

Allgrove syndrome: case report of 7 years old boy from Bahawalpur

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Abstract

Allgrove syndrome is a rare autosomal recessive syndrome of unknown prevalence. The first case of Allgrove syndrome was reported in 1978 by Allgrove. It is characterized by triad of achalasia, alacrima and adrenal hypoplasia. There are also associated autonomic and neurological manifestations. We report the case of a 7 years old boy being treated for achalasia cardia, presented with fits and altered sensorium which on further investigations was found to be due to adrenal insensitivity (Raised ACTH level, low Cortisol level, and normal Aldosterone and Renin ratio). He also had undiagnosed alacrima since birth, mild degree of hearing loss and autonomic instability in the form of episodic hypertension.

Keywords: Alacrima, Achalasia, ACTH (adrenocorticotrophic hormone).

Introduction

Allgrove syndrome is also known as Tripple A syndrome. It is a rare autosomal recessive disorder. It was first discovered by Allgrove in 1978 in two pairs of siblings.¹ This syndrome consists of triad of achalasia cardia, alacrima and adrenal hypoplasia.² Other signs and symptoms of progressive central, peripheral and autonomic nervous system involvement may also be present.³ Vahedi M has reported achalasia to be the first manifestation of Allgrove syndrome.⁴ Clinical presentation of this rare disorder comprise of weakness, fatigue, vomiting, anorexia, abdominal pain, constipation, postural dizziness, hypotension, hyperpigmentation, electrolyte imbalance, vitiligo, alacrima (absence of tear production or reduced tear production) and achalasia.^{1,5}

Case Report

We report the case of a 7 years old boy that came to the outpatient department in April 2017 with fits and altered sensorium for the last one day. On further enquiry, he was being investigated for suspected achalasia because of persistent vomiting for the last two years, and his surgery was planned but owing to the current condition, was

postponed. His mother gave the history of no tears on crying since birth and progressive darkening of the whole body. He was born by uneventful normal vaginal delivery to consanguineous parents. There is no family history of skin darkening, absent tears or persistent vomiting. On examination, he was sick looking, afebrile, with vitals: heart rate 98/min, respiratory rate 24/min, Blood Pressure (BP) 130/90 and Blood Glucose 169 mg/dL. His height was 104.5 cm (below 3rd centile), and weight was 13 kilograms (below 3rd centile). He had generalized hyperpigmentation involving oral mucosa, palmar creases (Figure-1) with normal external genitalia. His CNS (central nervous system) examination showed GCS (Glasgow coma scale) 11/15, with normal tone, power and reflexes and no signs of meningeal irritation. Fundoscopy and slit lamp examination of eye was normal except for blepharitis.

During his stay in Bahawal Victoria Hospital, he was monitored regularly in Paediatric ICU (intensive care unit), where he was found to have episodic hypertension (HTN) with BP fluctuating between 140/90 to 80/50. He was irritable with occasional facial flushing but there was no orthostatic hypotension and heart rate variability on valsalva maneuver. He was thoroughly investigated for Addison disease and episodic hypertension. His cerebrospinal fluid (CSF) examination and CT scan brain with contrast was normal. His ultrasound abdomen, ECG and CT scan abdomen were normal. His barium swallow was carried out which showed bird beak appearance suggesting achalasia cardia (Figure-2). Schirmer test was done showing less than 5 mm wetting of Whatman filter paper number 41 in 5 minutes suggestive of alacrima (more than 10 mm is normal). His hearing was assessed

Table: Investigations of the case.

Investigation	Value	Normal Range
S. sodium	134 mmol/L	135-145 mmol/L
S. potassium	2.7 mmol/L	3.4-4.7 mmol/L
Plasma ACTH	>1250 picogram/mL	46 picogram/mL
Cortisol level (At 7 AM)	3.2 microgram/dL	4.3-22.4 morning 3.09-16.66 evening
17 Hydroxy Progesterone	< 0.03 ng/mL	0.03-0.90 (Prepubertal child)
S. Urea	21 mg/dL	5-18 mg/dL
S. Creatinine	0.7 mg/dL	0.3-0.7mg/dL

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Figure-1: Child with darkening of lips and hands.

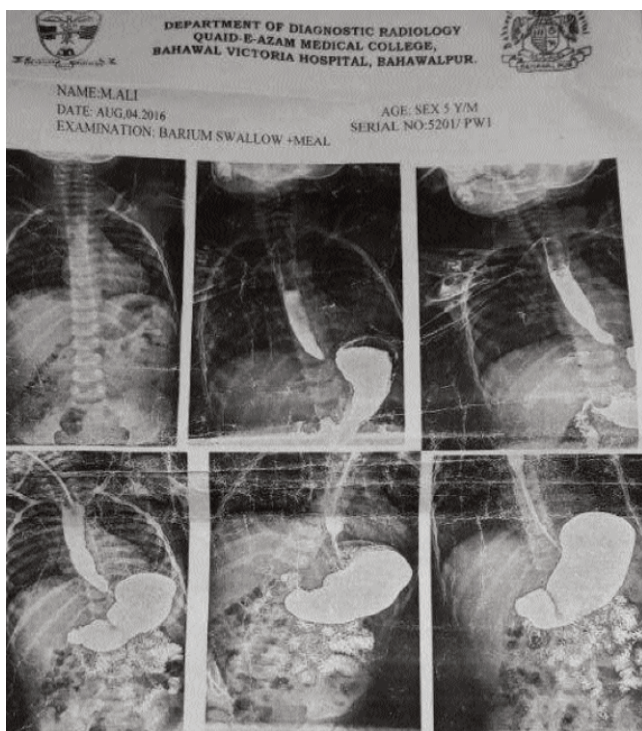


Figure-2: Barium Swallow showing bird beak appearance.

with BERA (brainstem evoked response audiometry) which showed bilateral mild degree of sensorineural hearing loss. The investigation results of the child are shown in the Table.

High ACTH, low cortisol, normal renin and aldosterone

prove ACTH insensitivity, which along with achalasia and alacrima makes him a case of Allgrove/ triple A syndrome. Molecular genetic study for triple AS gene could not be done as it is not available in Pakistan. His episodic HTN is due to autonomic instability, a feature of Allgrove syndrome. His low potassium level is due to persistent vomiting caused by achalasia cardia. He was started on hydrocortisone and beta blockers and responded well. His surgery is planned in the near future with stress dose of hydrocortisone. He is on regular follow up. His siblings were screened by detailed clinical and eye examination and found to be normal. This case has been reported after the consent of parents of the child.

Discussion

The prevalence of Allgrove syndrome is unknown, only few cases have been reported in literature.⁶ It has autosomal recessive pattern of inheritance. Since 1978, many cases have been reported and all of them have shown autosomal inheritance.³ The severity of symptoms of Allgrove syndrome varies at the time of presentation of the cases. These cases can present at variable ages with varying severity of symptoms. These symptoms are progressive.

Vahedi M mentioned achalasia to be the first manifestation of Allgrove syndrome.⁴ However Omek M attributed alacrima to be the first manifestation of this syndrome which is usually overlooked and is evident on careful history.⁷ In our case, the mother clearly said that "he cries with only few tears". Sarathi V also had reported alacrima to be most persistent and the earliest symptom.⁸ Alacrima is often ignored by the parents, as seen in our case.⁹

Achalasia is a grave problem of Allgrove syndrome. It often appears in these cases between 6 months to 16 years of age. Achalasia occurs in about 75% of all cases of this syndrome. The etiology of achalasia is not known but it is thought to be due to degeneration of autonomic plexus.⁵

Adrenal insufficiency is due to ACTH (adrenocorticotrophic hormone) insensitivity/resistance and often appears before puberty. ACTH level is normal or high in blood in this syndrome and cortisol level is low or showing diurnal variation.^{10,11}

Allgrove syndrome was also called as 4A syndrome by Gazzarian et al because of association with autonomic and neurologic association.¹² These autonomic and neurologic abnormalities include dysarthria, dysphagia, deafness, mild mental retardation, postural dizziness, muscle weakness, optic atrophy, cerebellar ataxia etc.⁵

Conclusion

Any case with combination of alacrima, achalasia, ACTH insensitivity and autonomic manifestations should arouse suspicion of Allgrove syndrome in the mind of physicians. As early identification and treatment can decrease mortality and improve quality of life.

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