis.

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