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Bhattacharyya S *

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Review Article

Infections Causing Hypothyroidism and Hypoadrenalism

Bhattacharyya S*, Kumar A

Associate Professor, Microbiology, AIIH&PH Kolkata.

*Corresponding Author: Bhattacharyya S, Associate Professor, Microbiology, AIIH&PH Kolkata.

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Abstract

Many infections can produce hypothyroidism and hypoadrenalism. Infections caused by M. tuberculosis, other bacteria, viruses as well as fungi are important causes of hormonal abnormalities due to affection of endocrine organs. These should not be neglected and looked for in cases of hypothyroidism and hypoadrenalism. IN this mini-review the authors have tried to address these issues.

Keywords: hypothyroidism; hypoadrenalism; endocrine

Introduction

Many infections cause derangements of the functioning of the endocrine organs. These can take place by various mechanisms.

The thyroid gland is generally resistant to microbial invasion due to its rich blood supply, Iodine content and presence of capsule.

Infectious thyroiditis is a rare condition, and is usually the manifestation of bacterial infection of the gland. Its sign is the classic tetrads of inflammation, like heat, pain, redness, and swelling, and some specific symptoms conditioned by local relationships, like dysphagia and a desire to keep head flexed on the chest so as to relax the paratracheal muscles.

Hypothyroidism may occur due to: -

Due to viral infections: -

Mumps, Influenza and other respiratory viruses can cause hypothyroidism. Here subacute thyroiditis is produced (1). Clinical features are sudden onset of pain in the region of the thyroid gland. It is commonly preceded by a viral infection**.** Various studies have reported that the occurrence of thyroid dysfunction (subclinical hypothyroidism) is much higher (about 36%-37%) in patients infected with HIV than in the general population. However, other researchers have suggested that the morbidity of overt thyroid dysfunction in HIV infected individuals is similar to that in the general population. HAART further increases the probability of thyroid dysfunction due to drugs like stavudine which can directly affect the production and/or metabolism of thyroid hormones. Bongiovanni et al demonstrated that the accumulation of the daily intake of stavudine and lamivudine is responsible for the occurrence of hypothyroidism.

Parasitic causes of hypothyroidism: S. stercoral is has been associated with hypothyroidism in one case report. Fasciola gigantica infection in buffaloes has been shown to lead to lymphocytic thyroiditis and hypothyroidism. Reports from Africa and Europe show that thyroid function may be affected in visceral leishmaniasis but the abnormalities detected are most likely a result of euthyroid sick syndrome or non-thyroidal illness with no clinical presentation of thyroid disease (2).

It can also occur due to bacterial infections. There are 2 presentations of bacterial thyroiditis, like acute suppurative thyroiditis (AST) and subacute (granulomatous) thyroiditis (SAT,) which is far commoner than AST. SAT is characterized by a more protracted course, generally involving the thyroid symmetrically. The gland is also swollen and tender, and systemic reactions may be severe, like fever and a high erythrocyte sedimentation rate. During the acute phase of the disease, tests of thyroid function often reveal a lowering of TSH, and elevated serum levels of T3, T4 and thyroglobulin (3). There may also be acute suppurative thyroiditis or AST leading to abscess, and these may be due to Staphylococcus aureus, Brucella spp., Escherichia coli, and Mycobacterium tuberculosis (4). There are some hallmark features like increased C-reactive protein (CRP) and measurable thyroglobulin which characterize this condition. However, AST has bene described to be a rare condition.

Acute suppurative thyroiditis (AST) occurring from a bacterial infection is a rare but potentially life-threatening endocrine emergency. Traditional management of this disease is surgery along with targeted chemotherapy (5).

b. Tuberculosis can often involve the thyroid gland, even in primary Tuberculosis. However thyroid hormone abnormalities occurring due to Tubercular involvement are very are. However sometimes initial thyrotoxicosis occurs followed by hypothyroidism occurring later due to extensive tissue destruction due to glandular involvement (6). Tubercular thyroiditis can present as a part of the spectrum of infections like:- a)Multiple lesions throughout the gland mimicking miliary TB, b)Enlargement of gland due to formation of caseating granulomas, c)Cold abscess formation with multiple sinuses; d)Chronic fibrosing tuberculosis, which is difficult to distinguish from DeQuervein's

thyroiditis, and e)Acute abscess formation, which can resemble carcinoma. A past history of tuberculosis along with cervical lymphadenopathy and the typical sites of tuberculous involvement can lead to the correct clinical diagnosis. FNAC assay along with tuberculin skin test and Chest X ray can help establish the diagnosis of Tubercular thyroiditis. Also, caseous necrosis along with simultaneous depiction of acid-fast bacilli (AFB) clinches the diagnosis. In this situation, a mycobacterial culture is also helpful.

c. Fungal thyroiditis: Patients suffering from Leukemia, lymphoma and autoimmune disorders can also suffer from fungal thyroiditis. Aspergillus spp. is by far the commonest cause of thyroiditis and affects the gland as a part of systemic affection. Local signs and symptoms of infection are similar to other infectious thyroiditis and include fever, anterior cervical pain, thyroid gland enlargement with occasional dysphagia and dysphonia, and clinical and laboratory features of transient hyperthyroidism due to release of thyroid hormone from follicular cell damage. This is followed by residual hypothyroidism (7). Pneumocystis jiroveci thyroiditis is also reported in patients with Acquired Immune deficiency syndrome (AIDS). Microscopy and culture of FNAC material can help establish the diagnosis (8). P. jiroveci is the commonest cause of fungal thyroiditis in individuals with AIDS (9). Fungal thyroiditis can also be caused by Coccidioides spp. and Candida spp, and also are a part of disseminated Histoplasmosis. But Histoplasmosis of Thyroid is rare even in areas endemic for Histoplasmosis. Fine-needle aspiration of the thyroid is an important diagnostic tool to confirm the diagnosis of histoplasmosis of Thyroid (10). Serologic testing of the patient's serum sample shows IgG-type immunodiffusion of H. capsulatum antibody to M antigen and H. capsulatum complement fixation test positivity. In case of Aspergillus thyroiditis, both hematoxylin -eosin and PAS stain may help in delineating the acute-angled branching hyphae of Aspergillus spp.

Adrenal gland involvement: -

Adrenal gland can be infected with bacteria and fungi as part of disseminated infection. Bacterial multiplication as well as production of endotoxins by the bacteria, lead to Adrenal gland damage (11). Waterhouse Friderichsen syndrome (WFS) is caused due to disseminated infection by Neisseria meningitidis. WFS was first described by Rupert Waterhouse and Carl Friderichsen as bilateral adrenal hemorrhage in cases of bacterial sepsis in children in the first part of the twentieth century. It is a cause of acute adrenal insufficiency (12). Here microthrombi and hemorrhages may occur in the Adrenal gland leading to impairment of secretion of hormones from this gland. WFS is caused not only by Meningococci but also by other pathogens like Streptococcus pneumoniae, Hemophilus influenzae, Group A beta-hemolytic Streptococcus, Escherichia coli, Staphylococcus aureus, Capnocytophaga canorous, Enterobacter cloacae, Pasteurella multicide, Leiomyomas shigellosis's, Neisseria gonorrhoeae and Moraxella duplex (13). Apart from WFS, other entities may cause adrenal insufficiency, like HIV, disseminated Mycobacterium avium-intracellular infection, severe Plasmodium falciparum malaria (end organ damage or >5% parasitemia), and Herpes simplex encephalitis (12). Clinically hypoglycemia and less secretion of steroid hormones are hallmark of the condition. Surgical management is often required.

Fungal infections may also cause hypoadrenalism. In Latin America, Para coccidioidomycosis leading to primary adrenal insufficiency, is the second most prevalent endemic mycosis. Because of the protection granted by estrogen to women, the prevalence in the chronic form of the disease as a male: female ratio is up to 22:1. In an autopsy series, the adrenal glands were observed to be affected in nearly 80% of patients with progressive disseminated histoplasmosis, which is even more common in immunosuppressed individuals (14). Other fungal infections that may provoke primary adrenal insufficiency include Pneumocystis gynoecia, Blastomyces dermatitis, Cryptococcus neoformans and Coccidioides imcites).

Viral: Viral infections that may lead to primary adrenal insufficiency are HIV, Cytomegalovirus and possibly SARS-CoV-2. In case of COVID-19, the mechanism could be that the virus expresses amino acids similar to human ACTH, and the antibody production by the immune system might impair endogenous ACTH function. Another theory might be related to cytokines. It has been demonstrated that tumor necrosis factor-α (TNF-α) reduces ACTH release and decreases its effect on adrenal tissue. However, the pituitary gland is not protected by the blood-brain barrier, and extensive cytokine production (interleukin (IL) 1, IL 6, TNF-α, monocyte chemoattractant protein 1(MCP1), and granulocyte-colony stimulating factor (G-CSF)) during COVID-19 infection might cause hypothalamic-pituitary adrenal axis dysfunction.

Parasitic: Primary adrenal insufficiency was reported in visceral leishmaniasis in a patient without HIV infection and a patient with HIV coinfection and was attributable to parasitic infiltration of the organ. A Brazilian Series has shown a prevalence rate of adrenal insufficiency to be about 50% in persons with visceral leishmaniasis. Adrenal insufficiency has also been reported in toxoplasmosis, S. stercoral is and F. gigantica.

Primary Adrenal insufficiency or Addison's disease, in fact, has been described first more than 150 years ago, by Thomas Addison. At that time, tuberculosis was the commonest cause of this disease. It can take place due to infection by many organisms, like Mycobacterium tuberculosis, Neisseria gonorrhoeae and Histoplasma spp. The hallmark features include hyponatremia and hyperkalemia. However initial features are often quite non-specific, like fatigue, anorexia and low blood pressure, and about 80–90% of the adrenal gland is lost before the patient shows full-fledged Addisonian symptoms; antemortem diagnosis is hence rare. Normally Addison's disease occurs due to autoimmune etiology in 70-90% cases in developed countries. However, in developing countries, 39%–51% of Addison's disease can happen due to infective etiology (15). Hormone disbalance and hypoadrenalism in these conditions occurs due to granulomatous infiltration of the gland, cytokine level elevation and also due to drugs like Itraconazole and Rifampicin. Dermatological, pulmonary and imaging findings can help the clinician in achieving a prompt diagnosis of specific infections causing hypoadrenalism, which is very important since early identification of any infectious cause of Addison's disease enables recovery of adrenal gland function.

Conclusion: -

Infection of endocrine organs can lead to initial hypersecretion of the hormones followed by less secretion, in case of Thyroid gland, or adrenal insufficiency from almost the very beginning, in case of Adrenal gland. So, in case of hormone disbalances in these 2 glands, infective etiology should always be looked into, especially in developing countries. More research and scientific information are needed in this interesting and intriguing area of medical science.

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