Osseous metaplasia in thyroid nodule: A case report and review of literature

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ABSTRACT

Objective: To present a case of osseous metaplasia in thyroid nodule. Introduction: Long standing thyroid nodules undergo changes. Sometimes they degenerate, may lead to hemorrhage or fibrosis and sometimes ectopic bone formation. Case report: 41 years old Yemeni married lady, presented to our surgical clinic with left thyroid nodule for 3 years duration. She had right thyroid lobectomy 6 years ago. She presented with left neck swelling and was taken to OR for thyroidectomy. histopathology came as extensive fibrosis and osseous metaplasia with small remnant of thyroid tissue. Discussion: Most thyroid stay longer with no complications but some undergo calcification or hemorrhage, fibrosis and sometimes osseous metaplasia. It may occur in benign or malignant thyroid swellings.

Keywords: Osseous metaplasia, Thyroid nodule ectopic bone

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**Introduction:**
Thyroid nodules are the commonest thyroid disease with incidence of 3.5% in adult population and 50% at autopsy [1,23]. Degeneration changes are frequent in thyroid nodules. Rupture of follicles often leads to granulomatous reaction with formation of foreign body giant cells and areas of hemorrhages and fibrous changes. These changes lead to calcification and sometimes ossification. There are studies which show mature bone formation in thyroid nodules [4,5]. Calcification and bone metaplasia are common findings and can be easily missed by pathologists. Virchow believed that osteoblast originate from fibroblast by metaplasia and termed them as modified fibroblasts [6]. It is not clear what triggers fibroblasts to change themselves to osteoblasts and start forming bone tissue. Local factors may stimulate osteoblasts to secrete collagen and ground substance and formation of hydroxyapatite crystal formation which ultimately lead to bone formation. Thyroid diseases are common but mature bone formation in thyroid tissue is rare. Extra-medullary hematopoiesis is defined as presence of hematopoietic tissue in the tissue other than bone marrow while osseous metaplasia is defined as presence of heterotopic normal bone tissue in soft tissue. Osseous metaplasia occurs outside skeletal system in fibro-dysplasia ossificans. We present a case of osseous metaplasia in thyroid nodules which is a rare entity.

**Case report:**
41 years old Yemeni married lady, presented to our surgical clinic with left thyroid nodule for 3 years duration. She had no voice changes, or compressive symptoms. She is dyslipidemic, has low vitamin D level for which she is on vitamin D drops. She had cervical and lumbar discs protrusions which were treated conservatively by analgesia and physiotherapy. She had a past history of right thyroid lobectomy done in another hospital 6 years ago for thyroid nodule. The histopathology of right lobectomy showed Hashimoto's thyroiditis with hyperplastic nodules, and suspicious focus for microscopic variant of papillary thyroid carcinoma. She received radioactive iodine therapy post operatively. She is on thyroxin 50 mcg once daily.

Examination of neck showed left thyroid nodule which was hard, slightly mobile, non-tender. No cervical lymphadenopathy. Her blood investigation including: CBC, thyroid, renal, liver function tests, Ca, P, and mg were normal. Thyroglobulin, and thyroid antibodies (thyroid peroxidase, thyroid globulin Antibodies) were also normal. She had neck ultrasound that showed a hyper-echoic nodule 2 by 2 cm in the left lobe with peripheral rim of calcification, no increased vascularity, no lymph nodes, and no residual tissue on the Right side. Fine needle aspiration cytology was done three times, all were insufficient for the diagnosis.

Decision was taken for left thyroid lobectomy, to exclude malignancy. Intra-operatively, it was difficult to identify the left lobe, there was a whitish, hard, small, egg like structure occupying the site of the left lobe, it was excised with a small jugular lymph node and sent for histopathology. The result came back as: extensive fibrosis and osseous metaplasia with small remnant of thyroid tissue (figure -1,2,3). The lymph node showed reactive lymphoid hyperplasia. There was no malignancy.

Post operatively, the patient was put on thyroxin replacement dose, she has her regular follow up in both the surgical and the endocrine clinics. She is euthyroid and has no more complaint.

**Discussion:**
It remains unclear which factor leads to the formation of bone in thyroid nodule. Various theories have been proposed but none has effectively showed the exact mechanism of osseous metaplasia in thyroid nodules. Bone morphogenetic factor (BMP) plays important role in synthesizing ground substance and collagen in presence of calcium and phosphate [7,8]. BMPs 1-7 induces ectopic bone formation [9]. BMP-1 converts pro-collagen 1,2,3 and 7 into mature...
forms which results in formation of extra-cellular matrix [10]. Calcified thyroid tissue has higher concentration of BMP-2[11]. Mesenchymal cells and capillaries in thyroid nodules provide favorable environment for the differentiation of hemopoietic tissue and formation of bone [12]. Our patient had low vit D level and she was receiving calcium supplements, further more she received radioactive iodine treatment, both of these facts shows that there was disturbance in calcium metabolism which may predispose to calcification and which ultimately led to bone formation.

Figure-1: Extensive fibrosis and lamillated bone in the lumen. Right arrow

Figure-2: Multinodular goiter- Variable sized thyroid follicles retaining colloid
Calcification is more common in papillary thyroid cancer\cite{13}. In our case there were foci of papillary thyroid cancer, so leading to more calcification. Papillary thyroid cancer is also associated with osseous metaplasia\cite{14,15}. Psammoma bodies are known to be associated with increased incidence of metastasis to lymph nodes and in presence of stromal calcifications there is gross lymph nodes metastasis and higher grade of tumor\cite{15}. Osseous metaplasia is more common with longer duration of thyroid disease\cite{16}. In our case duration of disease was 6 year which clearly shows more chances of developing osseous metaplasia. There is high level of osteocalcin in thyrocytes in papillary thyroid cancer patients, this shows that these are similar to osteoblasts which also have high level of osteocalcin\cite{17}. Ectopic bone formation is more common in older age group\cite{18}, in our case she was 41-year-old.

The presence of dystrophic calcification and bone formation may be seen in the necrotic areas of malignant neoplasm\cite{19}. Aurora et al stated that osseous metaplasia could be seen in benign lesions of thyroid as well as in malignant lesions like thyroid hyperplasia, follicular adenoma, papillary thyroid carcinoma and anaplastic carcinoma\cite{20}. Osseous metaplasia can also occur rarely in thyroid sarcomas or teratomas\cite{21}. There is another study which showed that osseous metaplasia is also associated with follicular carcinoma\cite{18}. Osseous metaplasia is extremely rare in benign thyroid neoplasm\cite{22}. In 1979 Tzankak described osseous metaplasia with ectopic bone formation, it was described as the presence of fresh and old hemorrhage cause fibrosis. Focal calcifications are common while osseous metaplasia is occasionally observed. Although dystrophic calcification in nodular goiter, osseous bone formation is very rare\cite{23}. Monckeberg sclerosing type calcification are found in perithyroidal vessels and may play a role in osseous metaplasia. In our case three attempts were given for fine needle aspiration and all came out as insufficient tissue, this emphasize the fact that any thyroid nodule which is hard and negative yield of tissue in FNAC should be suspected to have osseous metaplasia. In conclusion osseous metaplasia
is not a feature of malignancy or benignity, as it is very rarely seen in different lesions including benign and malignant, but it is not reported in normal thyroid tissue [23].

References:

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