

Dental Impairment in Allgrove Syndrome: A Case Report

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Abstract

Triple-A syndrome, also known as Allgrove syndrome, is a rare autosomal recessive disorder. The classical features of this syndrome are achalasia, adrenal insufficiency, and alacrima. Recently, dental impairment has been the subject of several case reports and reviews. However, this abnormality remains under-diagnosed. We represent the case of a 23-year-old male patient who was diagnosed with Allgrove syndrome at the age of 3. He suffered from many oral manifestations of this syndrome and especially premature loss of permanent teeth.

Keywords: Allgrove syndrome, triple A syndrome, oral manifestation, dental impairment, teeth loss.

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INTRODUCTION

Triple A syndrome or Allgrove's syndrome is a rare disease, first defined in 1978 (Allgrove *et al.*, 1978). It is a multisystemic disease with an estimated prevalence of 1 per 1,000,000 individuals (Brown *et al.*, 2016). Triple A syndrome is defined by 3 cardinal signs: Alacrima (absence of tears), achalasia and adrenal insufficiency. Autonomic nerve disorders have been also described in Allgrove's syndrome leading to the name 4A syndrome (Grant *et al.*, 1993a; Kimber *et al.*, 2003).

Recently, dental impairment has been the subject of several case reports and reviews. However, this abnormality remains under-diagnosed.

We report a patient with multisystemic features of the syndrome with particular attention to premature loss of permanent teeth.

CASE REPORT

A 23-year-old male patient, with no family medical history, born to consanguineous parents was referred to the endocrinology departement at the age of 16-year-old for hormonal evaluation. He was diagnosed with adrenal insufficiency at age 3. It was revealed by a hypoglycemic seizure with low cortisol and elevated ACTH level. He was treated with oral hydrocortisone and fludrocortisone.

Further interrogation identified alacrima (crying without tears from early age). It was confirmed by ophthalmologic evaluation and Schirmer test. Artificial tears were then prescribed. Furthermore, the patient had dysphagia and weight loss. An upper endoscopy was done and it confirmed the diagnosis of achalasia. He had esophageal dilatation on two occasions (2000 and 2011) leading to the improvement of dysphagia.

The Allgrove's syndrome was then confirmed with genetic analysis when mutation of the AAAS gene was identified (IVS14+1G).

At the age of 6, the patient started having dental caries and gingivitis. Due to tendency to eating sweet foods and poor oral hygiene, the teeth have decayed rapidly. Inadequate root length remained after the removal of decay leading to dental extraction. Because of economic problem, he had implant treatment for only his upper teeth when he was 20-years-old. However, the implant was only successful for 2 years and then the patient started losing his teeth again.

At the presentation to the endocrinology departement, physical examination showed hyperpigmentation, microcephaly, delayed developmental milestones and dysmorphic facial features: narrow face, long philtrum, down-turned mouth (fig1).

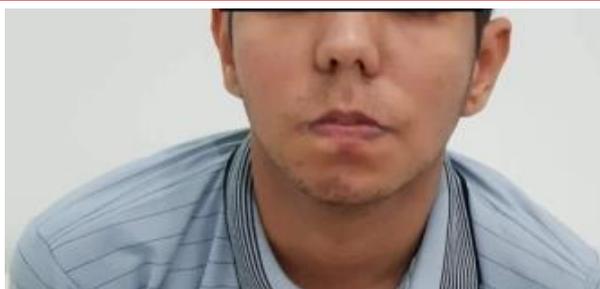


Fig-1: Dysmorphic facial features

The patient also presented mental retardation and normal sexual development (testicular volume 18 ml each and Tanner stage 5).

Neurological examination showed distal amyotrophy mainly of thenar, hypothenar and interosseous muscles (fig2). The patient also suffered from motor deficits of the four limbs and presented a pyramidal syndrome with diffuse polycinetic vivid stretch reflexes.

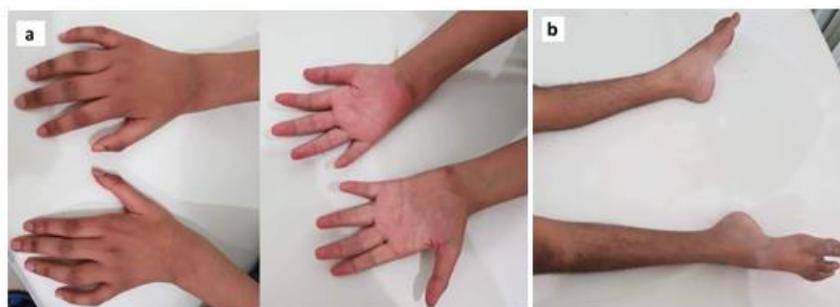


Fig-2: a- amyotrophy mainly of thenar, hypothenar and interosseous muscles. b- amyotrophy of the calves

In the oral examination, he had a very poor hygiene condition with severe caries and was partially edentulous (fig3, 4). Thus, a second dental implant is scheduled.



Fig-3: Dental caries

DISCUSSION

Allgrove syndrome is an autosomal recessive disorder characterized by achalasia, alacrima, adrenal insufficiency and progressive neurodegenerative disease. The disease gene called the AAAS gene (achalasia-addisonianism alacrymia syndrome) was localized at 12q13 in 1996. It codes the protein Alacrymia Achalasia Adrenal Insufficiency Neurologic disorder protein (ALADIN) (Handschug *et al.*, 2001; Tullio-Pelet *et al.*, 2000). This syndrome is characterized by significant allelic heterogeneity with more than 60 mutations according to the Human Gene Mutation Database (Cooper *et al.*, 1998).

In review of literature, alacrima was the earliest and most consistent clinical sign of Allgrove syndrome (Brooks *et al.*, 2004; Moore *et al.*, 1991). Achalasia is present in 75% of all cases and can occur at any age (Grant *et al.*, 1993b; Roucher-Boulez *et al.*, 2018). Adrenal insufficiency is usually present in the first decade of life. It could have mild symptoms as hypoglycemia, asthenia or could occur as sudden death (Milenkovic *et al.*, 2010; Roucher-Boulez *et al.*, 2018). For our patient, although alacrima was the first feature of the disease, the diagnosis was revealed by adrenal insufficiency signs.



Fig-4: Premature loss of permanent teeth

Many orofacial abnormalities associate with Allgrove syndrome were reported in the literature such as: down-turned mouth with thin upper lip, cleft palate, malar hypoplasia, mandibular malocclusion, relaxed speech musculature, high gothic hard palate, cross bite, (Dumić *et al.*, 2000a; Razavi *et al.*, 2010; Shetty *et al.*, 2018; Vucicevic-Boras *et al.*, 2003). In our patient, the orofacial findings observed were down-turned mouth and angular cheilitis. Intraoral abnormalities were also

described in literature. Li *et al.* reported a combination of xerostomia, caries, periodontal disease and premature teeth loss in three out of six patients with Allgrove disease (Tadini *et al.*, 2015). Our patient had xerostomia, dental caries and progressive teeth loss.

It is common that patients with Allgrove syndrome suffer from autonomic neuropathy. The innervation of lacrimal glands originates in the Superior Salivary nucleus of the brainstem, in common with the parasympathetic innervation of the sublingual salivary glands. Therefore, this abnormality could explain the xerostomia as well as alacrima (Dumić *et al.*, 2000a).

On the other hand, achalasia is responsible for gastric reflux, repeated vomiting inducing, thereafter, oral acidity almost consistently (Vahedi *et al.*, 2016). Gastric acid is a hydrochloric acid with a pH of 1–1.5 (Taji & Seow, 2010). Clinical manifestation resulting from this chemical erosion occurs after several months' exposure to gastric acid (Tolia & Vandenplas, 2009).

Razavi has reported premature loss of permanent teeth in a 10-year-old female patient who didn't suffer from xerostomia nor achalasia speculating teeth loss to be a feature of Allgrove syndrome. This points to the multisystemic character of the disease (Razavi *et al.*, 2010).

In our case, the common causative factors for premature teeth loss could be the consequences of the achalasia notably repeated vomiting and acid gastric reflux inducing oral acidity almost consistently. Furthermore, poor oral hygiene and tendency to bad eating habits are aggravating factors.

Consequently, it seems that the mismatch between dental age assessment and chronological age could have negative prognosis (Mazhuga *et al.*, 1987). Furthermore, the treatment by hydrocortisone inhibits protein and glycoprotein synthesis and decreases the amount of proliferating cells. Thus, a delay of teeth growth could be explained (BD *et al.*, 2017).

Nowadays, no guidelines of dental impairment management in triple a syndrome were published in literature. But, the treatment of achalasia and especially xerostomia with artificial saliva were essential to prevent and delay teeth loss (Dumić *et al.*, 2000b; Onat *et al.*, 2007). Flykos *et al.* has recently recommended a dental visit at least twice a year. He also provided some preventive measurements as accurate oral hygiene, toothpaste with fluoride and low-sugar diet (Flokas *et al.*, 2019).

CONCLUSION

Triple a syndrome is a multisystemic disease needing multidisciplinary management including endocrinologists, gastroenterologists, ophthalmologists, neurologists and dentists. The prevention and

management of bucco-dental complications associated with xerostomia and achalasia are essential to minimize the loss of permanent teeth and improve the quality of life.

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