Postpartum Thyroiditis

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Postpartum thyroiditis is a disorder which is morphologically similar to Hashimoto's thyroiditis, but differs clinically. The disorder presents with a transient period of thyrotoxicosis which may be so mild that it is clinically missed. Many of these patients subsequently develop hypothyroidism which also spontaneously resolves. Documentation that the hypothyroidism is transient would be necessary to establish the diagnosis. There is a proclivity for this disorder to develop in the postpartum period. Two patients are presented with this disorder, one with a transient hypermetabolic state and one with a transient hypothyroid state.

Thyroiditis in the postpartum period is an uncommon disorder which has been reported infrequently in the literature.[1,2] Two such cases were encountered in less than one year and are described along with a review of the literature on postpartum thyroiditis.

There are four major types of thyroiditis: Hashimoto's (also called autoimmune); Reidel's fibrosing; pyogenic; and subacute (or de Quervain's).[3] Hashimoto's thyroiditis is associated with a diffusely enlarged, non-tender, rubbery goiter. It occurs with a marked female predominance, and is especially frequent from ages 30 to 50 years. It is nearly always associated with positive antithyroglobulin antibodies. Reidel's thyroiditis is a rare disorder manifested by a very firm gland which must be distinguished from carcinoma. Pyogenic thyroiditis is also quite rare and is characterized by a very tender, inflamed gland usually secondary to an acute streptococcal or staphylococcal infection. Subacute thyroiditis is also usually marked by a painful gland with some nodularity, but the painless form of the subacute disease seems to be more common than previously realized.[4] Subacute thyroiditis generally is antibody negative, but can be associated with low levels of anti-thyroid antibodies.

The two case reports in this paper illustrate one of the unusual effects pregnancy can have on the thyroid gland. Mild thyroid enlargement and hyperplasia are common in normal pregnancy. The cause of this hyperplasia is not well established, but may be related to increased renal clearance of iodine resulting in a relative iodine deficiency.[5] The thyroid gland responds by undergoing some degree of hyperplasia, causing a mild goiter. This theory is supported by epidemiologic data suggesting that pregnancy induced goiters occur less frequently in areas where the dietary intake of iodine is high.[6] On the other hand, research conducted in the United States suggests that there is no significant difference in iodine balance between pregnant and nonpregnant patients.[7] An alternative explanation for the pathogenesis of pregnancy induced goiters involves a possible thyrotropic substance which has been identified in placental tissue.[8] Since mild thyromegaly is physiologic in pregnancy, thyroid function tests are essential in de-

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termining whether any pathologic condition requiring therapy is present.

Classically, postpartum thyroiditis may involve four phases: (1) an initial thyrotoxic phase, (2) leading to a short-lived euthyroid phase, (3) passing to a prolonged hypothyroid phase, and (4) eventually in most cases going through a recovery phase and returning to normal function.[9] However, any of these phases may be missed clinically.

Methods

Serum thyroxine (T_4) testing was performed by a competitive binding assay (Clinical Assay Gamma Coat; normal values: 4.5 to 11.5 μg/100 ml). The triiodothyronine resin uptake (T_3RU) test was performed using the Nuclear Medical Lab Kit (normal values: 35 to 45 percent). The free thyroxine index (FTI) is a product of the T_4 and T_3RU values (normal values: 1.58 to 5.18 μg/100 ml). Serum thyrotropin (TSH) was determined by an immunoradiometric assay (Biorad kit; normal values: less than 5.7 μU/ml). Thyroid autoantibody titers (anti-thyroglobulin and anti-microsomal antibodies) were determined by the tanned sheep erythrocyte hemagglutination method (Upjohn Laboratories; normal anti-thyroglobulin values are less than or equal to 1:160, normal anti-microsomal values are less than 1:100). Nuclear medicine studies included a qualitative technetium 99m pertechnetate scan and a radioactive iodine uptake (RAIU) using NaI-131 (normal uptake at 24 hours: 10 to 30 percent).

Case Reports

S.B., a 28-year-old primiparous white woman presented to the family practice center six weeks after a normal pregnancy and delivery with a history of an enlarging goiter. She has a previous history of a small euthyroid goiter for four years, and there is a positive family history of goiter in the patient's mother. Thyroid function tests obtained during pregnancy, because of the past history of goiter, were within normal limits. On presentation, she described some heat intolerance, and pain in the thyroid area, but was otherwise asymptomatic. Examination revealed a 6 × 6 cm, somewhat nodular, non-tender goiter, a resting pulse rate of 112 beats per minute, and a blood pressure of 135/85 mmHg. A diffuse goiter was demonstrated on technetium scan. Radioactive iodine uptake at 24 hours was less than one percent. Other laboratory data disclosed the following values: Wintrobe sedimentation rate, 48 mm/hr (normal values: 0 to 20 mm/hr); T_4, 17.8 μg/100 ml; T_3RU, 60 percent; FTI, 10.7 μg/100 ml; TSH, 0 μU/ml; anti-thyroglobulin antibodies, negative; anti-microsomal antibodies, positive at 1:6400. A diagnosis of postpartum thyroiditis with thyrotoxicosis was made. Two weeks after obtaining these initial studies, the patient developed increased heat intolerance, marked tremor, hyperreflexia, and a resting pulse rate of 144 beats per minute, and a blood pressure of 150/90 mmHg. The thyroid gland had increased in size to 7 × 8 cm, and she had lost weight. Propranolol, 10 mg four times daily, was prescribed for the patient. Within one week, her symptoms had greatly improved, and she subsequently became asymptomatic on 80 mg of propranolol daily. Six weeks after the onset of symptoms, thyroid function tests and sedimentation rates were within normal limits (T_4, 4.9 μg/100 ml; T_3RU, 36 percent; FTI, 1.81 μg/100 ml; erythrocyte sedimentation rate, 18 mm/hr). The thyroid gland had decreased in size to 4 × 4 cm. She continued to be asymptomatic and thyroid function tests six months later were within normal limits (T_4, 5.1 μg/100 ml; T_3RU, 38 percent; FTI, 1.80 μg/100 ml).

L.H., a 37-year-old primiparous white woman, presented with a two-week history of extreme fatigue, four months after delivering a stillborn infant at seven months gestation. Physical examination at six weeks postpartum was normal. Her present illness began abruptly with fatigue which became progressively worse. Her symptoms consisted of marked decrease in her ability to concentrate, difficulty in staying awake, hair loss, dry skin, and constipation. There was no personal or family history of goiter. Examination revealed a resting pulse of 95 beats per minute, a blood pressure of 110/60 mmHg, and a non-tender, rubbery thyroid gland which was three times normal size. Laboratory data were as follows: T_4, 0.7 μg/100 ml; T_3RU, 32 percent; FTI, 0.21 μg/100 ml; TSH, greater than 100 μU/ml; anti-thyroglobulin antibodies, 1:160, anti-microsomal antibodies, positive at 1:6400. She was treated initially with L-thyroxine, 0.025 mg daily with progression to 0.20 mg daily. After three months, she noted marked relief of her symptoms and the thyroid

gland had returned to normal size. Thyroid function studies were within normal limits while taking L-thyroxine (T_4, 7.7 μg/100 ml; T_3RU, 38 percent; FTI, 2.95 μg/100 ml). Twelve months later the L-thyroxine was stopped and thyroid studies done three months after cessation of the L-thyroxine were within normal limits (T_4, 7.7 μg/100 ml; T_3RU, 38 percent; FTI, 2.95 μg/100 ml).

Differential Diagnosis

Amino observed 23 patients with postpartum hypothyroidism of which 14 were definitely associated with thyroiditis.[1] He noted six characteristics which were associated with these 14 patients: (1) 50 percent previously had a goiter; (2) thyroid enlargement occurred at one to four months postpartum; (3) hypothyroidism was noted at three to five months postpartum; (4) spontaneous recovery usually occurred five to ten months postpartum; (5) a high titer of antithyroid microsomal antibodies was found, along with variable titers of the anti-thyroglobulin antibodies; and (6) persistence of a small goiter. In addition, two of Amino's patients who were followed in subsequent pregnancies developed thyroiditis with a transient thyrotoxic phase.

Ginsberg and Walfish observed five patients with transient thyrotoxicosis and thyroiditis in the postpartum period.[2] They noted the following characteristics: (1) thyrotoxicosis developed within one to six months of delivery; (2) all had non-tender goiters; (3) radioactive iodine uptake was suppressed; (4) thyrotoxicosis resolved in four months; and (5) transient hypothyroidism appeared in four of the five patients.

Postpartum thyroiditis shares features of both Hashimoto's thyroiditis (non-tender gland, frequently positive anti-thyroglobulin antibodies) and subacute thyroiditis (antibodies often negative; lack of pain, however, can still be consistent). The diagnosis should be suspected when a woman in the postpartum period presents with an enlarging goiter and/or signs and symptoms of hypothyroidism or thyrotoxicosis. Thyroid function tests can show abnormal or normal function depending on the phase at time of presentation. Confirmatory tests include an elevated erythrocyte sedimentation rate and strongly positive antithyroid antibodies (anti-thyroglobulin in about 50 percent and anti-microsomal in almost all patients). The radionuclide scan and radioactive iodine uptake are very helpful in the diagnosis.[10] In thyroiditis, the gland will be large with a diffusely *decreased* uptake as opposed to the enlarged gland with *increased* uptake seen with Graves' disease. In addition, Amino utilizes a serum triiodothyronine to thyroxine ratio (T_3/T_4) as a means of differentiating thyrotoxicosis in Graves' disease from that in thyroiditis (either subacute or Hashimoto's). In Graves' disease, the ratio is usually greater than 20, whereas in thyrotoxic thyroiditis the ratio is usually less than 20.[11] A thyroid biopsy would also be confirmatory, but is generally not needed to make the diagnosis.

Treatment

Since postpartum thyroiditis is usually a self-limited disease, the treatment should be conservative. If symptoms of thyrotoxicosis are present, drugs such as propranolol and mild sedation are helpful. Anti-thyroid medications like propylthiouracil or methimazole, commonly used in Graves' disease, are ineffective in treating thyroiditis.[12] When symptoms of hypo-function are present, thyroid replacement may be used. Thyroid hormone therapy has been shown not to inhibit recovery, nor will it disturb the regression of the goiter (according to a letter from N. Amino, MD, March 12, 1979, regarding unpublished data). If there is significant goiter pain, aspirin, or rarely corticosteroids, may be useful.

Although this disease is self-limited, it comes at a time in the patient's life which is already very stressful. Another burden is added to the tasks of caring for a new child or grieving the loss of a stillborn child. Working with the family and using all possible support systems is an important part of the therapy.

Discussion

The etiology of postpartum thyroiditis is not known. In fact, it is possible that the occurrence of thyroiditis during the postpartum period is merely coincidental. However, the evidence implies a causal relationship involving abnormalities in both humoral and cell mediated systems. Certainly the finding of high titers of anti-thyroid antibodies in both postpartum and Hashimoto's thyroiditis im-

plies a B-cell abnormality. Nevertheless, in autoimmune thyroiditis, transfer of these antibodies does not induce thyroiditis in animal recipients.[13] Thus, the antibody rise may be secondary to some original inciting agent. In support of humoral pathogenesis, Amino observed the changes of thyroid antibodies during and after pregnancy in 17 patients with autoimmune thyroid disease.[14] The patients with positive antibodies at the onset of pregnancy were observed to have a gradual decrease in titers, with two patients showing negative titers at the end of pregnancy. Transient or permanent increases in the antibodies were observed in all patients within two months of delivery. They also observed a gradual reduction in IgG and IgM levels during pregnancy and a subsequent rapid rise after delivery in one of their patients with thyroiditis. Amino suggests that "antibody production is suppressed in pregnancy." He postulates that "immunosuppression may disappear at delivery and that 'transient enhancement' of the immune reactions may occur after delivery by a somewhat similar mechanism to the 'rebound phenomenon' observed after withdrawal of immunosuppressive glucocorticoid therapy."[14]

Cell mediated immunity also seems to play an important role in the pathogenesis of Hashimoto's disease.[15] There is some evidence to suggest that T-lymphocytes require specific antibodies to become cytotoxic "killer T-cells."[16] Thus, an interaction between humoral and cellular systems may be involved in the pathogenesis of autoimmune thyroiditis. Billingham suggests that cellular immune reactions are suppressed to some degree during pregnancy:

> It has been shown that multiparity may lead to the production of humoral isoantibodies corresponding to important histocompatible antigens of their progeny. It remains to be resolved whether a female confronted by an intrauterine alien fetus is only capable of the humoral component of the normal homograft response or whether there is an associated cellular response that is concealed or blocked by the influence of these antibodies.[17]

Perhaps release of the blockage of the cellular response after delivery activates postpartum thyroiditis.

In cases of other autoimmune diseases such as rheumatoid arthritis and idiopathic thrombocytopenia purpura, there is noted relief of symptoms during pregnancy with relapse of the disease two to six months postpartum.[14]

One may conclude there are immunologic changes that occur in some pregnancies and predispose patients to develop thyroiditis. The natural immunosuppression of pregnancy may halt the development of a cellular or humoral response until after delivery. Then, in the postpartum period there may be an immunological "rebound" resulting in thyroiditis.

In conclusion, the disorder appears to be only one small example of the normal and pathologic immunologic changes which occur during and after pregnancy. Furthermore, the occurrence of two cases of postpartum thyroiditis in a small, family practice setting indicates that this disorder may not be as rare as previously suggested.

References

1. Amino N, Miyai K, Kuro R, et al: Transient postpartum hypothyroidism: Fourteen cases with autoimmune thyroiditis. Ann Intern Med 87:155, 1977
2. Ginsberg J, Walfish PG: Postpartum transient thyrotoxicosis with painless thyroiditis. Lancet 1:1125, 1977
3. Robbins SL: Pathologic Basis of Disease. Philadelphia, WB Saunders, 1974, pp 1326-1331
4. Wolf PD, Daly R: Thyrotoxicosis with painless thyroiditis. Am J Med 60:73, 1976
5. Burrow GN: The thyroid in pregnancy. Med Clin North Am 59:1089, 1975
6. Crooks J, Tullock MI, Turnbull AC, et al: Comparative incidence of goiter in pregnancy in Ireland and Scotland. Lancet 2:625, 1967
7. Dworkin HJ, Jacques JA, Beierwaltes WH: Relationship of iodine ingestion to iodine excretion in pregnancy. J Clin Endocrinol Metab 26:1329, 1966
8. Hershman JM, Starnes WR: Placental content and characterization of human chorionic thyrotropin. J Clin Endocrinol Metab 32:52, 1971
9. Volpe R, Johnston W, Huber N: Thyroid function in subacute thyroiditis. J Clin Endocrinol Metab 18:65, 1958
10. Volpe R: Thyroiditis: Current view on pathogenesis. Med Clin North Am 59:1163, 1975
11. Amino N, Miyai K, Asukizawa M, et al: Differentiation of thyrotoxicosis induced by thyroid destruction from Graves' disease. Lancet 2:344, 1978
12. Evered DC: Treatment of thyroid disease: Part 2: Goitre. Br Med J 1:335, 1976
13. McMaster RB, Lerner EM: The transfer of allergic thyroiditis in histo-compatible guinea pigs by lymph node cells. J Immunol 99:208, 1967
14. Amino N, Kuro R, Tanizawa O, et al: Changes of serum anti-thyroid antibodies during and after pregnancy in autoimmune thyroid diseases. Clin Exp Immunol 31:30, 1978
15. Lamki L, Row VV, Volpe R: Cell mediated immunity in Graves' disease and Hashimoto's thyroiditis as shown by the demonstration of migration inhibition factor (MIF). J Clin Endocrinol Metab 36:358, 1973
16. Brown J: Autoimmune thyroid disease. Ann Intern Med 88:379, 1978
17. Billingham RE: The transplantation biology of mammalian gestation. Am J Obstet Gynecol 3:469, 1971