Case Report

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Diffuse Follicular Variant of Papillary Thyroid Carcinoma (DFVPTC) - "A Challenging Diagnostic Entity"

Pathology Section

ANSHU GUPTA, SWAPNIL AGARWAL, PRATIMA KHARE, KARSING PATIRI, MUKTA AHUJA

ABSTRACT

Diffuse Follicular Variant of Papillary Thyroid Carcinoma (DFVPTC) presents unique challenges to the pathologists with respect to its histological diagnosis, as it closely mimics nodular colloid goitre. Herein we present a case of FVPTC-diffuse follicular type initially diagnosed as adenomatous colloid goitre with cystic change on FNAC. The patient was a 35-year-old female with complaints of progressively increasing swelling in right anterior neck for two years. Clinical examination revealed thyroid swelling measuring 7x5cm, more on the right side. CT-scan showed multiple well defined heterogeneously enhancing masses with shifting of trachea and larynx to left side. Histopathological examination revealed follicles of varying sizes lined by cells showing typical papillary nuclear features, intrafollicular haemorrhage and multinucleated histiocytes in the lumen of follicles. In view of these microscopic findings especially presence of multinucleated histiocytes, final diagnosis of diffuse follicular variant of papillary thyroid carcinoma was rendered. The aim of this case report is to highlight and put forth distinctive histo morphological features that helps to distinguish between DFVPTC and nodular colloid goitre.

Keywords: Adenomatous colloid goitre, Intrafollicular haemorrhage, Thyroidectomy

CASE REPORT

A 35-year-old female presented in ENT OPD with complains of gradually increasing midline neck swelling for 2 years. It was more on right side, measuring 7x5cm, moving with deglutition confirming its thyroid origin. The patient was referred to Pathology Department for FNAC. On the basis of cytomorphological findings, the presumptive diagnosis of adenomatous colloid goitre with cystic changes was given.

Computed Tomography (CT) demonstrated diffuse asymmetric enlargement of thyroid with multiple well defined heterogenously enhancing masses. Trachea and larynx were displaced to left side by enlarged thyroid along with posterolateral displacement of carotid and jugular vessels on right side with no evidence of obstruction. The CT-scan findings were suggestive of multinodular goitre.

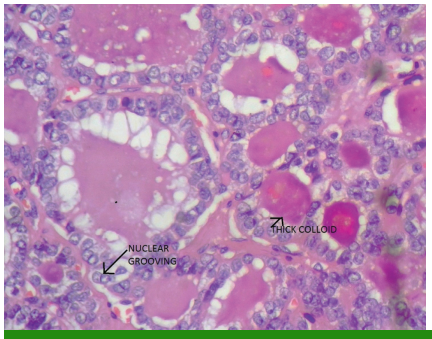
The patient underwent total thyroidectomy under general anaesthesia and the resected specimen was sent for histopathological examination. Grossly the specimen consisted of two globular pieces, larger one measuring 8x7x5cm and smaller one measuring 4.5x2.5x2cm. On cutting the larger piece three nodules were identified - cut section was greyish white, firm with variegated appearance. Cut section of smaller one was brownish with areas of haemorrhage [Table/Fig-1].

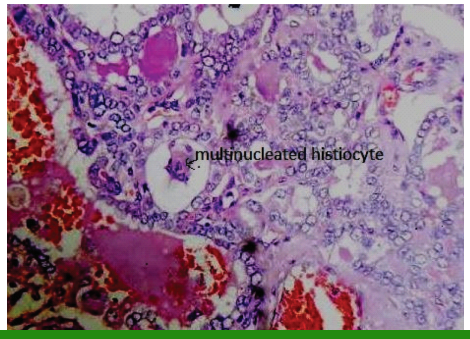
Microscopic examination revealed thyroid neoplasm composed of follicles of varying sizes ranging from microfollicular to normo to macrofollicular pattern lined by

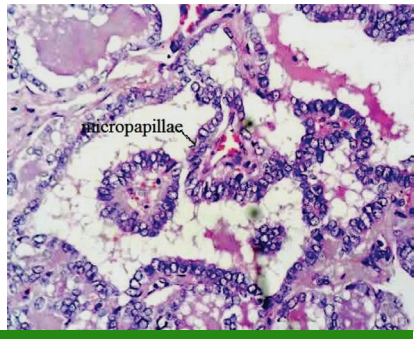
[Table/Fig-1]: Total thyroidectomy specimen bisected, showing whitish nodules replacing the gland.

columnar cells with oval ground glass empty looking nucleus ("Orphan Annie") showing overcrowding, loss of polarity and occasional nuclear grooving [Table/Fig-2]. There were areas showing intrafollicular haemorrhage, scalloping, focal dark colloid and characteristic multinucleated histiocytes in the lumen [Table/Fig-3]. Focal areas showing micro papillae were also seen [Table/Fig-4]. On the basis of above mentioned findings the diagnosis of DFVPTC was rendered.

The patient made an uneventful recovery and was discharged







[Table/Fig-2]: Diffuse follicular variant of papillary thyroid carcinoma showing characteristic papillary nuclear features (H&E, 40X).
[Table/Fig-3]: Diffuse follicular variant of papillary thyroid carcinoma with multinucleated histiocyte in follicular lumen in centre (H&E, 40X).
[Table/Fig-4]: Diffuse follicular variant of papillary thyroid carcinoma showing micropapillary structure in centre (H&E, 40 X).

on the 8th postoperative day. Thereafter she was referred to higher centre for radioactive iodine therapy. Further follow-up of the patient is still awaited.

DISCUSSION

Papillary carcinoma of thyroid accounts for 85.3% of all thyroid malignancies. It is a malignant epithelial tumour showing follicular cell differentiation with distinctive nuclear features i.e., clear or pale nuclear chromatin, overlapping oval nuclei with grooves and /or pseudo inclusions, arranged in the form of papillae and follicles [1]. It shows female preponderance with most patients presenting with neck mass with or without nodal metastasis and can present at any age. Many predisposing factors have been implicated namely - radiation exposure, Hashimoto's thyroiditis and familial adenomatous polyposis [2].

Follicular Variant of Papillary Carcinoma (FVPTC) is a distinct subset of papillary carcinoma with respect to its diagnosis, prognosis and treatment. Especially, its Diffuse Follicular Variant (DFVPTC) is often confused with colloid goitre. The aim of this case report is to highlight and put forth distinctive histomorphological features that help to distinguish this entity from nodular colloid goitre.

FVPTC accounts for 15-20% of papillary thyroid carcinoma. There are several subtypes, such as encapsulated follicular, diffuse follicular and macrofollicular variant [3]. Encapsulated and macrofollicular have an indolent course. In contrast, DFVPTC is a distinct aggressive variant that occurs primarily in young women that demonstrates higher rate of extrathyroid extension, multicentricity, lymph node involvement and distant metastasis. Grossly the tumour resembles multinodular goitre with distinct white nodules replacing the entire gland [4]. Studies have shown that DFVPTC also exhibits higher BRAF V600E mutation [1].

Although, ultrasound imaging and fine needle aspiration cytology play an important role in management of thyroid malignancies there are some limitations, it is difficult to comment on the nature of follicular lesions on cytological grounds, therefore histological examination is must to arrive at definitive opinion. Furthermore, histopathologists still face difficulty in clearly distinguishing between cases showing overlapping features of nodular colloid goitre, follicular adenoma versus DFVPTC. Studies have also pointed towards the fact that significant inter-observer disagreement exists to the extent of 40% of such cases [1]. This problem may be due to absence of consensus on the minimum criteria required to definitively diagnose and label lesions with intermediate features as FVPTC in particular diffuse follicular type. As far as FVPTC is concerned histopathology still remains the last resort for accurate diagnosis as immunohistochemical markers, either positive or negative are not 100% diagnostic of FVPTC [5].

In this case in order to arrive at a conclusive opinion, we followed the criteria proposed by Chen et al., [1], wherein four major and five minor features were taken into consideration. The four major features to be looked for are: (a) Oval rather than round nuclei; (b) Crowding of nuclei with lack of polarity; (c) Clear/pale nuclear chromatin pattern throughout the lesion or prominent nuclear grooves; and (d) Presence of psammoma bodies. According to Chen, in the presence of any one of these major features, the presence of all the five minor features listed subsequently is necessary to establish a diagnosis of FVPTC. These minor features are: (a) Presence of abortive papillae; (b) Predominantly elongated or irregularly shaped follicles; (c) Dark staining colloid; (d) Presence of rare nuclear pseudoinclusions; and (e) Multinucleated histiocytes in the lumen of follicles.

In this case three major features except psammoma bodies were present and all the minor features could be appreciated focally thus establising a diagnosis of FVPTC. In another study by Radina Ivanova et al., following morphologic criteria listed subsequently were followed to diagnosed DFVPTC [6]: (a) Involvement of whole thyroid gland or entire lobe; (b) Exclusive follicular growth pattern; (c) No psammoma bodies; (d) No fibrosis; and (e) Discrete or no lymphocytic infiltration. Present case discussed fulfilled all the above criteria and therefore, we labelled it as diffuse follicular type.

Another feature which we took seriously was to look for the presence of multinucleated histiocytes in follicular lumen. In a study by Guiter GE et al., in which they analysed 76 cases

of papillary thyroid carcinoma for presence of this particular feature and could appreciate it in approximately 50% of them [7]. They concluded, that their presence can aid in diagnosis of papillary carcinoma as they are rarely found in other thyroid lesions and tumours. In our case also we could demonstrate their presence focally, so in cases wherein there is diagnostic dilemma they can tilt the balance in favour of papillary carcinoma pushing other benign and inflammatory conditions behind.

CONCLUSION

DFVPTC presents unique challenges regarding its histomorphological diagnosis. Proper attention to major and minor histological features helps in arriving at conclusion to label FVPTC. Involvement of entire thyroid/lobe with follicles having characteristic papillary nuclear features, no fibrosis and partial/ no encapsulation favours diffuse variant.

Presence of multinucleated histiocytes in the follicular lumen can tilt the balance in favour of DFVPTC versus colloid goitre. A thorough search for the same is therefore warranted in all suspicious cases. It is important to distinguish this variant of FVPTC from other variants of papillary carcinoma, as well as from colloid goitre because of its aggressive nature and further management.

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AUTHOR(S):

1. Dr. Anshu Gupta
2. Dr. Swapnil Agarwal
3. Dr. Pratima Khare
4. Dr. Karsing Patiri
5. Dr. Mukta Ahuja

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Pathology, Baba Saheb Ambedkar Medical College and Hospital, Rohini, Delhi, India.
2. Medical Officer, Baba Saheb Ambedkar Medical College and Hospital, Rohini, Delhi, India.
3. HOD, Department of Pathology, Baba Saheb Ambedkar Medical College and Hospital, Rohini, Delhi, India.
4. Assistant Professor, Department of Pathology, Baba Saheb Ambedkar Medical College and Hospital, Rohini, Delhi, India.
5. Senior Resident, Department of Pathology, Baba Saheb Ambedkar Medical College and Hospital, Rohini, Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Anshu Gupta,
Flat No. C- 601, ATS Haciendas, Ahinsa Khand -1,
Indirapuram, Ghaziabad-201014, U.P., India.
E-mail: amitanshu75@gmail.com

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