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Case History

Extramedullary Hemopoiesis in a Thyroid Nodule with Extensive Bone Metaplasia and Mature Bone Formation

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Thyroid nodules may undergo a wide range of degenerative change such as infarction, hemorrhage, or fibrosis, which may be localized or extensive and associated with calcification or even ossification. However, the detection of true bone formation in a thyroid nodule is a very rare occurrence. Extramedullary hemopoiesis (EMH) has been described in almost every organ of the body, mainly in tissues active in hemopoiesis in embryonic life. It is extremely rare for EMH to occur in the thyroid gland especially in patients without known chronic anemia. We describe a case of a cold thyroid nodule with histologically proven extensive bone metaplasia and formation of mature bone with foci of hemopoietic tissue in a young woman without chronic anemia, which, to the best of our knowledge, is the first to be reported in the English language literature.

Introduction

COLLOID NODULES OF THE THYROID are usually well circumscribed and often sharply demarcated from adjacent tissues. They vary in size from approximately 1 mm in diameter to several centimeters. Hemorrhage, fibrosis, and cystic changes may be evident. Microscopically chronic inflammation, groups of macrophages, hemosiderin, fibrosis, and even calcification or ossification can be found (1). However, mature bone formation in a thyroid nodule is a rare occurrence (2,3). Extramedullary hemopoiesis (EMH) has been described in almost every organ of the body, especially in tissues that were active in hemopoiesis in embryonic life such as the spleen, liver and lymph nodes (4,5). It is extremely rare, however, for EMH to occur in the thyroid gland. Until now only very few cases of EMH in the thyroid have been described in the English language literature. Two occurred in patients with chronic myelofibrosis (6,7), and one in a patient with chronic iron deficiency anemia (8). We describe a case of a cold thyroid nodule with histologically proven extensive bone metaplasia and mature bone formation with foci of hemopoietic tissue including megakaryocytes and myeloid blasts in a young woman without chronic anemia.

Case History

A 34-year-old woman was investigated for a palpable lesion in the thyroid gland. She had a 2-year history of nodular goiter. She reported no compressive symptoms. She had no history of previous irradiation to the head or neck, and she was on no medication. She had never smoked. She had never had any serious hematologic or other chronic disease in the past.

On examination she appeared well with a body mass index of 42 kg/m^2, and normal pulse rate and blood pressure (120/180 mm Hg). Palpation of the neck revealed a hard lesion approximately 7 cm in diameter in the right lobe of the thyroid gland, with well-defined margins and nodular surface. There was no cervical lymphadenopathy, and no evidence of tracheal compression or mediastinal syndrome.

Her complete blood count showed a hematocrit of 42.5%, hemoglobin level of 14.1 g/L, white blood cell count of 8.4×10^3 per microliter with normal differential count, and a platelet count of 316×10^3 per microliter. The peripheral blood smear was normal. Serum iron was 72 μg/dL (normal, 50–160) and ferritin 64 ng/mL (normal, 12–161). Her thyroid hormone levels were also normal. The patient tested negative for thyroid antimicrosomal and antithyroglobulin

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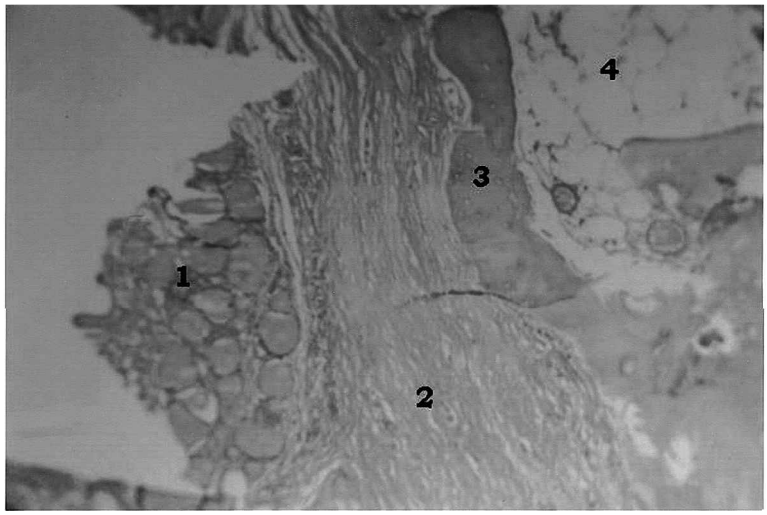

FIG. 1. Section from the right lobe—pathologic findings. (1) thyroid follicles; (2) fibrosis with sclerosis; (3) bone formation; (4) intertrabecular spaces filled with mature fat cells.

antibodies. Plain neck and chest radiographs showed mild deviation of the trachea to the left and an osseous appearance in the lower right part of the neck, corresponding to the anatomic site of the palpable thyroid nodule.

Thyroid gland scintigraphy with 6 mCi ^{99m}Tc showed increased size of the gland and a cold area in the lower part of the right lobe. Ultrasound examination revealed increased volume of the right lobe, with a hyperechogenic solid lesion measuring 6.8 cm in its maximum diameter. The left lobe was of normal size with a micronodular architecture. The trachea was slightly deviated to the left and appeared normal; no cervical nodes were detected.

Fine-needle aspiration biopsy (FNAB) of the nodule proved impossible because of the stone-like hardness of the mass. In view of the size and unusual consistency of the nodule the patient underwent total thyroidectomy under general anesthesia.

Pathologic Findings

The surgical specimen consisted of the entire thyroid gland, which weighed 52 g and had brown-tan coloration and nodular surface. The capsule was intact. The right lobe, which was measured $7.5 \times 4.0 \times 3.0$ cm, had an extremely hard consistency, which made it impossible to obtain sections before demineralization. The left lobe, which was measured $2.5 \times 3.0 \times 1.5$ cm, had soft micronodular consistency.

Microscopic examination of the left lobe showed features compatible with a nodular goiter. Thyroid follicles of variable size were separated by fibrous tissue bundles into multiple nodules. The follicular cells were cuboidal and uniform without atypia. Sections from the right lobe after decalcification for about 10 days, showed largely the same histopathologic features with sclerosis, calcification and mature bone formation. The inter trabecular spaces were filled

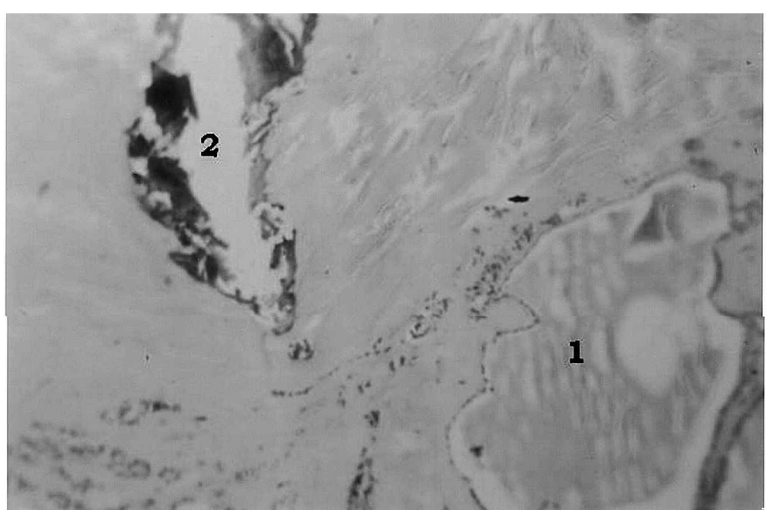

FIG. 2. Section from the right lobe—pathologic findings (1) Thyroid follicles; (2) calcification.

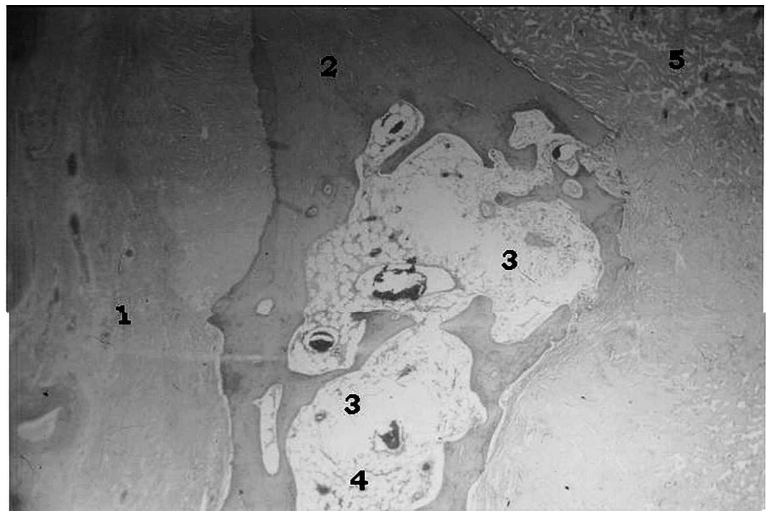

FIG. 3. Section from the right lobe—pathologic findings. (1) Fibrosis with sclerosis; (2) bone formation; (3) bone marrow spaces; (4) hemopoietic cells; (5) thyroid follicles.

either with mature fat cells or hemopoietic elements including a number of megakaryoblasts and blasts of the myeloid series (Figs. 1–4).

Discussion

Degenerative changes of the thyroid are mostly observed in nodular goiter. Areas of hemorrhage (recent or old), cholesterol crystals, deposition bands of fibrous tissue or colloid lakes occasionally filled with fat, may alternate with normal foci of thyroid tissue. Distinct areas of calcification and even ossification may also be noted. Rarely, these degenerative changes will reach the stage of calcinosis (1). This last feature is called metaplastic calcification because it arises on a sclerotic tissue rather than a cartilaginous matrix; it is a frequent finding in areas of hemorrhage or sclerosis of any origin (3,4). Similar degenerative changes can be observed in both benign and malignant neoplasms of the thyroid gland. However, they occur more frequently in papillary carcinomas than in adenomatous follicular nodules (1).

Although calcific deposition may often be detected in a nodular goiter, maturation of this calcified tissue to mature bone is extremely rare. A specific osteogenic factor, known as bone morphogenetic protein (BMP [3]), is essential for appropriate orientation to calcified trabeculae and for formation of spaces filled with bone marrow or adipose tissue, as shown in our case.

EMH or myeloid metaplasia is defined as the process of blood cell formation in sites other than those that are normally active (4). It has been described in cases where there is increased demand for blood cells after severe and continuing hemorrhage or hemolysis in newborn or young children (5) and in patients with severe chronic disease of hemopoietic tissue such as chronic granulocytic leukemia,

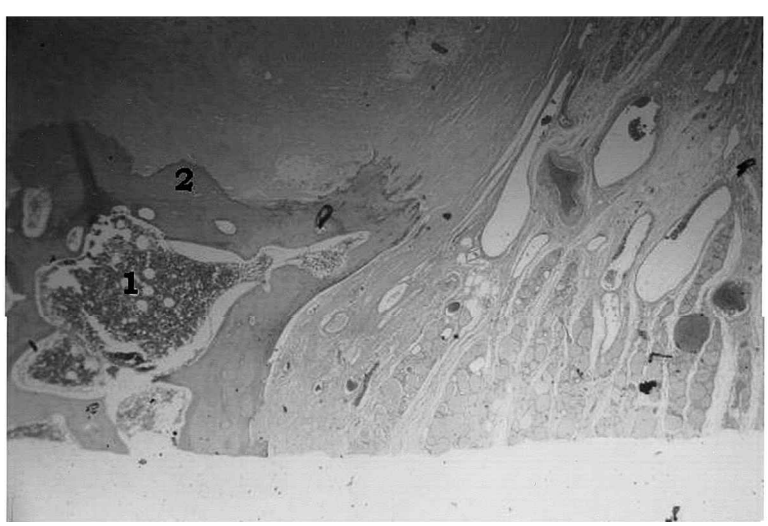

FIG. 4. Section from the right lobe—pathologic findings. (1) Mature bone marrow with hemopoietic cells; (2) bone formation.

Hodgkin's disease, primary polycythemia, thalassemia, sickle cell anemia, pernicious anemia or hereditary spherocytosis (9). It has also been described in chronic iron deficiency anemia (8). Myelofibrosis, however, particularly in the context of agnogenic myeloid metaplasia, is one of the most important causes of EMH (10). The most common sites of EMH are tissues active in hemopoiesis in embryonic life such as the liver, spleen and lymph nodes (5). However, EMH can occur in almost every organ and in numerous locations (4).

Development of EMH in the thyroid gland is extremely uncommon and has been described in only three reports (6–8). In all these cases the diagnosis of EMH was based on FNAB findings, which showed bone marrow elements containing all three hemopoietic cell lines as in our case. However, two of these patients had myelofibrosis (6,7) and the third had chronic iron deficiency anemia with long-term use of methotrexate in the past for treatment of psoriatic arthritis, which could produce occult myelodysplasia (8). It should be noted that FNAB may yield false-positive results in some cases and, for this reason, an experienced cytolopathologist in this field is required (11).

According to current concepts, EMH foci arise from local transformation of cells that have hemopoietic potential (4). Thus, it is believed that in a suitable microenvironment consisting of blood precursor cells, neighboring cells, extracellular matrix, growth factors such as granulocyte-macrophase colony-stimulating factor, other cytokines and/or hormones, these pluripotent hemopoietic cells can differentiate into various cell lines (7). The reactive changes accompanying degenerative alterations within the nodule (such as inflammation, necrosis, extensive fibrosis and hypervascularity) may have played a contributary role for focal EMH (7).

The interesting and extremely unusual finding in our case was the formation of mature osseous tissue made up of bone trabeculae containing bone marrow and characteristic hemopoietic cells such as megakaryocytes and myeloid blasts. Megakaryocytes were clearly observed, while the red cell and granulocyte series, although present, showed degenerative changes due to demineralization of the surgical specimen. Osteoid was also found in the vicinity of the bony structure, entrapped in fibrous tissue.

In conclusion, we describe a very rare case of multinodular goiter with extensive bone metaplasia and mature bone formation with the presence of foci of hemopoietic tissue such as megakaryocytes and myeloid blasts in a young female without any obvious stimulus for EMH.

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