CASE REPORT

Highly raised serum lipid levels in a child with autoimmune polyglandular syndrome type III A: A novel experience

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ABSTRACT

Autoimmune polyglandular syndrome (APS) type III A refers to the coexistence of autoimmune thyroiditis and immune-mediated diabetes mellitus. Although diabetic lipemias in APS type III have been described in medical literature, the degree of metabolic derangements in our patient, especially in the lipid profile is an extremely rare scenario. In this case report, we share this valuable experience.

Keywords: Autoimmune, autoimmune polyglandular syndrome, diabetes mellitus, hypothyroid

INTRODUCTION

Autoimmune polyglandular syndrome (APS) type III refers to the coexistence of autoimmune thyroid dysfunction along with at least one other autoimmune pathology; with the exception of autoimmune Addison's disease.[1] APS type III A is a combination of autoimmune thyroiditis and immune-mediated diabetes (IMD) mellitus.[2]

In the present case, a 14-year-old male with autoimmune type I diabetes mellitus (DM) had autoimmune thyroiditis, and therefore we diagnosed his illness as APS type IIIA. Although diabetic lipemias in APS type III have been described in medical literature,[3] the degree of metabolic derangements in this patient, especially in the lipid profile is an extremely rare scenario. As it is, the findings can neither be explained by any of the known hyperlipidemia syndromes nor as a consequence of the APS. Accordingly, we report this valuable experience.

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CASE REPORT

A 14-year-old male patient was admitted with complaints of low-grade fever for a week, along with recurrent episodes of spasmodic abdominal pain and repeated episodes of loose motion for a day. He had been suffering from easy fatigability, inability to concentrate in studies, breathlessness on exertion and anorexia for last 3 months. He weighed 37 kg and his height was 145 cm, body mass index being 17.6 kg/m^2.

The routine investigations on day 0 (on admission) showed microcytic hypochromic anemia and leukocytosis with lymphocytosis. Erythrocyte sedimentation rate (Wintergreen's method) was 30 mm in 1st h and the value of C-reactive protein was 8.2 mg/L. Thick and thin smear of blood did not reveal any malaria parasite. Renal function test revealed uremia and hypercreatinemia. Electrolyte assessments showed hyponatremia.

The lipid profile on day 0 was as follows: Total cholesterol: 1068 mg/dL (high-density lipoprotein [HDL] cholesterol: 466 mg/dL, low-density lipoprotein [LDL] cholesterol: 422 mg/dL, very low-density lipoprotein [VLDL] cholesterol: 180 mg/dL) triglyceride (TG): 15,810 mg/dL. Liver function test revealed serum glutamic oxaloacetic

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transaminase (SGOT) of 2080 IU/L, Serum glutamic-pyruvic transaminase (SGPT) of 2720 IU/L and alkaline phosphatase of 800 U/L. Serum amylase and serum lipase were within normal limits. The random plasma glucose was 605 mg/dL. Urine for routine investigations (including ketone body) revealed no abnormality. The acetoacetate and hydroxybutyrate levels were normal, ketosis was absent, and no acidosis was observed on an arterial blood gas analysis. Serum iron, ferritin, total iron binding capacity, Vitamin B12, folic acid were all within normal limits. The chest radiography showed haziness and coarse vascular markings in the middle and lower zones of the right lung, suggesting infective changes. Urine for culture and sensitivity showed no growth.

The patient was administered cefepime (a third generation cephalosporin) intravenously according to his body weight. Intravenous infusion of regular soluble insulin 40 U dissolved in 50 mL normal saline was initially infused at 2 mL/h. Capillary blood sugar was checked every hour till check blood glucose was 250 mg/dL. After the capillary blood sugar level of 250 mg/dL was reached regular insulin was infused at 1 mL/h.

He became afebrile on day 1 and continued to remain so throughout. Repeat blood tests on day 3 showed normalization of the leukocytosis, hyponatremia, uremia, hypercreatinemia and raised hepatic enzymes. Chest radiography on day 3 showed clear lung fields. Patient was put on fixed dose regular insulin 16 units before breakfast, 10 units before lunch and 6 units before dinner along with glargine 20 units subcutaneously after dinner. Atorvastatin and fenofibrate (20 mg and 145 mg/day respectively) were now administered as SGPT and SGOT had reduced to less than 3 times of upper normal limits. Relevant blood biochemistry reports were summarized in Table 1

Meanwhile, the anti-glutamic acid decarboxylate antibody titer was very high, and anti-insulin antibodies were positive. Glycosylated hemoglobin was 7.9%. A C-peptide response test showed serum C-peptide concentrations of 0.5 ng/mL after an overnight fast and 3.1 ng/mL 2 h after a meal, thus indicating a reduced capacity of endogenous insulin secretion. Based on these results, the patient was diagnosed with DM type IA. Thyroid function tests revealed the following: Thyroid stimulating hormone (TSH) of 17.97 μIU/mL, free T3 of 1.88 ng/dL and free T4 of 0.82 ng/dL, and positive anti-thyroid peroxidase (>500 U/mL) and anti-thyroglobulin antibodies. There was no enlargement of the thyroid gland on thyroid ultrasonography; however, mild attenuation and heterogeneity of the internal echo were observed, which were consistent with chronic thyroiditis. Therefore, a diagnosis of hypothyroidism due to chronic thyroiditis was made, and later, the cytological examination showed autoimmune thyroiditis [Figure 1]. Treatment was initiated with levothyroxine sodium hydrate at a maintenance dose of 100 μg/day.

Ultrasonography of the whole abdomen, done on day 5, revealed hepatomegaly, mild ascites and bilateral slightly bulky kidneys. Serological examination for anti-nuclear antibodies, Rheumatoid factor, antibody against autoimmune gastritis (anti-cellular parietal antibodies, intrinsic anti-factor), celiac disease (antibody type immunoglobulin A tissue transglutaminase, endomysium) and Addison's disease (anti-21-hydroxylase, the adrenal cortex anti-cellular antibody) were negative. Serum iron, folic acid and Vitamin B12 were normal. Values of plasma aldosterone, renin, and 8 A.M. cortisol were normal, and they allowed us to exclude hyperaldosteronism and Cushing's syndrome. The patient was nonreactive for HIV (I and II), hepatitis C virus and HB_SAg.

Repeat lipid profile for day 5 was as follows: Total cholesterol: 785 mg/dL (HDL cholesterol 150 mg/dL, LDL cholesterol 250 mg/dL, VLDL cholesterol 385 mg/dL) and TG 905 mg/dL. Genetic testing could not be done because of financial constraints. The boy was discharged on day 7 with advice to take atorvastatin/fenofibrate (20/145 mg/day), Levothyroxine 100 μg/day and fixed dose regular insulin 16 units before breakfast, 10 units before lunch and 6 units before dinner along with glargine 20 units subcutaneously after dinner. He was asked to visit us after 2 weeks with reports of repeat serum lipid profile, fasting blood glucose and TSH.

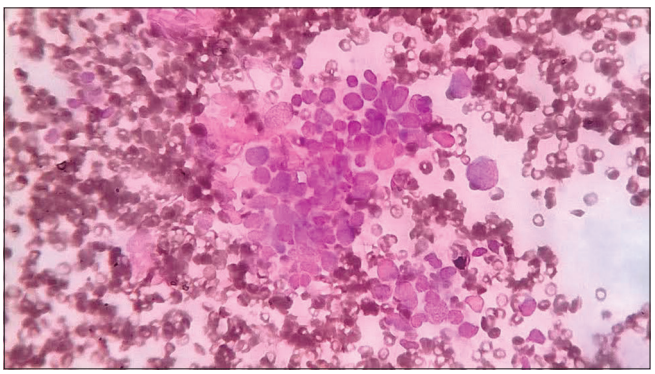

Figure 1: Cytological examination showing autoimmune thyroiditis

DISCUSSION

Autoimmune polyglandular syndrome essentially includes the presence of two autoimmune disorders, at least one being endocrinological. The association between autoimmune endocrinopathies has been described in medical literature since the late 19th century, through the works of Addison, Claude, Gougerot and Schmidt and ultimately in 1980, Neufeld and Blizzard promulgated the first classification of APS. The classification has undergone revisions and currently four distinct types of APS are recognized.[4] The following is the classification of APS:

- Type I: Atleast 2 of chronic mucocutaneous candidiasis, idiopathic hypoparathyroidism and autoimmune Addison's disease
- Type II: Autoimmune Addison's disease and autoimmune thyroiditis and/or type I DM
- Type III: Coexistence of autoimmune thyroiditis with at least 1 other autoimmune pathology (excluding Addison's disease)
- Type IV: ≥2 autoimmune entities (not classifiable under type I, II or III).

The exact prevalence of APS is unknown; it has been calculated that 3.5–4% of the total population has a complete or incomplete APS type III.[5] APS III again is abscinded as follows:

- APS IIIA: Autoimmune thyroiditis with IMD mellitus
- APS IIIB: Autoimmune thyroiditis with pernicious anemia
- APS IIIC: Autoimmune thyroiditis with vitiligo and/or alopecia and/or other organ-specific autoimmune disease.

Considering that autoimmune thyroiditis is most frequently seen in patients with other autoimmune diseases (present in 10–30% of patients),[6] it is easy to appreciate why APS III is the most important and frequent among those described to date.

Our patient demonstrates a constellation of clinical entities suggestive of APS type IIIA, which may be a random association, but may also indicate a common immunological and/or genetic disturbance. APS III was previously reported to have association with diabetic lipemia, eruptive xanthoma, anti-MuSK positive myasthenia gravis, and portal hypertension.[3,7,8] However, the gross derangements in lipid profile, as seen in this patient, have never been reported. It does not fit any of the hyperlipidemia syndromes. It was neither associated with eruptive xanthomas, xanthelesmas or pancreatitis. The hepatic transaminases were also distinctly raised, but abdominal ultrasonography was largely normal.

Autoimmune polyglandular syndrome III is a multifactorial disease in which diverse genetic and environmental factors may modulate the immunological activity. Several family and population studies have hypothesized a strong genetic predilection for APS type III, but establishing a specific genetic basis continues to remain elusive. Due to financial constraints, genetic study of this patient could not be undertaken; but the study of HLA haplotypes increasing susceptibility in autoimmune thyroiditis, e.g. HLA-DQB1*0602

Table 1: Results of blood tests during hospital stay

	Day 0	Day 1	Day 3	Day 5
Hb%	9.9			
RBC	3.05			
PCV	29.7			
MCV	80.7			
MCHC	33.3			
Total iron				
Ferritin				
TIBC				
Vitamin B12				
Folic acid				
ESR	30			
CRP	8.2			
TC	12,300	9900	7200	
Neutrophil	48			
Lymphocyte	49			
Eosinophil	1			
Monocyte	2			
Basophil	0			
Na^+	129.7	131.6	136	
K^+	4.09		4.6	
Ca^{++}	9.2			
Urea		70	42	30
Creatinine		2.2	1.2	0.7
TSH	17.97			
Free T4	0.82			
Free T3	1.88			
Anti-TPO	>5000			
SGOT	2080		109	
SGPT	2720		70	
Alkaline phosphatase	800		268	
Amylase	43			
Lipsae	52			
Lipid profile				
TC	1068			785
LDL-C	422			250
HDL-C	466			150
VLDL	180			385
TG	15,810			905

Hb: Hemoglobin; RBC: Red blood cell; PCV: Packed cell volume; MCV: Mean corpuscular volume; MCHC: Mean cell hemoglobin concentration; TIBC: Total iron-binding capacity; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; TC: Total cholesterol; Anti-TPO: Anti-thyroid peroxidase; TSH: Thyroid stimulating hormone; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic-pyruvic transaminase; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; VLDL: Very low-density lipoprotein; TG: Triglyceride

HLA-DQB1*0301, increasing susceptibility in IMD e.g. DRB1*04/DQA1*0301/DQB1*0302 or decreasing it e.g. HLA-DQB1*0602[9] and also the ones most important for common disease susceptibility genes are human leukocyte antigen (chromosome 6), protein tyrosine phosphatase nonreceptor type 22 (chromosome 1), cytotoxic T-lymphocyte–associated antigen 4 (chromosome 2), forkhead box P3 (X chromosome), and the interleukin 2 receptor alpha/CD25 gene region (chromosome 10) remains a major crux in further study of the case,[10] for which funding has been sought from government authorities.

CONCLUSION

Although APS IIIA is a rare disorder, the clinician must search associations in type I DM or autoimmune thyroiditis patients. Abnormal dyslipidemia reported, in this case, is probably a new manifestation of APS IIIA. As the genetic analysis was not performed, in this case, the possibility of a new genetic dyslipidemic syndrome cannot be ruled out.

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