CASE REPORT

SCHMIDT'S SYNDROME IN A 32 YEARS OLD FEMALE

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In polyglandular autoimmune (PGA) syndromes, there is immune dysfunction of two or more endocrine glands. Immunity mediated disorders of non-endocrine organs may also be seen. These syndromes are of two main types: type I and type II. We are reporting this case of a 32 years old lady who presented initially with hypothyroidism for many years and received thyroid replacement therapy. After that she was married and had children. After an interval of about seven years of the initial diagnosis of hypothyroidism, she was hospitalized in first trimester of pregnancy for severe vertigo, syncopal episodes and hypotension. She responded well to intravenous fluids **and** steroids. Further endocrine related investigations revealed Addison's disease and the above episode were retrospectively diagnosed as Addisonian crisis. Thus the patient was diagnosed as Schmidt's Syndrome (Autoimmune polyendocrine syndrome type 2) since 2009.

Keywords: Schmidt's syndrome, autoimmune, Addison's disease, hypothyroidism

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INTRODUCTION

In polyglandular autoimmune (PGA) syndromes, immune dysfunction affects two or more endocrine glands and other non-endocrine immune disorders may also be present. The PGA syndromes are classified into two main types: PGA type I and PGA type II.[1] We describe this case in which a young female patient initially had hypothyroidism for many years and subsequently had primary adrenal insufficiency, which was diagnosed when she presented in a comatose state with Addisonian crisis as a medical emergency. She was then diagnosed as a case of "Schmidt's syndrome" (PGA type II). We are reporting this case as very few cases of Schmidt's syndrome have been reported because of its rare and atypical presentation.

CASE REPORT

A 32 years old female patient was brought in Emergency Department of Combined Military Hospital, Murree with history of sudden onset of generalized weakness, fatigability, vertigo, dizziness, paraesthesia both lower limbs for the last one week and loss of consciousness for the last two hours. There was no polyuria or polydipsia. She was found to be hypothyroid in 2002 and after that she was on regular oral Thyroxine replacement therapy. She subsequently got married and had children. In 2009 she was hospitalized in first trimester of pregnancy on account of severe vertigo, syncopal episodes and hypotension and at that time she had a dramatic response to Intravenous fluids and intravenous Hydrocortisone. This led to further endocrinological investigations (Table-1) and she was diagnosed as a case of Addison's disease and the above episode was retrospectively diagnosed as Addisonian crisis. Thus the patient was diagnosed as Schmidt's Syndrome (Autoimmune polyendocrine syndrome type 2) since 2009. The baby boy was delivered by Caesarean section in December 2009. After that she had regular episodes of postural hypotension, vertigo and depression after every 4–5 months. These episodes lasted for 5–7 days. She was then treated with oral Hydrocortisone, Fludrocortisone along with Thyroxine. On this therapy her episodes of anxiety depression, vertigo, fatigability, dizziness, syncope and hypotension were much reduced, however these episodes were observed 3–4 times in a year. She was presently living in Murree, a hill resort, due to her husband being a government servant and currently posted there. Relatives, guests and visitors thus frequented her home and she remained overworked looking after the guests and household chores including her three children (boys aged 8, 6 and 3 years). So at times she missed her medicines leading to the above mentioned episodes and hospitalizations.

On examination she was drowsy (Glasgow coma scale 12/15) but arouse able, her Pulse was 78/min regular; Blood pressure was 70/40 mm of Hg. Patient did not have history of weight loss and her body mass index was 26.3 kg/m^2. There was no oedema or jaundice. There were no features of myasthenia gravis (ptosis, diplopia, difficulty in swallowing, slurred speech, etc). Bilateral rotatory nystagmus was positive, while rest of examination was unremarkable. There was no vitiligo. She was admitted in Intensive Care Unit and treated with intravenous Hydrocortisone, Omeprazole, Ceftriaxone, Fludrocortisone, Betahistine and Intravenous fluids, along with oral Thyroxine, Calcium supplements and Escitalopram. She completely recovered and was discharged on the fifth day with oral medications including tablets:

Hydrocortisone 50 mg daily, Fludrocortisone 100 mg daily, Calcium/Vitamin D, Esomeprazole, Escitalopram and Betahistine.

She was further investigated and magnetic resonance imaging of brain with multi-planer imaging done through brain with special techniques (T_1 and T_2 weighted) and fluid attenuated inversion recovery (FLAIR) sequences in axial, coronal and sagittal images taken at regular intervals without gadolinium contrast. This revealed normal brain and pituitary. Endoscopy of upper gastrointestinal tract revealed normal study.

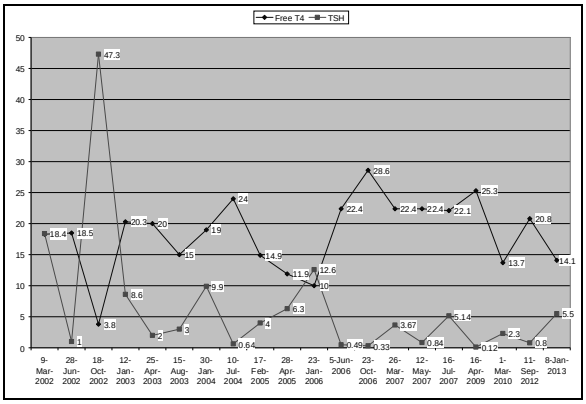

Figure-1: Serial thyroid functions of the patient

Table-1: Patients haematological investigations

Complete Blood Counts	Patient	Reference Rangel
RBC	4.6	4.5–5.5x1012/L
Haemoglobin	14.4	13.5–17.5 g/dL
Hct	43.8	39–51%
MCV	95.1	77–97 fL
MCH	31.2	27.5–32.5 pg
MCHC	32.8	31.5–34.5 g/dL
WBC	7.2	4.0–10.0x10^9/L
Neutrophils	65	40–75%
Lymphocytes	29	20–45%
Monocytes	4	2–8%
Eosinophils	2	1–5%
Platelets	240	150–400x109/L

Table-2: Patients biochemical investigations

Investigations	Patient	Reference Range
Total bilirubin	8	Up to 17 µmol/l
Alanine aminotransaminase	29	Up to IU/l
Alkaline Phosphatase	194	65–303IU/l
Serum Urea	5.5	3.3–6.7mmol/l
Serum Creatinine	76	63–120 µmol/l
Serum Sodium	137	135–148 mmol/l
Serum Potassium	4.1	3.5–5.0 mmol/l
Fasting Plasma Glucose	5.4	3.3–5.6 mmmol/l
Total Cholesterol	4.8	Desirable <5.2 mmol/l
High density lipoprotein	1.2	Desirable >0.9 mmol/l
Low density lipoprotein	2.4	Desirable <3.4 mmol/l
Triglycerides	1.0	Desirable <2.3 mmol/l

Her serial thyroid function tests are depicted in figure-1 (Reference range for free T4=8–24 pmol/l, TSH=0.4–4.0 miu/l). Her serum cortisol (morning) on 11 September, 2012 was 143 nmol/l, and on 8 January 2013 was 673 nmol/l (Reference range for serum cortisol (morning) was 138–690 nmol/l). This may be explained by her poor compliance to medications. Her serum ferritin level was at lower limit of reference range 11.2 (11–375 ng/ml). Her anti double stranded DNA antibodies were negative.

DISCUSSION

Schmidt's syndrome is the most common entity among immune mediated endocrine syndromes. Its diagnosis requires autoimmune Addison disease plus thyroid diseases and/or insulin-dependent diabetes mellitus, or IDDM). Other features of this syndrome are primary hypogonadism, myasthenia gravis, and celiac disease.[1] The characteristic feature of this syndrome is Addison disease and Hashimoto thyroiditis, as was present in this case. Other features of this syndrome cited above were not present in our patient

The prevalence of this syndrome in America is 14–20 people per million. However, if subclinical cases are also included, then the disease prevalence will increase. The disease usually occurs in the 3rd or 4th decade of life and is more common in females.[2]

The exact pathogenesis of Schmidt's syndrome is not fully understood.[3] Immune dysfunction against the target tissue-specific antigens is well known. Genetic predisposition has also been described.[4] What exactly triggers the autoimmunity against target tissue antigens is not exactly known. Both the extrinsic and intrinsic factor could be involved. Molecular mimicry has also been postulated. All or some of these mechanisms may initiate the formation of autoantibodies in the subclinical phase of this syndrome. Later on these antibodies are responsible for tissue or organ dysfunction and clinical manifestations of this syndrome. The amount of immune mediated damage is of variable severity and is progressive. Class II HLA molecules are also considered to play important role, like in many other autoimmune diseases.[5]

There is no single curative treatment of polyendocrine autoimmune syndromes. Hormonal replacement therapy in the form of glucocorticoids and thyroxine is the mainstay of treatment as it was done in our patient.[3] Most of the component disorders of this syndrome have long prodromal phases before overt disease develops.[6,7] Treatment may be delayed if patients do not seek medical advice during this phase

The disease may manifest in stressful situations like infections, surgery, trauma and pregnancy. This happened in our case as she presented with Addisonian crisis. Administration of thyroid hormones to such patients without cover of glucocorticoids may precipitate life-threatening

adrenal insufficiency. Therefore initiation of thyroid replacement therapy may be preceded by assessment of adrenal function. This is due to the action of thyroxine in enhancing hepatic corticosteroid metabolism. Initiation of glucocorticoids in a patient with both deficiencies may initially lead to improvement in thyroid function or mask its clinical manifestations.[8]

As already mentioned our patient initially had hypothyroidism for many years and subsequently had primary adrenal insufficiency, which was diagnosed when she presented in a comatose state with Addisonian crisis as a medical emergency which was probably precipitated by her pregnancy and poor compliance with thyroid replacement therapy. Subsequently she was diagnosed as a case of "Schmidt's syndrome" (PGA type II). Practically it is important to consider "Schmidt's syndrome" in a patient who is having two endocrine deficiencies. Presently our patient is being monitored and followed up to detect any new disorders before overt clinical features develop. In addition she, her husband and family are being given psychosocial support and motivation for compliance with medications.

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