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Oral and Dental Manifestations of 4 "A" (Allgrove) Syndrome: Report of A Pediatric Case

Jomaa Nermine[1*], Zaroui Jihène[2], Jemmali Badiaa[3]
[1]Resident in Pediatric Dentistry, Dentistry Department, Hospital La Rabta, Tunis, Tunisia
[2]Assistant professor on Pediatric Dentistry, Dental Faculty of Medicine of Monastir, Monastir, Tunisia
[3]Professor in Pediatric Dentistry, Head of Dentistry Department, Hospital la Rabta Tunis, Tunisia

Case Report

***Corresponding author**
Jomaa Nermine

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Abstract: Allgrove syndrome which is known as the triple A syndrome, is a rare autosomal recessive disease. It has an estimated prevalence of 1 per 1,000,000 individuals. The triple A stands for the three most prominent features of the syndrome, alacrimia, achalasia and adrenocorticotropic hormone (ACTH)-resistant adrenal insufficiency. It may be associated with autonomic, central and peripheral nervous system abnormalities then the name 4 A syndrome has been introduced. In this paper, we report the case of a 14-year-old girl with the 4 A syndrome who was referred to the Oral Medicine Department of hospital La Rabta (Tunisia). She suffered from many oral manifestations of Allgrove's syndrome as well as general abnormalities. Through this observation, we will show that the Knowledge of the oral manifestations is important and it leads the dentist to the right prevention and management of bucco dental complications of these patients.

Keywords: Allgrove syndrome, oral manifestations, Xerostomia, tooth loss, erosion, fissured tongue, gingival pigmentation, oral candidiasis.

INTRODUCTION

Triple A syndrome or Allgrove syndrome is a rare autosomal recessive disease whose first cases were reported by Allgrove in 1978 [1]. The incidence of this rare multisystemic disorder is unknown [1]. It has an estimated prevalence of 1 per 1,000,000 individuals [2]. The triple A stands for the three most prominent features of the syndrome: alacrimia (absence of tears), achalasia (esophageal motility disorder) and adrenocorticotropic hormone (ACTH)-resistant adrenal insufficiency [1].

It may be associated with autonomic, central and peripheral nervous system abnormalities then the name 4A syndrome has been introduced (autonomic abrnormalities) [3, 4].

The disease-causing gene (AAAS) encodes a protein of 546 amino acids called ALADIN (for alacrima–achalasia–adrenal insufficiency neurologic disorder) [5, 6]. ALADIN is a protein that belongs to the WD tryptophane-aspartic acid repeat-containing protein (WD) family [6, 7]. The function of ALADIN is not clear, but it could be shown that it is supposed to regulate nucleo-cytoplasmic transport of specific proteins including DNA repair proteins [7, 8].

The early onset disease usually presents with hypoglycemic episodes, hyperpigmentation or hypolacrimia [6] while the adult onset disease has been reported to be more neurological, with the endocrinologic or gastro intenstinal signs being minor [3, 8].

This article reports a case with broad clinical features of the syndrome with particular attention to oral manifestations.

CASE REPORT

A 14 year old femal patient diagnosed with Allgrove's syndrome was referred to the Department of Oral Medicine, LA RABTA hospital (Tunisia), with the chief complaint of oral dryness and extensive decays in teeth (Fig-1). She was born to non-consanguineous parents and there was no family history of the disease.

Fig-1

Allgrove's syndrome was diagnosed at six years old when she developed achalasia. Other than alacrimia, achalasia and adrenocorticotropic hormone (ACTH)-resistant adrenal insufficiency, this case has progressive neurological disability. She exhibits signs of multisystem neurological disease including walking disorder, Spastic Paraparesis, hyperreflexia, muscle wasting, intellectual impairment, dysarthria and nasal speech (Fig-1). So the 4A syndrome has been retained.

Besides, she had a deficiency in the growth hormone with stunted growth retardation, and a general cutaneous hyperpigmentation of Addisonian character mostly in sun exposed skin surfaces was detected.

Also at the age of 12, esophageal dilatation (ballooning dilatation) was performed, because of difficulty in swallowing.

At the presentation to the oral medicine department, careful extraoral and intraoral examinations were performed. Orthopantomogram was taken for the evaluation of caries (Fig-5). Extra oral examination showed down-turned mouth and angular cheilitis (Fig-2).

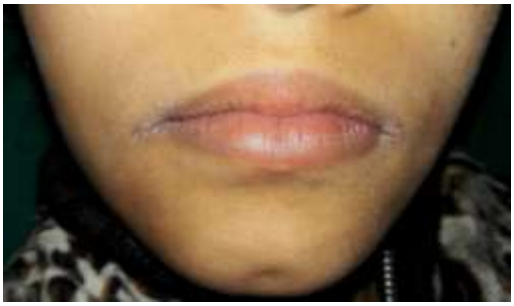

Fig-2: Down-turned mouth and angular cheilitis

In dental terms, CAD index is equal to 17. Two teeth had composite resin fillings: 37, 34 (Fig-3). Erosion, probably due to recurrent vomiting and gastroesophageal reflux, was common in most erupted teeth (Fig-3).

After a careful examination of the periodontal status by a periodontal probe, any periodontal diseases were found.

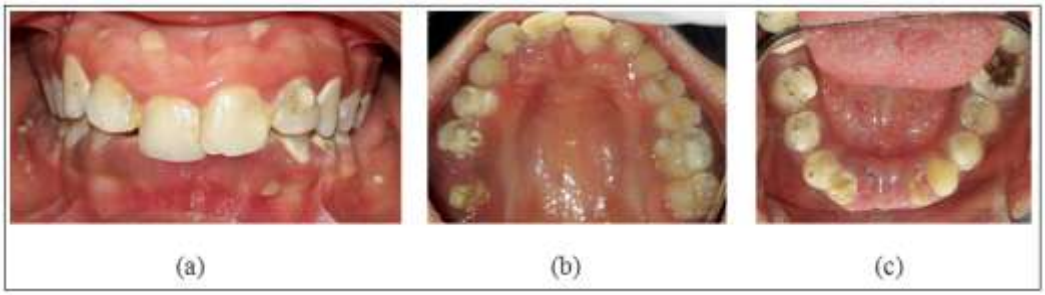

Fig-3: Intra oral examination

Careful inspection of the oral mucosal surfaces revealed oral candidiasis (Fig 3, 4), fissured tongue, macroglossia (Fig-4). Besides, Pigmented sites in the gum were found (fig-3).

For assessment of the patients' saliva secretion, whole salivary flow rate was measured in both resting and stimulated states in accordance with the method of Navazesh *et al.*, [9]. The measurement unit of the salivary secretions were expressed by gram/minute. The results of the sialometry are presented in table 1. This patient was considered Xerostomic. She suffered from oral dryness and difficulties in eating solid foods.

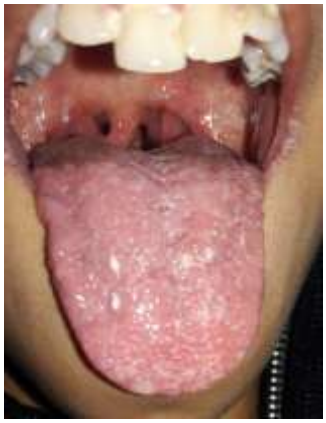

Fig-4: Fissured tongue and macroglossia

Table-1: Sialometry results of the patient

Salivary flow	
Unstimulated (grams/minute)	stimulated (grams/minute)
0.06g/minute	0.25g/minute

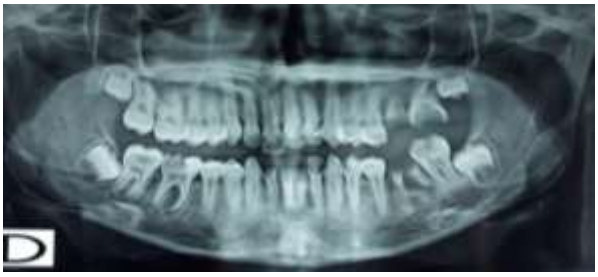

Fig-5: The orthopantomogram

DISCUSSION

Many orofacial abnormalities associate with Allgrove syndrome were reported in the literature such as: down-turned mouth with thin upper lip cleft palate, long narrow, malar hypoplasia, mandibular malocclusion, relaxed speech musculature, high gothic hard palate, cross bite, incompletely developed fungiform papillae of the tongue, atrophic tongue [4, 10-13]. In our patient, the observed orofacial abnormalities were down-turned mouth , macroglossia and fissured tongue.

The intraoral findings observed in our patient were Xerostomia, high rate of dental caries, erosion, gingival pigmentation and oral candidiasis.

In 2000, Dumic *et al.*, performed sialometry on 5 patients presenting this syndrome. All this patients

had oral dryness and reported the xerostomia as a newly recognized finding of Allgrove syndrome [12]. It is known that patient with Allgrove syndrome suffered from abnormality of automatic nervous system. This abnormality can explain the xerostomia. Besides, the innervation of lacrimal glands originates in the Superior Salivary nucleus of the brainstem, in common with the parasympathetic innervation of the submandibular and sublingual salivary glands [12]. Alacrima results in dryness of the eyes and reports suggest that an early manifestation of autonomic dysfunction exist [21]. Then Xerostomia, like alacrima, can be caused by progressive autonomic neuropathy [22] Thereafter dry mouth has been reported by others as a feature of this syndrome [3, 16, 17].

In fact, in his study patients reported, even after oesophageal dilatatin or myotomy, still have problems in swallowing could be explained partially by the reduced secretion of salivia [12].

Also dry mouth and gastric reflux can lead to high rates of dental decay and oral candidiasis [17]. Some teeth (16, 46, 31, 32, 41, 42) were too far destroyed from the decay process, and restore them was no longer indicated. This leads to a premature loss of permanent teeth. Razavi Z *et al*., speculate this premature loss to be also a feature of Allgrove syndrome [4].

As for gingival pigmentation, it can be a physiologic pigmentations caused by Addison's disease, hematologic disorders, drug induced... In Addison's disease, diffuse dark pigmentations of the oral mucosa can be explained by the deficient production of cortisol results in increased production of adrenocorticotropic hormone (ACTH) [18]. This can also be observed in Triple A syndrome due to adrenocorticotropic hormone (ACTH)-resistant adrenal insufficiency. Then this oral finding can be the first revealing in the earlier detection of the syndrome.

The management of Allgroves is multidisciplinary. Various specialties are concerned such as: endocrinology ophthalmology gastrology and obviously dental medicine.

Among the healthcare professional, the dentist has an important role in the diagnosis and management of these patients. In Fact, their dental treatment needs and assessment of the relevant intraoral complaints can be the first indication of this disease. Also the dentist have an important role in the prevention and management of dental complications associated with a poor salivary flow..

The loss of buffering capacity due to Xerostomia and gastric reflux increases the risk of caries and periodontal diseases. Prevention measures must be taken such as meticulous oral, prescription hygiene with a low sugar diet, and topically-based fluoride application for protection of the remaining teeth. Fissure sealants are also useful in these 'at-risk' groups [23]. The patients were advised for strict dental visits every 3 months [19]. Saliva substitutes may reduce discomfort during speech and mastication. Saliva substitute preferred for the patients is a mixture of 20cc 4% carboxymethyl cellulose, 1 drop of lemon oil, 60cc normal saline and 10cc glycerin [14].

The onset of Allgrove's syndrome is often at a young age and the need to visit multiple medical clinicians may make oral health care a low priority. This may delay preventive advice. However, it is vital to emphasis the importance of these measures and the dental management, along with regular oral health reviews to parents and carers even though they may already feel they have a lot to cope with.

The important of this patient's care is the preparations made for any future dental treatment. It is obligatory to contact the patient's medical specialists from the first consultation, to confirm any special precaution.

In Allgrove's syndrome where adrenal hypofunction can be variable, The patient is exposed to a syncopal risk due to stress. Acute hypoadrenalism can present with confusion, weakness, nausea, abdomen pains and signs of acute hypovolaemia with circulatory collapse. It can quickly progress to sudden loss of consciousness with rapidly falling blood pressure. Then a regime for each individual patient will depend on the proposed treatment, level of adrenal hypofunction, level of exogenous steroid supplementation and the anxiety/stress level of the patient. The type of precaution or the amount steroid supplementation required for an individual patient requires close liaison with the relevant medical specialist [20].

CONCLUSION

In conclusion, it is advised that all patients with Xerostomia and mucosal pigmentation be referred to hormonal tests and medical evaluation in looking for more signs of Allgrove.

The prevention and management of bucco dental complications associated with a poor salivary flow and gastric reflux are mandatory to limit the damage and improve the quality of life.

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