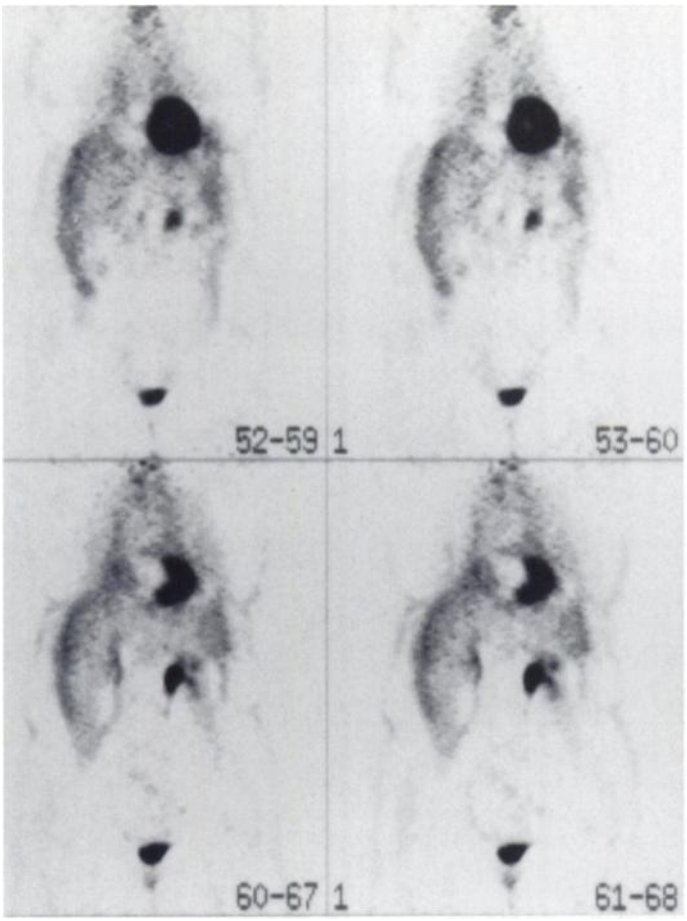

FIGURE 4. Coronal images of a whole-body PET scan with [^{18}F]FDG-PET shows no evidence of disease 11 mo after the initial therapy with radiolabeled anti-CEA antibodies. The images proceed from left to right, starting from the anterior to the posterior part of the body.

CONCLUSION

This case demonstrates the prospect of achieving excellent targeting and antitumor responses in ovarian cancer with intravenously administered antibodies directed against carcinoembryonic antigen. Therefore, further studies are in progress to confirm this finding and to elucidate the mechanisms involved in tumor response.

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Graves' Disease Triggered by Autoinfarction of an Autonomously Functioning Thyroid Adenoma

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A patient whose nontoxic autonomously functioning thyroid adenoma had been stable for at least 3 yr developed enlargement of the nodule and hyperthyroidism. It was assumed the hyperthyroidism was caused by evolving toxicity in the autonomous adenoma, but imaging showed the nodule had undergone infarction and the hyperthyroidism was secondary to Graves' disease. This case demonstrates the necessity of thyroid imaging in patients with nontoxic autonomously functioning thyroid adenomas when there is a change in nodule size or thyroid function which requires treatment.

Key Words: autoinfarction; autonomously functioning thyroid adenoma; Graves' disease

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Hyperthyroidism can be caused by autoimmune Graves' disease (GD) or be secondary to increased function in nodules

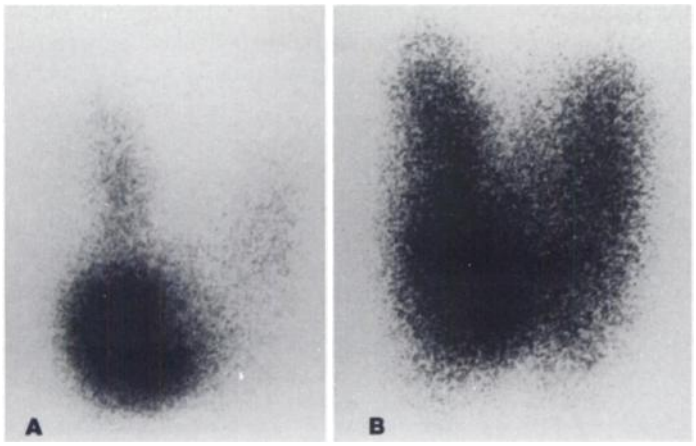

FIGURE 1. Functional nodule is demonstrated with [^{99m}Tc]pertechnetate tracer (A) and with ^{123}I (B).

that function autonomously from normal thyroid stimulating hormone (TSH) control. Nontoxic autonomously functioning thyroid adenomas (AFTA) can remain stable, enlarge with increasing function leading to hyperthyroidism or undergo degeneration (*1*). When this patient became hyperthyroid and her previously stable AFTA enlarged, we considered whether repeat imaging was necessary for the presumably now-toxic AFTA. Scanning showed infarction of the AFTA and a pattern of GD in the extranodular tissue. A literature search revealed four cases of GD developing after ^{131}I therapy of toxic AFTA. We raise the possibility that the destruction of the follicular cells in the toxic adenoma in these cases results in the release of antigenic material that stimulates an immune response. This response, in turn, activates TSH receptors in the extranodular tissue, causing the GD.

CASE REPORT

A 31-yr-old woman was found to have a 2.0-cm right thyroid lobe nodule during examination for a sore throat. The nodule was functional on [^{99m}Tc]pertechnetate and ^{123}I scans (Fig. 1). At a follow-up visit 2 yr later, her right-side nodule was 2.5 cm and extended into the midline. Thyroid function studies were normal, with a TSH of 0.26 uIU/ml (normal 0.25–4.0), free T4 of 1.4 ng/dl (normal 0.6–2.2) and a free T3 of 3.6 pg/ml (normal 1.4–4.7). A suppression ^{131}I uptake and image was performed approximately 1 mo later, after she had been on triiodothyronine 25 μg twice daily (Fig. 2). The 24-hr radioiodine uptake (RAIU) was 16%, and the scan demonstrated persistent radioiodine uptake in the right lobe nodule with good suppression of extranodular tissue, confirming that the nodule was an AFTA. Her nodule and function studies were stable for about 2 yr. Five years after her initial evaluation, she was having symptoms of heat intolerance and palpitations. Her TSH was now suppressed at 0.05 uIU/ml and the free T4 was elevated at 3.8 ng/ml as was the free T3 at 7.7 pg/ml. The right thyroid nodule was now 3.0 cm. A [^{99m}Tc]pertechnetate scan demonstrated that the prior functional nodule was now completely photopenic and the remainder of the gland was excellently visualized (Fig. 3). Initially, she elected antithyroid drug therapy, but after 4 mo of methimazole treatment, she requested definitive ^{131}I therapy. The methimazole was stopped. Five days later, her 24-hr RAIU was 47% and she received 12.0 mCi of ^{131}I.

FIGURE 2. Radioiodine suppression scan shows suppression of the extranodular tissue, proving the nodule was an AFTA. Beginning degeneration is suggested in the small photopenic area.

DISCUSSION

It is generally accepted that GD is an autoimmune disorder in which thyroid stimulating immunoglobulins (TSI) are produced, resulting in thyroid hyperplasia and increased hormone secretion. Autonomously functioning thyroid adenomas (AFTAs) are generally benign neoplasms (*1*). Miller was the first to suggest that the development of autonomous function occurs at an early stage in the evolution of the clinical AFTA (*2*). Recent studies have shown the presence of genetic alteration in these lesions that result in constitutive activation of the TSH receptor (*3–5*). This probably occurs within the first cell that will eventually develop into the AFTA. At least two types of somatic mutations have been identified, either in the $G_s\alpha$ (stimulating guanine nucleotide binding protein alpha) gene or in the TSH receptor gene, that contribute to the activation of adenylate cyclase (*5*).

AFTAs appear hyperfunctional on both radioiodine and [^{99m}Tc]pertechnetate scans with the degree of extranodular activity dependent upon the secretory capacity of the AFTA and the resultant level of TSH. Most AFTAs are nontoxic and, when less than 2.5 cm in size, remain stable in size and function (*1*). AFTAs 3.0 cm or larger are more likely to be toxic (*6*). Degeneration of AFTAs is also common and is often seen on thyroid scanning as a central area of reduced activity. This can relate to some hemorrhage into the nodule. Figure 2 suggests beginning degeneration 2 yr after our patient's initial visit. This degenerative phenomenon can offset the tendency of larger AFTAs to increase in size and function. Infarction of AFTAs has been reported associated with transient thyrotoxicosis secondary to the release of stored thyroid hormone into the circulation (*7*). These authors pointed out the need for imaging to differentiate between the evolution of toxicity in a prior nontoxic AFTA and hemorrhagic infarction, as was shown by bloody needle aspiration from the AFTAs in their two patients. Although we did not perform a needle aspiration, Figure 3 clearly shows loss of function in the prior functional AFTA consistent with degenerative infarction. In our patient, it was originally assumed that the hyperthyroidism was the result of increasing function in the AFTA, and the question was raised as to whether a repeat scan was even necessary before ^{131}I therapy. Although a TSI assay was not obtained, it is clear from Figure 3 and the elevated 24-hr RAIU, done 4 mo later, that the hyperthyroidism was caused by GD rather than a toxic AFTA.

Some investigators, especially in Europe, have shown the presence of autoimmune thyroid disease features in some patients with AFTAs. Grubeck-Loebenstein et al., using a cytochemical bioassay with high sensitivity, found the presence of TSI in 10 patients with a single toxic AFTA (*8*). Diffuse lymphocytic infiltration of the extranodular tissue was found in all 10 patients, and they suggested an overlap in the pathogenetic background of GD and AFTAs. Sellschopp et al. found a lymphoplasmacellular infiltrate in the extranodular tissue in 23 of 30 patients with AFTAs (*9*). By using immunochemical techniques, they found a positive staining reaction for thyroid-related antibodies in 12 of the 23 patients.

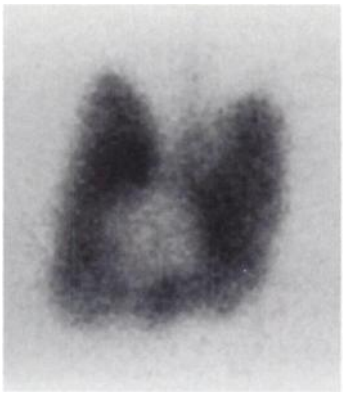

FIGURE 3. Technetium-99m-pertechnetate scan demonstrates infarction of the AFTA and shows the hyperthyroidism caused by Graves' disease.

Four cases of hyperthyroidism of the Graves' type occurring after ^{131}I therapy for a toxic AFTA have been reported (*10–13*). In one case, TSI was present at a low titer before the ^{131}I and rose after the patient became hyperthyroid from GD (*12*). In another case, TSH receptor antibodies or TSI were undetected before ^{131}I therapy, although there was a low level of thyroid peroxidase antibody (1500 U/ml) (*13*). These cases suggest that when susceptibility for GD exists in the extranodular tissue, the release of antigenic material from the ^{131}I-damaged follicular cells of the toxic adenoma stimulates an immune response that activates the TSH receptors in the extranodular tissue resulting in GD. In our patient, a similar pathogenesis could exist with autoinfarction of the autonomous nodule being the triggering mechanism.

CONCLUSION

This patient had a long-standing nontoxic AFTA and then became hyperthyroid secondary to GD after infarction of the autonomous nodule. The necessity of thyroid imaging to determine the etiology of the hyperthyroidism is discussed, as well as the possibility that the destruction of the follicular cells in the adenoma released antigenic material that evoked an immune response in the extranodular tissue causing the GD.

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Technetium-99m-MDP Uptake in Hilar Lymph Nodes in Sarcoidosis

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We describe a patient with unexplained hypercalcemia who underwent bone scintigraphy, which demonstrated marked tracer uptake within the hilar lymph nodes. The pattern strongly suggested sarcoidosis, which was subsequently confirmed by bronchoscopy-directed biopsy.

Key Words: sarcoidosis; bone scintigraphy; lymphadenopathy

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Sarcoidosis is a worldwide multisystem disorder of unknown etiology characterized by noncaseating granulomas at sites of disease activity (*1*). Although many organs of the body may be affected, the lungs are the most common sites involved (90%) and account for the greatest morbidity and mortality. There are several extra thoracic sites of involvement of sarcoidosis, including the eyes, kidneys, liver, spleen, bone marrow, skin, lymph nodes, nervous system, musculoskeletal system and others. Hypercalcemia is a rare complication (*2*).

The diagnosis of sarcoidosis is based on clinical manifestations, radiographic findings, the demonstration of noncaseating granulomas and the exclusion of other causes of granulomatous inflammation (*3*). Serum angiotensin converting enzyme (ACE), bronchoalveolar lavage, pulmonary function tests and ^{67}Ga scanning have been used in the diagnosis and management of sarcoidosis. Clinical experience has been variable regarding the accuracy of these tests for detecting activity and monitoring therapy (*1,4*). The role of high-resolution CT scanning is under evaluation (*5*). The experience with ^{99m}Tc bone-seeking agents in sarcoidosis has been limited. There are only a few reported cases of abnormal

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