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Case Report

A Rare Form of Polyglandular Autoimmune Syndrome Type 2

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ABSTRACT

Polyglandular Autoimmune Syndrome type 2 (PGA-II) is the most common of the immunoendocrinopathy syndromes. It is characterised by the almost universal presence of adrenal insufficiency (Addison's disease) along with autoimmune thyroid disease, type 1 diabetes mellitus, hypogonadism, hypophysitis and other various non-endocrine manifestations like myasthenia gravis, celiac disease, rheumatoid arthritis, etc. Hashimoto's thyroiditis resulting in hypothyroidism is a far more common occurrence in PGA-II. Here we describe the case of a 40 year old man presenting with Addison's disease and Grave's disease causing hyperthyroidism as a presenting feature of PGA-II, which is a very rare clinical combination with respect to PGA-II.

KEYWORDS: Addison's disease, Grave's Disease, Polyglandular Autoimmune Syndrome type 2 (PGA-II), Schmidt Syndrome.

INTRODUCTION

Polyglandular Autoimmune Syndromes (PGA) is a heterogeneous group of disorders characterised by affection of one or more endocrine glands with various other non-endocrine manifestations. Adrenal insufficiency (Addison's disease)[1,2] is an almost universal presentation of PGA-II, the most common of the PGA syndromes. Hashimoto's thyroiditis is far more prevalent in the affected individuals than Grave's disease. Here we describe a rare case of a male patient who presented with Addison's disease and Grave's disease as a part of PGA-II syndrome without features of type-1 diabetes mellitus and other endocrine disorders.

CASE SUMMARY

A 40 year old male presented to the endocrine OPD with complaints of insidious onset, gradually progressive generalised hyperpigmentation of his entire body since the last 8 months. It was associated with generalised body weakness, lassitude, weight loss and decreased appetite. Since the last 10 days, his weakness had increased to the extent that limited his daily activities, associated with exertional breathlessness. He denied any history of fever, cough, altered bowel and bladder habits. There was no history of alcoholism, smoking or tubercular contact. Family history was unrewarding and negative for autoimmune disorders.

His pulse rate was 130/min, regular in rhythm and character. The blood pressure was on the lower side of normal range (104/60 mm Hg) with no postural variation. General examination was remarkable for generalised hyperpigmentation of the entire body, with darkened palmar creases and oral mucosa. (Figure 1) There was no evidence of pallor, pedal oedema, lymphadenopathy, neck vein engorgement, muscle wasting or any neurological deficit. Oral hygiene was good, and the examination of the chest, cardiovascular system and abdomen did not reveal any abnormal findings. Investigations revealed normal haemoglobin levels (13 g/dl), slight leucocytosis (13200 cells/mm^3) with normal differentials, raised serum potassium (7.3 mmol/l) and low serum sodium (124 mmol/l). Blood glucose (fasting & post-prandial), renal and liver function tests, ECG, chest roentgenogram and ultrasound study of abdomen were within normal limits. Basal serum cortisol was measured to be 21 nmol/l (Normal > 400 nmol/l). Co-syntropin stimulation test confirmed the presence of Adrenal Insufficiency. We further assessed his thyroid functions which showed features of primary hyperthyroidism (TSH <0.005 µIU/ml, fT4 = 76.3 pmol/l). Anti TPO antibodies were elevated (245 units/ml) and thyroid scan shows increased uptake suggestive of graves diseases. (Fig 2) Serum

Testosterone and Gonadotrophins (FSH/LH) were within normal limits; there were no clinical signs suggestive of hypogonadism. Anti-GAD 65 (Glutamic Acid Decarboxylase) and Anti tTg-IgA (anti tissue-transglutaminase) antibodies were undetectable. Serology for HIV, Hepatitis B & C antigens was negative.

We initially treated him with replacement doses of Hydrocortisone after adequate rehydration and correction of electrolyte abnormalities.

After 3 days, Methimazole and Propranolol was added to his regimen. He is being followed up for symptoms of recovery and signs of appearance of other autoimmune diseases.

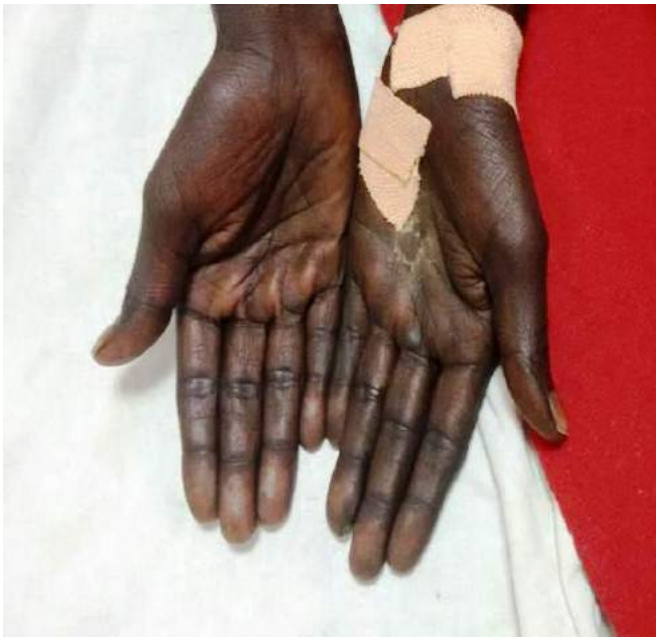

Fig 1: Generalised hyperpigmentation of the entire body, with darkened palmar creases

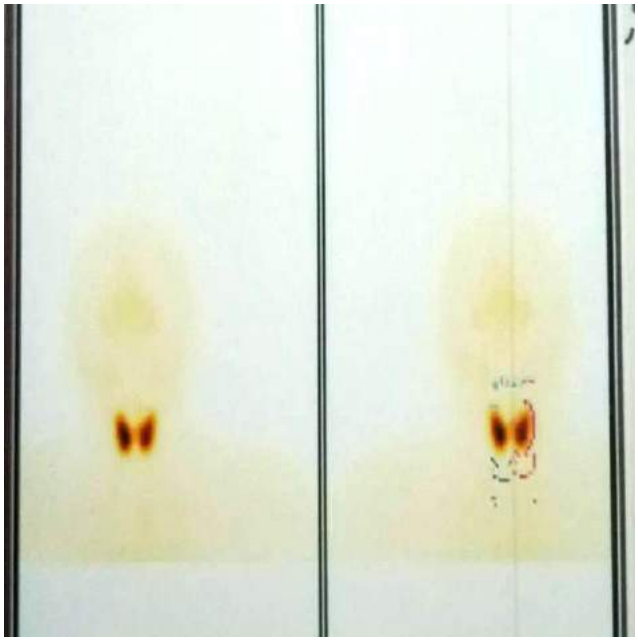

Fig 2: Thyroid scan shows increased uptake suggestive of graves diseases

DISCUSSION

Polyglandular Autoimmune Syndrome type 2 (PGA-II), also known as "Schmidt Syndrome", is the commonest immunoendocrinopathy syndrome. It is characterised by the presence of autoimmune adrenal insufficiency[1,2] (Addison's disease) in combination with autoimmune thyroid disease and type-1 diabetes mellitus. Other autoimmune features like celiac disease, primary hypogonadism, vitiligo, autoimmune hypophysitis, rheumatoid arthritis, antiphopholipid syndrome, thrombocytopenic purpura and myasthenia gravis are also commonly seen in patients affected with PGA-II. None of these additional features were present in our patient at the time of diagnosis.

PGA-II has several modes of inheritance, affects individuals mostly during adolescence and adulthood,[3] and is more common in women.[4] Addison's disease is usually the first manifestation, presenting with weakness, reduced appetite, weight loss, vomiting, fatigue along with generalised hyperpigmentation and orthostatic hypertension. Electrolyte abnormalities are commonly associated with adrenal insufficiency and may predispose to arrhythmias.[5] It may occur simultaneously or may be followed by development of autoimmune thyroid disease and type 1 diabetes mellitus. Various unusual form of PGA II had been reported in the past.[6,7]

Addison's disease is mostly caused by autoimmune destruction of the adrenal cortex, mostly mediated by anti 21-α hydroxylase and anti 17-α hydroxylase antibodies.

Besides these, thyroid peroxidase and thyroglobulin antibodies in thyroiditis, GAD, ICA-512, IA-2 antibodies in type 1 diabetes mellitus and anti-parietal cell antibodies in pernicious anaemia can also be present in PGA-II syndrome.[6]

The clinical combination of Addison's disease and Hashimoto's thyroiditis is the most common in PGA-II, while the least common combination is that of Addison's disease, Grave's Disease and type-1 diabetes mellitus.[8] This fact was also established in a recent retrospective review of case reports[9] where the number of patients presenting with hypothyroidism due to autoimmune thyroiditis was found to be greater than those presenting with hyperthyroidism due to Grave's Disease.

Thus, in such patients with one or more endocrine glandular hypofunction, a strong suspicion for the involvement of other endocrine glands along with other non-endocrine autoimmune phenomenon should be present. Autoantibodies are a good screening tool for the development of PGA syndromes, however regular clinical examination of affected patients during their follow up is also equally necessary.

CONCLUSION

Patients presenting with autoimmune endocrine glandular dysfunction should be periodically screened for other endocrine gland functions and non-endocrine autoimmune phenomenon as a part of the Polyglandular Autoimmune Syndromes.

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