AN UNUSUAL CASE OF ADRENAL INSUFFICIENCY – SCHMIDT’S SYNDROME

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ABSTRACT

Schmidt’s syndrome is a rare autoimmune endocrine disease in which the patient suffers from a combination of primary addison’s disease and autoimmune thyroid disorders. Schmidt’s syndrome is classified under inheritable Poly Glandular Autoimmune syndrome (PGA) as Type II. When immune dysfunction affects two or more endocrine glands and other non-endocrine immune disorders are present, the polyglandular autoimmune syndromes should be considered which are classified into two main types namely PGA type I and PGA type II. This syndrome is a very rare autoimmune disorder and difficult to diagnose because the symptoms of this syndrome depends on the endocrine gland that gets involved first. We report this case in which the patient had primary adrenal insufficiency, autoimmune hyperthyroidism and vitiligo and was diagnosed to have “Schmidt’s syndrome” (PGA type II). Our patient was treated with corticosteroid supplementation and anti thyroid drugs following which she recovered.

KEYWORDS: Polyglandular syndrome, PGA II, autoimmune syndrome, primary adrenal insufficiency

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INTRODUCTION

Schmidt’s syndrome is a rare (1.4 – 4.5 cases per 100,000 population) autoimmune endocrine disease, otherwise called as polyglandular autoimmune syndrome Type II. The patient usually suffers from a combination of primary adrenal insufficiency and autoimmune thyroid disorders with or without Type 1 diabetes, which was first reported by Schmidt in 2 patients in the year 1926. The primary adrenal insufficiency is due to an autoimmune process which leads to destruction of the adrenal cortex. When both the humoral and cell-mediated immune mechanisms are directed at the adrenal cortex, it is often associated with autoimmune destruction of other endocrine glands leading to development of the polyglandular autoimmune syndromes (PGA). PGA type II is more common than PGA type I. PGA type II is usually defined by the occurrence of two or more of the following: primary adrenal insufficiency (Addison's disease), type 1 diabetes mellitus, Grave's disease, autoimmune thyroiditis, and can be associated with other autoimmune disorders like myasthenia gravis, primary hypogonadism, vitiligo, alopecia and serositis.

The complete triad of Addison’s disease, thyroid autoimmune disease and Type 1 diabetes mellitus is also termed as Carpenter's syndrome. PGA Type I consists of Addison's disease, hyperparathyroidism and chronic mucocutaneous candidiasis. The condition is easily treatable if diagnosed early, but diagnosing such cases could be challenging and often misleading. Early recognition and treatment of such cases can often be life saving, or else mortality is common within one year of diagnosis.

CASE REPORT

A 38 year old female was admitted with history of generalized weakness, giddiness and weight loss for the past 6 months. There was no history suggestive of neurological involvement. She also complained of darkening of her palms and soles for the past one year associated with irregular menstrual cycles. Physical examination revealed hyperpigmentation of palmar creases (Fig 1) tongue, lips and mucous membrane (Fig 2) and hypopigmented patches (vitiligo) over the elbows, foot and trunk. Her pulse rate was 56 beats / min, and blood pressure was 90/70 mm Hg. Systemic examination was normal.
Complete blood counts, blood sugars, renal function tests, serum electrolytes, liver function tests and fasting lipid profiles were within normal limits. Thyroid function test revealed T3 – 23 ng/dL (N: 0.07 – 0.135 ng/dL), T4 – 34 ng/dL (N: 0.7 – 1.24 ng/dL), TSH < 0.01 µU/mL (N: 0.34–4.25 µU/mL) suggestive of hyperthyroidism. Anti TPO and anti thyroglobulin were positive. FNAC of the gland was normal. Since ACTH levels were high, co-syntropin test was performed (250 µg of co-syntropin was injected intramuscularly and the cortisol response failed to exceed 18 µg/dL) which was suggestive of primary adrenal insufficiency. Her CECT Abdomen showed a normal adrenal gland on the left side while on the right side it was thin and indistinctive which was suggestive of adrenal destruction. So a final diagnosis of autoimmune adrenal insufficiency with autoimmune hyperthyroidism was made which fit in to the diagnosis of Schmidt’s syndrome (PGA Type II). She was started on oral carbimazole 5mg three times daily, oral prednisolone 10mg in the morning and 5 mg in the evening. She improved symptomatically with the treatment. At follow up of three and six months, menstrual cycles became regular and her hyperpigmentation reduced. She continues to be on regular follow up and is continuing her medications with no demonstrable side effects. Her family members were screened and found to be normal.

DISCUSSION

Genetically mediated immune dysfunction leading to destruction of the endocrine glands and subsequent loss of glandular function is termed as Poly Glandular Autoimmunity syndromes (PGA). Patients also manifest with non-endocrine autoimmune diseases. The polyglandular autoimmune syndrome (PGA) is defined as the occurrence of at least two endocrine autoimmune diseases. PGA is classified as the rare juvenile type (PGA Type I) and the more common adult type (PGA Type II - IV). PGA Type I, also known as APECED (autoimmune polyendocrinopathy – candidiasis – ectodermal dys trophy), MEDAC (multiple endocrine autoimmune candidiasis syndrome), juvenile autoimmune polyendocrinopathy, is classically defined by the association of at least two of three major component diseases: chronic mucocutaneous candidiasis, primary hypoparathyroidism, and autoimmune adrenal insufficiency. Polyglandular autoimmune syndrome Type II is also known as Schmidt’s syndrome. Polyglandular autoimmune syndrome Type II (PGA Type II) is the most common of the immunoendocrinopathy syndromes. It is characterized by the occurrence of autoimmune Addison’s disease in combination with thyroid autoimmune diseases and/or Type I diabetes mellitus. Primary hypogonadism, myasthenia gravis, and celiac disease also are commonly observed in this syndrome. The pattern of inheritance in Schmidt’s syndrome is autosomal dominant; it is more frequently encountered in women. [M : F is 1: 3] PGA Type III comprises of autoimmune thyroid diseases associated with other autoimmune diseases (Type I diabetes, atrophic gastritis, pernicious anemia, vitiligo, alopecia, myasthenia gravis), excluding Addison’s disease and/or hypoparathyroidism. This syndrome has a peak incidence at ages 20 - 60 years, mostly in the third or fourth decade, and it is common for multiple generations to be affected by one or more component diseases. There is familial clustering and family members of patients are often affected. Thyroid disease is the most common glandular disorder to accompany adrenal insufficiency in individuals with Schmidt’s syndrome. Thyroid disease, as a part of Schmidt’s syndrome can occur in the form of chronic autoimmune thyroiditis (Hashimoto’s thyroiditis) or Graves’ disease. Hashimoto’s is much more common and occurs in 95 to 97 percent of patients with Schmidt’s syndrome who develop a thyroid disease. Graves’ disease occurs in 3 to 5 percent of patients who develop thyroid disorders. Adrenal insufficiency is the initial manifestation in about 50% of patients, occurring simultaneously with diabetes mellitus and autoimmune thyroid disease in about 30% and 20% respectively. Vitiligo is seen in 10 percent of patients with Schmidt’s syndrome. Patients with PGA are treated with hormonal replacement therapy. Starting steroids in a patient with deficiencies of cortisol and thyroxine shall lead to improvement in thyroid function or mask its clinical features. Diagnosis of Schmidt’s syndrome can be challenging and misleading too. Early recognition and treatment of such cases can be a bridge between life and death. Our reported case is unique, as our patient is a young female. Usually patients with PGA type II have autoimmune hypothyroidism, but our patient had autoimmune hyperthyroidism. In our case, patient did not have Type I diabetes. Although PGA Type II is often inherited in an autosomal dominant pattern, in our patient there has been no known family history of PGA. Adrenal insufficiency and autoimmune thyroiditis were the presenting endocrinopathies along with vitiligo. This combination constitutes rare manifestations of the syndrome, especially at a young age. Anyfantakis et al reported a case of PGA II with anxiety disorder but our patient did not have anxiety disorder. Wehbe et al reported severe hyponatermia in a patient with Schmidt syndrome but in our patient electrolytes were found to be normal. Das et al reported a similar case with hypogonadism which was not seen in our patient.

CONCLUSIONS

Atypical presentations are not uncommon and it is wise to screen for other endocrine deficiency in documented cases of adrenal insufficiency. A high degree of suspicion is needed for a speedy diagnosis and appropriate management for Schmidt’s syndrome. This rare syndrome can be a life threatening condition if not diagnosed and treated early.

CONFLICT OF INTEREST

Conflict of interest declared none.
REFERENCES


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