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Case Report

Allgrove syndrome: a case report

Marouf Alhalabi [1,*], Saddam Alsayd[2] and Ebtesam Alboushi[1]

[1]Gastroenterology Department, Damascus Hospital, Damascus, Syria
[2]Gastroenterology Department, Damascus Hospital, Damascus, Syria
*Correspondence address. Gastroenterology Department, Damascus Hospital, Almujtahed Street, Damascus 35044, Syria. Tel: +963952781278; E-mail: e.marouf@hotmail.com

Abstract

Allgrove syndrome (AS), or Triple-A syndrome, is a multi-system disorder characterized by alacrima (a decrease or absence of tear production), adrenal insufficiency and achalasia (absence of esophageal muscle peristalsis and failure to relax the lower esophageal sphincter). This syndrome may affect the autonomic nervous system, in which case it is called a 4A syndrome. It is a rare autosomal recessive inheritance, and early identification is difficult due to the rarity and wide phenotypic variation even among members of the same family. Endocrinologists, gastroenterologists, ophthalmologists, neurologists and surgeons are needed to coordinate care for these patients. We describe a case of AS that took several years to complete the diagnosis. She was diagnosed with alacrima at the age of 1-year-old, adrenal insufficiency at the age of 9 and achalasia at the age of 16. This case demonstrates the difficulty and delay in the diagnosis of AS.

INTRODUCTION

Allgrove syndrome (AS) is a rare autosomal recessive disorder. It is a multi-system disease first described in 1978 and characterized by the triad of alacrima, adrenal insufficiency and esophageal achalasia. Recognizing the clinical syndrome at the onset of the disease is difficult when there is only one presenting symptom and many diseases as a differential diagnosis. The presence of two cardinal clinical entities strongly suggests the diagnosis [1]. Neurological and dermatological manifestations have been reported, as well as short stature, microcephaly, osteoporosis and dysmorphic features [2]. We present an interesting case of AS that took several years to diagnose. She was diagnosed with alacrima at the age of 1-year-old, adrenal insufficiency at the age of 9 and achalasia at age of 16, which complete the syndrome trilogy. Although alacrima is an uncommon symptom, and that the adrenal insufficiency was diagnosed, doctors and other health care providers were unaware of AS.

CASE PRESENTATION

A 16-year-old Syrian girl was referred for evaluation due to short stature, progressive dysphagia to solids and liquids and a nocturnal cough that started several months ago. She had been diagnosed with alacrima since she was 1-year old, which was followed by adrenal insufficiency when she was 7 years old, confirmed by a review of adrenocorticotropic hormone (ACTH), cortisol and ACTH stimulation tests. Her weight was 28 kg, her height was 125 cm and she had a body mass index of 17.9 kg/m^2 and a body surface area of 0.986 m^2. Her mother informed us that she has three other short-statured children with alacrima. Furthermore, she had been treated with prednisolone 10 mg for 7 years for her adrenal insufficiency, her clinical examination was normal except for her low weight and short stature and her laboratory tests were normal. A gastroduodenoscopy revealed puckering of the gastroesophageal junction, requiring more pressure to traverse than the usual (Fig. 1). A barium esophagram/swallow revealed a dilated esophagus with a bird-breaking (Fig. 2). Manometry was characterized by a complete absence of peristalsis in the esophageal body and incomplete relaxation of the lower esophageal sphincter, which had a pressure of 73 mm/Hg. As a result, she was diagnosed with achalasia, which completes the manifestations of AS. The child's parents initially declined any therapeutic intervention. We adequately explained that both dysphagia and growth failure are irreversible unless she is managed appropriately. We started treatment with oral hydrocortisone (10 and 5 mg taken in the morning and noon) and nifedipine (1.5 mg/kg t.i.d). She continues to suffer from intermittent episodes of vomiting and a persisting failure to thrive. We advised her to eat small, low-fiber meals with more liquid, beside vitamin and mineral supplementation.

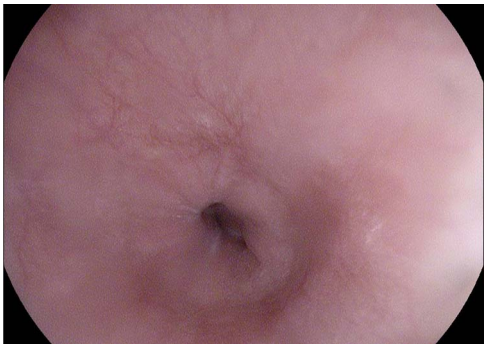

Figure 1. Puckering of the gastroesophageal junction necessitating more pressure than usual to traverse.

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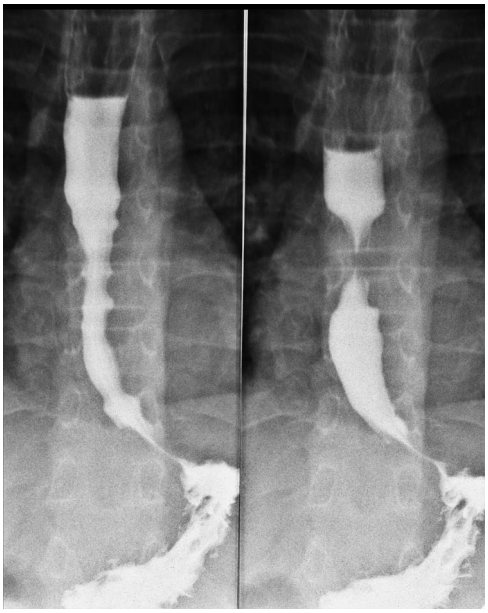

Figure 2. Bird's beak deformity and a dilatation of the body of the esophagus.

DISCUSSION

AS is a rare disorder with a prevalence of 10 cases per 100 000 people [3]. Alacrima is the most common early presenting sign occurring at birth or within the first year of life, but its significance is often overlooked, and attention is not sought until other symptoms emerge [2]. Schirmer's test confirms alacrima and each artificial tears, and lubricants can help in the treatment. If left untreated, it can cause keratopathy and corneal ulceration [2]. Glucocorticoid secretion affects up to 85% of patients, most of whom are in their first or, less frequently, the second decade of life. It is the leading cause of death due to severe hypoglycemia and can manifest as a variety of symptoms such as recurrent vomiting, hyperpigmentation of skin and mucous membranes, or developmental delays [2]. Cortisol levels at 8 a.m. along with concomitant ACTH measurements are used for confirming the diagnosis [2]. The preferred treatment is a short-acting glucocorticoid such as oral hydrocortisone, with 15–25 mg daily. For patients weighing less than 65 kg, a morning dose of 10 mg and a noon dose of 5 mg, or three doses of 10, 5 and 2.5 mg taken in the morning, noon and afternoon, respectively. Under-replacement symptoms such as myalgia, weight loss, nausea, fatigue, lack of energy and over-replacement symptoms such as central obesity, weight gain, hypertension, stretch marks, osteoporosis, osteopenia and impaired glucose tolerance must be identified [4]. Achalasia pathophysiology is characterized by failure to relax the lower esophageal sphincter and loss of esophageal peristaltic movement [5]. Gastroduodenoscopy, barium esophagram/barium swallow and esophageal manometry are well-established and complementary tests for the diagnosis of achalasia [6], and symptoms most commonly include regurgitation, dysphagia, weight loss and failure to thrive [7]. In up to 40% of cases, achalasia may also be accompanied by pulmonary symptoms such as cough, aspiration, hoarseness, dyspnea, wheezing or sore throat [8]. Achalasia in AS is distinguished by a more severe progression and a higher rate of treatment failure [9]. Treatment options include pneumatic dilation, which is the most effective non-surgical treatment option, laparoscopic Heller myotomy and peroral endoscopic myotomy [6]. To avoid pre-operative crisis, pre-operative measures should focus on preventing adrenal insufficiency and managing it with a stress dose of glucocorticoids on the morning of the procedure, while long procedures may necessitate continuous glucocorticoid infusion in the operating room. Blood glucose levels should be monitored throughout the procedure, as steroid administration may result in significant hyperglycemia, necessitating the administration of insulin. Hemodynamic stability in patients with impaired autonomic responses may be fragile, necessitating close cardiopulmonary monitoring for hypotension and arrhythmias, as well as caution during induction and position changes. To avoid keratopathy and corneal ulcers, eye protection in the form of lubrication should be provided [10]. Early identification of patients with suspected symptoms through genetic confirmation may allow proper monitoring and treatment [2]. The challenging conditions in Syria made it difficult for her to get appropriate medical consultation. Despite the long period of glucocorticoids treatment, the investigation of osteoporosis and opportunistic infections, including tuberculosis, was neglected.

AS can manifest in a variety of ways in timing, age of onset and coexisting disorders. This case demonstrates the difficulty and delay in diagnosis because the characteristic triad may not manifest concurrently. Although AS is uncommon, having a child present with a red-flag symptom such as alacrima should warrant further investigation.

ACKNOWLEDGEMENTS

None to declare.

CONFLICT OF INTEREST STATEMENT

None to declare.

FUNDING

None to declare.

ETHICAL APPROVAL

This case report did not require review by the Ethics Committee.

CONSENT

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

GUARANTOR

All authors have read and approved the manuscript, on behalf of all the contributors I will act and guarantor and will correspond with the journal from this point onward.

REFERENCES

1. Allgrove J, Clayden GS, Grant DB, Macaulay JC. Familial glucocorticoid deficiency with achalasia of THE cardia and deficient tear production. *Lancet* 1978;**311**:1284–6.
2. Flokas ME, Tomani M, Agdere L, Brown B. Triple A syndrome (Allgrove syndrome): improving outcomes with a multidisciplinary approach. *Pediatric Health Med Ther* 2019;**10**:99–106.

3. Sadowski DC, Ackah F, Jiang B, Svenson LW. Achalasia: incidence, prevalence and survival. A population-based study. *Neurogastroenterol Motil* 2010;**22**:e256–61.
4. Pazderska A, Pearce SH. Adrenal insufficiency – recognition and management. *Clin Med* 2017;**17**:258.
5. Furuzawa-Carballeda J, Torres-Landa S, Valdovinos MÁ, Coss-Adame E, Martín Del Campo LA, Torres-Villalobos G. New insights into the pathophysiology of achalasia and implications for future treatment. *World J Gastroenterol* 2016;**22**:7892–907.
6. Vaezi MF, Pandolfino JE, Yadlapati RH, Greer KB, Kavitt RT. ACG clinical guidelines: diagnosis and management of achalasia. *Am J Gastroenterol* 2020;**115**:1393–411.
7. Sarathi V, Shah NS. Triple-A syndrome. *Adv Exp Med Biol* 2010;**685**:1–8.
8. Sinan H, Tatum RP, Soares RV, Martin AV, Pellegrini CA, Oelschlager BK. Prevalence of respiratory symptoms in patients with achalasia. *Dis Esophagus* 2011;**24**:224–8.
9. Alhussaini B, Gottrand F, Goutet J-M, Scaillon M, Michaud L, Spyckerelle C, *et al.* Clinical and manometric characteristics of allgrove syndrome. *J Pediatr Gastroenterol Nutr* 2011;**53**:271–4.
10. Arun BG, Deepak BS, Chakravarthy MR. Anaesthetic management of a patient with allgrove syndrome. *Indian J Anaesth* 2014;**58**:736.