Carcinomatous pseudothyroiditis: a problem in differential diagnosis

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A 51-year-old woman presented with a painful, rapidly enlarging thyroid gland. The serum concentrations of the thyroid hormones were initially at the upper limit of normal, and the uptake of radioactive iodine by the thyroid was completely depressed. Although subacute thyroiditis was suspected, a biopsy specimen from the thyroid showed malignant disease and no evidence of inflammation. At the time of right subtotal lobectomy metastatic breast carcinoma was diagnosed. Thus, primary or secondary malignant disease of the thyroid can simulate thyroiditis and present a serious problem in differential diagnosis.

Une femme de 51 ans a présenté une glande thyroïde douloureuse, augmentant rapidement de volume. Les concentrations sériques des hormones thyroïdiennes étaient initialement à la limite supérieure de la normale, et la captation de l'iode radioactif par la thyroïde se trouvait complètement déprimée. Bien qu'une thyroïdite subaiguë ait été soupçonnée une biopsie de la thyroïde a révélé une maladie maligne sans signe d'inflammation. Lors d'une lobectomie subtotale du côté droit un carcinome mammaire métastatique a été diagnostiqué. Une maladie maligne primaire ou secondaire de la thyroïde peut donc simuler une thyroïdite et présente un sérieux problème de diagnostic différentiel.

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Subacute thyroiditis, which is nonbacterial and self-limiting, is usually accompanied by pain in the neck and very low 24-hour uptake of iodine-131.[1] The characteristic histologic findings include pseudotubercles and giant cells containing colloid. Recently a variant of subacute thyroiditis has been described in a few patients with a low uptake of ^{131}I, histologic evidence of lymphocytic thyroiditis and absence of pain.[2-4] Yet another variant has been described: a woman with advanced malignant lymphoma had clinical evidence of thyrotoxicosis without thyroid pain; the uptake of ^{131}I was very low and infiltration of the thyroid gland by the lymphoma was evident. There was no evidence of thyroiditis on examination of a thyroid specimen obtained by open biopsy.[5]

We report a case of painful pseudothyroiditis associated with metastatic breast carcinoma involving the thyroid gland, in which examination of a thyroid biopsy specimen on two occasions disclosed no evidence of inflammation.

Case report

A 51-year-old woman was admitted to hospital with a 3-week history of a progressive sensation of choking, swelling of the neck, nonradiating anterior neck pain and fatigue. For 2 weeks she had experienced dysphagia for liquids and dyspnea on exertion. She had had no recent infections of the upper respiratory tract and denied having palpitations or appreciable intolerance to heat. One week before admission the referring family physician recorded that the patient had experienced night sweats, had a pulse rate of 90 beats/min and had noted tenderness of the thyroid gland. Studies of thyroid function performed at another laboratory at that time had shown a serum thyroxine (T_4) value of 11.9 μg/dL (153 mmol/L) (normal for that laboratory 4.5 to 11 μg/dL [58 to 142 mmol/L]), a triiodothyronine (T_3) resin uptake of 32.8% (normal for that laboratory 25% to 35%) and a thyroid-stimulating hormone value of 1.3 μU/mL (normal for that laboratory less than 10 μU/mL).

The patient had had a hysterectomy for menstrual bleeding years earlier and a modified left mastectomy for infiltrating duct carcinoma with metastases to axillary lymph nodes 3 years before the current admission. One of the patient's sisters was reported to have had a thyroid disorder.

The patient was slightly obese and normotensive (blood pressure 110/80 mm Hg) and the pulse rate was 88 beats/min. The thyroid gland was diffusely enlarged (estimated weight 60 g), firm, slightly irregular and moderately tender; when the arms were raised above the head there was swelling of neck

Table I—Laboratory data

Variable	Method of measurement	Day of admission	One week later	Five weeks later	Normal values
Serum thyroxine concentration, μg/dL	Reference 7	11.0	6.8	1.7	4.6–11.6
Triiodothyronine Resin uptake, %	Silica talc resin	99	84	87	84–116
Serum concentration by radioimmunoassay, ng/dL	Reference 8	121	127	64	80–220
Thyroid-stimulating hormone concentration, μU/mL	Reference 9	—	—	94	0–6
Iodine-131 uptake in 24 h, %		1	—	—	9–26
Erythrocyte sedimentation rate, mm/h	Westergren	60	—	50	≤ 20
Tanned red cell agglutination antibody (thyroglobulin) titre	Sera-Tek thyroglobulin antibody test*	1:320	—	—	< 1:100
Complement fixing antibody (microsomal) titre	Sera-Tek thyroid microsomal test*	1:400	—	—	< 1:100
Hemoglobin concentration, g/dL		12.7	—	—	12–16
Leukocyte count, × 10^9/L		7.9	—	—	4.8–10.8

*Ames Company, Elkhart, Indiana.

veins (Pemberton's sign), indicating outlet compression by the goitre.[6] There was no eyelid sag, globe lag or stare. No masses were palpable in the right breast, and the neck and both axillary areas were free of lymph node enlargement. Subacute thyroiditis was suspected. Acetylsalicylic acid, 600 mg *q4h*, was prescribed.

Results of initial laboratory investigations (Table I) indicated that the serum T_4 value was at the upper limit of normal, the ^{131}I uptake was substantially suppressed, the erythrocyte sedimentation rate was elevated and the thyroid antibody titres were mildly elevated. No chest or bone lesions were visible on the roentgenograms.

One week later the neck pain was much less severe; there was also improvement in her tolerance to heat, appetite and general energy. The pulse rate was 80 beats/min. The thyroid gland was unchanged in size but was no longer tender. The serum T_4 and T_3 resin uptake values were lower than before but were within normal limits (Table I).

Five weeks later, while still taking acetylsalicylic acid, the patient reported recurrence of the pain in the thyroid area, especially along the lateral aspects of the neck, increased swelling of the neck, hoarseness, intolerance to cold, insomnia and malaise. Her weight was unchanged and her pulse rate was 76 beats/min. The thyroid gland was slightly larger (about three times the normal size) and very tender, especially on the left side, with extension of the pain to the left clavicle. The Achilles tendon reflexes were normal, and no other physical abnormalities were discerned. Prednisone, 40 mg/d, was added to her therapeutic regimen. Thyroid function studies were again performed and hypothyroidism was indicated (Table I).

Three weeks later her condition appeared to be much improved, and although the thyroid gland was not tender its size was unchanged. Thyroid biopsy with a 27-gauge needle on a 10-mL syringe was done, and examination of the specimen indicated papillary carcinoma with no evidence of thyroiditis (Fig. 1). Thyroxine replacement therapy was started and the patient was referred for surgery.

A right subtotal thyroid lobectomy was performed 3 weeks later. Metastatic breast carcinoma was diagnosed from examination of a frozen section (Fig. 2) and was later determined to be identical to the carcinoma removed from the left breast 3 years before (Fig. 3). Very little normal thyroid tissue was present, but we were unable to find evidence of inflammation.

Cobalt-60 irradiation (3000 rads over 3 weeks) was subsequently given to the neck area. Three months after irradiation the size of the neck had decreased, no new complications were reported and the patient was subjectively improved. She continued taking replacement therapy.

The patient remained well for about 8 months after radiotherapy, then pericardial and pleural effusions developed and bone, liver and lung metastases became evident. She died 4 months later, 16 months after the onset of thyroid problems, of cardiopulmonary insufficiency.

Discussion

Careful search for evidence of inflammation in the resected right thyroid lobe of our patient was unsuccessful. The thyroid specimen obtained by needle aspiration biopsy also failed to produce evidence of autoimmune or subacute thyroiditis. It is possible, though highly unlikely, that thyroiditis was present earlier in the course of the disease. This lack of histologic evidence of thyroiditis also characterized the case reported by Shimaoka, VanHerle and Dindogru,[5] in which pain was not a symptom and the disease was initially thought to fall into the category of painless thyroiditis, as recently reported.[2-4] Nonradiating pain in the thyroid was one of the presenting symptoms in our patient, both initially and later. This pain was obviously due to thyroid disease and not to pressure of other local structures, since it was relieved by acetylsalicylic acid initially and by prednisone later while the size of the thyroid increased. There is at least one similar report in the literature of thyroid pain, depressed ^{131}I uptake, increased protein-bound iodine and normal thyroxine iodine in a patient with rapidly enlarging anaplastic carcinoma of the thyroid gland; histologic examination of that

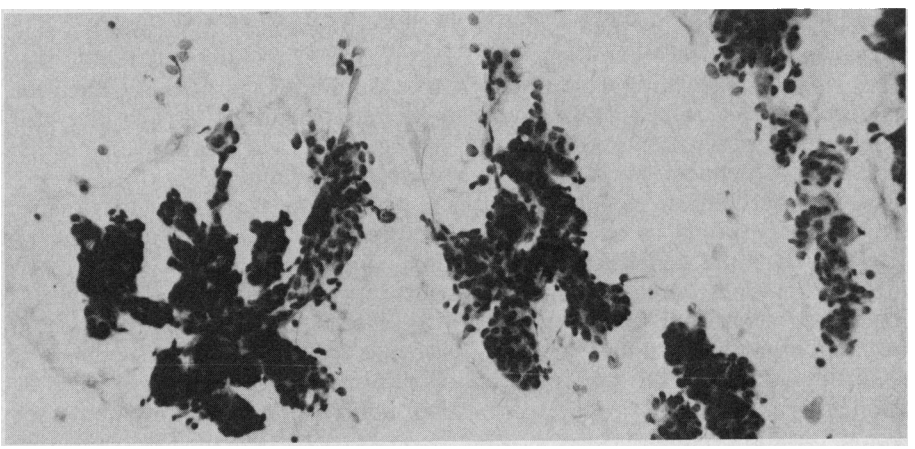

FIG. 1—Fine-needle aspiration biopsy specimen of thyroid: well differentiated papillary adenocarcinoma identical in configuration to original primary papillary carcinoma of breast (Papanicolaou stain; original magnification ×100).

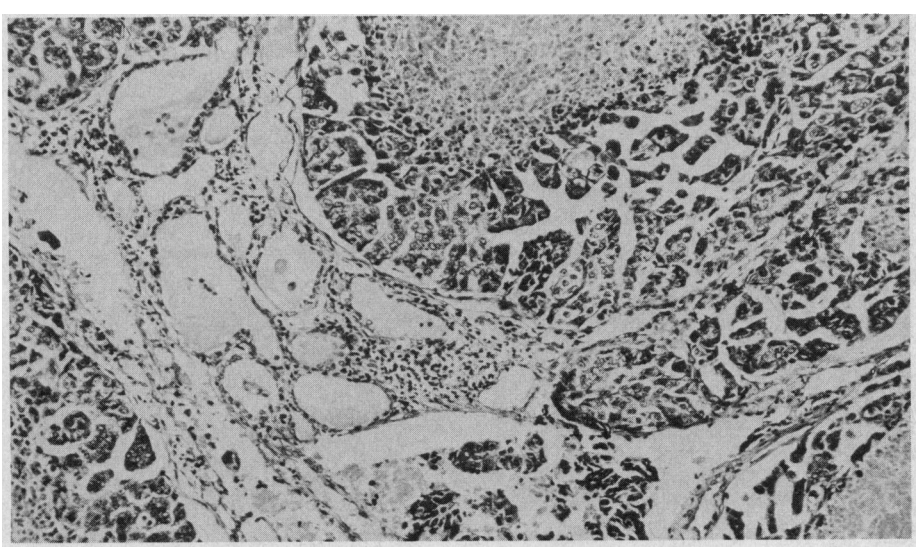

FIG. 2—Metastatic breast carcinoma in thyroid: identical pattern to that of breast primary (hematoxylin–eosin; original magnification ×100).

patient's thyroid gland was not possible.[10] Carcinomatous invasion of the thyroid gland apparently can give rise to a number of features suggestive of thyroiditis: depressed ^{131}I uptake and the absence of histologic evidence of thyroiditis appear to be constant; pain and hyperthyroidism appear to be variable. If the above combination of findings were to be reported in the future, a new entity causing hyperthyroidism might be established.

The most interesting aspect of our case and of similar reported cases[5,10] is the problem of differential diagnosis. The presence of pain and tenderness in the neck, combined with the nervousness and sweating, suggest a diagnosis of subacute thyroiditis, which appears to be confirmed by the low 24-hour ^{131}I uptake and the high or high-normal serum T_4 value. However, the goitre, as our case illustrates, may be larger than that usually seen in thyroiditis. Also, the progressive enlargement of the thyroid in spite of treatment should make one consider other diagnoses. The high or high-normal serum T_4 values appear to result from severe carcinomatous destruction of the thyroid and subsequent hormone leakage. This mechanism is involved in subacute thyroiditis as well, but inflammation is the underlying process in this condition. Abnormal circulating iodoproteins have been described in cases of both carcinoma and thyroiditis, confirming the mechanism of the leakage.[10]

Further observation of the thyroid disorder in our patient was not possible because the carcinoma was life-threatening and required immediate medical and subsequent surgical treatment.[11]

It is noteworthy that the thyroid specimen obtained by fine-needle biopsy was interpreted as showing primary carcinoma of the thyroid. This report was issued without knowledge of the previous breast carcinoma. The biopsy technique we used is accurate for the pathologic assessment of goitre, especially that due to thyroiditis.[12] Malignant lesions may be missed,[13] but infrequently.[14] The technique appears to be less accurate for the differentiation of the type of malignant lesion, but even with other methods of obtaining thyroid tissue for histologic examination, there occasionally is confusion about the type of malignant condition.[5] In spite of this deficiency, the fine-needle procedure is valuable because it is easily carried out in an office and it provides useful information on thyroid conditions, particularly when the specimen obtained is positive for malignancy, and can thus alter the course of treatment.[15]

In a patient with a previous malignant condition and a rapidly enlarging goitre, the possibility of a carcinomatous goitre simulating thyroiditis should be seriously considered when a syndrome of pain, a high or high-normal T_4 value and a low ^{131}I uptake develops. Carcinomatous pseudothyroiditis is probably infrequent, but its diagnosis is important to the institution of appropriate therapy.

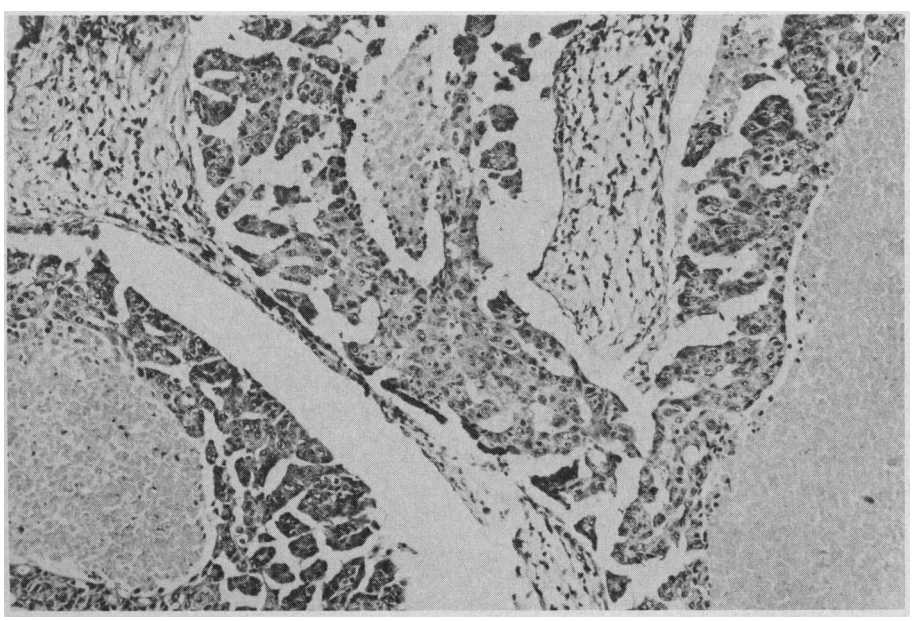

FIG. 3—Primary carcinoma of breast: striking papillary picture present in some but not all parts of infiltrating duct carcinoma (hematoxylin–eosin; original magnification ×100).

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