A Child with Weight Loss and Alacrimation: Triple A Syndrome

Qurat ul Ain, Naveed Asif, Noreen Shahzad and Waqas Hanif Sheikh

ABSTRACT

Triple A syndrome or Allgrove's syndrome is a rare autosomal recessive disorder usually manifested with three main clinical features, *i.e.* achalasia, alacrimation and adrenal inadequacy. Sometimes, it presents with polyneuropathy and neurological complications. Here, we report a case of a 7-year girl presenting with features of weight loss who was diagnosed with adrenal insufficiency at the age of 7 years while achalasia was diagnosed at the age of 3 years. First manifestation was achalasia and at that time, alacrimation was also defected. A 7-year XX female child presented at Endocrine Clinic of Armed Forces Institute of Pathology (AFIP) with hyperpigmentation, easy fatigue and weight loss. She had one sibling with same complaints and one brother died at the age of 3 years because of adrenal insufficiency. Her laboratory investigations revealed low cortisol level and high ACTH level, with inadequate response as well as short synacthen test (dynamic function test). This is a first case of Allgrove's syndrome reported in a tertiary hospital setting of Pakistan. Allgrove's syndrome should be considered in patients who report with adrenal insufficiency.

Key Words: *Triple A syndrome, Addison disease, Endocrinopathies.*

INTRODUCTION

Allgrove's syndrome, also known as Triple A syndrome, is an autosomal recessive disorder.[1] Allgrove's syndrome was first diagnosed in 1978 in two brothers with adrenal hormone deficiency and achalasia.[2] Allgrove's syndrome manifests by three main cardinal symptoms. Nervous system abnormalities due to involvement of focal, autonomic sensory and central systems are regularly noted in this rare disorder.[3] Adrenal deficiency and achalasia are generally present in patients with Allgrove's syndrome before first decade and neurological abnormalities later in life. Triple A disorder is uncommon and has been reported from various parts of the world. The genotypic presentation is due to mutation on chromosome 12q13, which is the site of protein for alacrimation, achalasia and adrenal insufficiency neurologic disorder (ALADIN) protein.

CASE REPORT

A 7-year girl, resident of Kashmir, was referred to this hospital with complaints of weight loss, hyper-pigmentation, weakness and fatigue for 2 years. The child was born at 39 weeks, full-term with consanguineous marriage and was delivered *via* vaginal delivery with an Apgar score of 8/10 and immediate cry at home. Her height and weight was more than 70th percentile at the time of birth. Systemic examination was unremarkable. Vaccination history was as per schedule of EPI programme. Soon after birth, she was fine and had no complaints; but after one month, parents brought her to local doctor after getting complaints of vomiting and skin color changes; and that physician asked that child was alright. One year later, the child started developing hyperpigmentation and was reluctant to take liquid food and then parents again consulted local doctor, but no cure after symptomatic treatment. At the age of 3 years, she started having vomiting, constipation, and off and on fainting spells. One sibling died with adrenal insufficiency and one sibling was diagnosed with primary adrenal deficiency.

Three years later, she presented with difficulty in swallowing, especially liquids. Barium meal examination was done and it showed narrowing of the distal end of esophagus near gastro-esophageal junction. At the age of 3 years, the patient was diagnosed with achalasia, which was managed with surgical intervention. After that, alacrimation was confirmed by Schrimer's test by ophthalmogist. Examination revealed thin lean body with loss of bulk of muscle and with pigmentation of tongue, buccal mucosa and skin; and it involved extensor surfaces of extremities. CNS examination revealed hyper reflexia, and tactile examination was not significant. Standard laboratory investigations revealed normal blood count, renal function tests and serum electrolytes (serum sodium, 138 mmol/L; serum K, 4.23 mmol/L and calcium level, 1.45 mmol/L, urea, 6.6 mmol/L, creatinine, 0.25 mg/dL). Basal serum cortisol (8:00 AM) was low (26 nmol/L) while normal range is 150-365 nmol/L, and failed to rise after intravenous infusion of 250 µg of tetracosactrin (30 minutes and 60 estimations of 38 nmol/L, individually), the dynamic function test for adrenal insufficiency. The plasma adrenocorticotropic hormone (ACTH) levels were raised (3150 pg/mL, while reference range, 10-85 pg/mL). A working diagnosis of adrenal deficiency was made. Workup was done to find out causes of adrenal insufficiency. Because tuberculosis is

Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan

Correspondence: Dr. Qurat ul Ain, Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan
E-mail: draaneiseera@gmail.com

Received: November 15, 2018; Accepted: January 31, 2019

considered the most common cause of adrenal deficiency, computed tomography (CT) of abdomen was performed and it showed bilateral atrophic adrenal glands. The tuberculin test was negative. Based on adrenal inadequacy, alacrimation, achalasia, and fringe neuropathy, a diagnosis of Allgrove's disorder was made. We have not carried out the genetic analysis of AAA5 gene due to non-availability of the test. Negative tuberculin test together with no signs of adrenal calcification on abdominal CT scan ruled out tuberculosis as the cause of adrenal deficiency in this patient. She was begun on oral hydrocortisone tablets and requested follow-up after a month.

DISCUSSION

In this case report, we presented the complete medical history, examination, and management of a patient who was diagnosed as Allgrove's syndrome, also known as Triple A syndrome, on the basis of triad of features alacrimation, adrenal insufficiency and achalasia. This patient presented with typical clinical features of adrenal insufficiency, such as hyperpigmentation, but with normal electrolytes, especially potassium and sodium.[4]

Allgrove's syndrome presents with adrenal insufficiency but a unique feature is the normal mineralocorticoid activity. The triad of clinical features of Allgrove's syndrome are ACTH resistant adrenal inadequacy, achalasia and alacrimation.[5] The first clinical picture in current case was achalasia and it was diagnosed after reluctance to feed and intermittent blacking out and fainting episodes. Adrenal deficiency and achalasia are normally present in first year of life. Achalasia of the cardia is found in about 75% of cases and in adults and children usual manifestation is difficulty in swallowing and it typically presents as dysphagia particularly to fluids. Adrenal deficiency and hypotension affect young adults which may cause sudden mortality. The demise of younger brother of our patient at 1 year was conceivably because of adrenal inadequacy as per given history of intermittent vomiting. Adrenal inadequacy in Allgrove's syndrome results from a dynamic issue prompting hypo functioning of the adrenals at a variable time after birth.

Allgrove's disease is a rare multisystem disease and the clinical manifestations may appear at any stage from birth to adulthood and it is not necessary that all symptoms appear at one time. In the current case, first the achalasia and then alacrimation was diagnosed. Gene mutation study is recommended for the diagnosis but was not carried out in this case due to non-availability.

REFERENCES

1. Stagi S, Cavalli L, Seminara S, de Martino M, Brandi ML. The ever-expanding conundrum of primary osteoporosis: Aetiopathogenesis, diagnosis, and treatment. *Ital J Pediatr* 2014; **40**:55.
2. Menon SK, Bangar TR, Kaba A, Shah R, Menon PS, Shah NS. Triple A syndrome. *Indian J Pediat* 2008; **75**:967.
3. Kimber J, McLean BN, Prevett M, Hammans SR. Allgrove or 4 "A" syndrome: An autosomal recessive syndrome causing multisystem neurological disease. *J Neurol Neurosurg Psychiatry* 2003; **74**:654-7.
4. Thomas J, Subramanyam S, Vijayaraghavan S, Bhaskar E. Late onset adrenal insufficiency and achalasia in Allgrove syndrome. *BMJ Case Rep* 2015; **2015**. pii: bcr2014208900.
5. Pandolfino JE, Gawron AJ. Achalasia: A systematic review. *JAMA* 2015; **313**:1841-52.