



CASE REPORT

Ahlstrom's Syndrome with Type IV Choledochal Cyst

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Abstract

Ahlstrom's syndrome is an autosomal recessive, single gene disorder with multisystem involvement with cone-rod retinal dystrophy leading to juvenile blindness, sensorineural hearing loss, obesity, insulin resistance and type 2 Diabetes mellitus. The other less common involvements may severely affect the prognosis and survival and include endocrine abnormalities, dilated cardiomyopathy(DCM) , pulmonary fibrosis and restrictive lung disease, progressive hepatic and renal failure. Apart from its typical, well known clinical features, hepatic & biliary involvement should be kept in mind. Though not known in literature, the biliary tract abnormalities might not be so uncommon. A routine MRCP in a child of AS with typical or atypical biliary tract involvement is thus advisable.

Key Words

Ahlstrom's Syndrome, Obesity

Introduction

Ahlstrom's syndrome is an autosomal recessive, single gene disorder with multisystem involvement with cone-rod retinal dystrophy leading to juvenile blindness, sensorineural hearing loss, obesity, insulin resistance and type 2 Diabetes mellitus. The other less common involvements may severely affect the prognosis and survival and include endocrine abnormalities, dilated cardiomyopathy(DCM), pulmonary fibrosis and restrictive lung disease, progressive hepatic and renal failure. Most patients have normal intelligence and females are mostly eumennorrhic. Life span rarely exceeds 40 years (1). Clinical features, time of onset, and severity can vary from patient to patient. We hereby describe very rare biliary tract abnormalities in patient of Ahlstrom's syndrome.

Case Report

16 year old girl obese since childhood, 10th standard student, with normal menstrual cycles attained menarche at age of 13 years, three years back evaluated by an endocrinologist for obesity and diabetes and put on oral hypoglycemic agents. A year later consulted an ophthalmologist for diminution of vision, diagnosed as Retinitis pigmentosa and underwent LASER treatment in Indore. She this time presented to us with recurrent

biliary colic's of one month duration. Her examination revealed generalized obesity with Body Mass Index (BMI) of 32kg/m², left divergent squint, normal intelligence, bilateral retinitis pigmentosa, short and stout hands, normal secondary sexual characters and normal rest of the systemic examination. On evaluation, her Haemogram, LFT, KFT, Thyroid profile, Blood gases, Electrolytes, Coagulation profile were normal, her sugars were controlled. Her ultrasonography showed grossly dilated Intra Hepatic Bile Ducts (IHDs) with stones (Fig1). Endoscopic Retrograde Cholangio Pancreaticography (ERCP) revealed dilated IHD and uniformly dilated Common Bile Duct (CBD) (Fig2).

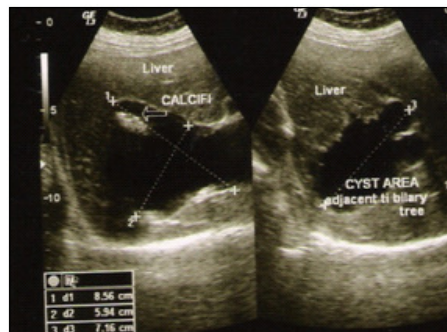


Fig.1 Grossly Dilated IHBDs with Stones

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Fig. 2 ERCP Showing Dilated both RIHD & LIHD & Non Uniform Dilatation of CBD

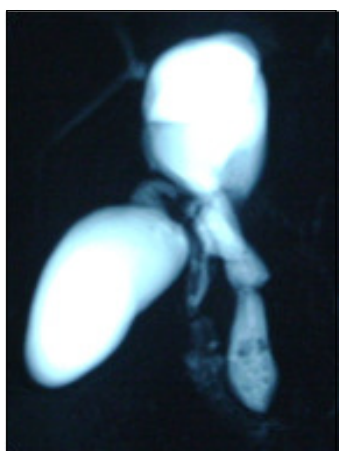


Fig.3 MRCP Revealed Type IV Choledochal Cyst with Stones in Dilated CBD

MRCP revealed type IV choledochal cyst with stones in dilated CBD (Fig 3).

Discussion

Ahlstrom's syndrome (AS) is an autosomal recessive, single gene disorder caused by mutation in ALMS (Chr. 2p13), a novel gene of currently unknown function. The clinical manifestations, onset of symptoms and severity of involvement vary greatly among the patients (1). Early diagnosis is difficult because the typical phenotypes are not present in infancy but develop over a period of time throughout the childhood and because the genetic testing for ALMS1, MIM #20380 is not routinely available in most of the centers in developing countries. Approximately 460 cases have been identified since the condition was identified in 1959 (2). The major phenotypes usually observed in children with Ahlstrom's syndrome include cone-rod retinal dystrophy, beginning in infancy and leading to eventual juvenile blindness, sensorineural hearing impairment, insulin resistance and

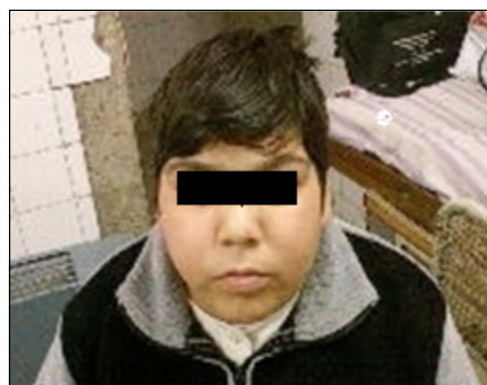


Fig 4. Typical Facial Features ; Round Face, Male Hair Pattern and Obesity

obesity (3). Dilated cardiomyopathy (DCM) occurs approximately in two-thirds of patients with AS. In many patients the cardiac function improves with age and patients reach adolescence, more of the major phenotypes develop including type 2 diabetes mellitus (T2 DM), hypertriglyceridemia and adolescent onset DCM, short stature, scoliosis, alopecia, male hypogonadism and hyperandrogenism in females also occur when patients reach adulthood. Pulmonary, hepatic and renal phenotypes are progressive. Fibrosis in multiple organs has been described (3).

The retinal dystrophy in Ahlstrom's syndrome usually develops within few weeks after birth and virtually all children exhibit low vision within first year of life. Eventually all children become blind by 9 years of age, approximately 90% of patients are totally blind by age 16 (3).

Most patients develop mild to moderate bilateral sensorineural hearing loss & 10% of patient's progress to profound deafness and may rely on tactile signing for communication. Cone-rod retinal dystrophy, beginning in infancy and leading to eventual juvenile blindness, sensorineural hearing impairment, as may remain stable for many years (3). Obesity is an early and consistent feature observed in all affected children. Weight gain starts at 6 months to one year and may be moderate after puberty. Insulin resistance and hyperinsulinemia have been observed in patients as young as one year (1). Most patients will eventually develop diabetes, though there is a great variability in the age of onset. Disturbances in growth hormone and insulin like growth hormone access have been reported in number of cases (4, 5).

Male adolescents have small testes and penises, impaired or delayed puberty, gynaecomastia and low



sperm count. Males are unlikely to be fertile but may have normal secondary sexual characters. In female adolescents, the sexual development usually progresses normally and menarche is not delayed. Few girls may have precocious puberty, secondary sexual characteristics and genitalia are normal. Increased androgen production and hirsutism are common. High frequency of ovarian cysts is reported.

Hyperlipidemia especially hypertriglyceredemia and hypothyroidism is seen in 20-30 percent of patients. There is no facial dysmorphism but patients have distinctive facial characteristics like rounded facies, deep set eyes, thick ears and thin hairs. Most children have wide thick flat feet and short stubby fingers with no poly or syndactyly; many patients have a buffalo hump (7). Hepatic involvement in AS is also variable. Initially only Gamma Glutamyl Transpeptidase may be elevated but overt clinical manifestations are absent, later in the course of disease patients may develop hepatosplenomegaly, portal hypertension, elevated INR, hepatic dysfunction and cirrhosis. Upper GI hemorrhage has led to death in several patients (7).

Slowly progressive nephropathy, progressive glomerulofibrosis and a gradual destruction of the kidneys are a major feature in adult patients with AS. Urethral stricture has been noted and fibrotic infiltration has been seen histopathologically (3, 8). Recurrent respiratory tract infection, chronic bronchitis, sinusitis, recurrent bouts of pneumonia and in older patients chronic obstructive pulmonary disease or acute respiratory distress syndrome have been seen (7). Hypertension is seen in 40% of patients, sometimes as early as 2 years of age. Neurological symptoms such as absence seizures, ataxia and unexplained muscular pain have been reported (7).

Clinical features such as early age of onset of cone dystrophy, hearing loss and obesity in childhood, dilated cardiomyopathy, type 2 diabetes mellitus, normal intelligence, absence of digital abnormalities and reduced final height can be helpful in distinguishing this syndrome from closely related disorders (9).

Conclusion

AS, an autosomal disorder can be diagnosed on clinical grounds in older children. Apart from its typical, well known clinical features, hepatic & biliary involvement should be kept in mind. Though not known in literature, the biliary tract abnormalities might not be so uncommon. A routine MRCP in a child of AS with typical or atypical biliary tract involvement is advisable. The management of a choledochal cyst with stones will for the time being attract eminence based approach, differing from person to person

References

1. Marshal JD, Beek S, Mafel P, Naggert JK. Ahlstrom syndrome. *Euro J Hum Gen* 2007; 15:1193-202
2. Ahlstrom CH, Hallgren B, Nilsson LB, Asander H. Retinal degeneration combined with obesity, diabetes Mellitus and neurogenous deafness: a specific syndrome (not hitherto described) distinct from Laurence-Moon-Bardet-Beidle syndrome: a clinical, endocrinological and genetic examination based on a large pedigree. *Acta Psychiatr Neurol Scand* 1959; 129:1-35
3. Marshal JD, Bronston RT, Collin GB *et al.* New Ahlstrom phenotypes based on evaluation of 182 cases. *Arch Intern Med* 2005; 165: 675-83
4. Alter CA, Moshang Jr T. Growth hormone deficiency in two siblings with Ahlstroms syndrome. *Isr J Dis Child* 1993; 147: 97-99
5. Maffei P, Munno V, Marshal JD *et al.* Characterization of the IGF system in 15 patients with Ahlstroms syndrome. *Clinical Endocrinol (Oxf)* 2007; 66:269-75
6. Koray F, Dorter C, Benderli Y *et al.* Alstrom syndrome: a case report. *J Oral Sci* 2001;43:221-24
7. Marshall JD, Beck S, Maffel P *et al.* Alstroms Syndrome. *Eur J of Hum Genet* 2007;15:1193-202
8. Charles S, Moore A, Yates J, Green T, Clark P. Ahlstroms syndrome: further evidence of autosomal recessive endocrinological dysfunction. *J Med Genet* 1990; 27:590-92
9. Hopkinson I, Marshall JD, Paisey RB, Carey c, MacDermott S: Alstrom syndrome <http://www.genetests.org>, 2007. Accessed on 2010