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RESEARCH ARTICLE

Difficult Thyroid Histopathology in Nodular Goitre: A Diagnostic Dilemma- Case series of two cases.

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Abstract

Fine needle aspiration cytology (FNAC) is a rapid, inexpensive procedure which is also highly sensitive and specific in categorization of thyroid lesions. Although,there is a large body of world literature claiming possible limitations and pitfalls of this procedure. Various types of histological alterations 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, capsular distortion (pseudoinvasion) & infarction, and chronic alterations such as fibrosis, metaplasia, infarction, cyst formation, papillary degeneration, papillary endothelial proliferation and calcification. This case report describes two cases of Colloid goitre with difficult and unusual histopathological features causing confusion in diagnostic confirmation. Therefore, a thorough knowledge of possible FNAC related alterations is essential for correct diagnosis and opting appropriate treatment to avoid misdiagnosis.

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]. Various types of 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 ultimo-bronchial 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]. The present study describes two cases of Colloid goitre with difficult and unusual histopathological features causing confusion in diagnostic confirmation.

Material and method:-

Case 1:-

A 30 year male presented with gradually increasing midline neck swelling for 2 years. On examination, swelling was firm, oval, 3X3 cm in shape and moved with deglutition. Overlying skin was unremarkable. Systemic examination was unremarkable and no regional lymphadenopathy was present. Routine blood examinations were normal. Thyroid function tests revealed euthyroid state. USG findings were suggestive of benign thyroid nodule with colloid degeneration. FNAC was performed and a diagnosis of benign thyroid nodule with colloid degeneration was made. After 1 month, hemithyroidectomy done.

Grossly, a single globular, encapsulated soft tissue piece measuring 3.5X2.5X1.5 cm was received. Outer surface was greyish-white with focal areas of haemorrhage. Cut surface showed one large cystic areas measuring 1 cm in greatest diameter, filled with haemorrhagic and colloid like material. Peripheral areas showed multiple, variable sized cystic areas surrounded by dense, homogenous areas [Fig. 1a]. Microscopically, areas of necrosis, hypocellular eosinophilic hyalinized areas with foci of cholesterol clefts formation and foreign body giant cell reaction were seen.

Other areas showed few variable sized cystically dilated follicles lined by cuboidal to flattened epithelium filled with colloid and cyst macrophages. Few follicles lying in hyalinized matrix showed a gradual metaplastic transition from follicular epithelium to squamous epithelium with lumen filled with colloid [Fig. 1b]. Stroma also showed focal chronic inflammatory infiltrate with foci of entrapped small solid nests of squamous cells with prominent intracellular bridges and having glassy eosinophilic cytoplasm [Fig. 1c]. Neither mitotic figures nor cellular features of malignancy were seen. Few foci shows degenerative atypia in metaplastic squamous cells as hyperchromatic enlarged nucleus, clumped chromatin with prominent nucleoli and cholesterol cleft formation [Fig.1d, 1e]. Histologic diagnosis of Nodular goitre with post haemorrhagic fibrotic nodule showing squamous metaplasia and cholesterol granuloma was made.

Case 2 :-

A 28 years female presented with complaint of thyroid swelling since 4 months. On examination, swelling was diffuse, 5X4 cm, firm, non-tender and moves with deglutition. Systemic examination was unremarkable and no regional lymphadenopathy was seen. Routine blood investigations were normal. Thyroid function tests revealed euthyroid state. USG findings were suggestive of cold abscess. FNAC was done and diagnosis of Colloid goitre with cystic degeneration was made. Patient underwent hemithyroidectomy. On gross examination, lesion showed single grey-white, cyst measuring 4.5X3.5X 2 cm in size. Outer surface was smooth with attached fibrofatty tissue and cut surface showed unilocular cystic area filled with friable grey-brown material. Wall thickness varied from 0.2 to 0.3 cm [Fig. 2a]. Microscopically, numerous variable sized dilated as well as compressed follicles lined by single layer of cuboidal epithelium and filled with dense eosinophilic homogenous colloid were seen. Focal areas show scalloping of colloid in the follicle. Surrounding stroma showed focal areas of fibrosis, hyalinization, calcification [Fig. 2b], and cholesterol cleft formation [Fig. 2c] with surrounding foreign body giant cells. Mild inflammatory infiltrate comprising of predominantly lymphocytes and few plasma cells were also seen. No neoplastic pathology was identified. Histologic diagnosis of colloid goitre with focal cholesterol cleft and foreign body giant cell reaction was made.

Discussion:-

FNAC is the primary choice of investigation in thyroid gland pathology among other diagnostic methods because of its high sensitivity, specificity and rare clinical complications [LiVolsi VA et al; 1994, Gordon DL et al; 1993, . Ersöz C et al; 1997], but the trauma inflicted by the aspiration needle may lead to various degrees of histopathological alterations in the thyroid gland. LiVolsi and Merino [2004] have defined these alterations as WHAFFT. These are confined to areas near the needle tract and hence could be differentiated from other common lesion. As in both of our case the specimen showed a central large area of hemorrhage which was surrounded by various histological alterations as hyalinization, fibrosis, squamous metaplasia and cholesterol clefts was seen. WHAFFT include acute changes, most prevalent are hemorrhage, fibrosis, granulation tissue (along with giant cells and siderophagia), mitosis and chronic alterations such as fibrosis, metaplasia, infarction, cyst formation, papillary degeneration, papillary endothelial proliferation, and calcification [LiVolsi VA et al; 1994]. Development of these changes depends upon the time interval between thyroidectomy and FNAC.

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 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.

Few authors also suggested that a subpopulation of pleuripotent stem cell exist with a goitrous thyroid. It appears that squamous metaplasia results from stem cell differentiation of inflamed or reparative follicular epithelium towards squamous type [LiVolsi VA et al; 1978]. There is presence of chronic inflammation and fibrosis. The requirement of the substratum or stromal matrix for support of stem cell metaplastic process has been proved in rabbit in tracheal epithelium by Jetten et al. However the role of stroma here is unclear although of interest is that squamous metaplasia in thyroid is most frequently associated with fibrotic areas in the thyroid gland.

Cholestrol 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 Cholestrol 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.

Figures:-

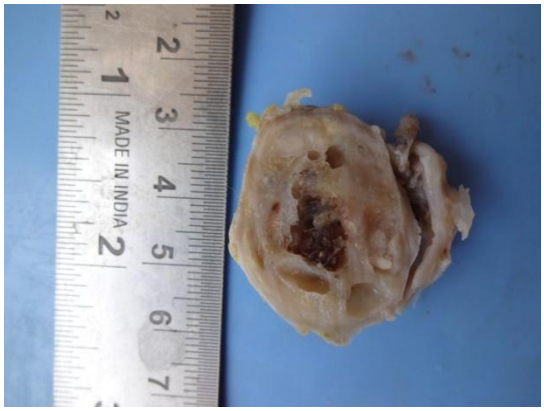

Fig. 1a

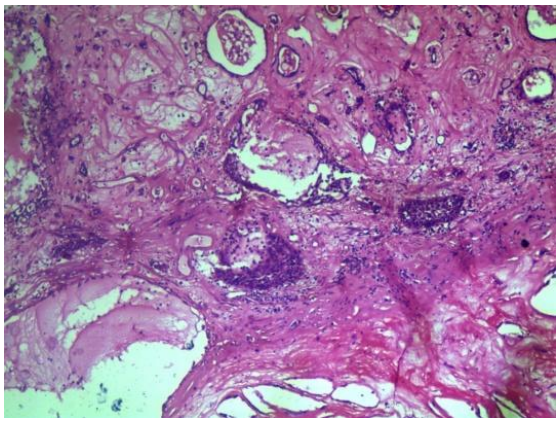

Fig. 1b

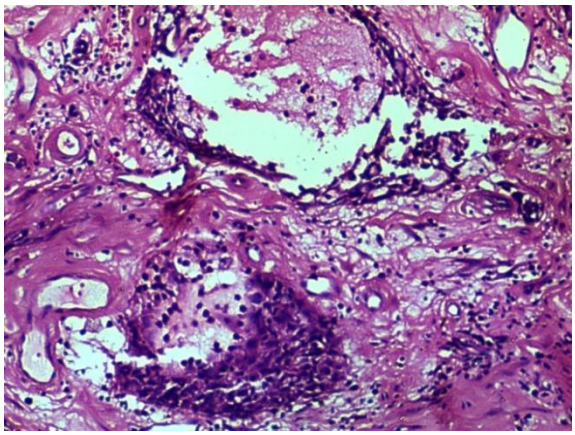

Fig. 1c

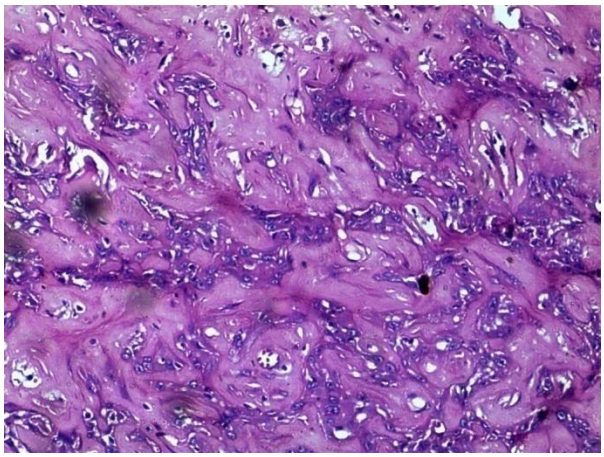

Fig. 1d

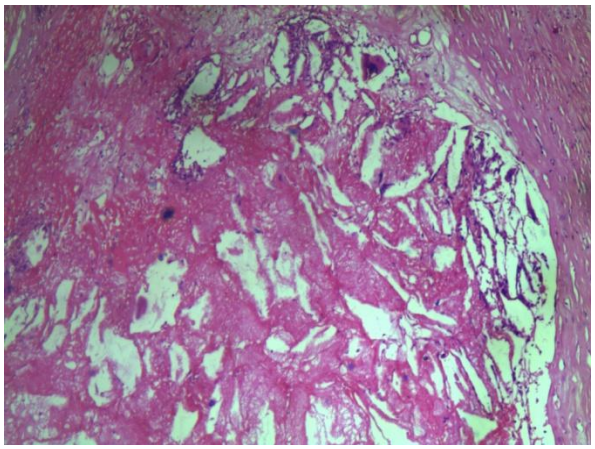

Fig. 1d

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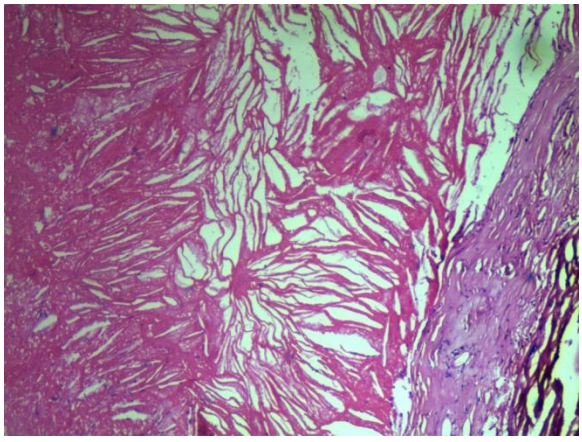

Fig. 1e

CASE 1- FIG. 1, [1a] shows one large cystic areas filled with haemorrhagic and colloid like material. Peripheral areas showed multiple, variable sized cystic areas surrounded by dense, homogenous areas.

[1b] shows Post FNAC changes showing hyalinization, haemorrhage, cholesterol cleft, squamous metaplasia and infarctions (100X)

[1c] shows thyroid follicles showing transition of columnar epithelium to squmaous epithelium (squamous metaplasia) (400X)

[1d] shows stromal hyalinization with entrapped squamous nests [100X]

[1e] shows cholesterol clefts with foreign body giant cell reaction [100X]

Fig. 2a

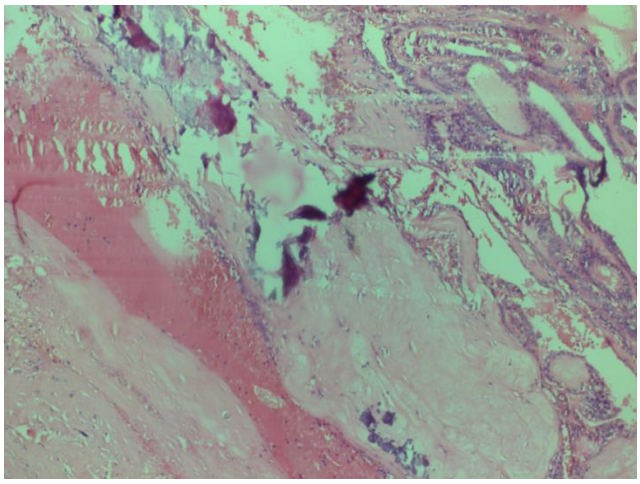

Fig. 2b

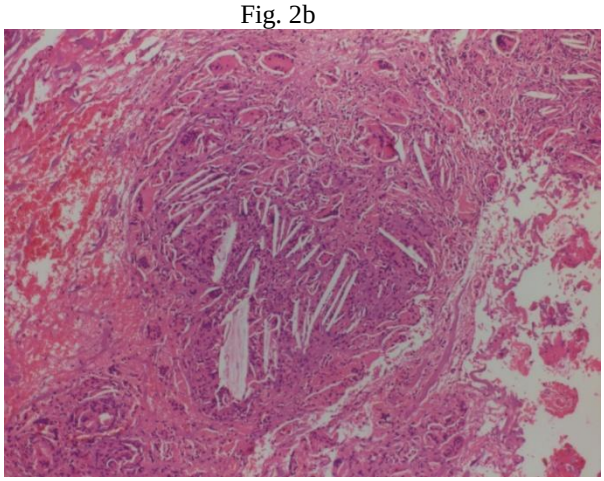

Fig. 2c

CASE 2- FIG. 2, [2a] shows unilocular cystic area filled with friable grey-brown material.
[2b] shows Post FNAC hyalinization and calcification (100X)
[2c] shows cholesterol cleft formation with surrounding foreign body giant cells (100X)

Conclusion:-

There is a large body of world literature claiming possible limitations and pitfalls of FNAC procedure [Hamburger JI et al; 1989, Ylagan LR et al; 2004]. As trauma inflicted by aspiration needle leads to various degree of histopathological alterations. 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. Streaming cohesive clusters with absence of mitosis and lack of obvious malignant features with background & awareness of the condition may readily assist in proper diagnosis. It is important to ask for history of the patient in case of aforementioned findings and avoid misdiagnosis. We report these cases because of its rarity & the pathologist should be aware of WHAFFT to avoid misinterpretation.

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