CASE REPORT

Metabolic Syndrome in Childhood: Rare Case of Alstrom Syndrome with Blindness

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Abstract Alstrom's syndrome (AS) is a rare autosomal recessive ciliopathic condition affecting 1:10,00,000 children. It's a single gene disorder of ALMS1 on chromosome 2 with multisystem involvement with cone-rod retinal dystrophy causing juvenile blindness, obesity, insulin resistance, type 2 Diabetes mellitus, hypogonadism and sensorineural hearing loss. Till now only 800 patients with this disorder has been identified so far. In this report, we describe the case of a 9-year old male boy from south India. He had been initially referred for polyphagia, polyuria, polydipsia, generalized weakness from 1 weeks. On examination he was demonstrated features suggestive of AS, including blindness, obesity, type 2 diabetes, altered lipid profile, hypogonadism, acanthosis nigricans, seborrheic dermatitis, right ear discharge and episodes of respiratory tract infections. So, diagnosis of AS is critical as it can easily be overlooked because of the many features associated with metabolic syndrome starting at age 7, a relatively early age.

Keywords Alstrom syndrome · Diabetes · Obesity · Metabolic syndrome

Introduction

Alstrom syndrome (AS) is a rare autosomal recessive disorder first described in 1959 by Carl Henry Alstrom. A wide range of clinical variation is observed in AS individuals and their siblings. The most common clinical findings are cone-rod dystrophy which results in childhood blindness, central obesity that manifests very early, insulin-resistant type 2 diabetes mellitus (T2DM), progressive sensorineural hearing loss and infantile or adolescent-onset dilated cardiomyopathy [1]. Only 800 cases of AS have been reported worldwide since 1959. The gene mutation involved is in ALMS1 gene located on chromosome 2p13. It becomes difficult to diagnose AS at an early age, since the characteristic features which resemble metabolic syndrome manifest only after the age of 6–8 years [2].

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Thus, clinical diagnosis of metabolic syndrome is usually made in AS cases based on the presence of abnormal glucose metabolism, obesity, hyperlipidemia and hypertension. The lipid profiles of patients with AS and metabolic syndrome are often characterized by hypertriglyceridemia, high LDL and low HDL cholesterol. Therefore cases with these defects from an early age have an increased risk of developing premature coronary artery disease and dilated cardiac myopathy which are the major causes of mortality in this syndrome [3]. Hence, knowledge about this rare syndrome is of vital importance for an early diagnosis and treatment.

Case Report

A 9-year-old boy from south Karnataka (India) presented with polyuria, polydipsia, polyphagia, weight gain and gradual weakness since 2 weeks. Child was unable to see since 5 months of age and had history of weight gain from 2nd year of life. He was the only child born to a consanguineous marriage, with no perinatal complications. He had birth weight of 2.6 kg after a full term elective caesarian section. The child was apparently normal for the first 5 months of life following which the parents noticed that the child was unable to follow objects (no eyeball movement). He was reported to have loss of vision in both eyes but no mental retardation or any signs of motor delay. There was no history of similar symptoms in the family.

On examination child was conscious, oriented, obese and having seborrheic dermatitis and acanthosis nigricans on the back of neck. His height was 117 cm (normal height at 9 years is 132 cm), weight 45.5 kg (normal weight at this age is 28.1 kg), BMI (body mass index) is 24.24 kg/m² (normal BMI at these age is 14–18.6 kg/m²), waist to hip ratio 1.01 and blood pressure of 130/80 mmHg (normal SBP is 95–115 mmHg and DBP is 60–80 mmHg). Genital examination showed bilateral atrophied testis. He also had itching in his right ear, on and off, discharge from 3 years for which he was given antibiotics. Rest of the systemic examination was normal.

Routine investigations, including complete blood count, hemoglobin, sedimentation rate, thyroid function test were within normal ranges. His laboratory tests were as follows [reference ranges in parentheses]: random plasma glucose was 354 mg/dL [70–140 mg/dL], fasting plasma glucose 246 mg/dL [70–100 mg/dL], HbA1c 9.8 % [<6 %], total cholesterol 232 mg/dL [<200 mg/dL], triglyceride 1183 mg/dL [<150 mg/dL], HDL 25 mg/dL [40–60 mg/dL], LDL 29 mg/dL [<100 mg/dL], VLDL 236 mg/dL [<40 mg/dL], urine albumin 89 mg/L [<30 mg/L], urine glucose 3+ [nil], ALT 95 U/L [5–40 U/L], AST 50 U/L [5–40 U/L], K⁺ 2.3 mmol/L [3.5–5.3 mmol/L] whereas

urea, creatinine, electrolytes and Ca²⁺ were within normal range. On the basis of these findings child was diagnosed with AS and continued on insulin and metformin therapy. Later on fenofibrate was added for lipid control.

Discussion

As mentioned above Alstrom Syndrome is an autosomal recessive, single gene disorder (ALMS1-2p13) presenting with childhood obesity, hyperinsulinemia, type 2 diabetes mellitus, progressive cone-rod dystrophy leading to blindness, sensorineural hearing loss and function loss of multiple organs [4]. In present case report child had loss of vision, obesity, T2DM and hearing impairment from the first year of life. Based on the diagnostic criteria mentioned by Marshall et al. [1] for this child between 3 and 14 years of age, a diagnosis of AS was made. In the present case 1 major criteria was loss of vision and 3 minor criteria were obesity, hearing impairment and hepatic dysfunction.

Diagnosis of AS is difficult because some features begin at birth and others develop as the child grows. As patients reach adolescence majority of the cases develop vision impairment, obesity, T2DM, hypertriglyceridemia and dilated cardiac myopathy. Short stature, male hypogonadism and hyperandrogenism in females may appear as they reach adulthood [5]. Obesity is an early and consistent sign seen in almost all affected cases of AS. Weight gain usually does not initiate until 6 months–1 year of age and may become moderate after puberty. Although hyperphagia and food fascination are common complaints but the exact cause of obesity is still unknown. The expression pattern of ALMS1 in mouse brain is suggestive of a hypothalamic cause for these features [1].

Diabetes may be present as early as the age of 4 years, with the median age of onset at 16 years. Almost one-third of AS cases present with acanthosis nigricans whether or not they have diabetes. Male adolescents mostly remain infertile because of small gonads which cause impaired or delayed puberty, gynecomastia, and low sperm count whereas sexual development is normal in female adolescents [1]. Hyperlipidemia, particularly hypertriglyceridemia presents usually from early childhood in these cases. In some patients, a sudden, rapid rise in triglycerides was also reported which increases the risk for pancreatitis in them [6].

Differential diagnoses include Bardet–Biedl syndrome, achromatopsia, Leber's congenital amaurosis, inherited mitochondrial disorders, Usher and Cohen syndromes [7]. Bardet–Biedl Syndrome (BBS) generally appears like AS but differs from AS in clinical features like polydactyly, brachidactyly, syndactyly, hypodontia, 50 % mental retardation and mutations of BBS gene [4].

The management of AS involves a multidisciplinary approach. Specific treatment is directed towards management of complications. If feasible, carrier testing for relatives and prenatal testing are advisable [7]. An interesting thing is that AS and BBS both are caused by genes that belong to the same biochemical pathway. Also, both syndromes are caused by different mutations at the same gene locus. So, localization and identification of the gene responsible for AS is very valuable because this not only would confirm the diagnosis but also would shed light on the causes of the isolated forms of cardiomyopathy, retinal dystrophy, diabetes, and deafness [8].

Phenotypic variations were observed in this case. In AS, symptoms of cone dystrophy usually begin in infancy and rod function is also impaired by five years [7]. But in the present case, complete loss of vision developed when the patient was only 4–5 months old that shows premature cone-rod dystrophy in this patient. The classic description by Alstrom et al. included obesity (98 %), insulin resistance (92 %), sensory neural deafness (88 %), T2DM (68 %) and cardiomyopathy (60 %) [7]. In our patient all these findings were present except for cardiomyopathy. However gradual weakness was reported by the patient which may be associated with myopathy. So creatinine kinase along with other routine investigation should be done frequently to follow the trends of associated complication of AS.

Childhood metabolic syndrome associated with other findings should be considered as AS because it shares the features of metabolic syndrome which is very common now a days in developing country like India. Early diagnosis will definitely help in the detection and effective

management of the complications. So, AS should be considered as a model for metabolic syndrome in children. It is to be expected that these findings will support clinicians to interpret the processes underlying the pathophysiology of AS, as well as of obesity and DM.

Compliance with Ethical Standards

Conflict of interest None.

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