CASE REPORT

When Dysphagia Leads to Diagnosis: A Case of Triple A Syndrome in a Malnourished Child

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ABSTRACT

Allgrove Syndrome, also called Triple A syndrome (TAS), is an uncommon autosomal recessive condition. We describe the case of a 12-year-old girl who developed progressively worsening dysphagia over six years, beginning with difficulty of swallowing solid foods and later progressing to liquids. Over time, she experienced significant muscle wasting and became severely malnourished. Upon hospital admission, she was also found to have adrenal insufficiency and had a history of alacrimia since early infancy. This case highlights the diagnostic challenges and delays commonly associated with TAS.

Key Words: *Allgrove syndrome; Triple A syndrome; alacrima; achalasia; adrenal insufficiency; dysphagia; pediatric case report*

INTRODUCTION

In 1978, Allgrove discovered a condition in two pairs of siblings [1]. Only fewer than 100 cases have been reported worldwide. Clinical presentation is variable and usually characterized by the triad of alacrimia, achalasia, and ACTH-resistant adrenal insufficiency[2]. It may include additional neurological or autonomic features. The condition usually presents in childhood, but the full triad may not appear simultaneously, making early diagnosis challenging. Because of its rarity and variable presentation, many patients experience delayed recognition and significant morbidity. The emphasis here is to remind clinicians about the existence of the disease in this country.

CASE REPORT

A 12-year-old girl presented with a three-month history of persistent, non-projectile, non-bilious vomiting associated with significant weight loss. She had no accompanying fever, cough, diarrhea, constipation, urinary symptoms, hematuria, headache, seizures, or history of drug intake. She also reported progressive difficulty swallowing over the past six years, beginning with solids and later involving liquids, with marked worsening in recent months. Previously developmentally normal, she had become bedridden due to extreme weakness and severe weight loss.On initial assessment, she was drowsy, pale, severely malnourished, and showed generalized hyperpigmentation involving the skin, palmar creases, and oral mucosa. She weighed 20 kg and measured 120 cm in height, both well below the expected centiles for her age. She was afebrile, with a pulse of 130/min, blood pressure of 90/60 mmHg, capillary refill time greater than three seconds, and a respiratory rate of 32–34/min. Conjunctival redness and marked

muscle wasting were noted, while the systemic examination was otherwise normal. Her mother reported the absence of tears since infancy, and there was a family history of alacrimia in two cousins. Investigations revealed normal CBC, sodium of 130 mmol/L, potassium of 2.8 mmol/L, a low morning cortisol of 80 nmol/L (reference range 133–557 nmol/L), and elevated ACTH at 127 pg./mL, consistent with primary adrenal insufficiency. A barium swallow demonstrated a classic “bird-beak” appearance of the distal esophagus, indicating achalasia cardia. The combination of alacrimia, adrenal insufficiency, and achalasia confirmed the diagnosis of Allgrove (AAA) syndrome. She was treated with hydrocortisone replacement after an endocrinology consultation and stabilized for adrenal insufficiency. She was then referred to pediatric surgery, where a Heller’s myotomy was planned and successfully performed once her condition improved. After postoperative recovery and optimization of steroid therapy, she was discharged home with follow-up arranged.





Figure 01. Pale, severely malnourished and generalized hyperpigmentation involving the skin and knuckles.

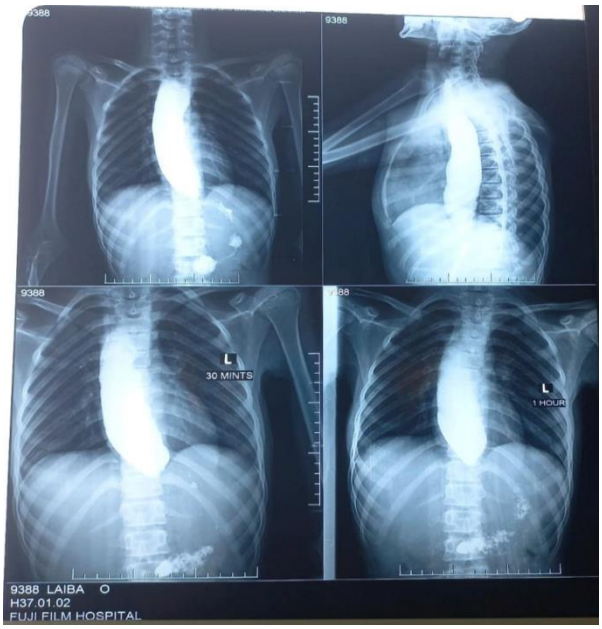


Figure 2. A barium swallow demonstrated a classic “bird-beak” appearance of the distal esophagus, indicating achalasia cardia

DISCUSSION

Allgrove (Triple A) syndrome is an uncommon autosomal recessive disorder caused by mutations in the AAAS gene on chromosome 12q13, which encodes the nuclear envelope protein ALADIN. The ALADIN protein is widely expressed in the body, with the highest levels found in the gastrointestinal tract, adrenal glands, and brain.[3,4] The exact role of the ALADIN protein remains uncertain; however, mutations appear to impair the function of nuclear pore complexes (NPCs) despite these structures remaining structurally normal.[5] This condition is identified by the triad of achalasia, alacrimia, and adrenal insufficiency, accompanied by progressive neurological impairment. Clinically, about two-thirds of affected individuals exhibit the full triad of primary symptoms, while roughly one-third present with only two features. Fewer than 10% manifest a single symptom alone. The true prevalence in children is unclear, as the condition

is often underdiagnosed and misreported. The median age at onset is 5 years, with lifetime frequencies of alacrimia, achalasia, and adrenal insufficiency estimated at 99%, 90.1%, and 79.4%, respectively.[6]

Alacrimia is typically the earliest manifestation, followed by the development of dysphagia, with adrenal insufficiency occurring later, although the severity and sequence of symptoms may vary among patients.[1]

Achalasia is often a hallmark of triple A syndrome and the most common reason for seeking medical consultation, occurring in 75% of cases. The onset of symptoms can start from infancy to 16 years. Patients typically present with repeated vomiting, progressive dysphagia, and bronchopulmonary complications due to aspiration. The underlying mechanism for this is due to the degeneration of cholinergic neurons within the autonomic nervous system. Diagnosis is primarily made through esophageal manometry and barium studies.[7]

Glucocorticoid deficiency due to ACTH resistance is the second important component of this syndrome.[8] As in our case, adrenal gland hypo-functioning is not present at birth; it gradually develops over time, and the median age of its presentation is 6 years. Adrenal function can range from inadequate to partially compensated. Depending on the adrenal status, patients can present with recurrent vomiting, hypoglycemic seizure, shock, hyperpigmentation of skin and mucous membrane and developmental delay.[6] The unique feature of adrenal insufficiency in Allgrove syndrome is that mineralocorticoid activity is preserved it can be impaired in 15% of patients. In our patient, a normal electrolyte level and normal plasma renin activity indicate normal mineralocorticoid activity.[7]

Alacrimia is the most prevalent symptom, reaching >90% of the patients. It usually starts at birth and is mostly ignored by parents until other symptoms appear or have some serious ophthalmological consequences. Schirmer's test confirms the absence of tears. Artificial tears and lubricants help to relieve the sensation of dryness in the eyes.[9]

Neurological involvement tends to occur late in the course of Allgrove syndrome. It can involve the central and peripheral autonomic nervous system. Distal sensory motor neuropathy is a common presentation. These patients can have spasticity, myopathy, optic nerve atrophy and sensory impairment.[10] A nerve conduction study can be helpful in diagnosing neuropathy. In some cases, cognitive defects, pyramidal syndrome, distal muscular dystrophy, hyperreflexia, and cerebellar dysfunction are also reported [11]. A genetic study is a definitive test for diagnosis. Although there is no curative treatment, a multidisciplinary approach can improve quality of life. Long-term management includes Hormonal replacement by hydrocortisone for adrenal insufficiency, lubricating drops for alacrimia and achalasia can be treated by surgical intervention. Allgrove syndrome is a difficult-to-diagnose disorder due to multisystem involvement and varying presentation. However, a timely diagnosis can reduce the morbidity of patients.

CONCLUSION

This case report aims to demonstrate that Allgrove syndrome is a very rare disorder. But always suspect it in any case presenting with alacrimia or dysphagia with adrenal symptoms. Early detection and timely management can prevent life-threatening complications. A multi-disciplinary team and long-term follow-up are needed in such patients to improve outcomes

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Authors' contribution

SQ: Literature Review & final approval.
MA: Literature Review and manuscript drafting.
TA: Manuscript drafting.
SMJ: Manuscript drafting.
ABR: Literature review

All the authors have approved the final manuscript draft and accept the responsibility of research integrity.