Aplasia of the Major and Minor Salivary Glands: Report of a Rare Case

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ABSTRACT

Background: Aplasia of the salivary glands, either partial or involving all the major and possibly the minor salivary glands, is a very rare cause of hyposalivation. The aim of this case report is to present a case of aplasia of the major and minor salivary glands and discuss the relevant literature.
Methods: A 23-year-old woman, with a non-contributory medical and family history was referred due to rampant caries, that could not be attributed to any obvious aetiology. No sicca symptoms, previous parotid gland swelling or general symptoms were reported. Clinically, oral mucosa dryness and extended dental erosions and caries were observed, while the orifices of the excretory ducts of the parotid and submandibular salivary glands were not evident. Unstimulated and stimulated saliva flow rates were severely diminished, while a diagnostic biopsy of the lower lip revealed absence of minor salivary glands. Detailed hematologic and immunological investigations to exclude systemic disorders were also within normal limits. Ultrasound and magnetic resonance imaging revealed the absence of all major salivary glands, confirming the clinical diagnosis of congenital aplasia of the salivary glands.
Results: Oral hygiene instructions and dietary advice were given while dental products with fluoride and saliva substitutes were administered and appropriate dental treatment was implemented. Regular dental follow-up was also advised.
Conclusions: Timely diagnosis of aplasia of the salivary glands is important, considering the detrimental effects of the absence of saliva on oral health. Management consists of the use of saliva substitutes, nutritional adaptation, maintenance of oral health and regular dental follow-ups.

Keywords: aplasia; salivary glands; xerostomia.

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INTRODUCTION

Chronic xerostomia, the subjective sensation of dry mouth, is a common symptom in the general population (10 to 46%) [1]. It accounts for 12 to 47% of elderly population and 10 to 19.3% of younger population (usually at their early 30s) [2].

In about 90% of cases, xerostomia is associated with the use of several xerostomic medications. In fact, more than 400 medications have been associated with xerostomia, the most common ones being anti-depressants, antihypertensives and antihistamines. Apart from the type of the drug, the number of medications received seems to be of major importance, since it has been estimated that the probability of xerostomia development increases 1.12 times with each medication added [1]. Less frequently, xerostomia may be caused by systemic diseases, such as diabetes mellitus and Sjögren's syndrome, or other systematic conditions, such as autoimmune thyroid disease, rheumatoid arthritis, graft-versus-host disease, viral and bacterial infections, granulomatous diseases, e.g. sarcoidosis, Parkinson's disease, and several others [2]. Congenital aplasia of the salivary glands, affecting either a subset or all the major (and possibly the minor) salivary glands, is a very rare cause of xerostomia [3]. Aplasia of the major salivary glands mainly affects the parotid salivary gland, unilaterally or bilaterally, and less frequently the submandibular salivary glands. In addition, it may often be associated with other ectodermal defects including several syndromes [4]. Hyposalivation caused by aplasia of the salivary glands may lead to several problems, such as dysphagia, dysgeusia, rampant dental caries, susceptibility to oral infections and even malnutrition and psychological problems [2]. Although congenital aplasia of the salivary glands is a rare condition, clinicians should be aware of this entity due to the detrimental effects on patient's quality of life.

The aim of this study is to present a rare case of aplasia of the major and minor salivary glands and discuss the relevant literature.

CASE DESCRIPTION AND RESULTS

A 23-year-old female, non-smoker, patient was referred by her dentist to the Department of Oral Pathology & Medicine and Hospital Dentistry (National and Kapodistrian University of Athens, Greece) on September 15th, 2014, due to rampant dental caries that could not be attributed to any obvious aetiology. The patient did not report xerostomia, xeropthalmia or general symptoms; there was no history of parotid or submandibular gland swelling. The physical examination was unremarkable while her medical and family history was non-significant.

Clinically, exfoliative cheilitis (Figure 1), extended dental erosions, rampant caries and multiple resin and sealant restorations throughout the upper and lower dentition were observed (Figures 2A, 2B). White striated lesions with features of lichenoid reaction and/or frictional keratosis were also noted on the buccal mucosa bilaterally, in contact with resin restorations and carious teeth (Figures 2C, 2D). Noticeably, it was not possible to identify the parotid papillae and their orifices on the buccal mucosa bilaterally (Figures 2C, 2D) nor the orifices of the excretory ducts of the submandibular salivary glands at the floor of the mouth (Figure 2B); further, no free saliva was present at the floor of the mouth (Figure 2B). In addition, the parotid and submandibular glands were not detected on palpation. Sialometry showed null unstimulated saliva flow rate (0 ml/5 min) and significantly reduced stimulated saliva flow rate (0.1 ml/5 min) [5]. Detailed hematologic, biochemical, and immunological investigations, were also carried out to exclude systemic disorders such as diabetes mellitus (glucose levels and HbA1C), Sjögren's syndrome (anti-SS-A and anti-SS-B antibodies), sarcoidosis (serum angioconverting enzyme, calcium levels etc.), but they were within normal limits [2]. A diagnostic biopsy of the lower lip was attempted in order to further investigate the possibility of Sjögren's syndrome, but it proved fruitless, since no minor salivary glands were found. With a possible diagnosis of congenital aplasia of the salivary glands, imaging was performed; both ultrasound (U/S) and magnetic resonance imaging (MRI) revealed the absence of all major salivary glands (Figure 3), confirming the clinical diagnosis of congenital aplasia of the major salivary glands.

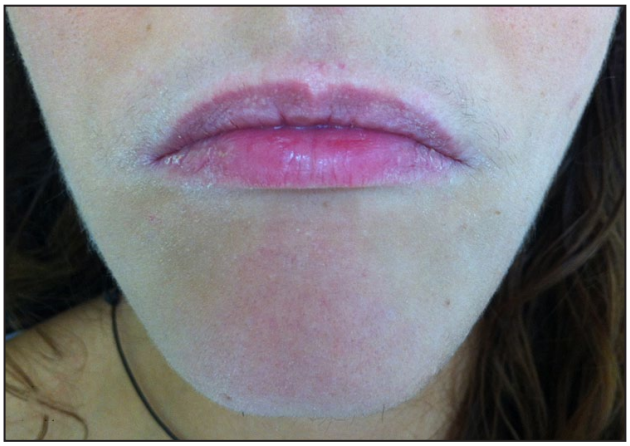

Figure 1. Patient's photograph showing exfoliative cheilitis.

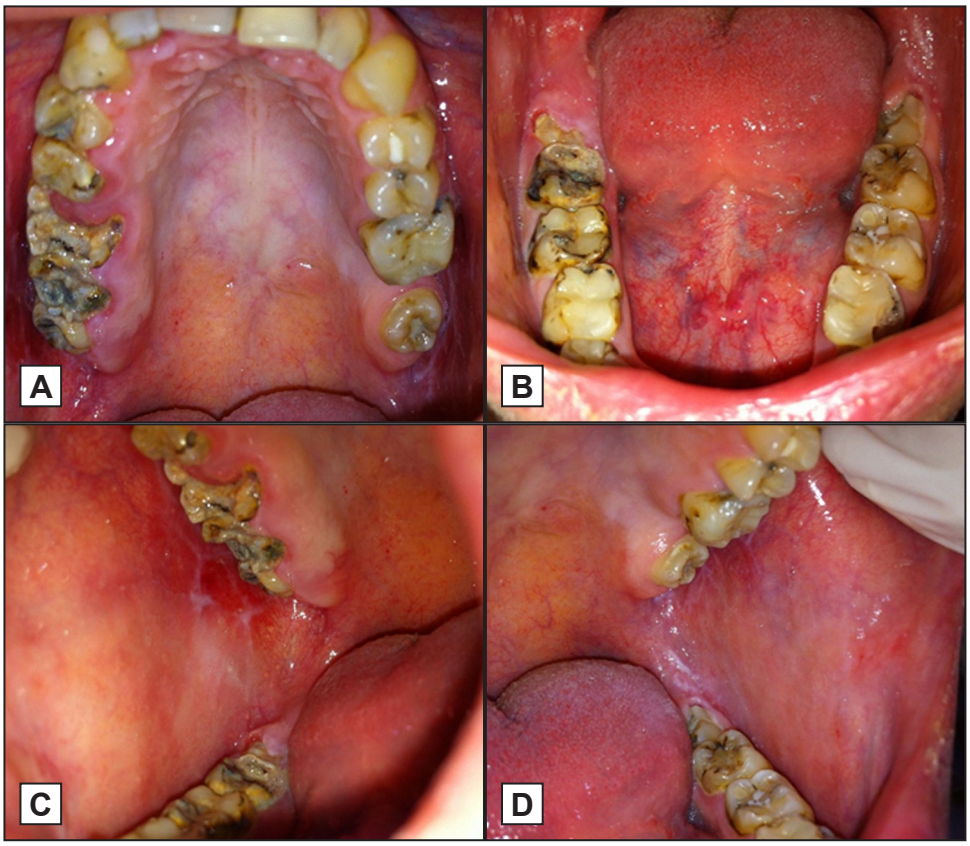

Figure 2. Photographs showing findings of clinical examination of the oral cavity.
A and B = extended dental erosions, rampant dental caries and multiple resin and sealant restorations are observed. Note the absence of free saliva at the floor of the mouth; also, the orifices of the Wharton's duct of the submandibular glands are not discerned (B).
C and D = white striated lesions of the buccal mucosa bilaterally in contact with resin restorations and carious teeth are noted; there is absence of the parotid papillae of the Stenson's ducts.

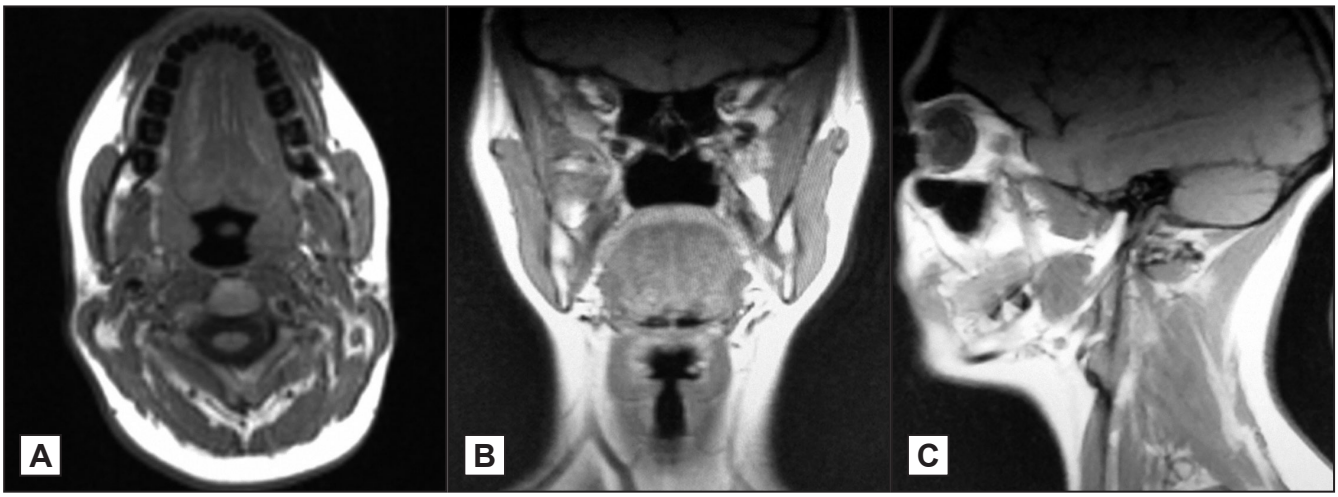

Figure 3. Magnetic resonance imaging examination revealing the absence of major salivary glands: A = axial; B = coronal; C = sagittal.

There were neither other dental abnormalities nor skin, hair or nail defects that could imply the presence of a syndrome. The patient was informed of the nature of the condition and the risks and complications associated with chronic xerostomia. Daily dental products with fluoride and saliva substitutes were administered and advice for nutritional modification was given. In addition, the patient received appropriate dental treatment and was advised for regular dental prophylaxis and follow-up.

DISCUSSION

The term xerostomia describes the subjective sensation of oral dryness, which is frequently,

but not always, caused by an actual salivary gland dysfunction with ensuing decrease in saliva flow (hyposalivation). In the latter case, the aetiology is multifactorial; in most patients, xerostomia is a drug-induced condition while, less frequently, it may be associated with systemic diseases, such as diabetes mellitus, Sjögren's syndrome, sarcoidosis, human immunodeficiency virus-infection etc., as well as with head and neck radiation [6,7]. However, xerostomia due to a congenital lack of salivary glands is very rare. Salivary gland aplasia was first described in 1885 by Gruber [8]. Since then, only a few cases of aplasia, incomplete aplasia or hypoplasia have been reported in the literature [3,4,9-19]. Pham Dang et al. [16] in 2010 reported 35 cases of agenesis of the major salivary glands while in a more recent literature review by Kuralt et al. [4], 148 radiologically confirmed cases of salivary gland aplasia were found; the median age of patients at the time of diagnosis was 21 years old and the majority were females (52.1%), as in our case who concerned a 23-year-old woman.

Salivary glands develop from the ectoderm between the sixth and eighth weeks of gestation. The parotid glands are the first to develop, followed by the submandibular glands; the sublingual glands begin their development later, at about the eighth week of gestation, while the minor salivary glands develop last. The ectodermal invagination forms a tubular duct plunging into the mesenchyme, while preserving a ventral opening in the oral cavity. The dorsal segment differentiates to form the gland and the ventral tract becomes the secretory duct [11]. However, a small part of the submandibular and the sublingual salivary glands may also grow from both the ectoderm and endoderm [3,10].

Reported cases of major salivary gland (ALSC) aplasia refer either to the parotid or the submandibular salivary glands or both; the former are involved more frequently, while aplasia of the submandibular glands is rather uncommon [10]. It should be mentioned that, in most reports, there is not enough information provided for the status of the sublingual salivary glands [11]. Major and minor salivary glands share the same ectodermal origin and as such, embryologic arrest of development could affect both types of glands. Unfortunately, there are no available data in the literature concerning minor salivary gland aplasia, either alone or in combination with aplasia of the major salivary glands, as in our case. Although it was not possible to confirm the complete absence of the minor salivary glands in our patient, be it that they are numerous and widely distributed throughout the oral mucosa, at least a paucity of them was evident since no glands were found during the biopsy procedure performed in the lower labial mucosa to rule out Sjögren's syndrome.

The exact pathogenesis of aplasia of the salivary glands is unknown and may occur either *de novo* or occur within a hereditary background [12]. Partial or unilateral aplasia of the major salivary glands may be associated with other ectodermal defects, more commonly abnormalities of the lacrimal apparatus [16,17]. Dental hypodontia and defects on hair, skin, and nails [10,12] may also be observed. None of the above features were noted in our patient. It has also been associated with several syndromes, such as Down, Treacher-Collins, hemi-facial microsomia, cleft lip and palate and Klinefelter syndrome [10,18].

Aplasia of the major salivary glands is frequently present in the context of aplasia of the lacrimal and major salivary gland, which is a rare autosomal dominant disorder. Its cause is a loss of function mutation on the fibroblast growth factor-10 gene [10]. The severity of lacrimal involvement varies from aplasia to hypoplasia and atresia of the nasolacrimal duct and absence of the lacrimal puncta [19]. Clinical examination reveals xerostomia, dental caries and irritable eyes.

Apart from ALSC, aplasia of the major salivary glands may be part of the lacrimo-auriculo-dento-digital syndrome (LADD) or else Levy-Hollister syndrome, which was first described in 1973 [20]. LADD includes nasal lacrimal duct obstruction, aplasia or hypoplasia of major salivary glands, cup shaped ears associated with a sensory or mixed deafness, small and sharp lateral incisors and agenesis of the upper lateral incisors, clinodactylia of the fifth finger and/or phalanx abnormalities [11]. In fact, Kuralt et al. [4] reported in their review that half of the cases of salivary gland aplasia were combined with craniofacial malformations and hereditary syndromes. In our case, none of the above findings were observed and the family history was not significant, so that aplasia of the salivary glands was considered an isolated feature.

Aplasia of the salivary glands results in hyposalivation, the severity of which varies between individuals, based on the number and type of the affected salivary glands [17]. Parotid glands are responsible for stimulated saliva secretion, which enables the normal functions of chewing, swallowing, speaking etc., while the submandibular/sublingual and minor salivary glands are responsible for the constant secretion of unstimulated saliva, ensuring wetness of the oral mucosa and the many positive effects (e.g., anti-microbial action) of saliva on oral health.

Hyposalivation increases the risk for oral mucosa infections, such as candidiasis [3]. In addition, it causes increased mucosal irritation and/or burning, difficulties with chewing, swallowing and speech, decreased taste acuity and severe dental caries [12]. However, patients with salivary gland aplasia do not always complain about hyposalivation, since they have never felt a hydrated mouth and may not be in a position to appreciate the difference, as in our case. On the other hand, dentists should be vigilent in recognizing hyposalivation and xerostomia and, especially in cases of young patients and severe xerostomia, prompt management (i.e. substitutional treatment) and further thorough investigation should be implemented. Unfortunately, there is insufficient awareness of general dentists about this rare entity and frequently patients remain undiagnosed for a long time, as in our case in which the patient was diagnosed at the age of 23.

Dryness of the oral mucosa and rampant caries are common, but the complete absence of the orifices of the excretory ducts of the parotids (Stenson's duct) and the submandibular glands (Wharton's ducts) has been rarely described, but, when present, it should raise the suspicion of an underlying aplasia, similar to our case [4]. Differential diagnosis encompasses the frequent causes of xerostomia, including diabetes mellitus, Sjögren's syndrome and xerostomia associated with medication. To reach the final diagnosis, a thorough medical and dental history is needed; biopsy of the minor salivary glands and blood and serum tests to rule out systemic diseases may also be required [10]. Genetic testing is not readily available in most clinical settings. Eventually, imaging with U/S, MRI or computed tomography is necessary to confirm the absence of salivary glands. In particular, MRI is thought to be the most appropriate imaging modality to evaluate and rule out other possible structural defects, especially in cases of suspected ALSC [19].

Patients with aplasia of the major salivary glands should undergo regular dental follow-ups because of the hyposalivation-associated side effects involving the dentition, as apparent in our case. Oral hygiene measures, daily fluoride toothpaste and nutritional adjustment are recommended. In order to manage xerostomia, saliva substitutes are administered, such as glycerine and lemon, lactoperoxidase, glucose oxidase and xylitol [3,10,12]. However, these agents may be of limited use in cases where stimulated saliva flow rate is close to zero, like in our case. In these severe cases, the treatment of choice is mainly the use of artificial saliva. Regular dental prophylaxis and follow-ups to detect and manage possible dental, periodontal and oral mucosal complications are also strongly recommended.

CONCLUSIONS

Pronounced dental and oral findings of hyposalivation in young patients are not common and should be thoroughly assessed, since appropriate investigation allows for a timely diagnosis of salivary gland aplasia. Patients should be given appropriate instructions and advised for regular dental prophylaxis and follow-ups in order to maintain optimal oral and dental health.

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All authors contributed to the study conception and design, acquisition of data, or analysis and interpretation. All authors revised critically and approved the final manuscript.

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