ACHALASIA IN CHILDREN: KEEP YOUR EYE OPEN FOR ADRENAL INSUFFICIENCY

Sarar Mohamed[1], Mohamed Ezz-Elregal[1], Abeer Salem[1], Iman Talat[1], Sadasivam Muthurajan[1], Ashraf Fouda[2]

Abstract:

Background: Triple a syndrome (Allgrove syndrome) is a rare autosomal recessive disorder characterized by the clinical triad of adrenal insufficiency, achalasia of the cardia and alacrima.

Methods and results: We report on a nine years old Saudi boy who presented with recurrent convulsions associated with hypoglycemia. Three years later, the patient developed difficulty swallowing and failure to thrive. Laboratory and radiology work up revealed achalasia and adrenal insufficiency. The clinical features were consistent with Allgrove syndrome.

Conclusions: High index of suspicion, early recognition and management of Allgrove syndrome can prevent life threatening complications, such as, adrenal crisis.

Key words: *Achalasia, Adrenal insufficiency, Alacrima, Allgrove syndrome, triple A syndrome*

Abbreviations:ACTH: adrenocorticotropic hormone, LES: lower esophageal sphincter

[1]*Department of Pediatrics, Saad Specialist Hospital, Alkhobar, Saudi Arabia.*
[2]*Department of Pediatrics, Faculty of Medicine, Mansoura University, Mansoura, Egypt.*
Correspondence to: *Dr Sarar Mohamed, Saad Specialist Hospital, Alkhobar 31952, P.O. Box 30353, Saudi Arabia. Email: sararmohamed@hotmail.com*

Introduction

Triple A syndrome, also known as Allgrove syndrome, is characterized by clinical triad of adrenocorticotropic hormone (ACTH)-resistant adrenal failure, achalasia of the cardia and alacrima.[1,2,3,4,5] Allgrove syndrom is associated with variable and progressive neurological impairment involving the central, peripheral and autonomic nervous systems. [6,7,8,9,10]

Case Report

We report on a nine year-old Saudi male who presented initially with recurrent convulsions associated with hypoglycemia. Perinatal history was uneventful. Parents are first cousins. There was no family history of developmental delay, hypoglycemia or chronic gastrointestinal problem. Clinical examination of the patient showed weight and height at the 25th and 50th percentiles respectively. Cardiovascular, abdomen and

neurological examination was normal. Developmental assessment revealed delayed expressive and receptive language with normal motor milestones.

Short ACTH stimulation test showed subnormal response (cortisone level was 16 µg/dl and 15 µg/dl 30 minutes and 60 minutes after intramuscular injection of 250µg tetracosactrin). MRI brain was normal. The patient was discharged home on no medication with a working diagnosis of partial adrenal insufficiency for follow up in outpatient department. The patient lost follow up for 3 years and then, he presented with chronic fatigability, tiredness, repeated vomiting, dysphagia and failure to thrive. Dysphagia was more to fluids than solids, which is a characteristic finding in achalasia. This raised the suspicion of triple A syndrome especially when the parents reported that the child used to cry without tears.

Growth assessment revealed failure to thrive with weight and height below 5th percentiles. Skin examination showed areas of hyperpigmentation on lower limbs together with hyperkeratotic skin lesions on planter aspects of both feet. Neurological examination revealed wasting of the muscles of the hands (thenar and hypothenar atrophy) and decreased peripheral sensation (peripheral neuropathy). Power, tone and reflexes were normal. The patient had no evidence of autonomic neuropathy. Decreased tear production was documented using Schirmer test (no tears on the filter paper from both eyes after 5 minutes (normal ≥15 mm of moisture on the filter paper in 5 minutes duration)). Barium swallows revealed dilation of the esophagus with narrowing of its lower end and tertiary contractions, suggestive of achalasia of the cardia (Figure 1). Esophageal manometry showed weak aprestaltic body contractions with incomplete relaxation of lower esophageal sphincter (LES) (Figure 2). .Prolonged ACTH stimulation test showed low baseline cortisol (7.3µg/dl) and lack of an increase in cortisol after daily injection of 0.5 mg/m^2 surface area of depot Synacthen for 3 days. Cortisol level on day 3 of the test was 8.2µg/dl which is consistent with adrenocortical insufficiency. Baseline ACTH was 98pmol/L (normal: less than 48pmol/L). Aldosterone level was 52ng/L (normal: 95-483ng/L). Mutation analysis of ALADIN gene revealed no mutation.

Heller myotomy together with laparoscopic fundoplication was done to avoid post-myotomy reflux. Barium study after the procedure showed improvement of esophageal passage of dye and the patient showed marked improvement of dysphagia. The

patient commenced on glucocorticoid replacement and artificial tear drops.

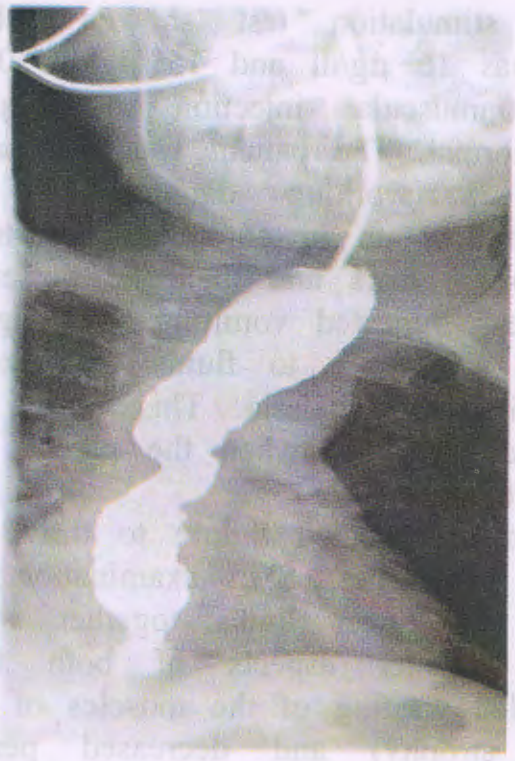

Fig. 1 Barium swallow shows a dilated esophagus with tapered lower end.

Discussion:

In 1978, Allgrove and colleagues first described two pairs of siblings with a combination of the symptoms of ACTH-resistant adrenal insufficiency, achalasia of the cardia and alacrima. Over the following years, many cases have been reported.[1-3]

Our patient presented at the age of nine years with predominant feature of achalasia. Achalasia is a rare condition in children. [4] The primary problems in achalesia are, failure of the LES to relax completely during swallowing together with failure of the esophageal smooth muscle to produce adequate peristalsis.[5] Achalasia of the cardia occurs in about 75% of all cases of Allgrove syndrome, and can be the dominant symptom of this syndrome.[6.]

ACTH stimulation test of our patient initially revealed normal basal cortisol level; however the lack of normal rise of cortisol in response to stimulation was suggestive for decreased adrenal reserve. This was documented by the prolonged ACTH stimulation test performed three years late. In Allgrove syndrome

adrenal insufficiency does not occur immediately in the post natal period, but presents at a variable time after birth as a progressive disorder leading to hypofunction of the adrenal gland.[7]

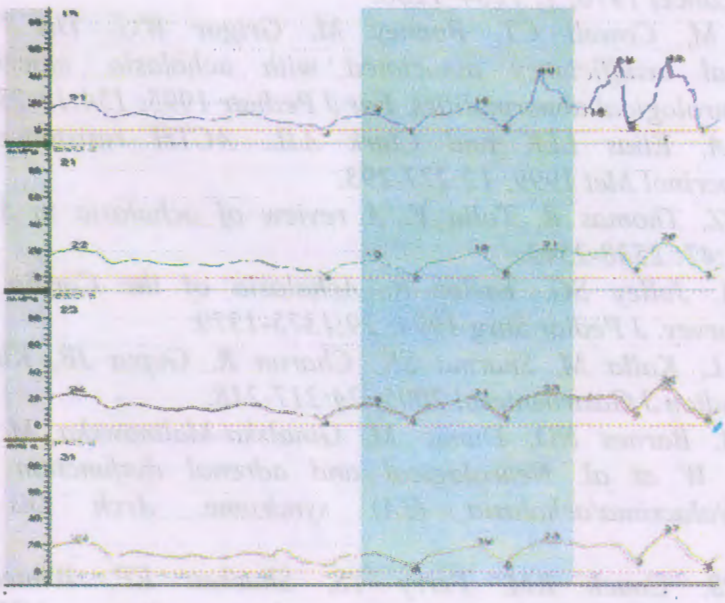

Fig. 2 Esophageal manometry shows weak a Peristaltic body contractions (ineffective peristalsis).

Alacrima, which is the earliest and most consistent clinical sign of Allgrove syndrome, is likely to be a manifestation of parasympathetic dysfunction. It is usually present early in infancy but is frequently missed by parents and physicians.[8]

Neurological manifestations are found in about 60% of all patients with Allgrove Syndrome[8]. About 30% of all patients suffer from autonomic impairment[2]. Our patient shows evidence of peripheral but not autonomic neuropathy.

Treatment of Allgrove syndrome is dependent on the symptoms. Artificial tears are used for alacrima and hydrocortisone is used for treatment of glucocorticoid deficiency.[7] The ideal treatment of achalasia in children remains controversial. Surgical treatment of achalasia remains the standard management.[9] Many data support the use of laparoscopic Heller myotomy for achalasia in children as an effective and safe procedure. Fundoplication can be carried out to prevent gastro-esophageal reflux.[10]

In summary, Allgrove syndrome is a rare multisystem disorder. High index of suspicion together with early recognition and management of the condition can prevent life threatening complications such as adrenal crisis and frequent aspiration.

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