Case Report

Allgrove syndrome: a case report

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ABSTRACT

Allgrove syndrome is an autosomal recessive disease which is characterized by Achalasia, Alacrimia and ACTH-resistant Adrenal deficiency with progressive neurological manifestations. Allgrove syndrome is caused due to mutations in AAAS gene, localized on chromosome 12q13. This report relates to an 8 years old female child who had complaints of vomiting, fever, cough, hyperpigmentation and poor weight gain. Barium swallow, ophthalmic examination and ACTH stimulation test proves that patient has Allgrove's syndrome. Management consisted of initiation of cortisone therapy which was successful in improving the hyper pigmentation. Patient was planned for surgical intervention for achalasia cardia on follow-up. Allgrove's syndrome may be an under diagnosed disorder. High index of suspicion is needed when patients present with such complex symptoms. Diagnosing and timely intervention helps in reducing the morbidity and mortality.

Keywords: Allgrove syndrome (Triple A syndrome), Achalasia, Alacrimia, Adrenal insufficiency

INTRODUCTION

Allgrove syndrome or triple A syndrome is a multisystem disorder which classically involves the triad of esophageal achalasia, alacrima and adrenal insufficiency due to adrenocorticotropin hormone insufficiency. It follows an autosomal recessive pattern of inheritance and is associated with mutations in the achalasia-addisonism-alacrima syndrome (AAAS) gene on chromosome 12q13 encoding the nuclear pore protein aladin.^{1,2} The clinical pattern is often accompanied by findings of autonomous nervous system involvement and therefore, it is sometimes named as 4 A-syndrome.³ Triple A syndrome is usually diagnosed in infancy and childhood. Here, we present an 8-year-old patient diagnosed to have triple A syndrome.

CASE REPORT

A 8 year old female child presented with complaints of recurrent vomiting, fever, cough and poor weight gain since 4 years and progressive darkening of skin since 6

months. Child was undernourished and developmentally normal. Patient had history of 1 episode of convulsion 1 month back.

On examination hyperpigmentation of skin (Figure 1) and mucosa was noticed, rest of general physical examination and systemic examination normal. Serum electrolytes and renal function test were within normal limits. Chest X-ray was s/o some air fluid levels with small gastric bubble. For further confirmation chest x-ray with barium swallow was done which was suggestive of gross Achalasia cardia (gross dilated esophagus) (Figure 2).

Schirmer's test on ophthalmological examination was positive, suggestive of severe dry eye.⁶ Suspecting Allgrove syndrome, Serum cortisol at 8am was done and was low at 1.82 ug/dl (normal:>14 ug/dl) following which ACTH stimulation test was done. Intramuscular injection corticotrophin 250 ug was given. After giving injection corticotrophin, serum cortisol levels were repeated after 1 hour and was still low at 1.82 ug/dl suggestive of primary adrenal insufficiency. Patient was

started on tab hydrocortisone 5 mg at 11 mg/m²/day in 2 divided doses.

Based on presentation of achalasia, alacrimia and ACTH resistant adrenal insufficiency, diagnosis of triple A syndrome was made. Patient was discharged on tablet hydrocortisone. Patient was planned for surgical intervention (Heller's myotomy) for achalasia cardia on follow up. On subsequent follow-up hyper pigmentation and complains of vomiting improved.

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Figure 1: A 8-year-old girl with hyperpigmentation due to ACTH resistant adrenal insufficiency.

Figure 2: Barium swallow of bird beak appearance.

DISCUSSION

Triple A syndrome is a hereditary autosomal recessive disease which is characterized by achalasia, alacrima,

adrenal failure, and neurological findings. Incidence is unknown and only scattered case reports are noted in the literature. No evidence suggests that gender affects the frequency and age at onset of symptoms varies. The patient can present with absent tears while crying, hyper pigmentation, developmental delay, seizures, dysphagia, hyper nasal speech, recurrent vomiting and orthostatic hypotension. Many cases present with classic symptoms of primary adrenal insufficiency, including hypoglycemic seizures and shock. Alacrima is typically present from early infancy, but is not the common presenting complaint.^{4,5} Recurrent vomiting and dysphagia occurs due to achalasia, which is a primary esophageal motility disorder characterized by the absence of esophageal peristalsis and impaired relaxation of the lower esophageal sphincter in response to swallowing which is caused by loss of inhibitory ganglion in the myenteric plexus of the esophagus. Our patient came to the hospital with symptoms, such as persistent vomiting, poor weight gain, fever, darkening in the skin and mucosa and had 1 episode of convulsion due to hypoglycemia.

For further evaluation, a baseline adrenocorticotrophic hormone (ACTH) and cortisol values must be taken and perform an ACTH stimulation test to assess adrenal function. Serum sodium, potassium, aldosterone, and renin levels are determined. Although aldosterone levels are usually normal in 4A syndrome, several cases of mineralocorticoid deficiency have been reported. In our patient Serum cortisol level were at 1.82 ug/dl and standard 250 µg corticotrophin stimulation test demonstrated no improvement in serum cortisol levels with normal aldosterone levels. So, the patient was diagnosed to have primary adrenal insufficiency. The primary cause of mortality in AS is unrecognized adrenal crisis. The most common presentation is a hypoglycemic seizure secondary to glucocorticoid deficiency. Careful replacement of glucocorticoids in patients with known adrenal insufficiency is critical to avoid an adrenal crisis and to allow for normal growth in children. Providing stress doses of corticosteroids during illness or injury is also important. Prednisolone and Dexamethasone are less preferred for maintenance than hydrocortisone which has balanced 1:1 effects of mineralocorticoid vs. glucocorticoid. Our patient was started on hydrocortisone therapy. Achalasia is best managed with surgical correction. Alacrima is managed with regular application of topical lubricants.

Provided the patient is effectively managed, a normal lifespan is possible. Cases of parkinsonism, peripheral neuropathy, and seizures developing in AS patients have been reported.⁷

CONCLUSION

Allgrove's syndrome may be an under diagnosed disorder. High index of suspicion is needed when patients present with such complex symptoms at variable stages that is vomiting, dysphagia, crying without tears

(alacrime), nasal speech, hyper pigmentation and hypoglycemic seizures. Diagnosing and timely intervention helps in reducing the morbidity and mortality.

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