

Case Report

Fine Needle Aspiration Cytology of the Thyroid Gland Following Methimazole Therapy

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Abstract

Carbimazole is widely used for treatment in patients with hyperthyroidism. Cytopathological and histopathological changes in patients with toxic goiter, following carbimazole therapy have been rarely documented. In this article, I report a case of 46-year-old female patient who clinically presented with features of hyperthyroidism.

Fine needle aspiration biopsy was performed on her thyroid gland. The absence of drug treatment history caused serious misinterpretation. She was referred to a surgeon, and total thyroidectomy was performed. After diligent search, no malignancy was found. However, on discussion with surgeon; it was found that the patient was on methimazole. Therefore, a final diagnosis of methimazole-induced changes was rendered.

Keywords

- Carbimazole
- Methimazole
- Hurthle cell
- Histopathological
- Cytopathological changes
- Toxic goiter
- Malignancy

INTRODUCTION

Diffuse toxic goiter is an autoimmune thyroid disorder occurring predominantly in women, characterized by thyroidmegaly, exophthalmos muscle weakness, weight loss, irritability, tachycardia and loss of appetite. The patients are generally treated with radioactive iodine, or antithyroid drug such as carbimazole [1]. Cytologically, radioactive iodine and carbimazole are known to induce cytological changes that often simulate malignancy [2-4]. Methimazole is a metabolite of carbimazole, and is also widely used as antithyroid drug, especially in country like USA where carbimazole is not approved by FDA. Yet, no report on methimazole-induced cytopathological, and histopathological changes simulating malignancy in patients with toxic goiter could be found in the medical literature. Here I present the first case of methimazole-associated cytopathological changes simulating malignancy in toxic goiter. In this patient, the absence of treatment history leads to a serious misinterpretation.

CASE PRESENTATION

A 46 year-old female went to see a cardiologist, complaining of hypertension, palpitation, weight loss with diffuse thyroid swelling for one year. The thyroid function tests revealed elevated free T4 (>7.77 ng/dl), and decreased TSH level (0.006 uIU/ml). TSH receptor antibody was 95%, antiperoxidase antibody was positive. Diagnosis of Hyperthyroidism was rendered. She started on methimazole 5mg daily for two months, and increased to 15 mg daily, because of no apparent clinical and laboratory effect. She was referred to an endocrinology for consultation. Ultrasonogram of thyroid showed diffuse enlarged thyroid glands with multi-goiter. Fine needle aspiration was performed.

Cytological findings

The smears were stained with Papanicolau stain. They appeared moderately cellular; discrete as well as clusters of thyroid follicular cells exhibiting anisokaryosis with moderate hyperchromatism were seen (Figure 1 a,b). Many Hurthle cells were observed in the background, some of which were bizarre looking with giant nuclei (Figure 2 a,b). In the absence of treatment history, the diagnosis of malignancy was rendered. The Bethesda System for Reporting thyroid cytopathology was classified as VI. The patient was referred to a surgeon for a total thyroidectomy.

Histopathological findings

The specimen consisted of a butterfly shaped thyroid, measuring 8.0 x 6.3 x 2.0 cm, weighing 49 grams (Figure 3). Its cut surface appeared multi-nodular. Microscopic features of the sections (30 in total) studied from both lobes manifesting follicles in different sizes and shape, and containing varying amount of colloid material. The acini were lined by large cuboidal to columnar cells with plenty of bright eosinophilic granular cytoplasm. The nuclei exhibited marked anisokaryosis, hyperchromatism, pleomorphism, and increased N/C ratio (Figure 4 a,b). These changes tended to occur in the sections taken from the periphery of the thyroid. They occurred in multiple foci, approximating 10% of the total volume. The lining epithelium occasionally showed papillary projections into the lumen (Figure 4 a,b). Here and there, pinocytosis was observed in the follicles within the nodules (Figure 5). Definitive diagnosis of malignancy could not be established. After discussion with the

clinician, it was found that the patient was on methimazole for seven months. Final diagnoses of methimazole-induced changes in toxic goiter were rendered.

After surgery, the patient has been on eltroxin 100 mcg daily. Her free T4 and TSH were within normal limits 2 months after surgery.

DISCUSSION

Cytomorphological and histopathological changes in patients with toxic goiter due to antithyroid drugs, such as radioactive iodine, lithium, carbimazole, amiodarone have been documented [5-8]. Methimazole, a metabolite of carbimazole, also is widely used as antithyroid drug; why similar cytomorphological and

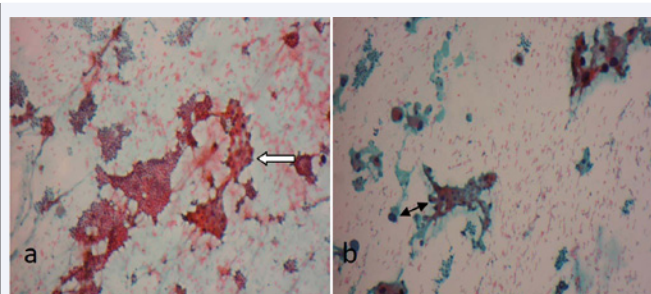


Figure 1 a) Hypercellularity of the smears, with Hurthle cell changes (white arrow). Papanicolaou stain x100. b) Discrete and cluster of follicular cells (black arrow). Papanicolaou stain x100.

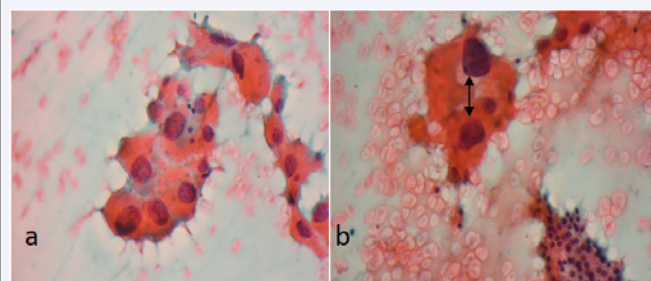


Figure 2 a) cluster of Hurthle cells displaying marked anisocytosis and moderate hyperchromatism. In the background are thin colloid and red blood cells. Papanicolaou stain x200. b) Some Hurthle cells contain bizarre-looking giant nucleoli (arrow). Papanicolaou stain x200.

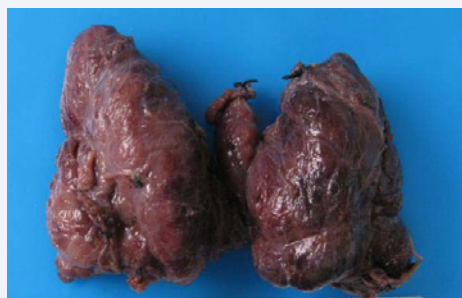


Figure 3 Gross specimen of the multi-nodular thyroid gland.

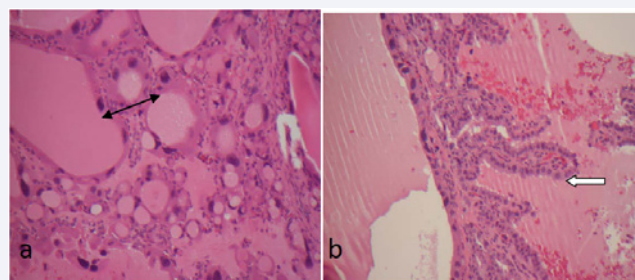


Figure 4 a) various sized and shaped follicles lined by large cuboidal to columnar cells with bright eosinophilic cytoplasm. Their nuclei manifested anisokaryosis, hyperchromatism, pleomorphism, and increased N/C ratio (black arrow). H & E stain X200. b) The lining epithelium occasionally showed papillary projections into the lumen (white arrow). H & E stain x 200.

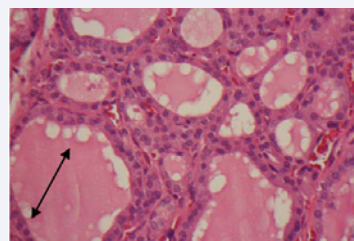


Figure 5 Pinocytosis was observed in the follicles in some nodules (arrow). H&E stain x200.

histopathological changes have never been reported in patients taking methimazole remained unexplained. My patient was on methimazole for hyperthyroidism for seven months. As a result, she developed changes in the thyroid gland identical to that induced by carbimazole. It is reasonable to link the changes to methimazole. In retrospect; perioperative frozen section may not be necessary in thyroid nodules diagnosed as Bethesda Categories V and VI [9].

CONCLUSION

Using antithyroid drug therapy on patients with toxic goiter occasionally caused cytomorphological and histopathological changes simulating malignancy that may result in a serious diagnostic confusion. A careful cytological interpretation, with complete clinical details, including that of hormonal levels, and the treatment history, can avoid unnecessary cytological interpretation confusion.

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