

## Case Reports

### Esophageal Achalasia and Alacrima in Siblings

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*Achalasia of the esophagus is a rare problem in children. It has been reported in siblings of consanguineous parents. Allgrove or AAA (triple-A) syndrome is an autosomal recessive condition associated with adrenal insufficiency, alacrima and achalasia of the oesophagus. We present two siblings with familial achalasia and alacrima treated at 3 months and 9 years respectively.*

**Key words:** Achalasia, Alacrima, Familial, Siblings.

Esophageal achalasia is a rare disease, manifested by absence of peristalsis in the body of the esophagus, failure of relaxation of the gastroesophageal sphincter and proximal esophageal dilatation. The incidence varies from 0.6 to 1.0 per 100,000 per year(1). Prevalence in siblings born from consanguineous marriage suggests a possible autosomal recessive trait(2). Allgrove and colleagues described 2 unrelated pairs of

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siblings with isolated glucocorticoid failure and achalasia of the esophagus(3). Three of these also had defective tear production. We present two siblings born of non-consanguineous parents with esophageal achalasia and alacrima treated successfully.

#### Case - 1

J.D., a 3-month-old boy was brought to us with history of frequent episodes of white vomiting immediately after feeds. The child had been losing weight over a period of 4 weeks. Abdominal examination was normal. A contrast meal showed a dilated esophagus with smooth abrupt narrowing in the region of lower oesophageal sphincter suggestive of achalasia. The child underwent esophagocardiomyotomy with fundoplication which relieved his symptoms. Four years after surgery, he has been thriving well. Follow up upper GI contrast showed a normal caliber esophagus, smooth passage into the stomach and no evidence of gastroesophageal reflux.

#### Case 2

Nine-year-old PD is the elder sister of JD. She had a history of recurrent pneumonitis requiring multiple hospital admissions. She also had dysphagia for solid food. At the age of 9 she underwent a CT scan of the chest to investigate the cause of her recurrent pneumonitis. CT scan showed a hugely dilated esophagus with bilateral pneumonitis and was hence referred to us for further management. A contrast swallow confirmed esophageal achalasia. She was also operated for abdominal esophagocardiomyotomy with fundoplication. Six months after the surgery, she has gained weight and has been relieved of her symptoms.

## Discussion

A worldwide survey of childhood achalasia has shown the disease to be unusual in infancy. Rao, *et al.*(4) reported two siblings with achalasia in infancy. Boys are affected more commonly than girls. The average age of presentation in familial achalasia has two peaks, one in the pediatric age group (average age 2.5 yrs) and one in the adult group (average age 46.5 yrs)(5). Familial achalasia has been known to occur in children born from consanguineous parents. There are reports of consanguineous marriages in five families that together account for 15 of all reported cases of affected children. In one report where 7 of the 8 siblings were probably affected, the father was the maternal uncle and the grand parents were consanguineous(6). Monning(7) has reported five siblings with achalasia with no history of consanguinity or of vertical transmission.

Allgrove syndrome, also called AAA (triple A) syndrome is an autosomal recessive condition which was first described in 1978. It is characterized by defective tear production, achalasia and adrenal deficiency(3). The disease gene, ALADIN localizes to 12q13, with mainly nonsense mutations resulting in expression of a truncated protein. Association with autonomic nervous system dysfunction also led to the suggestion to rename the syndrome as 4A syndrome (adrenal insufficiency, achalasia of cardia, alacrims and autonomic abnormalities).

In our case, it was only after presentation of J.D.'s sister that direct questioning led to the finding that neither JD nor PD had produced any tears since birth. Both siblings have undergone evaluation by pediatric ophthalmologist and are presently on tear substitutes. Neither of them had any evidence of hyperpigmentation or electrolyte disturbances.

Serum ACTH and basal cortisol levels were also normal. Lacrimal gland biopsies from children with alacrims have shown neuronal degeneration associated with depletion of secretory granules in the acinar cells. Haverkamp, *et al.*(8) also reported two brothers and one sister with a similar combination of only achalasia and alacrims and suggested that these cases may represent a different entity from the well described AAA syndrome.

Mayberry and Atkinson(9) studied 1012 first degree relatives of 159 adult achalasia patients, none of whom had achalasia. This excludes a dominant mode of inheritance and concludes that only 1 in 300-400 persons carry the predisposing recessive gene in the heterozygous state. It is not known if the same genetic influence is exerted in both childhood and adult forms of achalasia. It is interesting that an autosomal recessive disorder presents in infancy and again in adulthood. It could hence be possible that the penetrance of a single gene varies considerably in different families or more than one gene may cause the disorder. It is also possible that different types of mutations within the same gene may give rise to different phenotypes.

In view of the familial incidence, some investigators also recommend screening of all the family members by contrast swallow examination when achalasia is discovered in childhood(10). In children with associated adrenal deficiency, careful replacement of glucocorticoids is critical not only to avoid adrenal crisis but also to allow normal growth.

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