

Case Study

Triple-A (Allgrove) Syndrome



Triple-A (Allgrove) Syndrome

Case presentation

A 20 year old girl was diagnosed with motor neuron disease like illness at the age of 18 years. Her parents are consanguineously married and she has a younger brother who manifested with the same clinical features as her. She started having dysphagia and generalized muscle wasting over the face and hands about 3 years ago.

Detailed examination revealed microcephaly, Addison's disease, type 11 Achalasia cardia, alacrimia, nasal twang while talking, hypo-pigmented patches on lips, hyper-pigmented patches on extremities, hyperkeratosis, and gingival hypertrophy. All of these features are suggestive of Triple A syndrome also known as Allgrove syndrome.



Fig 1: Clawing of toes, hyperpigmentation



Fig 2: Hyperkeratosis of soles



Fig 3: Hyperpigmentation, muscle wasting

Previous workup

MRI, ECG, upper GI endoscopy, hormone level, blood evaluation, urine analysis, thyroid profile, serum electrolytes, DHEAS were evaluated.

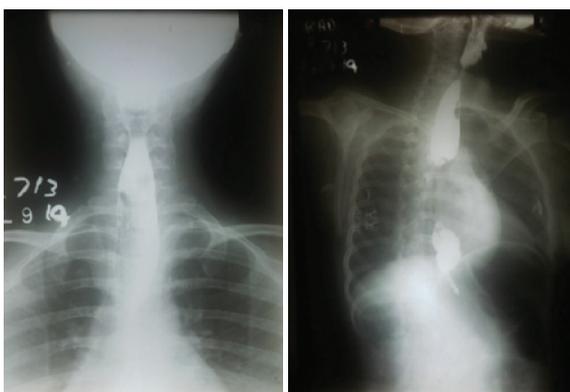


Fig 4: Filling defect in the middle 1/3rd and lower end of esophagus.

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Genetic testing

The Strand Rare Disease Test, a multi-gene panel (>460 genes) testing was initiated for this girl to confirm clinical diagnosis.

Results

A novel homozygous (two mutated copies) likely pathogenic variant was identified in AAAS gene. The brother was also found to have the same homozygous variant as his sister. Parents were identified to be carriers (having one copy of the gene each). This confirmed the clinical diagnosis of Triple A syndrome.

Treatment

Surgical correction of achalasia cardia was recommended. Apart from this, daily glucocorticoid therapy and mineralo-corticoid replacement therapy was put in place. The medical team has suggested use of artificial tear drops.

Conclusion

This genetic test helped the family in understanding the cause of the disorder in both children. The affected siblings were educated about their condition and prognosis was explained. A management protocol was put in place for both the siblings to ensure better quality of life. Both the siblings are now compliant with the management protocol in place.

Literature review

Defects in AAAS gene have been associated with Triple A- syndrome (also known as Allgrove syndrome) which is characterized by adrenocorticotropin hormone (ACTH)-resistant adrenal insufficiency, achalasia of the oesophageal cardia and alacrima. Autonomic dysfunction and intellectual disability have also been associated with Triple A-syndrome. The earliest manifestation of the syndrome is usually Alacrimia. It is a progressive disorder which can take many years to present all the clinical features and manifests with varying features within families.

It is inherited in an autosomal recessive fashion. Thus, carrier couples with deleterious variants in AAAS have 75% chance of having an unaffected child and 25% chance of having an affected child in every pregnancy.

Ref: <https://ghr.nlm.nih.gov/condition/triple-a-syndrome> retrieved on 25th March, 2016.

Physician comments about case

- How was the condition affecting the patient's day to day life before the diagnosis was made?
She had palpitation and sweating because of hypoglycaemic episodes, asthenia and difficulty in swallowing.
 - What are these siblings doing now?
He is studying
 - How is their quality of life?
Fair for both of them. Able to swallow well, no hypoglycaemic episodes.
 - How did this test help you in your clinical practice?
Even when we found all the three components of Triple A syndrome, it was necessary to obtain genetic confirmatory test positive, which is objective evidence of the root cause of the disease.
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