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Alstrom Syndrome with Bilateral Testicular Atrophy: A Rare Case Report

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ABSTRACT

Alstrom syndrome is a rare autosomal recessive, single gene disorder involving multiple systems. It was first described by Carl Henry Alstrom in 1959. With prevalence of less than one in one million children, approximately 700 cases have been reported worldwide out of which only about 20 cases have been reported from India. While previously case of Alstrom syndrome with unilateral absent testes had been reported, this case is an add on to the literature with combination of Alstrom syndrome with bilateral testicular atrophy.

Keywords: alstrom syndrome, diabetes mellitus, portal hypertension, retinitis pigmentosa, testicular atrophy

INTRODUCTION

Alstrom syndrome is a multiorgan disorder, characterized by single gene (ALMS1) mutation with autosomal recessive inheritance [1]. Alstrom syndrome exhibits a great degree of phenotypic variability, even within families, thereby creating difficulties for a universal definition of Alstrom syndrome [2]. It is diagnosed based on Marshall Criteria with usual manifestations like obesity, type 2 diabetes mellitus, progressive retinal dystrophy and sensorineural deafness. Diagnosis of Alstrom syndrome can be difficult because some features begin at birth and others emerge as the child develops. Here we report a case of Alstrom syndrome who presented with uncontrolled type 2 diabetes mellitus and portal hypertension. Bilateral testicular atrophy is another unique feature of our case.

CASE REPORT:

An 18-year-old male, only son of non-consanguineous parents from north Karnataka (India) presented with one episode of blood in vomitus. He had birth weight of 2.9 kgs after a full term elective caesarean section with no perinatal complications. The child was apparently normal until first seven months of life after which his mother noticed that the child was unable to follow objects. He was reported to have loss of vision in both eyes, mental retardation with no signs of motor delay. He also was known diabetic since 14 years of age and was on both insulin and oral hypoglycaemic agents. There was no history of similar complaints in the family. On general physical examination, he was conscious and oriented to time, place and person. His height was 148 cm (normal height at 18 years is 162 cm), weight 45.2 kg (normal weight at this age is 54.4 kg), BMI (body mass index) is 20.77 kg/m^2 (normal BMI at these age is 14-18.6 kg/m^2), pallor, round face, frontal balding with thick ears. Ocular examination revealed bilateral horizontal nystagmus and divergent squint. Fundus examination revealed optic atrophy and features suggestive of atypical retinitis pigmentosa. Genital examination showed bilateral atrophied testis. Rest of the systemic examinations were clinically within normal limits. Investigations

were done, that showed, total count 23680 cells/cu mm [4500-11000 cells/cu mm], neutrophils 67.3% [40-75%] haemoglobin 4.3gm% [11.6-14.5 gm%], platelet count of 2.31 lakhs/cu mm [1.5-4 lakhs], prothrombin time 13.6sec [10-14sec] and INR was 1.15. His biochemical tests results were [laboratory reference in parentheses]: random blood sugar was 596 mg/dl [upto 180 mg/dl], HbA1c 11.4 % [6 %], urine albumin - absent [15 mg/L], urine sugar - 2000 mg/dl [<25 mg/dl], SGOT- 108 U/L [15-43 U/L], SGPT 246 U/L [13-69 U/L], sodium - 126 mmol/L [137-145 mmol/l], potassium-5.3 mmol/L [3.5-5.1 mmol/L], calcium 7.9 mg/dl[8.5-11.0 mg/dl] whereas urea and creatinine were within normal range. Radiological investigations including ultrasonography of abdomen showed portal hypertension (Figure 1), ultrasonography of scrotum revealed bilateral testicular atrophy with minimal left hydrocele (Figure 2) and upper gastrointestinal endoscopy study concluded grade 2 and 3 oesophageal varices (Figure 3). Liver biopsy was performed and was suggestive of fatty change. The diagnosis of Alstrom syndrome was made based on Marshall Criteria (Table 1) [3]. The patient was prescribed propranolol 20 mg once daily for portal hypertension and insulin therapy based on glycaemic control.

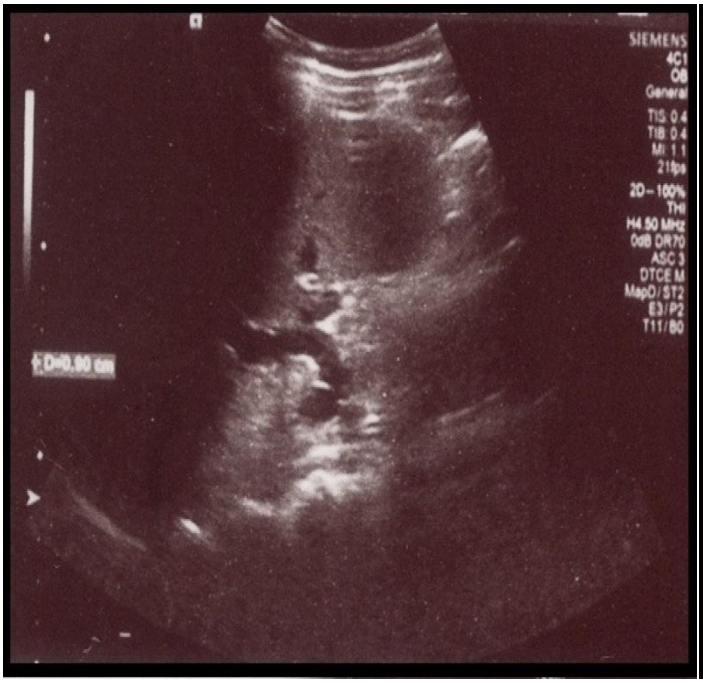

Figure 1: USG abdomen suggestive of Portal Hypertension

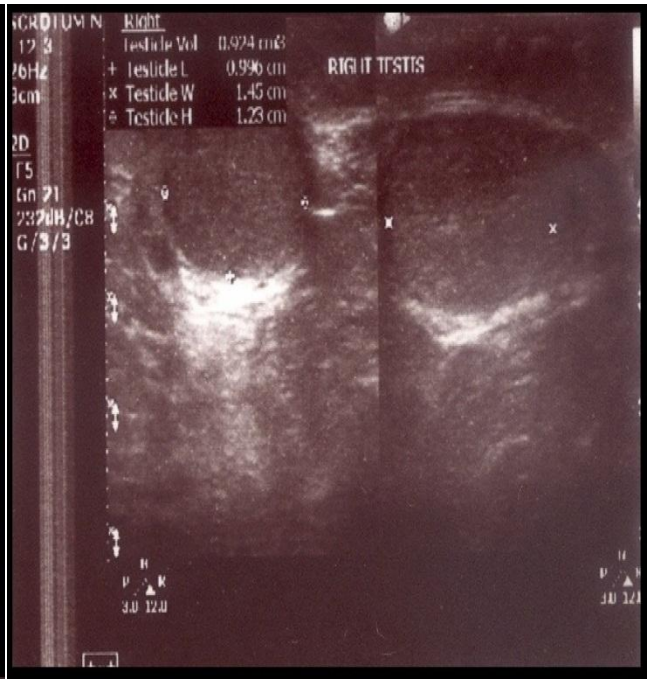

Figure 2: Scrotal USG suggestive of bilateral Testicular atrophy

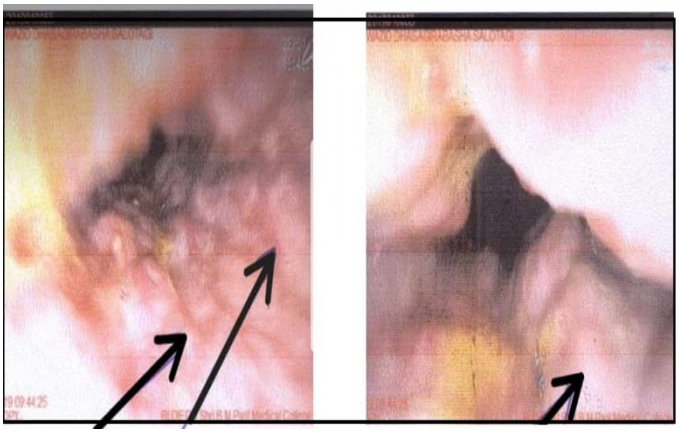

Figure 3: Endoscopy showing grade 2 and 3 Oesophageal varices

Volume 3, Issue 3; May-June 2020; Page No.22-25

DISCUSSION:

Alstrom syndrome is a rare genetic disorder caused by mutation of the ALMS1 gene. The gene mutation is inherited as an autosomal recessive trait. Approximately 700 cases have been reported worldwide out of which only about 20 cases have been reported from India [1]. With prevalence of less than one in one million children since the condition was first described in 1959, by Carl Henry Alstrom.

Alstrom syndrome presents with wide range of symptoms which are highly variable and progress with advancing age [2]. Diagnosis is done based on Marshall Criteria, which is classified into 3 groups as birth- 2 years, 3-14 years, and 15 years - adulthood [3]. Our case was a 18 year old male and we diagnosed him with criteria of third group (15 years- adulthood) satisfying one major and 4 minor criteria [4], which includes atypical retinitis pigmentosa with optic atrophy of both eyes, type-2 diabetes mellitus, portal hypertension, short stature and bilateral testicular atrophy.

Retinal dystrophy and hypogonadism is also seen in Bardet-Biedl, Lawrence-Moon, Kearns-Sayre and Wolfram syndromes. The absence of polydactyly, syndactyly, sensorineural deafness and spastic paraparesis, with normal mental health rules out Bardet-Biedl and Lawrence-Moon syndromes [5]. The genotyping of proband and the parents was not done, which remains a limitation of this case report, else a strong evidence to confirm the diagnosis could have been put forth.

Management requires a multidisciplinary approach and there is, thus far, no specific treatment that can cure Alstrom syndrome. Hence life span of patients affected with Alstrom syndrome rarely exceeds 40 years. In our case proband was treated with insulin and oral hypoglycaemic agents for diabetes mellitus and propranolol for portal hypertension and genetic counseling was done to parents.

CONCLUSION:

This case is reported to potentiate ongoing accumulation and sharing of information about Alstrom syndrome. It also intends to improve our ability to make valid diagnosis and to find different combinations with which patients with Alstrom syndrome can present. Though there is no specific treatment, but early diagnosis can help to delay the progression and improve the longevity and quality of life for patients.

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Volume 3, Issue 3; May-June 2020; Page No.22-25

	Birth - 2 years*	**3 –14 years**	**15 years – adulthood**
Proof+	2 ALMS1 mutations	2 ALMS1 mutations	2 ALMS1 mutations
Minimum diagnosis requires	(a) 2 major criteria or (b) 1 major and 2 minor criteria	(a) 2 major criteria or (b) 1 major and 3 minor criteria	(a) 2 major and 2 minor criteria or (b) 1 major and 4 minor criteria
Major criteria	▪ALMS1 mutation in 1 allele and/or family history of Alstrom Syndrome ▪Vision (nystagmus, photophobia)	▪ALMS1 mutation in 1 allele and/or family history of Alstrom Syndrome ▪Vision (nystagmus, photophobia, diminished acuity, if old enough for testing: cone dystrophy by ERG)	▪ALMS1 mutation in 1 allele and/or family history of Alstrom Syndrome ▪Vision (history of nystagmus in infancy/ childhood, legal blindness, cone and rod dystrophy by ERG)
Minor criteria	•Obesity •DCM/CHF	•Obesity and/or insulin resistance and/or T2DM •(history of) DCM/CHF •Hearing loss •Hepatic dysfunction •Renal failure •Advanced bone age	•Obesity and/or insulin resistance and/or T2DM •(history of) DCM/CHF •Hearing loss •Hepatic dysfunction •Renal failure •Short stature •Males: hypogonadism Females: irregular menses and/or hyperandrogenism
Other variable supportive evidence	○Recurrent pulmonary infections ○Normal digits ○Delayed developmental milestones	○Recurrent pulmonary infections ○Normal digits ○Delayed developmental milestones ○Hyperlipidemia ○Scoliosis ○Flat wide feet ○Hypothyroidism ○Hypertension ○Recurrent UTI ○Growth hormone deficiency	○Recurrent pulmonary infections ○Normal digits ○History of developmental delay ○Hyperlipidemia ○Scoliosis ○Flat wide feet ○Hypothyroidism ○Hypertension ○Recurrent UTI/urinary dysfunction ○Growth hormone deficiency ○Alopecia

1. *Diagnostic criteria in children should be re-evaluated when patient grows older.
2. +If two mutations are found, confirm one inherited from each parent.
3. Abbreviations: ERG, electroretinogram; T2DM, type 2 diabetes mellitus; DCM/CHF, dilated cardiomyopathy with congestive heart failure; UTI, urinary tract infections.

Table 1: Diagnostic criteria for Alstrom syndrome [3]

Volume 3, Issue 3; May-June 2020; Page No.22-25