Preoperative diagnosis of follicular variant of papillary carcinoma of thyroid-A retrospective study

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Abstract

Background: Follicular variant of papillary carcinoma is the second common variant of papillary carcinoma. The diagnosis of follicular variant pre-operatively has been really very challenging and the incidence of false diagnosis is also very high. So, an attempt has been made to study the cytological as well as ultrasound findings of histologically proven cases of follicular variant of papillary carcinoma of thyroid.

Materials and Methods: Sonographic findings and cytology findings of 20 histologically proven cases of Follicular variant of papillary carcinoma of thyroid are retrospectively reviewed.

Results: Only 50% of cases were diagnosed as malignant on ultrasound and only 25% cases were diagnosed malignant on cytology.

Conclusion: The sensitivity of diagnosis is more radiologically, so all the thyroid FNAC should be done under ultrasound guidance and also nuclear features of Papillary carcinoma should be more carefully looked into in all suspicious cases. With these initiatives, the accuracy of cytological diagnosis of FVPTC can be substantially increased.

Key words: FNAC(Fine needle aspiration Cytology), FVPTC(Follicular variant of papillary carcinoma of thyroid)

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Introduction

Among the various malignancies that occur in the thyroid, Papillary carcinoma is the fore-runner[1,2], and several pathognomonic variants have also been described[3]. Several studies show that Follicular variant of papillary carcinoma is the second most common variant[1-5]. Cytologically FVPTC shows nuclear features of papillary carcinoma like nuclear crowding, grooves and inclusions but lacks papillae[2,4,6,7]. The behavior of FVPTC with respect to metastasis is different from classical papillary carcinoma but prognostically behaves similar to the classical papillary carcinoma of thyroid[3,4,8,9,10,11]. Depending upon the similar biological behavior, the current treatment for FVPTC is similar to that given for classical variant.[3-5,11] Several studies have been done to prove the similar biological behavior of FVPTC to that of classical variety of PTC[3,4,6-8,10,11]. When compared to classical variant, Follicular variant of papillary carcinoma is more likely to be missed during diagnosis. Both the ultrasound and FNAC have not succeeded in rightly predicting this variant. Very few studies have been done to study the accuracy of Ultrasound and FNAC in predicting the diagnosis of FVPTC. In this study, the preoperative Ultrasound features, cytopathological characteristics in thyroid lesions diagnosed as FVPTC were evaluated so as to analyse whether any of these characteristics are useful in increasing the sensitivity of preoperative diagnosis of FVPTC.

Materials and Methods

Between January 2010 and January 2016 study period, all the cases diagnosed as FVPTC on histopathology were included. The ultrasound findings in all these cases were retrieved. The radiologists have defined malignant sonographic features as 1)pronounced hypoechogenicity (echogenicity that is lesser than that of the adjacent strap muscle), 2)micro lobulated or irregular margins, 3)more in length than width (greater in the longitudinal dimension than the horizontal dimension in any plane), and 4)micro calcifications. Thyroid swellings were labelled as suspicious for malignancy if any one of the above four findings was present radiologically. Suspicious for malignancy is considered positive predictability of the lesion by ultrasound and then the sensitivity of ultrasound in predicting malignancy in all the diagnosed cases of FVPTC were calculated.

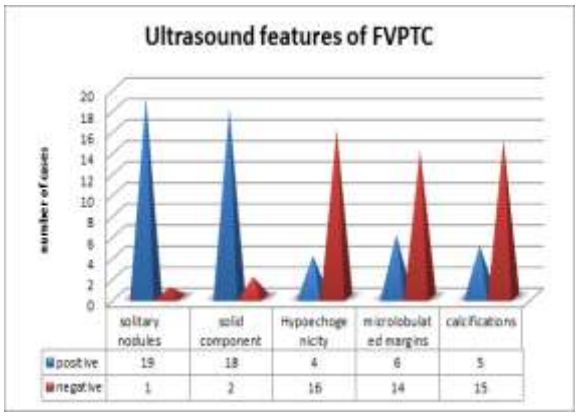
Fine-needle aspiration cytology findings were analysed in all of the thyroid lesions. The features that were looked into are cellularity of the smears, presence of sheets, syncytial clusters, papillary fronds, presence of colloid(thick/thin), Nuclear features including nuclear grooves, inclusions and presence of calcifications. Cytology findings were grouped according to the six categories in the Bethesda System for reporting Cytopathology: non-diagnostic group,

benign group, atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) group, follicular neoplasm or suspicious for follicular neoplasm group, suspicious for malignancy group, and malignancy group[12]. A result of papillary carcinoma or a diagnosis given as suspicious for papillary carcinoma was considered as a positive result, and the sensitivity of FNAC in detection of FVPTC is calculated.

Results

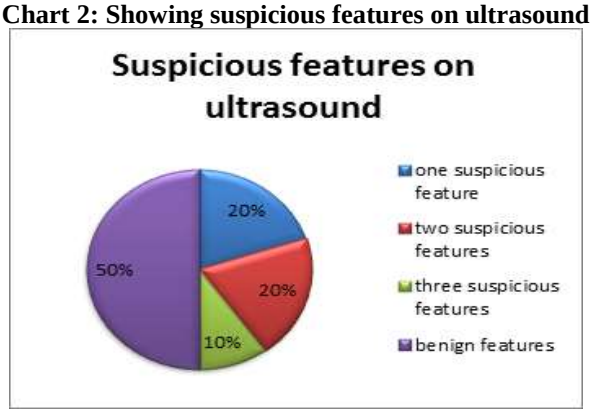
A total number of 20 cases were histologically diagnosed as FVPTC during the study period. The size of the thyroid swelling in confirmed cases of FVPTC varied from 3mm to 34 mm. Among the 20 cases, 19 cases(95%) presented as solitary nodules where as one case (5%)presented with multiple nodules. Eighteen nodules (90%) were solid, and 2 (10%) were having both solid and cystic areas(Chart 1).

Chart 1: Showing the ultrasound features of thyroid lesions



Among the various criteria laid down for a malignancy on ultrasound, 4 cases (20%) had 1 suspicious criteria; 4 (20%) had 2 suspicious criteria; and 2 (10%) had 3 suspicious criteria.(Chart 2)

Chart 2: Showing suspicious features on ultrasound



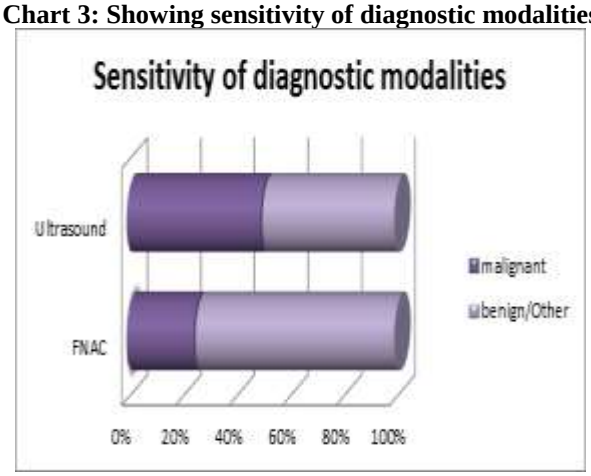
In the 10 cases(50%) with suspicious sonographic features, the most frequently seen sonographic finding was an irregular/ microlobulated margins seen in 6 cases(60%). Ten lesions (50%) were classified as malignant nodules as per the criteria accepted and described above and 10 (50%) were classified as benign. In terms of the cytologic results, that were grouped as per Bethesda system of reporting, 4 cases (20%) were non-diagnostic, 3 cases (15%) were diagnosed as benign (adenomatous goitre); 8 cases(40%) were diagnosed as follicular neoplasm,1 (5%) was diagnosed as suspicious for papillary carcinoma; and 4 (20%) were diagnosed as Follicular variant of papillary carcinoma.

Table 1: Bethesda System of reporting the FNAC findings

S. No	Bethesda reporting criteria	No of cases
1	Non diagnostic	4
2	Benign(Adenomatous goitre)	3
3	Follicular Neoplasm	8
4	Suspicious for Papillary carcinoma	1
5	Follicular variant of Papillary carcinoma	4

The diagnosis of FVPTC or suspicious findings for papillary carcinoma on FNAC were considered as positive results. Thus, the sensitivity of diagnosing FVPTC on FNAC was 25% (5 0f 20). (Chart 3).

Chart 3: Showing sensitivity of diagnostic modalities



The cytological pictures showing branching sheets, syncytial clusters and inclusions in the nucleoli are depicted(Fig.1, 2, 3).

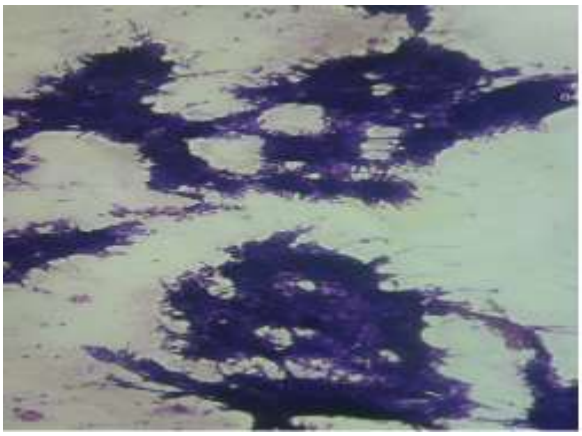


Fig. 1: Showing branching sheets of thyroid follicular cells

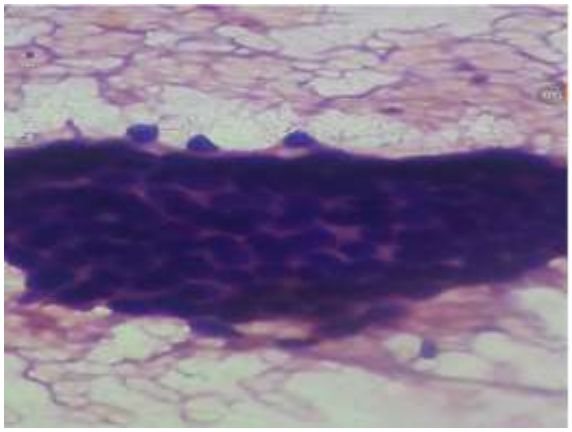


Fig. 2: Showing syncytial clusters of thyroid follicular cells

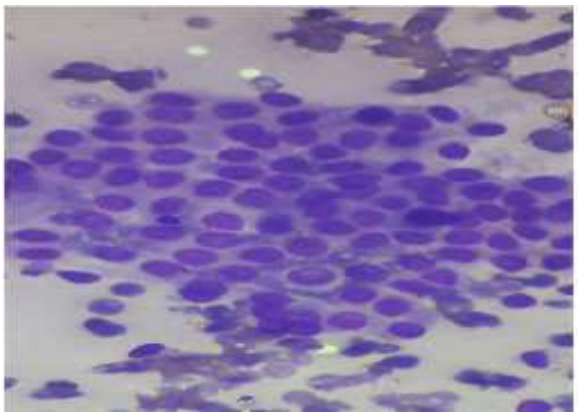


Fig. 3: Showing intranuclear inclusions in thyroid follicular cells

Three cases (15%) were diagnosed as benign nodules, and 4 (20%) were non-diagnostic samples on FNAC. Of the 10 nodules classified as malignant nodules on sonography, 3 were diagnosed as papillary carcinoma or suspicious for papillary carcinoma on FNAC, the rest of the 6 nodules though were given on ultrasound as malignant nodules, could not be diagnosed on FNAC. Among the 5 cases that were positive for diagnosis of FVPTC on cytology, the ultrasound findings were suspicious or diagnostic of malignancy only in 3 cases, the rest of the 2 cases had benign findings on sonography.

Discussion

Crile and Hazard get the credit of discovering the entity of FVPTC, although they named it as alveolar variant of PTC[13]. Lindsay was responsible for the designation of FVPTC. Chen and Rosai have firmly established the criteria for diagnosing this tumor saying that although the papillary architecture is absent, the presence of nuclear features is crucial in the diagnosis of this lesion[14]. The diagnosis is not straightforward as the follicular pattern seen here is noted in follicular adenoma, multinodular goiter also and careful observation of nuclei is crucial[15,16]. As the nuclear features carry the only clue, it is very likely to be missed on FNAC and a wrong diagnosis is possible[17]. When on FNAC, the nuclear features of papillary carcinoma are found focally, these lesions are put in the category of suspicious lesions and on resection such lesions more often than not harbor FVPTC and the tumor size also is found to be larger than for classical variant of PTC[18,19,20]. The studies of Shih and Shun et al show that the sensitivity of FNAC diagnosis of FVPTC was 42%[21]. Sensitivity of FNAC for the diagnosis of FVPTC was only 25% whereas the classic variant diagnosis had a sensitivity of 74% as per the studies of Lin HS et al.[22]

In our study, the sensitivity was low and was 25% which is similar to the results of Lin HS et al[22]. The misdiagnosis of FVPTC as follicular adenoma or adenomatoid goiter would result in revision thyroidectomy and increased morbidity for the patient. Cytological criteria for foolproof diagnosis of FVPTC in FNAC are yet to be established[23]. Apart from the nuclear features, other corroborative features have been studied by various authors. The studies of Aron et al[24] indicate nucleomegaly to be a significant feature apart from nuclear clearing and grooving. The studies of Wu et al[23] showed that branching syncytial sheets and thick colloid are other corroborative features in addition to nuclear features.

In our study apart from the nuclear features that were seen in all the diagnosed cases, microfollicular and syncytial clusters were the other dominant patterns and a thick colloid was seen in 2 cases. As per the studies of Powari et al,[25] FVPTC should be suspected in all cases showing follicular arrangement with syncytial clusters and thick colloid. Shih SR et al,[21] concluded in their study that whenever the diagnosis of follicular neoplasm is being given, the smears have to be diligently searched for nuclear features and the study also showed the fact that classical PTC and FVPTC also cannot be differentiated on FNAC. The studies of Yan et al.,[26] showed that whenever one encounters branching sheets of follicular cells, careful search has to

be made for nuclear features. In our study we analyzed H&E slides and identified nuclear grooves in 4 cases, pseudoinclusions in 5 cases. The study indicates that in all cases where one encounters cellular smears with features like branching sheets, syncytial clusters, nucleomegaly and thick colloid one has to deligently search for more specific nuclear features of papillary carcinoma. This approach will help in not missing the diagnosis of FVPTC on cytology. Right diagnosis on cytology would help in application of more appropriate treatment modalities.

When the role of ultrasound is considered, FVPTC presents with more benign features than classical PTC[2,9]. The common ultrasound features of FVPTC observed in our study were a solid texture, presence of hypoechogenicity, microlobulated margins, absent calcifications, and an oblong shape, corresponding to the results obtained in the previous studies[2,9]. Though most of the above said features are not diagnostic of malignancy, 50% (10 of 20 lesions) had more than one suspicious ultrasound feature. This indicates that Thyroid ultrasound plays an important role for predicting the diagnosis of malignancy in FVPTC to some extent. This study brings to light the fact that the sensitivity of Ultrasound is higher in predicting malignancy in cases of FVPTC when compared to cytology alone.

Based on the above facts, we arrive at a conclusion that as to increase the sensitivity of FNAC, all thyroid FNAC should be performed under ultrasound guidance and the lesions found to be suspicious on Ultrasound should be subjected to multiple pokes from various areas to obtain representative sampling and this procedure along with diligent search for the cytological features of FVPTC, suspecting its possibility in all smears with branching sheets, syncytial clusters, thick colloid and nucleomegaly would definitely rise the sensitivity value in general and particularly in our institution.

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