

**Varied histopathological changes in thyroid lumps mimicking carcinoma radiologically: a Diagnostic Dilemma**

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**Correspondence Author:** Neema Tiwari, Eras Lucknow medical college and hospital, Lucknow, U.P. India**Type of publication:** Original Research Paper**Conflicts of Interest:** Nil**Abstract****Introduction**

Fine needle aspiration cytology (FNAC) of the thyroid gland is a first-line diagnostic test for evaluation of diffuse thyroid lesions as well as of thyroid nodules with the main aim of differentiating benign from malignant lesions and reducing unnecessary surgery [Orell SR, et al.,2005]. One of the common modalities in determining the diagnosis of thyroid lesions is fine needle aspiration. It is minimally invasive and cheap with good patient compliance and gives around 80 to 90% diagnostic yield.<sup>[4]</sup> However there are diagnostic difficulties in a post FNAC thyroidectomy specimen. TB in India is extremely common especially in young, adults than other age group. It is more common in female population in India where women remain poor and neglected.<sup>[1]</sup> Tuberculosis [TB] burden continues to remain huge with more than half cases not getting registered under Revised National Tuberculosis Programme [RNTCP]. Tuberculosis commonly is pulmonary where it exists as primary ,primary progressive, secondary and disseminated. Common extrapulmonary TB sites are the intestine skin, liver spleen meninges etc. In meninges tuberculosis commonly occur as abscess. When those abscesses rupture and release bacteria, tuberculosis meningitis occurs.<sup>[2]</sup> Thyroid is one of the lesser known organs to be affected by

tuberculosis. The thyroid gland maybe involved in two forms , first, and the more common, is miliary spread to the thyroid gland as a part of generalized dissemination. Second is the focal caseous tuberculosis of thyroid presenting as a localized swelling mimicking a tumor , a cold abscess, or a multinodular goiter with rarely an acute abscess.<sup>[3]</sup>

Thyroid undergoes secondary changes due to introduction of the needle. These changes can be schematically divided into two major groups--recent ones (intranodal bleeding and/or necrosis) and subacute/late ones (proliferation of granulation tissue with predominance of myofibroblasts or endothelial cells, resorptive pseudoxanthomatous granulomas, formation of sarcoid-like granulomas, capsular pseudoinvasion and scarring).<sup>[5]</sup> These varied histological alteration also called as Worrisome histological alterations following fine needle aspiration (WHAFFT) are seen in thyroid tissue due to trauma caused by the aspiration needle in FNAC. These include acute changes such as hemorrhage, granulation tissue, mitosis, granuloma, capsular distortion (pseudoinvasion) and infarction, and chronic alterations such as fibrosis, metaplasias, infarction, cholesterol granuloma, cyst formation, degeneration, papillary endothelial proliferation and calcification [LiVolsi VA et al;1994]. They cause difficulty in diagnosis of histopathological specimen received thereafter. Squamous epithelium in

thyroid lesions is an unusual finding and their presence has been attributed to metaplastic change in follicular epithelium by some authors or persistence of ultimobronchial body by others in areas of fibrosis and inflammation, secondary to hemorrhage. If it is extensive with associated degenerative epithelial changes, it can be easily confused with primary or metastatic malignancy. When metaplasia is extensive, they can present as thyroid nodule. Differentiation of FNAC related squamous metaplasia from malignancy is very necessary to choose appropriate treatment. Cholesterol granulomas are extremely rare in thyroid. Cases have been reported as Cholesterol granuloma in association with primary lipid metabolism disorders like Erdheim-Chester disease (ECD), can also be post inflammatory finding or some reported literature say it can be a part of WHAFFT [Pandit AA et al;2001].

We aimed our study to determine the incidence of secondary changes seen in cases undergone a previous FNAC as well as secondary diagnosis missed on FNAC. We reviewed cases over a period of one month where we had the FNAC findings as well as the biopsy findings and found total 10 cases where we had both the diagnosis out of which 6 showed the desired secondary changes and 1 showed secondary finding missed on FNAC.

**Keywords:** FANC, ECD, WHAFFT, TB, RNTCP

### **Material And Method**

We retrospectively reviewed cases over a period of one month where we had the FNAC findings as well as the biopsy findings and found total 10 cases where we had both the diagnosis. The cases were taken from dept of surgery and ENT Era's Lucknow medical college and analyzed in the department of pathology ELMCH.

### **Results**

We analyzed 10 cases of thyroid lesion where we had both cytological as well as histological diagnosis

available. 6 out of these 10 cases showed the desired secondary changes and 1 showed secondary finding of tuberculosis missed on FNAC.

### **Table In Separate File**

### **Discussion**

Starting with the benign lesions of the thyroid gland common lesions that we found in our study could be divided into non inflammatory and inflammatory. All 10 cases showed colloid goiter with 2 out of 10 cases showing multi-nodular goiter and 4 cases showing cystic degeneration with 1 showing secondary diagnosis of tuberculosis. Inflammatory lesion most commonly diagnosed are thyroiditis like hashimotos, Graves, autoimmune, de quervians etc. A rare cause of inflammation is thyroid tuberculosis. Tuberculosis thyroid is a very rare entity with less than 0.3% cases each year. The exact prevalence of TTB varies from 0.1 to 1% of all cases, and ranges from 0.6 to 1.15% of FNAC's results when performed for isolated thyroid nodule in endemic areas (India). The incidence of extrapulmonary tuberculosis is showing a progressive increase with time. Mean age of onset is around third to fourth decades with females being the most affected [4]. The scarcity of this entity may be explained by so many resistive mechanisms of the thyroid gland including bactericidal property of colloid material, increased vascularity, the presence of iodine in the thyroid gland and the anti-tuberculous activity of thyroid hormones [5-6]. Recently, the incidence of thyroid tuberculosis seems increasing due to the routine practice of fine-needle aspiration cytology (FNAC) which had an important impact on its diagnosis and management. TTB may be primary when isolated or secondary when associated with a disseminated disease which spreads directly from adjacent organs or by hematogenous route [6-7]. It presents as disseminated or less commonly as focal caseous tuberculosis of thyroid,

presenting as a localized swelling mimicking carcinoma [2]. It can also present as a cold abscess appearing superficially, as multinodular goiter [5, 6], or very rarely as an acute abscess [4]. Thyroid tuberculosis can also manifest itself as a common thyroid nodule, lump or with a cystic component [7]. The clinical presentation is often subacute, but it may be acute in case of abscess or thyroiditis [5, 8]. The patient may also be asymptomatic [7]. The thyroid function is preserved in the vast majority of cases although it can present as hyperthyroidism which occurs generally at the beginning of glandular involvement due to its destruction [3, 9]. The hypothyroidism is caused by extensive glandular destruction by caseous necrosis. In the literature, to the best of our knowledge, only three cases of hypothyroidism due to thyroid have been reported. The thyroid tuberculosis is usually not investigated because of its rare occurrence. If mycobacterial infection is suspected, a chest X-ray and a tuberculin skin test (PPD) should be performed [10-12]. The diagnosis is made only after fine-needle aspiration cytology (FNAC) or after histopathological examination of the surgical specimen when FNAC is negative [13-15]. The diagnosis of TTB remains difficult except when clinical or biological indications (Tuberculosis contagion, personal or family history of tuberculosis, cutaneous fistula on physical examination, long duration of fever, associated inflammatory syndrome or other tuberculous sites such as pulmonary or lymph node tuberculosis) are present. Moreover, TTB may take several clinical aspects of a thyroid involvement, the patient may present with subacute thyroiditis, thyroid abscess or fever of unknown origin, multi nodular goiter or only an isolated nodule. It can also mimic thyroid malignancy as patient may have dysphagia, dysphonia and laryngeal nerve palsy [8]. An anaplastic carcinoma's presentation is exceptional [9]. An interesting point to note is that general signs may be

lacking during the course of the disease. At the onset of the disease, hyperthyroidism may occur as a result of the destruction of the parenchyma and the massive release of thyroid hormones. Subsequently, hypothyroidism may appear by a total destruction of the gland. Dysfunction of the thyroid gland in TTB is rarely reported. In most cases, thyroid function is normal (10), only 3 cases of hypothyroidism have been described [6-11], and one patient presented transient thyrotoxicosis preceding hypothyroidism [11]. The imaging techniques (Ultrasonography, thyroid CT or MRI) are not very useful in diagnosis. USG may show a frank abscess with internal echoes or hypoechoic or heterogeneous lesion similar to neoplastic lesion [12]. Most often, Cervical CT findings show an isolated nodule or heterogeneous multifocal goiter or a hypodense lesion with peripheral enhanced contours after contrast material injection. The presence of cervical lymphadenopathy is possible [13]. Radiological imaging still indicate precisely the thyroid origin of the lesion, specify its solid or liquid nature and its extension to the adjacent structures.

The characteristic histological findings include epithelioid cell granulomas with central caseous necrosis, peripheral lymphocytic infiltration, and Langhan's giant cells [16]. In fact, *caseous necrosis* is a cytologic finding specific to tuberculosis. The simultaneous demonstration of acid fast bacilli (AFB) makes diagnosis almost certain. In this situation, a mycobacterial culture is helpful [15]. The imaging techniques are not very helpful in establishing the diagnosis and have been described only sporadically due to the disease's rare occurrence [17]. Many diseases may cause granulomatous inflammation in thyroid, like granulomatous thyroiditis, palpation thyroiditis, fungal infection, tuberculosis, sarcoidosis, granulomatous vasculitis, and foreign body reaction. However, caseation necrosis is seen only in tuberculous inflammation. In the

event where pain is absent, thyroid tuberculosis might be falsely diagnosed as thyroid malignancy; the two conditions may even coexist [20].

Other inflammatory lesion is Hashimoto's thyroiditis which histopathological presents with inflammatory infiltrate comprising of lymphocytes with some cases showing germinal centers and at times giant cells and granulomas. Hurtheloid/Oncocytic changes are seen in the lining epithelium. De Quervian's presents with granulomatous inflammation with mixed inflammatory infiltrate and giant cells and gives a dirty background on FNAC. [18-20]. Initially, treatment of thyroid tuberculosis consisted of antituberculous drugs combined with surgical removal of the affected parts of the thyroid gland or surgical drainage [3]. In cases with large abscess, surgical drainage or resection followed by antituberculous treatment is considered as sufficient, and further surgery is rarely required. FNAC associated changes may complicate the diagnosis of thyroiditis however in our case with the changes we saw clear cut granulomas so no diagnostic confusion was created.

WHAFFT changes associated with thyroid lesion due to FNAC have varied presentation. These varied histological alteration also called as Worrisome histological alterations following fine needle aspiration (WHAFFT) are seen in thyroid tissue due to trauma caused by the aspiration needle in FNAC. These include acute changes such as hemorrhage, granulation tissue, mitosis, granuloma, capsular distortion (pseudoinvasion) and infarction, and chronic alterations such as fibrosis, metaplasias, infarction, cholesterol granuloma, cyst formation, degeneration, papillary endothelial proliferation and calcification [LiVolsi VA et al;1994].

Squamous epithelium in thyroid is an unusual finding mostly seen in association with inflammatory & neoplastic conditions. Squamous metaplasia is reported in

normal thyroid gland, nodular goiter, thyroiditis, adenomas and carcinomas. Following FNAC, there may be oncocytic, squamous and spindle cell metaplasia. In one of our case; we can see squamous cells abutting upon recognizable follicular cells making a possibility of metaplasia occurring in colloid goiter. Squamous metaplasia is one of the rare alterations following FNAC. This term is first reported in human thyroid gland by Nicholson in (1922) who attributed it by severe chronic inflammatory and fibrotic change in the gland. Although the finding of squamous and oncocytic metaplasia may suggest malignancy, FNAC also cause similar changes, therefore it is important for the a pathologist to ask for patient history in order to differentiate these potentially malignant changes from the benign post FNAC process. Squamous cells can be derived from several sources: ectopic thymic tissue, remnants of ultimobranchial body, thyroglossal duct, metaplasia in thyroid tumors, and metaplasia of follicular cells.

Cholesterol granuloma of thyroid is extremely rare finding. Isolated cholesterol granuloma is generally seen with abnormal lipid metabolism suggestive of Erdheim-Chester disease (ECD), but can also present without it [Schmidt HH et al; 1997]. Here, cholesterol granuloma was thought to be secondary to post FNAC or as a part of WHAFFT lesion [Pandit AA et al; 2001]. It is suggested that thyroid puncture may have caused inflammation of the thyroid (subacute thyroiditis) leading to acute exacerbation of pre-existing Cholesterol granuloma or accumulation of cholesterol crystal incited a foreign body giant cell reaction. It is difficult to distinguish cholesterol granuloma of thyroid from carcinoma by clinical course and imaging finding. Even in cholesterol granuloma, surgery is necessary to control inflammation. It is a diagnostic pitfall and should not be misdiagnosed as malignancy. Calcification, fibrosis and hyalinization are

chronic alteration seen in chronic phase, usually developing within two months of FNAC and are generally accompanied by cholesterol clefts as seen in our case.

### **Conclusion**

FNAC related changes can cause a diagnostic dilemma with associated changes being marked. These features create diagnostic confusion and should be differentiated from more ominous lesions. Differentiation of metaplastic squamous cells from malignant squamous cells and anaplastic carcinoma is very important. Also important is to find missed secondary diagnosis once we receive the histopathological changes. Prompt diagnosis and treatment is a life saver for the patient.

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#### List of Figure

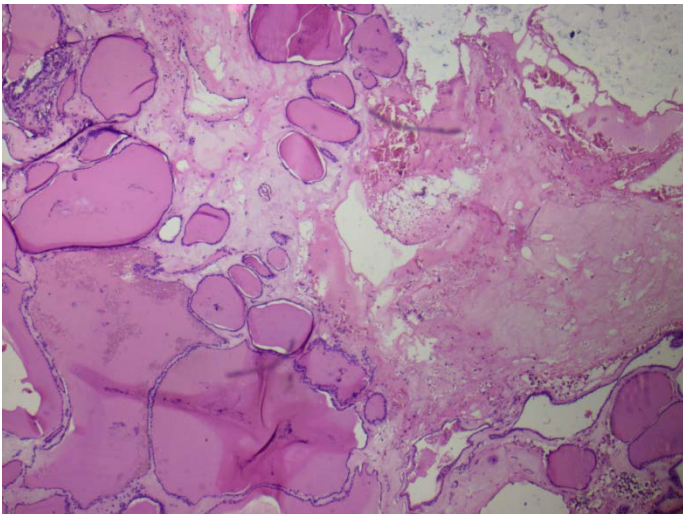


Fig 1- WHAFF changes in thyroid gland

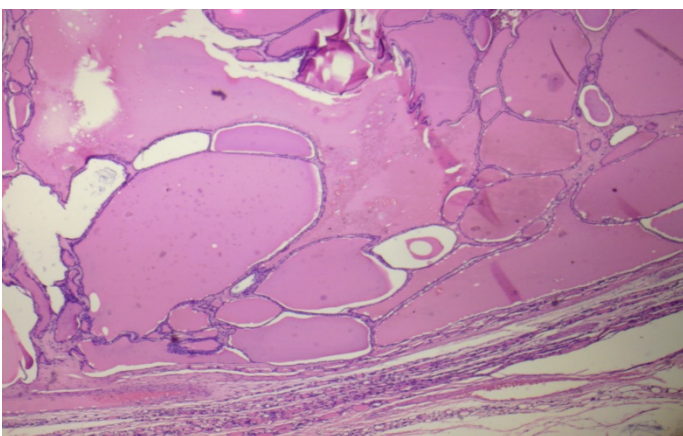


Fig 2- Dilated follicles with colloid

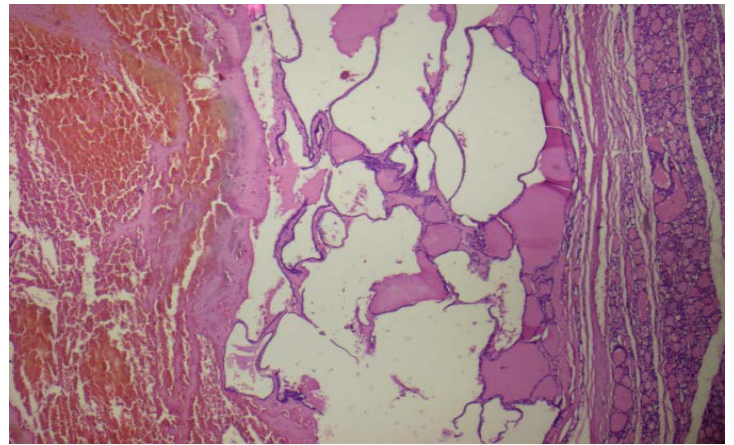


Fig.3- WHAFF changes with haemorrhage in thyroid

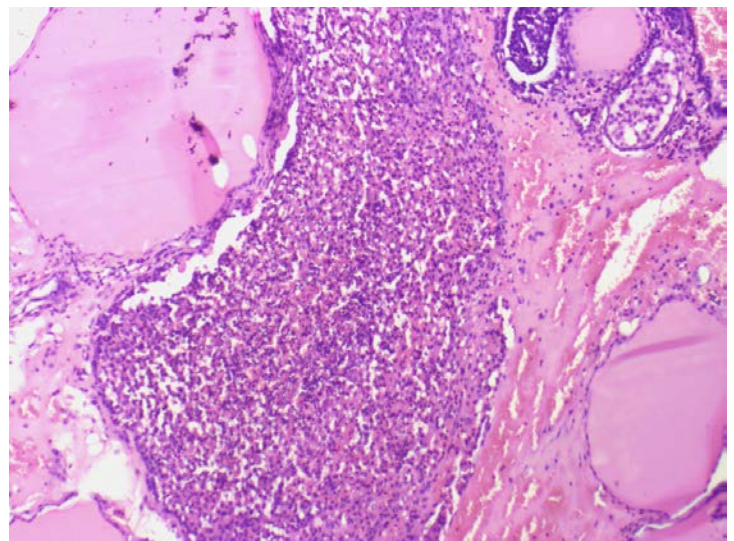


Fig 4-Inflammation admixed with haemorrhage in thyroid

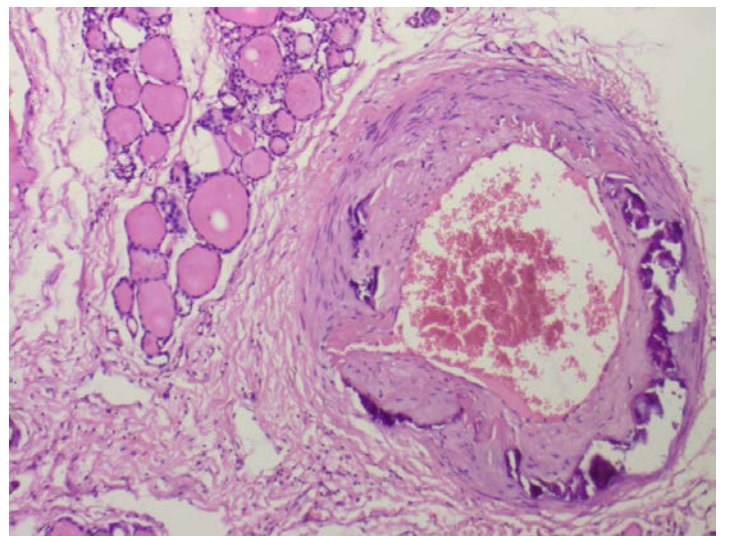


Fig 5- Calcification in vessel wall in thyroid



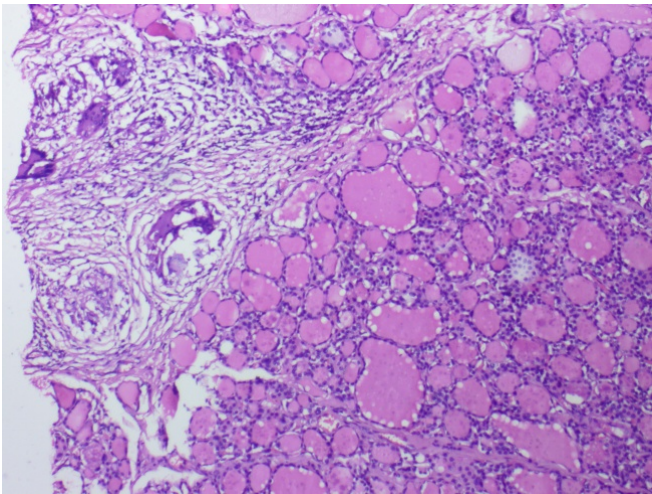


Fig.6- Tuberculous granuloma with giant cells in thyroid

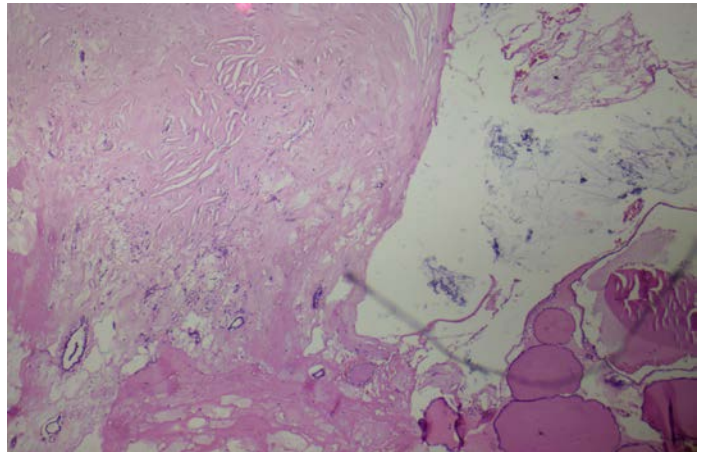


Fig.9-FNAC changes in thyroid

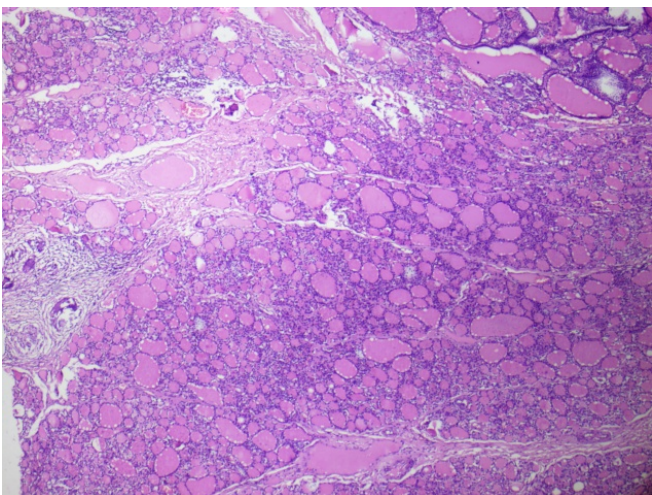


Fig 7- Granuloma as well as multiple nodules being formed in thyroid

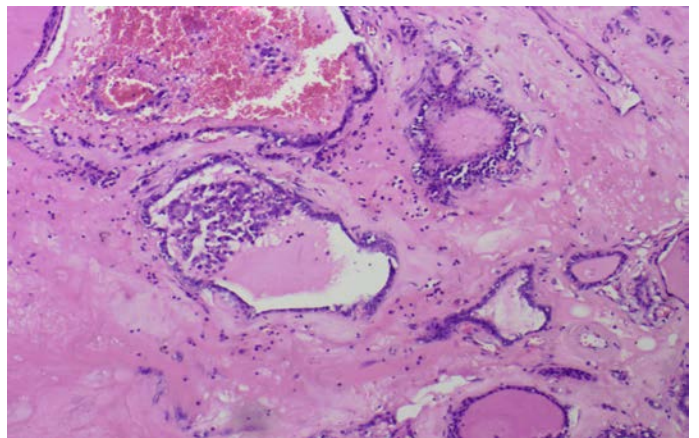


Fig.10-FNAC changes in thyroid

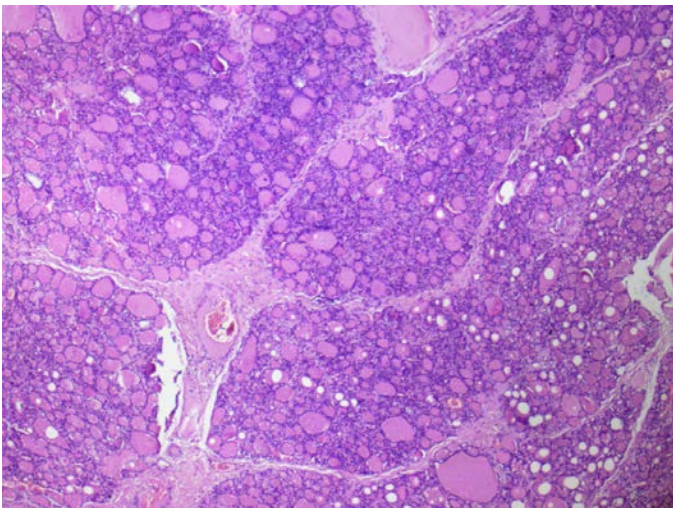


Fig 8-Multiple nodules thyroid



Fig 11- Gross of the thyroid with solid variegated area measuring 3x2 cms with normal looking thyroid circumferentially.

AGE/SEX	CF	USG	GROSS	FNAC diagnosis	Histopath. diagnosis	WHAF FT	SECONDARY DIAGNOSIS
60 YRS/F	left mid neck swelling x 2 months breathlessness X3yrs.Euthyroid	MNG	Solid areas resembling tumor with partially preserved thyroid gland.	Colloid goitre	MNG with WHAFFT changes and Tubercular thyroiditis	Present	Tuberculosis
38YRS/F	Midline neck swelling x 2yrs.Euthyroid	Cold abscess	Single globular, encapsulated soft tissue piece with variegated cut surface	Benign thyroid nodule with colloid degeneration	Colloid goitre with focal cholesterol cleft and foreign body giant cell reaction	present	-
42YRS/F	Left neck swelling x3months.Euthyroid	Colloid goitre with cystic degeneration	Multiple cysts largest ms.3x2x1 cm. Thick capsule and haemorrhage.	Colloid goitre with cystic degeneration	Nodular goitre with post haemorrhagic fibrotic nodule showing squamous metaplasia and cholesterol granuloma	present	-



AGE/SEX	CF	USG	Gross	FNAC diag.	Histopath diag.	WHAFFT	Secondary diagnosis
55YRS/M	left mid neck swelling x 2 months breathlessness X5yrs.	Benign nodule	Encapsulated, large cyst with colloid	Colloid goitre	Goitre with WHAFFT	Present	-
38YRS/F	Midline neck swelling x 1yrs.	MNG	Multiple encapsulated nodules	MNG	MNG	Absent	-
40YRS/M	Left neck swelling x3months.Euthyroid	Nodule with cystic degeneration	Cut surface variegated	Colloid goitre with cystic degen.	Goitre	Absent	-
60YRS/F	left mid neck swelling x 2 months	Benign nodule with cyst	Cyst measuring 3 cms in largest diameter	Colloid goitre with cystic degen.	Goitre with WHAFFT	Present	-
45YRS/F	Midline neck swelling x 1yrs.Euthyroid	Multiple cysts	Multiple colloid filled cysts	MNG	MNG	absent	-
50 YRS/F	left mid neck swelling x 6months breathlessness X3yrs.	Cold abscess	A solid area measuring 3x2 cms with normal thyroid parenchyma showing few cysts	MNG with haze and cyst macrophages	MNG with WHAFFT	Present	-
30YRS/M	Midline thyroid swelling x4 months.Hypothyroid	Benign nodule	A cyst with haze. ms 2x2 cms	Colloid goitre	Goitre	absent	-