Polyglandular Autoimmune Syndrome Type II

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Introduction
Polyglandular deficiency syndromes (PDS) are characterized by sequential or simultaneous deficiencies in the function of several endocrine glands that have a common cause. Etiology is most often autoimmune. They consist of two distinct types: Type I and Type II polyglandular autoimmune syndrome. Type II is also known as Schmidt’s syndrome. PGA Type II is more common than PGA Type I. This case report describes an 18 year old unmarried female who presented with diabetic ketoacidosis.

Case Report
Eighteen years old unmarried female, diagnosed case of hypothyroidism for 11 years and on medication (Thyroxine tablets 50 mcg BD) with good compliance, presented to emergency room, Benazir Bhutto Hospital with complaints of polyuria for 4 days and Vomiting for 1 day. The frequency of urination was > 20 times/day with nocturnal awakening and sleep disturbance. It was associated with polydipsia, anorexia and generalized weakness. There were 3 episodes of vomiting which were watery, contained no blood or food particle, not associated with food intake, headache, abdominal pain or neck stiffness. On systemic inquiry there was undocumented weight loss, irritable mood and anorexia. Patient was having primary amenorrhea. There was no family history of tuberculosis, diabetes, hypertension, asthma, epilepsy or any other significant illness. There was history of consanguineous marriages in family. Clinical workup showed that patient was having diabetic keto acidosis (blood sugar random = 547 mg/dL, serum ketones= 2.0 mM/L, pH= 7.219 HCO3= 8.5 mM/L) for which she was managed accordingly, and was admitted for further work-up. On further investigations patient was found to be having multiple endocrine deficiencies. HBA1C was 15.1% (normal 4-6% in non diabetics), serum Cortisol(AM) was 21.64 mM/L (normal 260-710 mM/L), Serum prolactin was 119.81 mIU/mL (normal 0.4-6.0 uIU/mL), Serum FSH was 0.43 mIU/mL, serum LH was 0.03 mIU/mL.

Further investigations regarding autoimmune disorders associated with PGA were done. Results revealed Anti tTG IgA was 152 AU/mL (reactive) (Positive: >9 AU/mL), Anti tTGIgG was 80.2 U/mL (reactive) (Positive: >11 U/mL), Vitamin D levels were 3.96 ng/mL (Deficiency: <10 ng/mL). X-ray chest was normal, Endoscopic duodenal biopsy showed Giardia organism and was negative for malignancy or celiac disease. Patient was started on regular Insulin subcutaneous according to sliding scale, tab Thyroxine was continued along with tablet Cefixime 400mg for 5 days before the labs came out and was scheduled for follow up.

Discussion
Historically, the interest in these syndromes began in the 19th century and essentially focused on the adrenal cortex. In 1849, Thomas Addison first described the clinical and pathologic features of adrenocortical failure in patients who also appeared to have coexisting pernicious anemia. In 1981, Neufeld and colleagues distinguished two major polyglandular autoimmune (PGA) syndromes, and other authors subsequently began to add to our knowledge of these conditions. In 2004, Eisenbarth and Gottlieb extended the discussion on the classification of these syndromes. The frequency of Type II PGA in humans is rare, being described in about 1.4-4.5/100,000 inhabitants. Approximately 14-20 people per million population are affected by polyglandular autoimmune syndrome type II. 

Polyglandular autoimmune syndrome type II is characterized by immune dysfunction of two or more endocrine glands. This disease can cause multiple endocrinopathies including: primary adrenal insufficiency (Addison’s Disease), Type 1 diabetes mellitus, autoimmune hypothyroidism and primary hypogonadism. Rarely, this disease can also cause hypophosphatemia, celiac disease (2-3%), atrophic gastritis, pernicious anemia (13%), vitiligo and can also cause late-onset hypoparathyroidism. The most frequent clinical combination association is Addison disease.
and Hashimoto thyroiditis, while the least frequent clinical combination is Addison disease, Graves disease, and type 1 diabetes mellitus. The complete triglandular syndrome is sometimes referred to as Carpenter syndrome.

Our patient had been suffering from hypothyroidism for last 14 years, now she was diagnosed to have type 1 Diabetes Mellitus, Addison’s disease, as well as celiac disease (which is a very rare presentation in cases of PGA type 2 syndrome). Thyroiditis occurs in about 50% of patients with Addison's, while T1D occurs in about 15% of Addison's patients. T1D is frequently associated with autoimmune endocrine and non-endocrine diseases and patients with T1D are at a higher risk for developing several glandular autoimmune diseases. Familial clustering is observed, which suggests that there is a genetic predisposition. Various hypotheses pertaining to viral and bacterial-induced pancreatic autoimmunity have been proposed, however a definitive delineation of the autoimmune pathomechanism is still lacking.

Basically the defect in self tolerance mechanism of immune system leads to destruction of multiple endocrine glands, which results in endocrine insufficiencies and thus causes the disease. Thymus and bone marrow help to delete hyperactive T & B cells, respectively, during their development. Defect in this function leaves T & B cells against the self antigens undeleted. A persistent defective capacity has recently been described in CD4+ CD25+ regulatory T cells, a subset of specialized T lymphocytes involved in suppression of autoreactivity, in patients with Type 2 APS but not in patients with single autoimmune endocrinopathy or in normal healthy controls. Females are affected more than males and disease is familial in nature. Inheritance is autosomal dominant, with defect in HLA-locus.

It is now well established that organ-specific diseases frequently occur in privileged clusters of association and Type 2 APS is considered one of the most typical. Clinically overt syndrome is considered only the tip of the iceberg, since latent forms are much more frequent. Organ-specific autoantibody screening in patients with monoglandular autoimmune endocrinopathies undoubtedly facilitates the identification of those at risk of developing a future APS. Early identification and treatment of another autoimmune endocrine disease may be critical and even life-saving. Currently, management of these disease is restricted to the pharmacological replacement therapy. However, progress in understanding the inner immunological mechanisms implicated in these conditions, should allow common treatments aimed to prevent or at least dampen the progression to irreversible multiple organ damage.

References