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Case Report

Allgrove syndrome: Case report of 18 years old male:the first case report from Syria

Nagham Hanino [a], Sarya Swed [b,*], Mohammed Deeb Zakkor [a], Abdullah Hindawy [a], Hidar Alibrahim [b], Hachem Alhussein [a]

[a] Department of Endrocinology Medicine, University Aleppo Hospital, Aleppo, Syria
[b] Faculty OF Human Medicine, Aleppo University, Aleppo, Syria

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ABSTRACT

Triple A syndrome 3A (Allgrove syndrome) is a rare autosomal recessive multiorgans dysfunction characterized by alacrima, achalasia which is the absence of esophageal muscle peristalsis and lower sphincter failure to relax and adrenal insufficiency.

About third of patient additional features like neurological and autonomic manifestations reported (making the syndrome 4A), the spectrum of neurological symptoms varies including gait disturbances, parkinsonism, muscle wakeness, mental retardation, peripheral sensory and motor neuropathy.

Here we reported A 18 years old male, who had postnatal recurrent conjunctivitis so alacrima was diagnosed, in the sventh years he developed achalasia signs; dysphagia and regurgitation and laparscopic surgical myotomy and fundoplication were done, when he became 16 he presented to our clinic for poor appetite, weight loss,and failure to thrive.

Assessment of ACTH, cortisol, ACTH stimulation test confirmed he had adrenal insufficiency and physical examination showed he had foots deformity due to muscular atrophy caused by neuropathy.treatment performed by managing symptoms of the condition(replacement of glucocorticoids, surgical correction of achalasia, artificial tears).The follow-up was over a period of 6 months and we noted a great improvement of patient's condition.

1. Introduction

The combination of ACTH-resistant cortisol deficiency, achalasia, and absent lacrimation is known as the triple A syndrome (AAAS), also known as Allgrove syndrome [1].Allgrove syndrome, or AAA syndrome, is a rare autosomal recessive endocrine disorder with an estimated prevalence of 1 per 1,000,000 individual.The molecular basis of this rare autosomal recessive disorder is the mutated gene, located on chromosome 12q13, that codes for ALacrima Achalasia aDrenal Insufficiency Neurologic disorder (ALADIN) protein [2].There is a significant gap between initial symptoms and the diagnosis of the triple A syndrome [3].The clinical presentation of classical signs and symptoms of the syndrome is dependent on the age of the patient.The classic history and reasons for consultation include frequent complaints of the absence of tears while crying/dry eyes at birth due to alacrima, feeding difficulties, repeated vomiting, weight loss due to underlying achalasia, or seizure secondary to hypoglycemia resulting from the adrenal crisis, and delayed growth/milestones.In addition, neurological abnormalities were frequently described [4].The main aim of our work is to report a case of AAA syndrome that presents with weight loss,General fatigue, generalized pigmentation, caries and peripheral Neuropathy.This is the first report of this rare syndrome from Syria.

This case report has been reported in line with the SCARE criteria 2020 [9].

1.1. Case presentation

A 18 year old male attended to Endocrinology clinic at Aleppo University Hospital with a complaint of general fatigue, difficulty in walking and Weight loss. By taking the clinical history, The family noted that since birth they noticed a lack of tears when crying. There is also a history of the patient's brother dying at an early age for an unknown

* Corresponding author.
E-mail addresses: nagham1992hanino@gmail.com (N. Hanino), saryaswed1@gmail.com (S. Swed), mohmmedzakour12345@gmail.com (M.D. Zakkor), Abdull.hindawe91@gmail.com (A. Hindawy), haideralibrahem1999@gmail.com (H. Alibrahim), Hachem917@yahoo.FR (H. Alhussein).

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reason, but he was suffering from alacrima, so they consulted the ophthalmologist. Ophthalmological examination, including.

Schirmer's test was positive, wetting was 3 mmin right eye and 2.5 mm in left eye at 5 min, whereas, normal wetting at 5 min is > 5mm.So he had dry eyes and alacrima. We re-tested the Schirmer test and the result was positive, which confirmed the previous diagnosis. But there were no other complaints at that age. At the age of seven years, the patient started to have recurrent attacks of vomiting with dysphagia. So, he consulted a gastroenterologist, and many investigations were requested, including: upper gastrointestinal endoscopy, It showed severe stenosis of the lower esophageal sphincter, as well as dilatation of the upper esophagus(Fig. 1), also barium swallow test was performed and The result was that the child swallowed the barite bite with great difficulty and returned it immediately(Fig. 2). From the above, achalasia was diagnosed and treated by dilatational surgery.Returning to the National Center for Chronic Disease Prevention and Health Promotion, we found three standard deviations in length. On clinical examination, we noticed the presence of skin pigmentation on different areas of the skin like skin and folds, This raises the suspicion of adrenal insufficiency. So, we performed a morning cortisol assay, and the result was 7.17 Ug/dl. To confirm the diagnosis, we performed a synacthen induction test, and the result was positive. The laboratory values were as follows: Serum sodium was low at 135 mEq/L, potassium mmol/L,3.5 and Serum glutamic pyruvic transaminase was less than 30 U ml.On the other hand, the rest of the tests were normal.

This confirmed the presence of adrenal insufficiency (Addison's disease). Thus, we have a patient suffering from Triple A syndrome (allgrove syndrome).The clinical examination also revealed the presence of dental caries(Fig. 3) and lack of saliva secretion. Following the examination, we found a deformity at the level of the foots, and this suggests either the presence of a bony deformity or atrophy at the level of nerves or muscles associated with Triple A syndrome.

But by requesting an X-ray of the foots, we did not find any bony deformity(Fig. 4), and to confirm the diagnosis, we performed an electrocardiogram of the nerves feeding the muscles of the right foot, and it was found that there was a peripheral neuropathy that led to atrophy of the muscles of the right foot(Fig. 5). From the above, we conclude that the patient suffers from Triple A syndrome (Allgrove syndrome) with neuropathies.

Treatment includes the following: Giving hydrocortisone at a dose of 10 mg in the morning and 5 mg in the evening for the management of adrenal insufficiency (Addison's legendse)

Alacrimia is treated with artificial tears While to manage the deformity of the toe caused by neuropathy, we recommended physical therapy.

The follow-up was over a period of 6 months, where we noticed an improvement in the general condition in addition to gaining weight, and the physiotherapy sessions helped reduce the deformity caused by neuropathy.

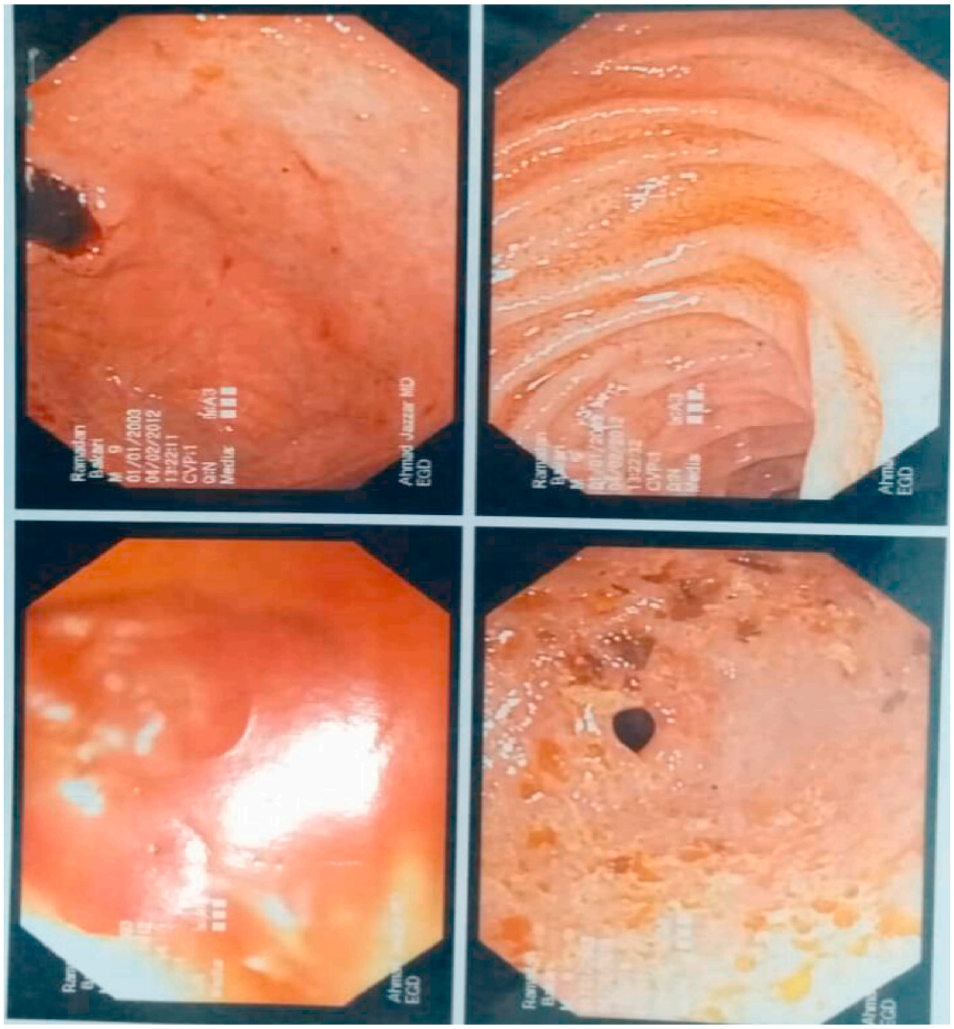

Fig. 1. Gastrointestinal endoscopy showed stenosis of the lower esophageal sphincter and dilatation of the upper esophagus.

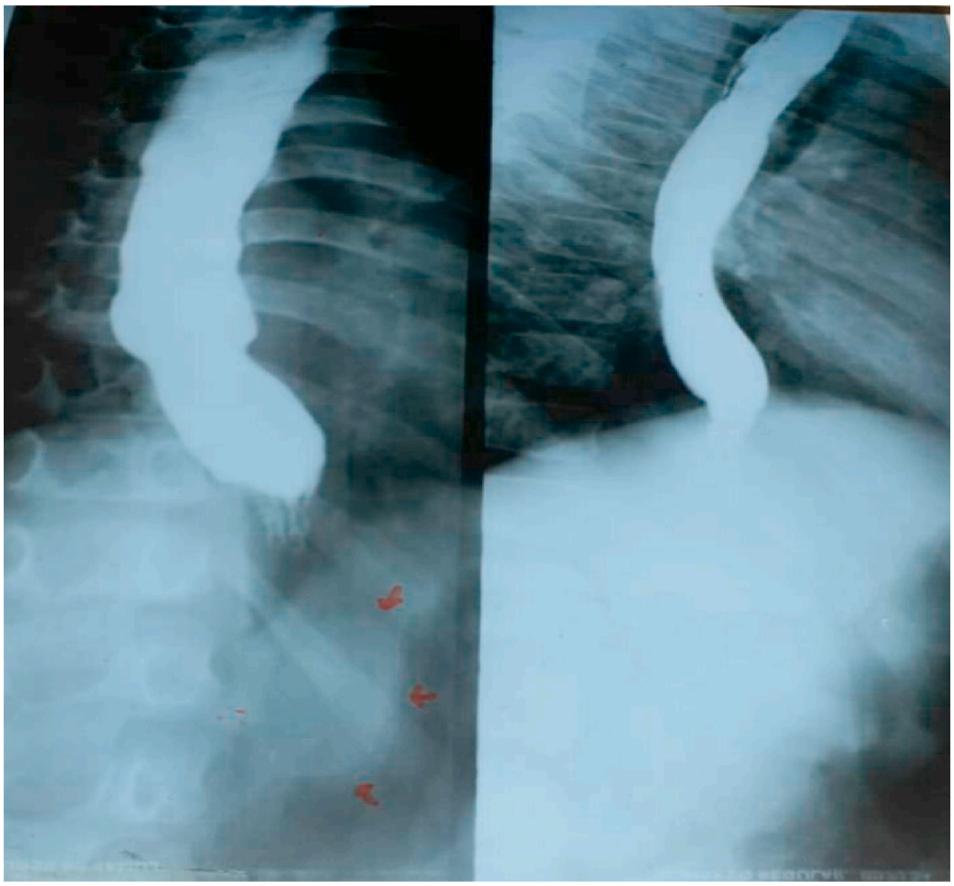

Fig. 2. Barium swallow test informed the presence of achalasia.

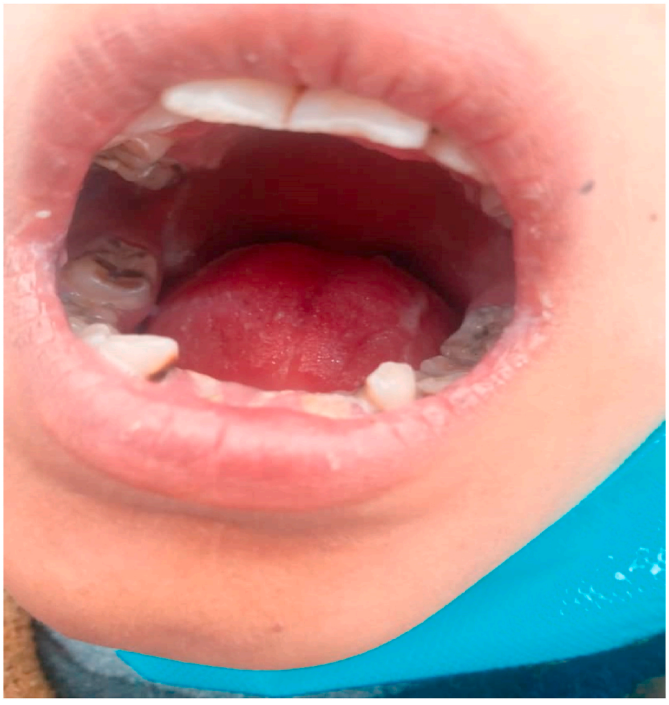

Fig. 3. Dental caries.

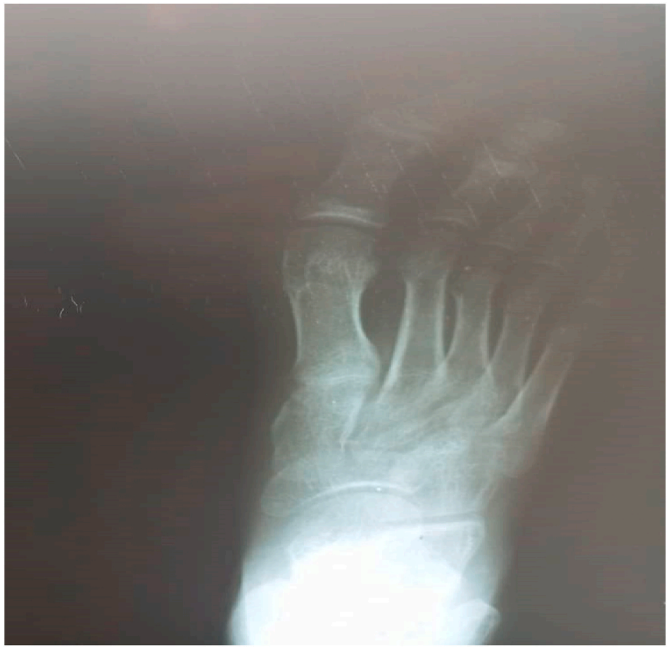

Fig. 4. Picture of x-rays for foots:thereis no bony deformity.

2. Discussion

Triple A Syndrome:The triple A (Allgrove) syndrome was first described in two pairs of siblings by in 1978 [5].The description of

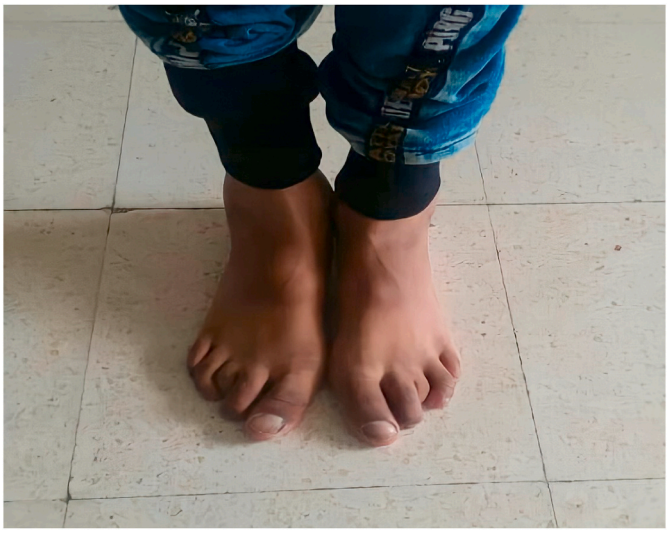

Fig. 5. Atrophy of the muscles of the foots.

Allgrove syndrome is limited to case reports because, since its first description in 1978, about 100 patients with the clinical triad of alacrimia, achalasia and adrenal insufficiency have been described.

The earliest feature is alacrimia as was in our patient. Achlarimia is the most consistent finding, with prevalence reaching >90% of the patients affected [6].Schirmer's test confirms the presence of reduced or absent tears. Administration of artificial tears and lubricants help relief the sensation of dryness. Achalasia of the cardia occurs in about 75% of cases and in older children/adults it usually manifests as dysphagia especially for liquids.Achalasia present in 3A is caused by absent lower esophageal sphincter relaxation and impaired esophageal motility.Adrenal insufficiency due to deficient glucocorticoid secretion affects up to 85% of patients with 3A.It is the main cause of mortality among patients with 3A, mostly due to severe hypoglycemia [7].Adrenal insufficiency is also an early manifestation and manifests as severe hypoglycemic or hypotensive attacks during childhood which may lead to sudden death. Neurological dysfunction from the involvement of central, peripheral or autonomic nervous systems is often associated with Allgrove syndrome [8].

Our case is an 18-year-old patient diagnosed with alacrimia since birth by doing Schremer test and artificial tears were performed to avoid dry eyes constantly and at the age of 7 years, the patient complained of dysphagia and vomiting of undigested food. The presence of achalasia was confirmed by upper gastrointestinal endoscopy and esophageal motility study. He was treated by surgical dilation.At the age of 18 years, the patient complained of weight loss, general fatigue and generalized pigmentation,so we assested Adrenocorticotropic hormone(ACTH), cortisol, ACTH stimulation test and we informed the presence of adrenal insufficiency and we had to constantly replace with hydrocortisone.

Based on above, we have a rare case of Allgrove A syndrome, in addition to the patient's latest complaints, dental caries due to a lack of saliva production with muscular atrophy in the foots as a result of peripheral neuropathy confirmed by neuro grammetry.

There is no cure for triple A syndrome at this time; treatment typically focuses on managing individual signs and symptoms of the condition(replacement of glucocorticoids, surgical correction of achalasia, artificial tears).We emphasize that Allgrove syndrome is a multisystem disease and the cardinal manifestations may appear at any time from infancy to adulthood.

3. Conclusion

Triple A syndrome is a rare disease; however many cases still undiagnosed or misdiagnosed, Thus, Triple A syndrome should be expected in any child presents with one of the three cardinal features, and these children should be closely surveillanced.

Early diagnosis and management improves quality of life and survival rates.

In addition; neurological assessment and follow up the patient should be made, because the neurological symptoms are very varied, and then refer patient with neurological symptoms to the appropriate specialists to provide proper care.

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Ethical approval

This case reports didn't require review by Ethics committee .The National Ribat University hospital/Ribat/Sudan.

Consent

Written informed consent was obtained from the patient for publication of these two case reports and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author contributions

Nagham Hanino: contributed in study concept and design, data collection.

Sarya Swed:contributed in data interpretation and writing the paper.

Mohammed Deeb Zakkor:contributed in writing the paper.

Abdullah Hindawy:contributed in writing the paper

Registration of research studies

Not applicable.

Guarantor

Sarya Swed

Declaration of competing interest

All authors declared no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.103009.

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