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Case Report

Allgrove syndrome in childhood: a case report and review of the literature

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ABSTRACT

Allgrove syndrome is an autosomal recessive disease which is characterized by Achalasia, Alacrimia and adrenocorticotropic hormone (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 a 5 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, was first described in 1978 by Allgrove and colleagues in two sibling pairs presenting with adrenal insufficiency, achalasia, and alacrima.[1] This rare autosomal recessive disorder results from pathogenic variants in the AAAS gene on chromosome 12q13, which encodes the nuclear pore complex protein ALADIN.[3] The syndrome exhibits marked phenotypic variability, ranging from isolated involvement of the classical triad to extensive multisystem disease. Neurological abnormalities—including central, peripheral, and autonomic dysfunction—are increasingly recognized, often as later manifestations.[2] Typically, adrenal insufficiency and achalasia manifest by the end of the first decade, whereas neurological features appear subsequently.[3] Herein, we describe an unusual pediatric case in which neurological manifestations preceded overt adrenal dysfunction, underscoring the importance of early recognition, multidisciplinary evaluation, and long-term follow-up.

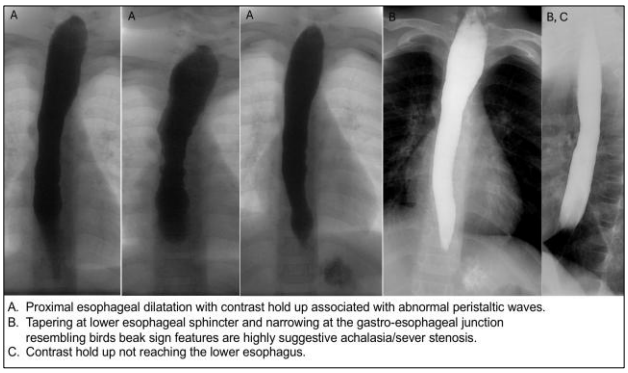
CASE REPORT

A 5-year-old boy was referred by pediatric endocrinology for evaluation of chronic vomiting and progressive dysphagia. His history was notable for recurrent symptomatic hypoglycemia and diffuse hyper-pigmentation, suggesting adrenal dysfunction. Ophthalmology had previously documented keratitis; however, no unifying diagnosis was made until surgical evaluation was sought.

On admission, growth parameters were within the normal range (weight: 21 kg). Examination revealed cheilitis, gingivitis, and poor oral hygiene, with ocular findings consistent with keratitis. Abdominal and systemic examinations were unremarkable. Baseline hematological and biochemical investigations were normal. Endocrine

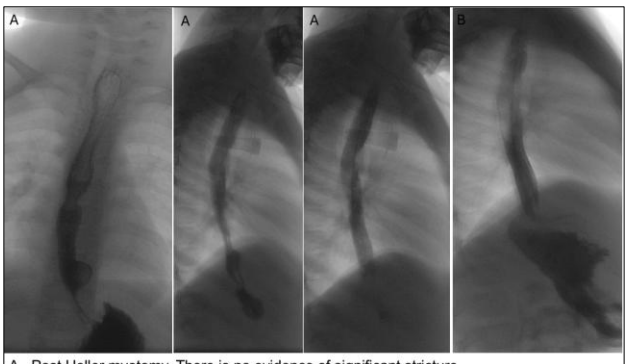
testing confirmed primary adrenal insufficiency, with markedly elevated adrenocorticotropic hormone (ACTH) (700 pg/ml, later 2000 pg/ml) and low cortisol levels. The patient had been initiated on glucocorticoid replacement prior to surgical referral.

Persistent vomiting and dysphagia prompted gastrointestinal workup. Chest radiography was normal. An upper gastrointestinal contrast study revealed distal esophageal narrowing with a classic 'bird-beak' appearance, suggestive of achalasia (Figure 1), which was subsequently confirmed by endoscopy. Given the triad of ACTH-resistant adrenal insufficiency, alacrima with keratitis, and achalasia, a diagnosis of Triple A (Allgrove) syndrome was made. The patient underwent Heller myotomy, which was well tolerated. He was discharged in stable condition and, on follow-up (Figure 2), demonstrated appropriate weight gain and clinical improvement, with continued ophthalmic care for keratitis.



A. Proximal esophageal dilatation with contrast hold up associated with abnormal peristaltic waves.
B. Tapering at lower esophageal sphincter and narrowing at the gastro-esophageal junction resembling birds beak sign features are highly suggestive achalasia/sever stenosis.
C. Contrast hold up not reaching the lower esophagus.

Figure 1: Pre-operative images.



A. Post Heller myotomy. There is no evidence of significant stricture.
B. Persistent residual contrast reaching the upper and middle one thirds of the esophagus, not passing within 10 minutes post study observation.

Figure 2: Post-operative images.

DISCUSSION

Allgrove syndrome is an exceptionally rare multisystem disorder, with fewer than several hundred cases reported worldwide. Its true prevalence remains unknown due to under-diagnosis and phenotypic variability. The molecular basis lies in mutations of the AAAS gene, which encodes ALADIN, a nuclear pore complex protein involved in nucleocytoplasmic transport. Most reported mutations are truncating variants, leading to dysfunctional protein products.[4]

Clinically, the syndrome is defined by the triad of ACTH-resistant adrenal insufficiency, achalasia, and alacrima. Alacrima is usually the earliest feature and may be present from infancy, though often overlooked. Achalasia occurs in approximately 75% of cases and manifests as progressive dysphagia, more prominent for liquids, frequently within the first decade.[5] Adrenal insufficiencies typically presents with hypoglycemia, hyperpigmentation, or hypotensive crises, sometimes culminating in sudden death if undiagnosed. In our patient, the unexplained death of a younger sibling with recurrent vomiting and shock was retrospectively consistent with unrecognized adrenal insufficiency.

Adrenal involvement in Allgrove syndrome is unique among causes of primary adrenal insufficiency because mineralocorticoid secretion is usually preserved, although up to 15% of patients may eventually develop mineralocorticoid deficiency.[6,7] In our case, normal electrolytes suggested preserved mineralocorticoid function, though plasma aldosterone was not measured.

Neurological manifestations represent an increasingly recognized component of the syndrome's expanded phenotype. These include sensorimotor polyneuropathy, autonomic dysfunction, intellectual disability, optic atrophy, and movement disorders such as dystonia or parkinsonism.[8]

Our patient demonstrated keratitis secondary to alacrima and was at risk of progressive neurological complications, necessitating continued surveillance. Non-neurological associations—including dysmorphic features, growth retardation, osteoporosis, and cardiac conduction abnormalities—further highlight the syndrome's heterogeneity.[9]

The diagnosis of Allgrove syndrome requires a high index of suspicion, particularly in children with unexplained combinations of adrenal insufficiency, esophageal dysmotility, and ocular abnormalities. Early multidisciplinary management, including endocrinology, gastroenterology, ophthalmology, and surgery, is crucial in reducing morbidity and mortality.

CONCLUSION

This case emphasizes the clinical variability of Allgrove syndrome and illustrates the potential for neurological or ophthalmic features to precede endocrine manifestations. Recognition of the cardinal triad, together with broader systemic associations, is essential for timely diagnosis. Multidisciplinary evaluation and long-term surveillance are critical to improving outcomes in this rare but potentially life-threatening disorder.

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