Case Report

Polyglandular Autoimmune Syndrome Type-II (Schmidt's Syndrome): A Case Report

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Abstract:
Schmidt's syndrome refers to the combination of autoimmune adrenal insufficiency (Addison's disease) with autoimmune hypothyroidism and/or type 1 diabetes mellitus and is part of a larger syndrome known as autoimmune poly endocrine syndrome type II or poly glandular autoimmune syndrome type II (PAS II).The condition was first described by Schmidt's in 1926 reporting two patients with Addison's disease and chronic lymphocytic thyroiditis and was subsequently named after him. PAS II is a polygenic disorder which may include autoimmune thyroid disease (hypothyroidism or hyperthyroidism), IDDM, Addison's disease, primary hypogonadism and less commonly hypoparathyroidism or hypopituitarism. More common than other poly glandular autoimmune disorders1 Associated non-endocrine autoimmune conditions may be present including vitiligo, alopecia, pernicious anemia, myasthenia gravis, idiopathic thrombocytopenic purpura, Sjogren's syndrome and rheumatoid arthritis. In terms of the sequence of the development of endocrine gland insufficiency in the Schmidt's syndrome, it has been reported that in one half of the cases, autoimmune adrenal insufficiency is the abnormality that occurs first while Hashimoto's thyroiditis tends to occur simultaneously or after the emergence of autoimmune Addison's disease.

Keywords: Polyglandular, Schmidt's syndrome, autoimmune, primary adrenal insufficiency, autoimmune hypothyroid, insulin dependent diabetes mellitus

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Introduction:
When the body's immune system affects two or more endocrine glands and other non-endocrine immune disorders are present, the Polyglandular Autoimmune Syndromes (PAS) should be considered. The PAS are classified as two main types: PAS type-I and PAS type-II. PAS type-II is more common than PAS type-I [1]. We are reporting this case in which a patient had primary adrenal insufficiency, autoimmune hypothyroidism and insulin dependent diabetes mellitus and was diagnosed as Schmidt's syndrome (PAS type-II). This syndrome is a very rare autoimmune disorder and difficult to diagnose because the symptoms of this syndrome depends on the gland which gets involved first. Our patient was treated and improved with corticosteroid, thyroxine and insulin therapy[2].

Prevalence of Schmidt's Syndrome is 1:20,000 in general population with 3:1 ratio of females to males affected[3]. Peak incidence occurs in 3rd to 4th decade of life. Familial clustering with multiple family members often affected. Autosomal dominant inheritance with variable penetrance associated with certain HLA antigens HLA-DR3, HLA-DR4, non HLA gene M-ICA and CTLA-4.

Diagnosis of component disorders of PAS type-II is the same as that of the individual disorders[4]. Diagnosis of Addison's disease (primary adrenal insufficiency due to autoimmune adrenalitis) is based on the following: 1) early morning (i.e. 7-9 am) serum cortisol <3 mcg/dL or a serum cortisol less than 18 mcg/dL 60 minutes after a 250 mcg IV bolus of cosyntropin (ACTH), is strongly suggestive; 2) elevated basal serum ACTH level; 3) early morning 8 AM salivary cortisol <5 nmol/L (testing only recommended if high suspicion for falsely low serum cortisol due to low cortisol binding globulins); 4) Abdominal CT to evaluate for other causes of adrenal insufficiency (infection, hemorrhage, metastases) is recommended; 5) presence of other autoimmune disorders[5].

Diagnosis of primary hypothyroidism is based on an elevated serum TSH and low (or normal in subclinical disease) serum T4 level, whereas hyperthyroidism is diagnosed based on a low TSH

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with elevated (or normal in subclinical disease) serum T4.

Until now very few cases have been reported on poly glandular autoimmune syndrome because of its atypical presentation and because it is a very rare syndrome.

Case report:

A 43 years old rural female, attended in outpatient department of Z. H. Sikder Women's Medical College and Hospital, Dhaka complaining of generalized weakness with feeling of undue tiredness and tingling sensation in hands and feet for two months, inability to walk for ten days, abdominal fullness and puffiness of face for one month. She has history of Diabetes Mellitus since her teens, she also complain of that her period was very irregular for last six months, difficulty in concentrating, insomnia and intermittent fatigue, progressively worsening over the last six months. She attributed her state to an excessive, uncontrollable almost daily, worry about the financial status of her family caused by the economic crisis. Her symptoms compromised her daily activities. Personal background was negative for depression, social phobia, obsessive-compulsive disorder or post-traumatic stress disorder.

The patient's prior medical history was unremarkable except for a hypothyroidism and Diabetes Mellitus, treated with levothyroxine 100 µg daily and taking insulin (Mixtard) along with a sitagliptin tablet. The diagnosis of hypothyroidism was made 9 years ago and was based on thyroid ultra-sonographic features, raised thyroid stimulating hormone and lower free thyroxine, as well as anti-thyroid antibodies (anti-antithyroid peroxidase and anti-antithyroglobulin antibodies).

Current physical examination revealed that she is overweight, there were hyper pigmentation on her buccal cavity as well as in the palmar creases of both hands, and she had a caesarean scar which is also become darkened. Her blood pressure was 110/75 lying and 90/70 on standing. Her abdomen was distended but no organomegally was detected. She has bilateral non pitting oedema in the legs, light touch and pin prick sensation was impaired in both legs up to the mid-thigh.

From the laboratory work-up, complete blood count, folate and vitamin B12 levels were normal. Thyroid function tests were within normal limits as she was getting levothyroxine except for the presence of anti-thyroid antibodies. Early morning serum cortisol was 2.1 mcg/dl, serum cortisol was 12 mcg/dl after 60 minutes of 250 mcg I/V bolus ACTH, RBS was 18.2 mmol/dl, HbA1c was 8.1 %. Serum electrolytes showed Na+ 125 mmol/dl, K+ 5.5 mmol/dl. Other routine blood, urine, X-ray chest, USG of whole abdomen was absolutely normal.

Initial fluid resuscitation included I/V administration of 0.9% Normal saline solution with rate 1 liter/hour. Hydrocortisone administration was initiated 100 mg I/V 8 hourly for three days than switch over to oral prednisolone 10 mg P.O. in the morning, 5mg P.O. at lunch time and 5 mg in the early evening. Furthermore, 0.1 mg fludrocortisone was given. For hypothyroidism her levothyroxine was continued as earlier dose and for her glycemic control dose of insulin was modified along with linagliptin was added during day time. On discharge, the patient's physical status was significantly improved within 1 week. During a 12-month follow up the patient's physical and psychological status was normal without recurrence of symptoms.

Discussion:

PAS type-II (Schmidt's syndrome) is a disorder with polygenic inheritance. This is more common than type-I and is seen from infancy through adulthood[1]. Most cases develop after the age of 20 years during the 3-4th decades[2,3]. Male female ratio is 1:3 [4]. It has autosomal dominant inheritance, with familial clustering and family members may manifest different diseases[3]. HLA-DQ2 and HLA-DQ8 are the alleles usually associated with PAS1. When compared to the general population, patients with PAS and Addison's disease have 30-50 times increased risk of developing additional autoimmune diseases[1]. Addison's disease is a rare component of PAS and is usually symptomatic albeit diagnosed after many years. The classic presentation is of hypotension due to adrenal insufficiency with intermittent episodes of hypoglycemia and fatigue. Adrenocortical insufficiency is the initial abnormality in 50% of cases and is required for diagnosis[4]. Addison's disease develops in stages, with metabolic parameters like elevated renin, reduced basal and stress cortisol levels developing prior to symptoms. Diabetes usually heralds the syndrome in most cases. Diabetes is observed in 20% of patients, while 10% of PAS type-II have ovarian failure. Frequency of individual diseases depends upon the population being studied[2].

Other component of diseases may include vitiligo, hypergonadotropic hypogonadism, Graves' disease, pernicious anaemia, alopecia, chronic thyroiditis, chronic atrophic gastritis and autoimmune chronic hepatitis[2]. Increased pigmentation of not only normal skin, but also pre-existing naevi is observed in patients with Addison's disease in Schmidt's syndrome. Hyponatremia is related to the presence of both hypothyroidism and hypoadrenalism and was also seen in our patient.

The patient may have other associated disorders such as primary hypogonadism, myasthenia gravis, and coeliac disease but in our patient none of these disease manifestations were seen.

Conclusion:
PAS type-II (Schmidt's syndrome) can present to the obstetrics & gynecology department with infertility. Care needs to be taken to rule other coexisting conditions, since autoimmune antibodies can predict development of diseases even if asymptomatic at time of presentation. Absence of antibodies does not exclude disease. Patients should be counseled regarding future risk of autoimmune diseases.

Conflict of interest:
The authors declare that there is no conflict of interests regarding the publication of this paper.

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