



## Schmidt's syndrome – Case report

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### CASE REPORT

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### Abstract

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When immune dysfunction affects two or more endocrine glands and other non-endocrine immune disorders are present, the polyglandular autoimmune (PGA) syndromes should be considered. The PGA syndromes are classified as two main types: PGA type I and PGA type II. 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" (PGA 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.

#### Key Words

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

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### Implications for practice

1. **What is known about such cases?** Very few cases of Schmidt's syndrome have been reported because of its rare and atypical presentation.

2. **What is the key finding reported in this case report?** This case was diagnosed as chronic meningitis with initial presentation of headache, vomiting and altered sensorium

3. **What are the implications for future practice?** In cases with two or more endocrinopathies, the possibility of polyglandular syndrome should be considered and treated accordingly.

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### Background

Type II polyglandular autoimmune syndrome (PGA type II) consists of Addison's disease, autoimmune thyroid disease and type 1 diabetes. The idiopathic primary adrenal insufficiency is due to an autoimmune process which destroys 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 also called polyglandular autoimmune syndromes (PGA). PGA: II is more common than PGA: I.<sup>1</sup> This syndrome is very rare, and may occur in both sexes at any age of their lifetime but it commonly affects middle-aged females. PGA type 2 is also known as Schmidt's syndrome. The prevalence of Schmidt's syndrome is 1.4-2.0 per 100,000 population. PGA 2 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. Pernicious anaemia also occurs with increased frequency in patients with this syndrome. Addison's disease is a component of both polyglandular autoimmune syndromes. Type 1 polyglandular autoimmune syndrome (PGA type I) consists of Addison's disease, hyperparathyroidism and chronic mucocutaneous candidiasis. Type II polyglandular autoimmune syndrome (PGA type II) consists of Addison's disease, autoimmune thyroid disease and type 1 diabetes. We are reporting a case of a 42-year-old lady who was misdiagnosed with chronic meningitis because of her

atypical presentation. She was given incorrect treatment with multiple courses of various antibiotics regimen with no improvement in her symptoms for six months and was referred to the psychiatry department. On follow-up she was diagnosed with Addison's disease and subsequently she developed type 1 diabetes mellitus and autoimmune hypothyroidism. Until now very few cases have been reported on polyglandular autoimmune syndrome because of its atypical presentation and because it is a very rare syndrome.

### Case details

A 42-year-old lady presented to the Emergency Department with complaints of weight loss (14kg in six months), anorexia, hyperpigmentation over the body and face (Figures 1-4), headache and vomiting for six months and altered sensorium for seven days. There were no complaints of fever, seizures and focal neurological deficit during her illness.

Her past history revealed that in the last six months, she was hospitalised four times and misdiagnosed with chronic meningitis of unknown aetiology and treated with multiple antibiotics and anti-cerebral oedema measures. However there was no improvement in her symptoms, there was no past history of vitiligo, hair loss joint pain and other features of autoimmune disease. But during her last admission she was presented with significant postural drop in her blood pressure, uncontrolled blood sugar that raised the possibility of Type II polyglandular autoimmune syndrome (PGA type II).

Figure 1: Hyperpigmentation over the dorsum of hands.



Figure 2: Hyperpigmentation over the palmer aspect of hands



Figure 3: Hyperpigmentation over the foot



Figure 4: hyperpigmentation over the face



Physical examination on admission revealed, she was afebrile, no alopecia, no vitiligo, BMI-17.5kg/mt<sup>2</sup>, her pulse was 114/mins, supine position her BP-80/60mmHg (postural drop of systolic 30 mmHg and diastolic 16 mmHg) and respiratory rate-22/mins. Hyperpigmentation was present over the face, limbs (Figures 1-4) and oral mucosa. Glasgow



coma scale (GCS) score -12, CNS examination was normal and other systemic examinations were normal.

Initial laboratory studies showed Hb-14.8g/dl, packed cell volume-45%, total leucocyte count-8200cells/mm<sup>3</sup>, neutrophils 56%, lymphocytes 37%, monocytes 4%, eosinophils 3%. Platelet count-242000cells/mm<sup>3</sup>, erythrocyte sedimentation rate-47mm/hr, fasting blood sugar -180mg/dl, postprandial blood sugar-340mg/dl, GlyHb-9.0, peripheral smear study, renal function tests, liver function tests, serum electrolytes and fasting lipid profiles were within normal limits. Free T3 -2.5pg/ml, Free T4-0.539ng/dl, TSH-17.4IU/ml, random cortisol-0.018UG/DL, anti TPO levels-200IU/ml, cosyntropin test was suggestive of primary adrenal insufficiency. Two blood cultures were sterile, chest X-ray, echocardiography and ECG were normal. Serology for HIV, Hepatitis B and C were negative.

Abdominal sonography revealed normal study. Brain CT scan with contrast and MRI was normal and CSF analysis was normal.

By concluding the history and laboratory findings, the patient was diagnosed to have primary adrenal insufficiency, autoimmune hypothyroid and insulin dependent diabetes mellitus.

She was diagnosed as polyglandular autoimmune type 2 (or Schmidt's syndrome). She was started on insulin, thyroxin therapy and steroid replacement therapy. At discharge the patient was symptomatically better, her blood pressure was 130/80 mm of Hg with no significant postural drop, Glasgow coma scale (GCS) score improved to 15. During her follow-up after one month she was completely normal and a weight gain of 2.5 kg.

## Discussion

Polyglandular autoimmune syndrome type II (PGA-II) is the most common of the immunoendocrinopathy syndromes. It is characterised by the obligatory occurrence of autoimmune Addison's disease in combination with thyroid autoimmune diseases and/or type 1 diabetes mellitus (also known as insulin-dependent diabetes mellitus, or IDDM). Primary hypogonadism, myasthenia gravis, and coeliac disease also are commonly observed in this syndrome. The definition of the syndrome depends on the fact that if one of the component disorders is present, an associated disorder occurs more commonly than in the general population. The most frequent clinical combination association is Addison's disease and Hashimoto thyroiditis, while the least frequent clinical combination is Addison's disease, Graves disease, and type 1 diabetes mellitus.

Approximately 14-20 people per million population are affected by polyglandular autoimmune syndrome type II. Observations have revealed, however, that the disease is much more prevalent if subclinical forms are included. Polyglandular autoimmune type 2 (or Schmidt's syndrome) syndrome diagnosis was made because of the presence of Addison's disease, autoimmune thyroid disease and type 1 diabetes and this syndrome is usually missed because of their atypical presentation and the clinical symptoms of the patient depend upon the gland which is involved first and the severity of that gland dysfunction. 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. Dr Thomas Addison, a British physician, described Addison's disease, that now bears his name.<sup>2</sup> Addison's disease results from the damage to the bilateral adrenal cortex and tuberculosis was the most common cause. Now tuberculosis accounts for only 7 to 20% of cases and autoimmune diseases are responsible for 70 to 90% of cases, with the remainder being caused by other infectious diseases, metastatic cancer or lymphoma and adrenal haemorrhage or infarction.

The primary adrenal insufficiency is because of an autoimmune process that destroys the adrenal cortex. When there is evidence of both humoral and cell-mediated immune mechanisms directed at the adrenal cortex, it is often associated with autoimmune destruction of other endocrine glands referred as polyglandular autoimmune syndromes.

In 86% of patients with autoimmune primary adrenal insufficiency, their serum contain the antibodies that react with several steroidogenic enzymes and all three zones of the adrenal cortex but rarely in patients with other causes of adrenal insufficiency, or in normal subjects.<sup>3</sup> However, first-degree relatives of patients with autoimmune primary adrenal insufficiency express these antibodies and have an increased risk of developing adrenal insufficiency of up to 10%.

The type II syndrome (PGA2) is much more prevalent than the type I syndrome. It is associated with HLA-DR3 and/or HLA-DR4 haplotypes. The pattern of inheritance is autosomal dominance with variable expressivity and a female-to-male ratio of 3-4:1, it occurs in the third or fourth decade of life.<sup>4</sup> Primary adrenal insufficiency is the principal manifestation of<sup>5,6</sup> PGA type II, plus autoimmune thyroid disease, usually chronic autoimmune thyroiditis but occasionally Graves' disease, and type 1 diabetes mellitus are also common. The clinical features consist of a constellation of the individual endocrinopathies. 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. This syndrome can be associated with other non-endocrine autoimmune disorders, such as vitiligo, myasthenia gravis, Sjögren's syndrome, rheumatoid arthritis and primary antiphospholipid syndrome. Patients with autoimmune thyroid disease or diabetes mellitus who have adrenal autoantibodies but do not yet have adrenal insufficiency, and relatives who have one or more components of the syndrome should also be screened and considered as having the disorder.

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## PEER REVIEW

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None

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## PATIENT CONSENT

The authors declare that:

1. They have obtained written, informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees.