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CASE REPORT

Fungal Granulomatous Thyroiditis in A Renal Transplant Recipient

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ABSTRACT

Fungal granulomatous thyroiditis is a relatively rare entity. Aspergillus is the fungus that most commonly affects the thyroid gland and is generally missed until autopsy. Aspergillus granulomatous thyroiditis diagnosed antemortem and treated in renal transplant recipients is extremely rare. We report a 35-year-old female renal transplant recipient who presented with fever, generalized weakness, and loss of appetite; her clinical examination revealed a left thyroid lobe nodule. Fine needle aspiration cytology (FNAC) microscopic examination of the nodule revealed fungal granulomatous thyroiditis. Subsequent examination of FNAC material with special stain Gomori`s Methenamine Silver (GMS), 10% KOH (potassium hydroxide) mounting, and culture confirmed the presence of fungus Aspergillus flavus. This case emphasizes the need for thorough clinical examination and the utility of FNAC in examining thyroid nodules. *J Microbiol Infect Dis 2021; 11(4):233-237.*

Keywords: *Granulomatous fungal thyroiditis, Aspergillus species, Fine-needle aspiration cytology*

INTRODUCTION

Granulomatous thyroiditis is commonly associated with viral, bacterial, or autoimmune etiologies. Granulomatous thyroiditis caused by a fungus is unusual; this is due to the encapsulated structure of the thyroid gland along with a high iodine concentration, hydrogen peroxide production coupled with high vascularity, and lymphatic drainage [1]. Among fungal infections, Aspergillus is the most common cause of granulomatous thyroiditis. Fungal thyroiditis is often seen in immunocompromised patients. Patients with hematological malignancies, recipients of bone marrow or solid organ transplants, and patients with HIV are vulnerable. Disseminated Aspergillus infections originate in the lungs [2]. We report a renal transplant recipient presenting to us with granulomatous thyroiditis due to Aspergillus.

CASE

A 35-year-old woman had undergone a deceased donor renal transplantation in 2016 and was receiving standard triple immunosuppressive therapy comprising Prednisolone, Tacrolimus, and Mycophenolate-Moefitil. She developed Banff 1A T cell-mediated rejection (TCMR) after four years. She received three doses of methylprednisolone 500 mg each, resulting in improved graft function. The dose of tacrolimus was simultaneously increased. Unfortunately, she developed two more episodes of TCMRs over the next three months, and methylprednisolone was repeated in the same dose for each episode. One month later, she presented with fever, loss of appetite, and asthenia. The physical examination of the neck revealed a palpable nodule of 3x2 cm in size in the left lobe of the thyroid. The nodule was non-tender, mobile, and firm in consistency, and there was no evidence of regional lymphadenopathy.

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Ultrasound examination revealed an irregular hypoechoic lesion measuring 21 x 17 x 17mm in the left lobe of the thyroid (Figure 1a). It had minimal vascularity (Figure 1b) and was consistent with a thyroid neoplasm. The right lobe of the thyroid and soft tissues of the neck was normal. There was no evidence of cervical lymphadenopathy.

Microscopic examination of the material obtained from fine-needle aspiration of the nodule showed a cohesive cluster of follicular epithelial cells with regular round nuclei (Figure 2a), many tufts of fungal hyphae (Figure 2b), and a granuloma composed of epithelioid cells (Figure 2c) suggestive of fungal granulomatous thyroiditis. Smears stained with Gomori`s methenamine silver (GMS) stain showed septate hyphae with dichotomous branching (Figure 2d). KOH mount was positive for fungal hyphae, and fungal culture revealed *Aspergillus flavus*.

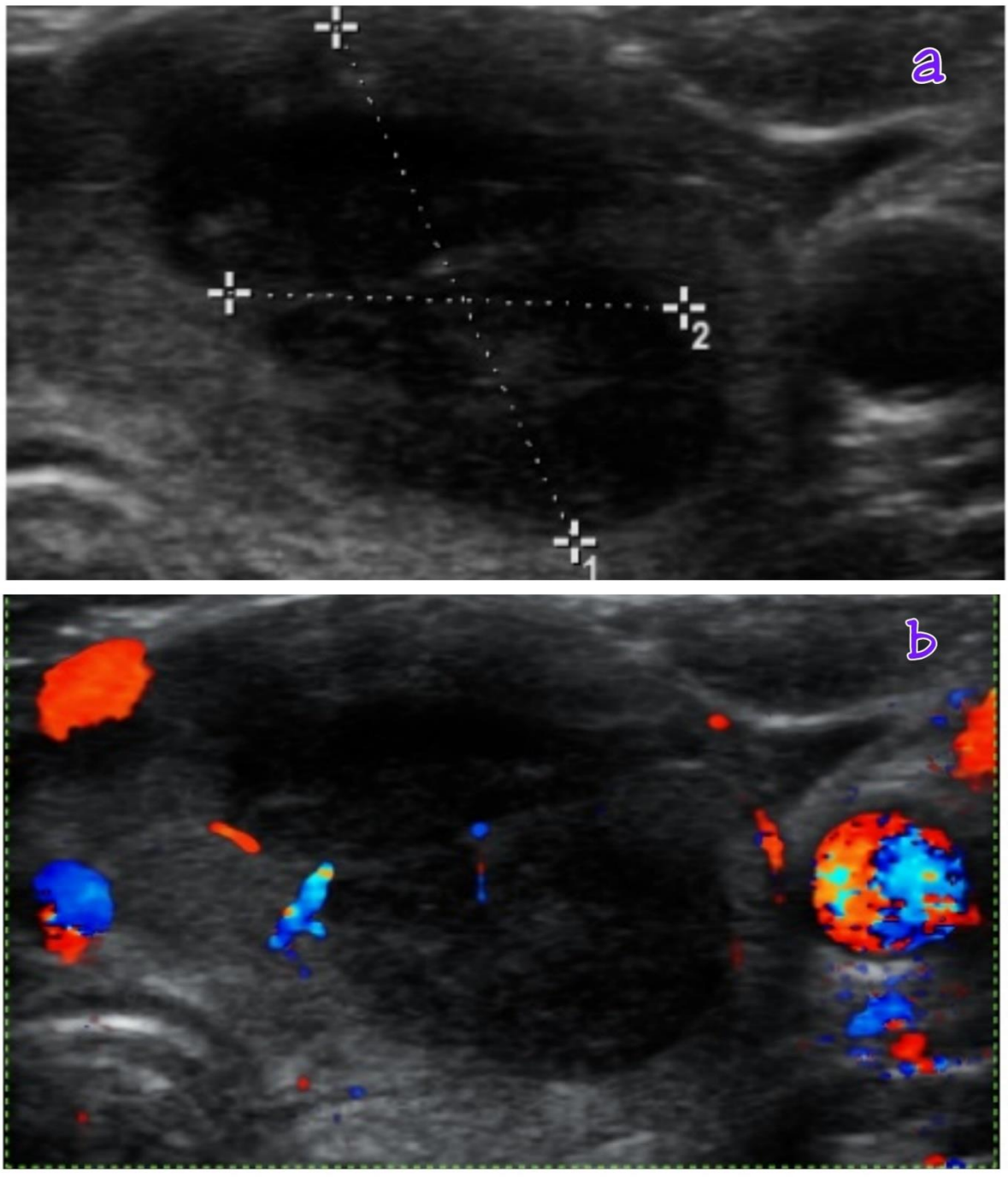

Figure:1. Ultrasonography Thyroid

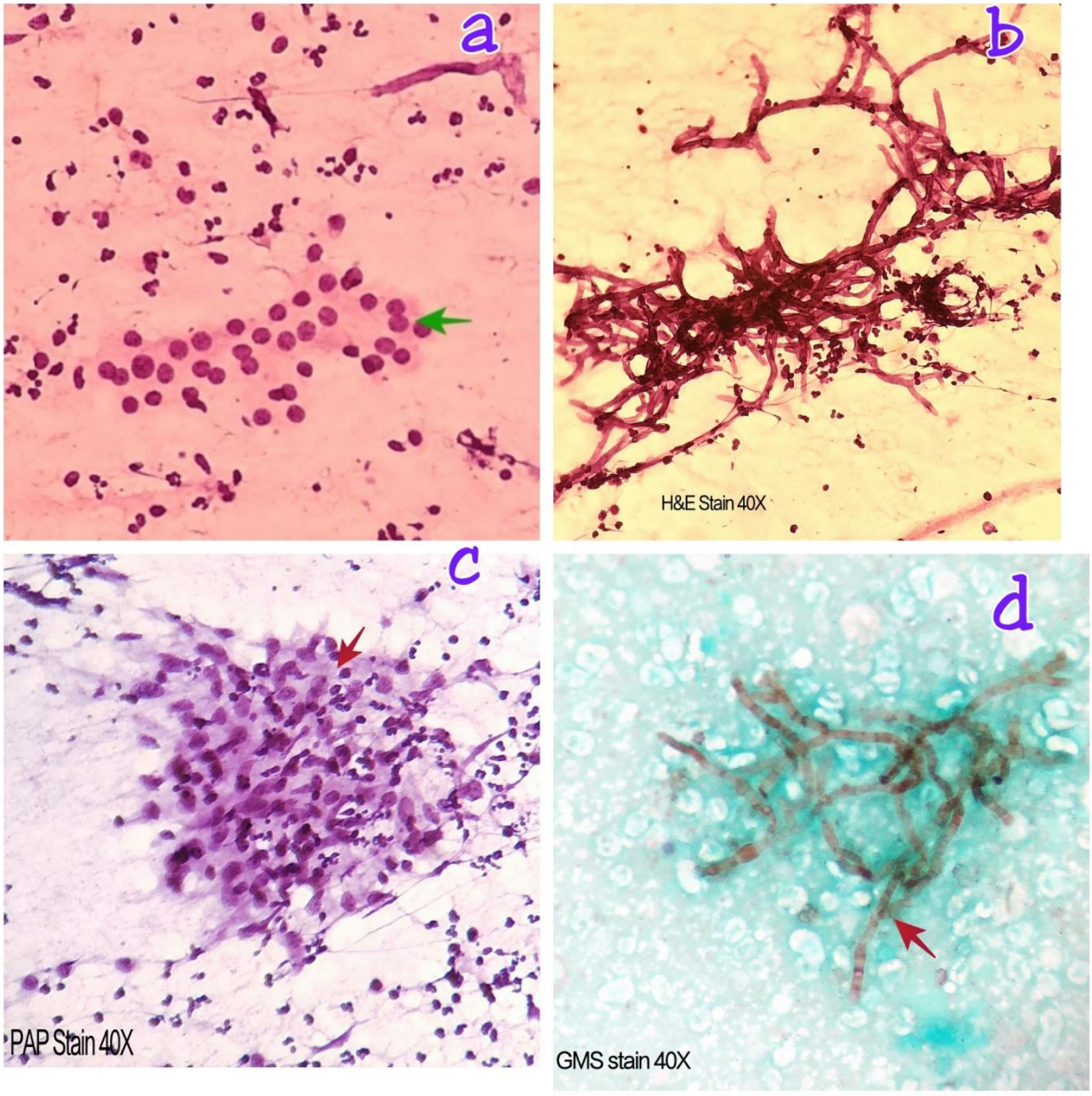

Figure:2. Fine needle aspiration cytology (FNAC) left thyroid lobe nodule showed thyroid follicular cells (Figure 2a), tufts of fungal hyphae (Figure 2b), granuloma composed of epithelioid cells (Figure 2c), and Gomori`s methenamine silver (GMS) stain showed septate hyphae with dichotomous branching (Figure 2d).

Another laboratory parameter of significance was a high serum creatinine (7.8 mg/dl), signifying renal allograft dysfunction. The serology for HIV-1, HIV-2, anti-hepatitis C antibody, hepatitis B surface antigen, Ebstein Barr viral capsid antigen, Dengue NS1, Dengue IgM, malarial parasite antigen test, Typhi IgM, Weil-Felix test, and Scrub typhus IgM were negative. The blood and urine cultures did not reveal any bacterial growth.

The patient was started on voriconazole, and hemodialysis was initiated. Mycophenolate mofetil was completely stopped at presentation. The doses of other immunosuppressive medications were reduced initially but eventually stopped to save the patient. The fever disappeared over the next ten days. The thyroid nodule size gradually decreased, but unfortunately, there was no improvement in allograft kidney function, leaving her dialysis-dependent.

DISCUSSION

The most common form of granulomatous thyroiditis is De Quervain's thyroiditis or subacute granulomatous thyroiditis, self-limiting, inflammatory disease of the thyroid, believed to be caused by a viral infection [3]. Fungal granulomatous thyroiditis is rare. However, *Aspergillus species* are the most common cause. Other fungal species causing thyroiditis are Candida, Cryptococcus

neoformans, Coccidioides immitis, and Histoplasma capsulatum[4]. Fungal granulomatous thyroiditis is typically associated with disseminated infection in immunocompromised individuals, some of whom had a pre-existing thyroid disease. Hematogenous dispersion mechanisms include neutrophil recruitment, cell-mediated immunity activation, host defense inhibition, and suppressed T cell response. Fever, neck pain, enlargement of the thyroid gland, dyspnoea, and dysphonia are the most common symptoms. Thyroid function test results are noncontributory and can vary from hyperthyroidism to hypothyroidism or euthyroidism. Initially, a hyperthyroid period is seen, caused by the destruction of follicles and colloid release. Subsequently, a hypothyroid state will ensue due to decreased thyroid-stimulating hormone from the pituitary gland [5]. In our patient, thyroid nodules were incidental findings during a clinical examination. There were no symptoms related to the thyroid gland, and thyroid function tests were within normal limits. The presence of granulomas with tufts of fungal hyphae in cytosmears directed pathologists to initiate workup for fungal species. Further submission of FNAC material for special stain and culture confirms the diagnosis.

Aspergillus thyroiditis (AT) is most commonly a postmortem diagnosis. The first case report of Aspergillus infection involving the thyroid gland was described in 1950 by Grekin et al. in an autopsy [6]. The postmortem study conducted by Hori et al. on 107 invasive aspergillosis patients found that 12% had fungal thyroiditis [7]. Similar incidence, in an autopsy series, of thyroid gland involvement in disseminated Aspergillus was noted in a review by Denning and Stevens [8]. Solak et al. published a case of AT, confirmed histologically, in a post-renal transplant patient presenting with hypoactive nodules and thyrotoxicosis [9]. Our patient had a painless thyroid nodule which on cytological examination revealed Aspergillus thyroiditis.

Ultrasonography (USG) is an essential diagnostic modality to evaluate thyroid disease. However, a specific sonographic finding of fungal thyroiditis has not been reported. The sequential sonographic features can help differentiate primary invasive aspergillosis from subacute thyroiditis[10]. Fine-needle aspiration cytology (FNAC) is widely considered the diagnostic technique of choice in assessing thyroid lesions. The mandatory diagnostic test for fungal thyroiditis includes FNA and aspirated samples for culture[11]. The serum galactomannan assay can detect aspergillosis, but its sensitivity and specificity in solid organ transplant patients are lower than in patients with hematological malignancies [12]. In the retrospective analysis of 26 cases of fungal infection by Das et al., it was noted that fungal etiology was not suspected clinically in 71% of the patients but was diagnosed following the cytological examination of the aspirated specimens [13]. Similarly, in our patient, the diagnosis of AT was made solely based on cytological examination of FNA specimens emphasizing the importance of using FNA-based cytology as a diagnostic tool.

Voriconazole (200 mg twice a day) is the drug of choice to treat aspergillosis. Other drugs that can be used are amphotericin B, caspofungin, posaconazole, or micafungin. Surgical drainage is necessary for Aspergillus thyroiditis presenting a thyroid abscess [14]. Aspergillus thyroiditis carries a high rate of morbidity, extended hospital stay, and mortality in recipients of solid organ transplantation. Sometimes the mortality rate can be as high as 70% [15].

Conclusion

Granulomatous thyroiditis due to a fungus is a rare entity and is frequently missed antemortem. It is often seen in immunocompromised patients and is caused by Aspergillus. The present case highlights the need to have a high index of suspicion to diagnose fungal thyroiditis and the importance of FNA in achieving it.

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