

FNAC of the Thyroid following Carbimazole Therapy in Hyperthyroidism: A Diagnostic Dilemma

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ABSTRACT

Antithyroid drug therapy is routinely used for treatment of hyperthyroid patients. Therapy induced changes in hyperthyroidism can cause serious diagnostic dilemma on FNAC and have been rarely documented. We present a case of 45-year-old female patient who clinically presented with diffuse thyroid swelling and features of hyperthyroidism. FNAC from thyroid swelling showed features of Hashimoto's thyroiditis / Grave's disease / Colloid goiter with follicular hyperplasia and at places raising the suspicion of malignant transformation. Further clinical evaluation of patient, it was found that she had carbimazole therapy. Correlating the clinical and cytomorphologic features, a diagnosis of "therapy induced (carbimazole) changes in hyperthyroidism was given.

Key words: Carbimazole, FNAC, Grave's disease, Therapy, Thyroid.

INTRODUCTION

Grave's disease (also known as Basedow disease, thyrotoxicosis, diffuse toxic goiter, and exophthalmic goiter) is an autoimmune thyroid disease which classically present in young adult females with thyromegaly, exophthalmos, muscle weakness, weight loss, irritability, tachycardia, goiter, often a great increase of appetite and other features of thyrotoxicosis.^[1] These patients have elevated T4 and T3 levels, along with an increased radioiodine uptake, in the presence of TSH levels less than 0.1 mU/L. The patients are treated with radioactive iodine (RaI) / anti-thyroid drugs / subtotal thyroidectomy. Histologically, radioactive iodine is known to induce changes that often simulate malignancy.^[2] Here we are reporting the cytologic changes in the thyroid of a rare and unique case of a Graves' disease treated with carbimazole. In the absence of treatment history, these changes have led to a serious misinterpretation, sometimes even as papillary thyroid carcinoma. The drug induced changes in the thyroid aspirates of our case caused a diagnostic dilemma.

CASE REPORT

A 45-year-old female patient, a known case of Graves' disease presented with diffuse thyroid swelling since 3 years (Figure 1). Thyroid function tests revealed triiodothyronine (T3) – 3.23, thyroxine (T4) – 17.33 µg/dL, and thyroid stimulating hormone (TSH) - 0.01 µIU/mL. With a clinical diagnosis of Graves' disease she was referred to us for FNAC. Non guided fine needle cytology using a 25 gauge needle was done. Blood mixed aspirated material was stained with

Giemsa and Papanicolaou stains. Cytology revealed discrete as well as clusters of thyroid follicular cells exhibiting anisokaryosis with mild hyperchromasia, few clusters have fire flare changes and infiltrated by lymphocytes. Prominent hurthle cell changes were also seen in the background of thin colloid and mature lymphoid cells. (Figure 2) This varied cytomorphology caused a diagnostic dilemma. Re-evaluating the patient's treatment history it was found that she was on carbimazole therapy for 3 years. Correlating the clinical and cytologic findings, a cytodiagnosis of "carbimazole induced change in Graves' disease" was given.

DISCUSSION

Grave's disease is considered among the autoimmune thyroid diseases together with Hashimoto's thyroiditis and idiopathic myxedema. The changes resulting from different therapeutic modalities of thyrotoxicosis have been described by various authors.^[1-4] Certain medications like lithium and amiodarone may induce thyroiditis, hypothyroidism or hyperthyroidism and are associated with morphological changes. It is often not possible to determine if the drug has induced thyroiditis or has uncovered pre-existing subclinical thyroid disease.^[3] Radioactive iodine (RaI) induced histologic patterns are not uniform and range from loss of follicles to fibrosclerosis.^[4] The FNAC findings described in RaI cases include cellular enlargement, nuclear hyperchromasia, intranuclear pseudoinclusions, cytoplasmic metaplasia, oxyphilia, and vacuolization. These changes are sometimes erroneously interpreted

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Figure 1

Figure 1: Patient with diffuse thyroid swelling.

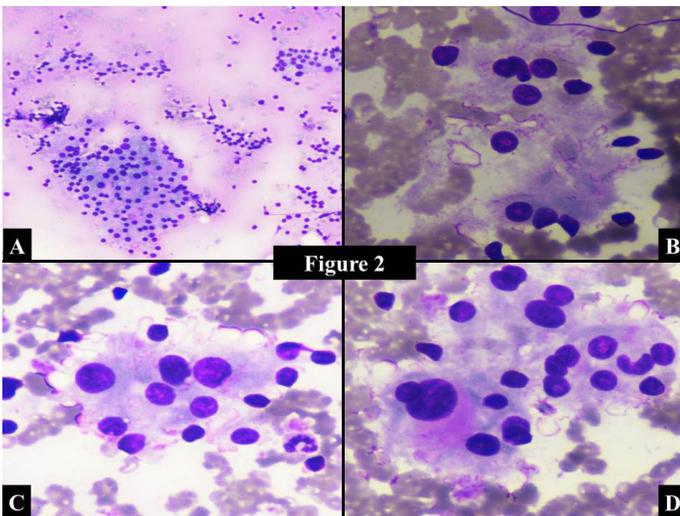


Figure 2

Figure 2: Cytosmears were (A) moderately cellular with discrete, as well as clusters of thyroid follicular cells exhibiting (B,C,D) marked anisokaryosis, mild hyperchromasia, few clusters show fire flare changes and infiltrated by lymphocytes. (C,D) Prominent hurthle cell changes are also seen in the background of thin colloid and mature lymphoid cells. (Giemsa, x10, x40).

as papillary carcinoma, especially when the clinical data on prior RaI are not provided.^[2]

The characteristic cytomorphologic features of untreated toxic goiter's include a fine cytoplasmic granularity with fire flare like vacuoles and distinct anisonucleosis; these features are better appreciated on MGG stained smears.^[5] Using toluidine blue staining Smejkal *et al.* have demonstrated an increased number of nucleoli in these cases; they also described the cytoplasmic positivity of hyperplastic cells for acid phosphatase. These features are said to indicate an increased proteosynthetic activity. The variation in nucleolar morphology is considered as a factor in determining the growth and activity of the thyroid follicular cells. Ring shaped nucleoli are indicative of a reversible inhibition of ribonucleic acid (RNA) synthesis and therefore, a low proteosynthetic activity;

compact nucleoli with homogeneous distribution of RNA indicate an increased activity of growth or secretion. Small compact nucleoli are demonstrated in thyrotoxic goiter, while large compact nucleoli are seen in cancer cells or in a proliferating benign adenoma.^[5]

Carbimazole-induced histological changes in thyroid among experimental albino rates showed reduced number of thyroid follicles with scanty homogenous colloidal material.^[1] Siddaraju *et al.*, reported carbimazole-induced cytological changes in Graves' disease; showed a prominent Hurthle cell change with anisokaryosis, unusually large hyperchromatic nuclei.^[2,6]

The cytologic change described in toxic goiter's treated with carbimazole is the presence cellular, monolayer sheet, microfollicles pseudopapillae, plenty of bare nuclei, sudden bizarre pleomorphic nuclei, coarse chromatin, occasional paravacuolar granules, mild Hurthle cell change, minimal lymphocytes, absent colloid. Serology for anti TPO is positive.^[7]

Cytologically, Smejkal *et al* demonstrated ring shaped nucleoli by toluidine blue staining, and the cytoplasmic negativity for acid phosphatase in the follicular cells of Graves' disease patients treated with carbimazole. These changes were similar to those of benign conditions and were noted even in large, bizarre nuclei, indicating that a malignant origin of such nuclei was unlikely. It was also noted that these changes did not have any relation to the length of treatment, the age of the patient, or the dose of the drug used.^[5]

We also excluded the possibility of a dysmorphogenetic goiter/malignant suspicion by the mode of clinical presentation, such as age of the patient and features of thyrotoxicosis cytologic picture lacking macronuclei and a colloid background of the cytologic smears.

The therapy induced cytologic change in Graves' disease as well as a dysmorphogenetic goiter may often simulate malignancy in which case knowledge of complete clinical picture with hormonal levels is highly essential for an accurate interpretation and diagnosis. In our case, hormonal levels were indicative of primary thyrotoxicosis. As we were aware of the fact that the patient was a known case of Graves' disease, an attempt to obtain further clinical details was made and we learnt that the patient had carbimazole treatment for Graves' disease.

The cytologic changes described in our case were somewhat similar to those described for RaI induced change though our patient had not received RaI. The bizarre nuclei are the only finding described in Graves' disease treated with carbimazole^[2] which of course was seen in our case too.

CONCLUSION

Together with clinical-biochemical evaluation, FNAC remains the first-line diagnostic test in the management of thyroid nodules. A varied cytomorphologic features can present in patients receiving carbimazole therapy in Graves' disease leading to serious diagnostic dilemma. A careful cytologic interpretation with complete clinical details, including that of hormonal levels and the treatment history can avoid unnecessary cytologic interpretive confusions.

Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee. Informed consent was obtained from individual participant included in the study.

Consent for publication: Written consent was obtained from individual participant included in the study.

Availability of data and materials: All the data regarding the findings are available within the manuscript.

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AUTHORS' CONTRIBUTIONS

TS carried out concepts & design, literature search, participated in clinical study and will stand as guarantor also. HP carried out data acquisition, data analysis & manuscript preparation. BK carried out concepts & design, literature search. YS participated in clinical study & manuscript review. RA participated in clinical study & manuscript review. NH carried out literature search & data acquisition. All the authors have read & approved the final manuscript.

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Nil

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