AUTOIMMUNE POLYENDOCRINOPATHY TYPE II IN FIRST DECADE - A CASE REPORT
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Abstract: Auto immune polyendocrine syndrome type II with its multisystem involvement and its varied presentation is usually diagnosed in third decade of life and is very uncommon in pediatric population. We highlight its early presentation in children and the need for further investigations and regular follow up in all children with suspected polyendocrinopathy. 9 year old child born to 3rd degree consanguineous parents diagnosed with diabetes at the age of 7 years was on follow up in our diabetic clinic. During follow up, the mother complained of increased pigmentation of face and upper limbs. Investigation revealed normal electrolytes and blood counts. ACTH stimulation test revealed hypo adrenalism. Further investigations revealed presence of Thyroid anti microsomal antibodies but no biochemical evidence of hypothyroidism. The child was diagnosed with Autoimmune Polyendocrine syndrome 2, started on steroids, insulin does was modified and the child is currently followed up in our diabetic clinic.

Keyword: Addison disease, Diabetes mellitus, Thyroid dysfunction

Type 1 Diabetes mellitus is associated with other autoimmune diseases. Neufeld and Blizzard organized and classified these clinical conditions as polyglandular autoimmune diseases, also termed autoimmune polyendocrine syndromes (APS) (1). APS-I is diagnosed when a patient presents with at least two of its three cardinal clinical features: hypoparathyroidism, chronic mucocutaneous candidiasis and hypoadrenocorticism. Autoimmune polyendocrine syndrome (APS) type II is defined by the coexistence of autoimmune Addison disease with autoimmune thyroid disease and/or type 1 diabetes mellitus (2). A fraction of the patients also present with or later develop other organ specific autoimmune disorders like hypogonadism, vitiligo, chronic atrophic gastritis, pernicious anemia, autoimmune chronic hepatitis and celiac disease. It is a rare syndrome that may occur at any age and in both sexes but it is most common in middle-aged females and very rare in childhood (3). We report a 9 year old child, a known diabetic, who on follow up, developed Adrenal insufficiency.

Case Report: 11 years old child second born to 3rd degree consanguineous parents was diagnosed with Type 1 Diabetes mellitus at the age of 7 years, when he presented with polyuria, polydipsia and abdomen pain. He was treated as per DKA protocol, was started on split mixed regime and is being followed up in diabetic clinic. During follow up, the child began to develop hypoglycemic episodes necessitating insulin dose reduction to 25% of the prior dosage over three months. His mother also complained of increased pigmentation of face and limbs over two months. He did not complain of asthenia or fatigue. There was no family history of endocrine disease including Addison’s disease. No contact with tuberculosis. On examination, the child had increased pigmentation over face, limbs, trunk, creases. There was no pallor, icterus. No signs of Vitamin deficiencies were noted. He was normotensive and hydration was adequate. Examination of other systems was normal, his SMR was Stage – 1 prepubertal. A possibility of Adrenal insufficiency was thought and worked up. Investigations revealed normal hemoglobin, blood counts, serum electrolytes, Calcium, Phosphorous, liver function tests. Mantoux, Chest xray, Echocardiogram were normal. ACTH stimulation test revealed basal cortisol levels of 1.60 mcg/dl and 1 ½ and 3 hours levels of 1.50 and 1.40 mcg/dl respectively, indicating hypo adrenalism. Thyroid profile. Parathoromone estimation were normal. Anti thyroid microsomal antibodies was 60.83 which was elevated. He tested negative for anti tissue transglutaminase antibodies. Insulin dose was modified, and was started on Hydrocortisone and fludrocortisones supplements and being followed up.
Discussion:
Autoimmune polyendocrine syndrome, type 2 (APS-II) is the most common form of the polyglandular failure syndromes. In patients with APS-II, Addison’s disease is present in 100% of the cases, autoimmune thyroid disease in 69-82% and type 1 diabetes mellitus in 30-52% of the syndrome (4). Before the advent of effective chemotherapy, tuberculosis was the most common cause worldwide, but current reports indicate that autoimmune disease accounts for 44 to 94 percent of primary adrenal insufficiency. (5). APS-I is a rare childhood disease affecting males and females equally, but more is prominent in certain races such as in Finns, Sardinians and Iranian Jews. APS-II is more heterogeneous and has not been linked to one gene. Rather, patients are at a higher risk when they carry a particular HLA genotype DQ2, DQ8 and DRB1*0404. Many circulating organ-specific antibodies directed against endocrine organs are detected in patients with APS II. These antibodies include 21 hydroxylase autoantibodies against adrenal cortex, thryeroxidase, thyroglobulin and TSH receptor autoantibodies against thyroid, thymus and adrenal cortex, thyroperoxidase, thyroglobulin and TSH receptor autoantibodies against the endocrine pancreas. (6).

In APS II there is an association between organ specific autoantibodies and the presence of pre-existing disease. Autoantibodies may be detected before the symptomatic phases of the autoimmune diseases. The detection of autoantibodies and appropriate interventions prevent morbidity and mortality from other diseases such as diabetic ketoacidosis and Addisonian crisis. APS II typically occurs in early adulthood with a peak onset during the third of fourth decades, however, our patient presented at 9 years, which is quite uncommon. A high index of suspicion for additional autoimmune disorders patients who have APS I or APS II, and their relatives, is essential. Patients should be advised of the symptoms of the disorders for which they are at high risk: hypothyroidism (especially when they are receiving insulin therapy), fatigue, and hyperpigmentation (in some cases) for Addison’s disease; polyuria, polyphagia, polydipsia, and nausea and vomiting with ketoacidosis for diabetes; coordination difficulties for perrnicous anemia; and anemia, osteopenia, abdominal pain and diarrhea for celiac disease. In the patients who have type 1 diabetes and adrenal failure together, an unexpected fall in insulin requirement may be the earliest sign of adrenal failure (7). Also, abnormalities of growth velocity, family history of Addison’s disease should alert one to look for hypoadrenalism. Hypoglycemia attacks are considered to be caused by enhanced insulin sensitivity secondary to glucocorticoid deficiency. The standard test for primary adrenal insufficiency is the cosyntropin test (synthetic adrenocorticotrophic hormone), which has 95% sensitivity and 97% specificity (8). Electrolyte disturbances are not invariable in Addison’s disease – 20 to 30% do not have hypokalemia or hyperkalemia at any time, as in our patient. Autoimmune thyroid diseases – Hashimoto’s thyroiditis, primary myxedema, asymptomatic autoimmune thyroiditis, Graves disease, isolated ophthalmopathy occur in 60-70% of patients with APS II (9). This patient had high titers of anti microsomal antibodies but not biochemical evidence of hypo or hyperthyroidism. The treatment for polyglandular autoimmune syndrome, type II, is targeted at whatever organ is affected. Thyroxine therapy may precipitate Addisonian crisis in patients with APS – II through increasing cortisol clearance and metabolic rate (10) and so, simultaneous investigation of thyroid and adrenal functions become necessary. Hydrocortisone is better for treating Adrenal insufficiency because of its additional mineralocorticoid benefit, most of the time, a mineralocorticoidfludrocortisone also is added to the regimen. The glucocorticoid dose is changed according to the patient’s symptoms. Electrolytes and the activity levels of plasma rennin are monitored to assess the efficacy of treatment with fluorocortisones. Periodic monitoring of blood pressure, growth velocity is need to identify side effect of the drugs. In case of intercurrent illness, the doses of hydrocortisone is increased. The children need to carry a medical identity card indicating their illness. In conclusion, one should think of autoimmune polyendocrine syndrome in all age, especially with presence of Addison’s disease and we need lifelong follow up of these children for early identification and appropriate management of other endocrinopathies and autoimmune disorders.

References:

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