CASE REPORT

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Triple-A or Allgrove Syndrome

Dharmander Singh, Sanjay Pandit**, DP Bhadoria***, Prashant Thandi**

Abstract

Background: Triple-A or Allgrove syndrome is a rare inherited disease classically seen in children less than 10 years of age. Triple-A consists of achalasia, alacrimia, and primary adrenal insufficiency. Surprisingly, very few cases have been reported in Indian population that present with all three components[1].

Objective: To report a rare case of Allgrove syndrome to create awareness amongst physicians for early diagnosis and management.

Key words: Allgrove syndrome, Triple-A syndrome, achalasia, ACTH insensitivity syndrome, alacrimia.

Case presentation

A 13-year-old male child presented with chief complaints of nausea, vomiting, abdominal pain, loose stools and dizziness for the last 4 days. The patient reported that he had similar recurrent episodes of gastrointestinal complaints for the last 4 months. He also complained of fatigue, weight loss and generalised hyperpigmentation of skin involving palms, knuckles, and oral mucosa. He also had raised body temperature documented as 100-degree Fahrenheit persistently. The fever had no diurnal variation and was not relieved by antipyretics. The patient had bilateral dry eyes since childhood. No other symptoms were indicative of sicca syndrome or any other autoimmune illness. Tuberculosis and other systemic illnesses were ruled out clinically. The patient had undergone surgery at the age of 7 years for achalasia. The child has been completely immunised for his age. He was born by normal vaginal delivery and attained developing milestones later than his elder brother.

On physical examination, the patient's blood pressure was 90/ 60 mmHg. The temperature recorded was 101.5° F. There were signs of mild dehydration. Hyperpigmentation was also confirmed. On ancillary investigations, random blood glucose levels were 70 mg/dl (reference range: < 140 mg/dl), blood sodium levels were 128 mmol/l (reference range: 133 - 148 mmol/l) and serum potassium levels were 5.7 mmol/l (3.5 - 5.5 mmol/l). Investigations including haemogram, kidney function test, liver function test, erythrocyte sedimentation rate, C- reactive protein, Mantoux, hepatitis B, hepatitis C and HIV serology and thyroid profile did not reveal any abnormality. Arterial blood gas analysis revealed metabolic acidosis. No abnormality was detected on a chest X-ray and ultrasound abdomen. Schirmer's test and fluorescent staining on slit lamp examination confirmed alacrimia. Basal serum cortisol level was 0.25 ug/dl (reference range: 4.30 - 22.40 ug/dl). After 60 minutes of stimulation by Adrenocorticotrophic hormone (ACTH), cortisol levels were 0.20 ug/dl (reference range: > 20 ug/dl). Contrast enhanced computed tomography (CECT) of the chest and abdomen showed bilateral adrenal atrophy. Noncontrast enhanced computed tomography (NCCT) of orbit revealed bilateral atrophic lacrimal glands. Patient's records showed subtle abnormal contractility of the distal half of the thoracic esophagus with transient holdup of contrast followed by complete emptying suggestive of achalasia on barium swallow. Based on the history of achalasia and investigations indicating primary adrenal insufficiency and alacrimia, the patient was diagnosed with Allgrove syndrome. The patient was started on tablet fludrocortisone 0.1 mg once daily. For dry eyes, punctal occlusion was done and topical lubricants were prescribed. Clinical recovery was noticed.

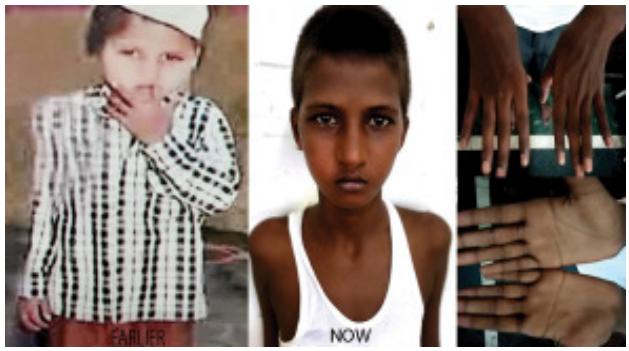

Fig. 1: *Shows generalised hyperpigmentation as compared to earlier photo; hyperpigmentation involved palmar surface too.*

****Post-Graduate Student, **Professor, ***Director Professor, Department of Medicine, Maulana Azad Medical College, Lok Nayak Hospital, New Delhi - 110 002.***

Corresponding Author: Dr Dharmander Singh, Post-Graduate Student, Department of Medicine, Maulana Azad Medical College, Lok Nayak Hospital, New Delhi - 110 002. Phone: 8860968415, E-mail: dr.dharmander@gmail.com.

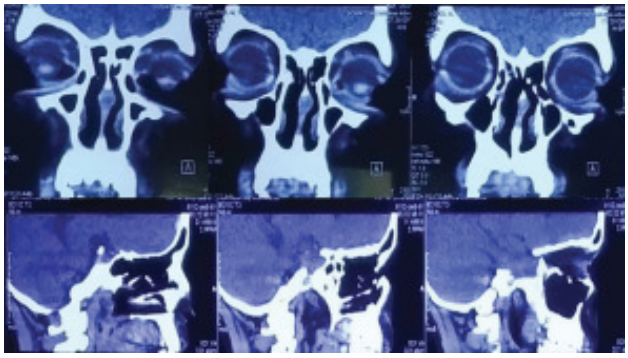

Fig. 2: *Shows non-visualisation of bilateral lacrimal glands, likely atrophic.*

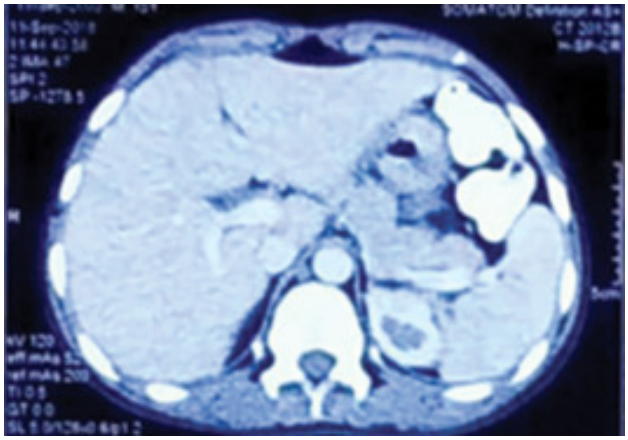

Fig. 3: *Shows bilateral atrophic adrenal glands.*

Discussion

Triple-A syndrome or Allgrove syndrome was described by Allgrove and his colleagues in 1978 as a syndrome consisting of achalasia (involving distal thoracic oesophagus), primary adrenal insufficiency and alacrimia[2]. Later on, with addition of autonomic disturbances, the disease was termed as 4 A syndrome[3]. Studies have shown that the syndrome is due to mutation of ADRACALIN or AAAS gene present on chromosome 12q13 that encodes for the protein ALADIN that is part of the nuclear protein complex[4,5]. This syndrome does not have any gender predilection and the exact frequency is not yet known. Alacrimia is the early manifestation of the disease which may be present in infancy or childhood. Primary adrenal insufficiency has a variable onset; however, it is important to diagnose it early in the disease course as it can be life-threatening because of possible progression to Addisonian crisis. The exact reason for delayed onset adrenal symptoms and involvement of the above three specific tissues is not yet clear. Interestingly, very few cases have been reported with a patient presenting with all three symptoms.

The disease is treated by managing the symptoms. For achalasia, balloon dilation or surgery is the treatment of choice which is usually needed in childhood. Lifelong fludrocortisone therapy at the dose of 0.1 - 0.3 mg is the drug of choice for primary adrenal insufficiency. In adolescence, addition or replacement with an equipotent dose of prednisone or dexamethasone is needed, for the appearance of sexual characters. Alacrimia is treated symptomatically with topical lubricants and punctal occlusion.

References

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