International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 01 Issue 10 December 2021

Page No: 350-353

DOI: https://doi.org/10.47191/ijmscrs/v1-i10-07, Impact Factor: 5.276

Signet Ring Cell Adenoma Thyroid – A Case Report

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ABSTRACT

Signet ring cell adenoma is a rare thyroid neoplasm which usually present as a solitary nodule. Histopathologically it can very well be mistaken for a metastatic signet ring cell lesion, as both of them shows cells with intracytoplasmic vacuole and eccentrically pushed nucleus. The intracytoplasmic vacuole in signet ring cell adenoma stain positive for thyroglobulin which help in confirming the diagnosis. Here we describe a case of signet ring cell adenoma of thyroid in a 46-year-old female with its cytological, histological and immunohistochemical features.

KEYWORDS: Signet ring cell adenoma, Follicular adenoma, Thyroid

ARTICLE DETAILS

Published On:
17 December 2021

Available on:
https://ijmscr.org

INTRODUCTION

Signet ring cell adenoma of thyroid is a variant of follicular adenoma which is very rare but well described. Patients usually present with asymptomatic or mildly symptomatic thyroid nodule[4]. Histopathology shows signet ring cells arranged in microfollicles, which can simulate other primary and secondary lesions with signet ring cell morphology[3,4]. Other lesions in thyroid with signet ring cells include, follicular carcinoma, follicular variant of papillary thyroid carcinoma, secretory carcinoma, metastatic signet ring cell carcinoma and metastatic renal cell carcinoma.

CASE REPORT

We would like to report a case of signet ring cell adenoma thyroid.

A 46year old female presented with complaints of swelling in front of neck of 1 year duration, which was progressively increasing in size. This was associated with dysphagia. On physical examination a 3 x 3 cm irregular firm nodule was palpable in the left lobe of thyroid which was not crossing the midline. Right lobe appeared normal and no cervical lymph node was palpable.

Laboratory investigations revealed an elevated thyroglobulin level (Thyroglobulin – 88.04µg/dl) and unremarkable free thyroxine and TSH levels.

The ultrasonogram demonstrated a partially exophytic relatively large, mildly hypoechoic nodule Measuring 3 x 2.8 x 1 cm in the upper pole of left lobe of thyroid with peripheral and internal vascularity, likely TIRADS IV nodule **(figure.1).** A fine needle aspiration cytology of the thyroid nodule was performed and the report came as follicular lesion of undetermined significance in a background of lymphocytic thyroiditis, Bethesda category 3 **(figure 2)**.

Following this a total thyroidectomy was carried out. On gross examination, thyroid weighs 20grams, right lobe with isthmus measures 3.5 x 2 x 1.2cm and left lobe measures 3 x 3 x 1.5cm. Also, upper pole of left lobe shows a pedunculated nodular mass measuring 3.5 x 2.4 x 1cm. On cut section, nodular mass on the upper pole of left lobe shows a well circumscribed encapsulated grey white lesion with specks of haemorrhage. There is no capsular infiltration grossly. Cut section of rest of the left lobe, right lobe and isthmus is grey brown glistening **(figure.3)**. On histopathological examination the nodule shows a well encapsulated neoplasm, composed of cells arranged in microfollicles and sheets. Individual cells are round to ovoid with pale vacuolated cytoplasm and eccentrically pushed irregular vesicular nucleus with fine chromatin. Stroma shows foci of haemorrhage. No vascular or capsular invasion seen **(figure.4)**. On immunohistochemical examination thyroglobulin shows intracytoplasmic positivity **(figure.5)** and TTF1 intranuclear positivity **(figure.6)**.

Patient had uneventful post-operative period and was discharged and is on regular follow up since February 2021.

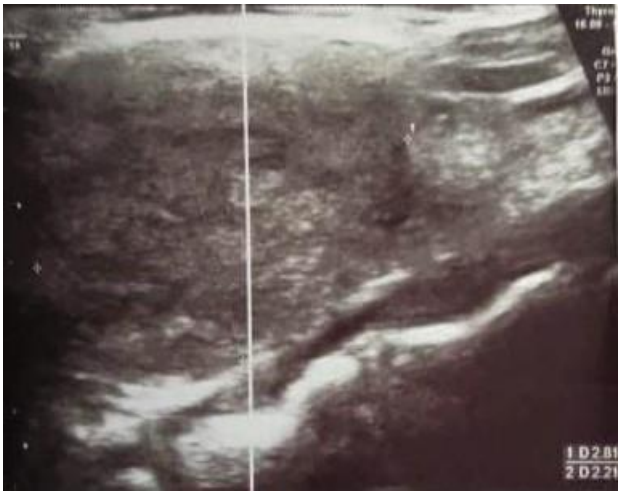

Figure 1: USG Image of Thyroid Nodule

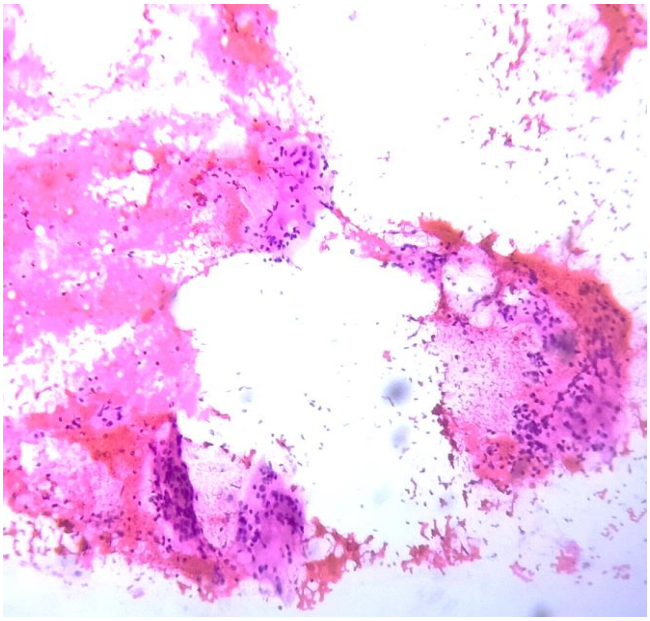

Figure 2: Fine needle aspiration cytology (100x)

Figure 3: Gross Image

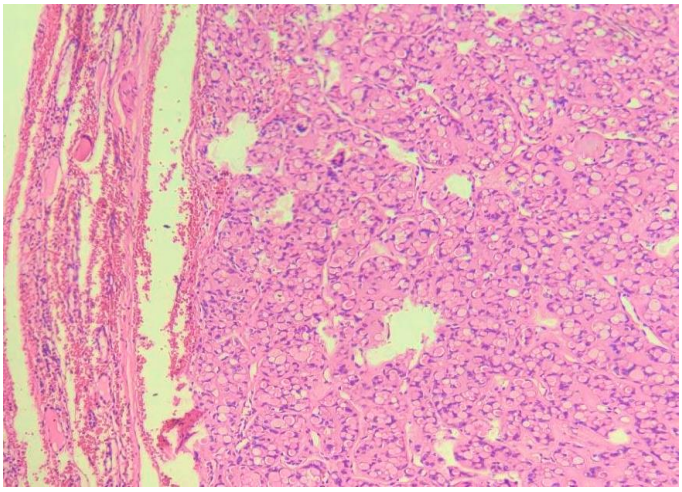

Figure 4: Microscopy (100x)

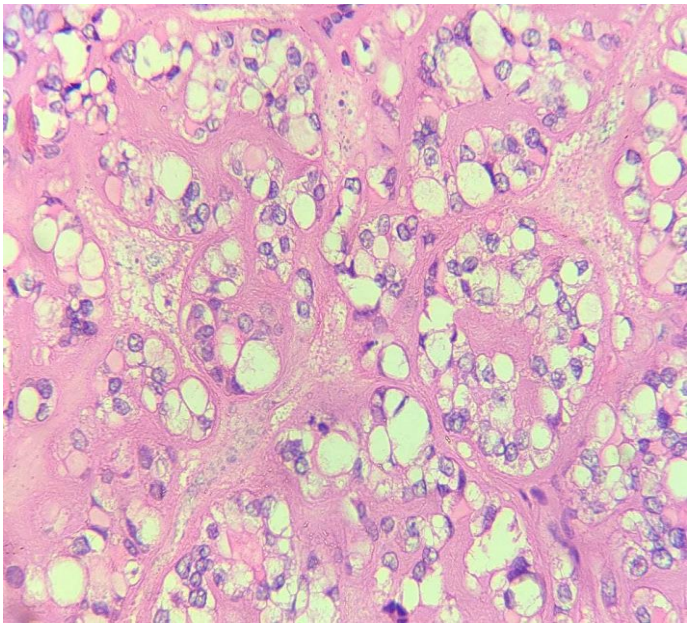

Figure 5: Microscopy (400X)

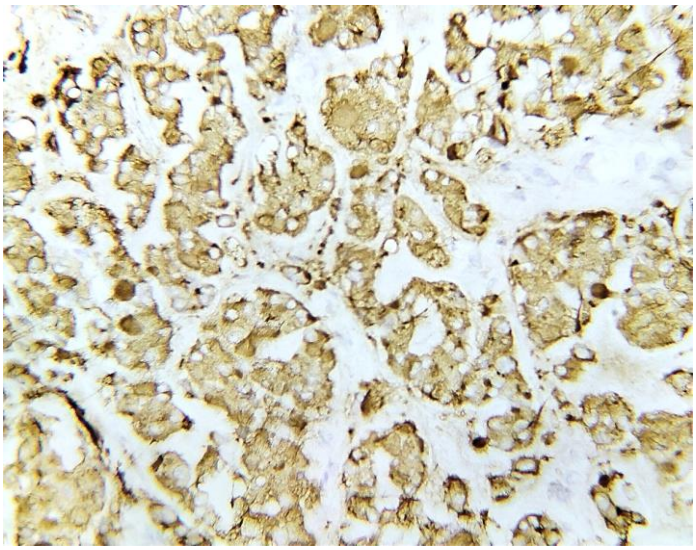

Figure 6: Immunohistochemistry for thyroglobulin

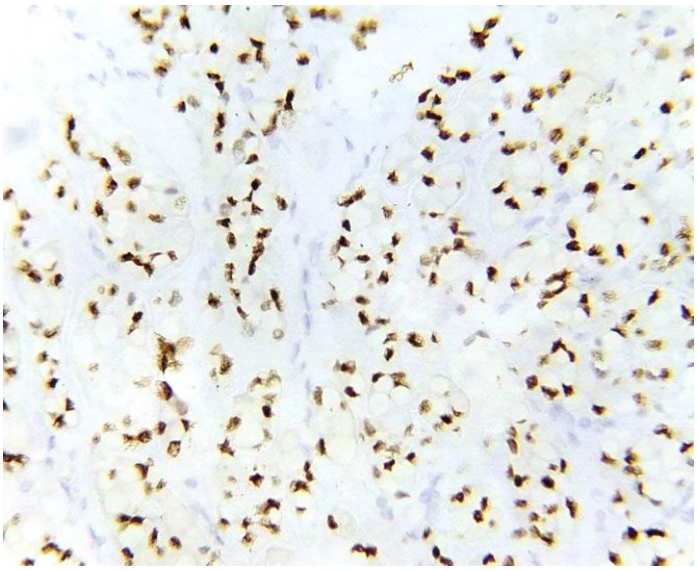

Figure 7: Immunohistochemistry for TTF1

DISCUSSION

Signet ring cell adenoma of thyroid is a very rarely encountered variant of follicular adenoma of thyroid. The WHO classification of tumours of endocrine organs describes it as a follicular neoplasm characterized by cells with discrete cytoplasmic vacuole and peripherally pushed nucleus, producing a signet-ring appearance. According to the reports the content of intracytoplasmic vacuole varies, includes thyroglobulin, mucin, lipid and glycogen.[1]

It was first described by Mendelsohn in 1984, and only few cases have been reported in literature since then[2].The affected age group ranges from 17 to 81 years and there is a female preponderance.[3] Patients usually present with palpable solitary neck mass with no or minimal symptomatology due to its non-invasive nature[4].

Macroscopically lesion is well encapsulated, firm, tan, or brown in colour. There can be cystic or haemorrhagic changes.[3] Microscopy is characteristic, shows a well encapsulated lesion composed exclusively or partially of pale, eosinophilic cells arranged in micro follicular, micro vesicular, papillary, trabecular or solid pattern separated by a capillary network and fibrous septae. Individual cells are round to oval have abundant vacuolated cytoplasm and eccentric hyperchromatic nucleus. No capsular or vascular invasion will be seen.[3,4]

Intracytoplasmic vacuole can be positive for mucin stains like Alcian blue, mucicarmine and periodic acid-Schiff stain with diastase. Alcian blue and mucicarmine give only weak reactivity. The mechanism of positivity for mucin stains is not exactly known, but it has been proposed that it could be due to aberrant intracellular accumulation of thyroglobulin and its partial degradation into protein-polysaccharide complexes.[2,5,6] So immunohistochemical study with thyroglobulin, which gives intracytoplasmic positivity, is mandatory to differentiate it from other metastatic mucin secreting signet ring cell tumours. Other immunohistochemical stain include TTF1 which gives intranuclear positivity.[6]

On electron microscopy vacuoles are identified as intracellular lumina lined by microvilli which suggests arrested folliculogenesis.[7]In a study by Mochizuki M et al, cells showed many cystic and dilated rough endoplasmic reticulum in the cytoplasm. Coupling with the finding of immunohistochemical positivity for thyroglobulin, this may represent accumulated non-carbohydrated immature thyroglobulin in the dysfunctional dilated rough endoplasmic reticulum or Golgi appratus.[8]

Diagnosis of signet ring cell adenoma thyroid in cytology is challenging. Most of the cases, as in ours, were reported as follicular neoplasm and were identified as signet ring cell variant only retrospectively. The characterizing features include microfollicular or cord like arrangement of tumour cells associated with signet ring cells and mucin globules. [5,6]The appearance of signet ring cells can be misleading and raise a suspicion of metastatic signet ring cell carcinoma. Cytologic diagnosis of metastatic signet ring cell carcinoma to thyroid has been reported in literature.[9]

Molecular studies of signet ring cell adenoma thyroid is mere. A case with PTEN mutation has been reported.[10]

Differential diagnosis comprises many benign, primary and secondary malignant thyroid tumours with signet ring cell appearance, most important being metastatic signet ring cell carcinoma. The tumours to be considered include follicular carcinoma thyroid signet ring cell variant,[11] non-invasive follicular thyroid neoplasm with papillary-like nuclear features, secretory carcinoma thyroid, metastatic signet ring cell carcinoma, metastasis from renal cell carcinoma. From the reports studied secondary malignant tumours of the thyroid gland comprise 1.9 -26% in autopsy series, reflecting the importance of ruling out metastatic carcinoma.[3] . Similarly, care should be taken to not label a benign signet ring follicular adenoma as a metastatic tumour.

CONCLUSION

Signet ring cell adenoma of thyroid is a rare neoplasm with a benign course. The presence of signet ring cells can be alarming if the pathologist is unaware of this rare entity. It is of great importance that, a benign follicular adenoma should be distinguished from a metastatic signet ring cell carcinoma.

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