Case Report

Congenital Aplasia of the Major Salivary Glands: Literature Review and Case Report

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Abstract: *Congenital aplasia of the major salivary glands is rare, and there have been few cases of the condition reported to date. In many cases, absence of the salivary glands is associated with syndromes involving the ectodermal tissues. The xerostomia encountered in affected children is usually associated with increased risk for caries and infections of the soft tissues. The purpose of this paper was to describe the case of a 10-year-old boy with bilateral aplasia of the submandibular and parotid salivary glands and the preventive and restorative treatment rendered. This case study demonstrates the importance of timely diagnosis of this condition in order to prevent the serious oral complications from xerostomia. (Pediatr Dent 2011;33:113-8)*
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The parotid gland is the first salivary gland to commence development at the sixth week of intrauterine life, followed by the submandibular gland during the seventh week and sublingual gland during the eighth week.[1] The minor salivary glands develop last, between the ninth and 12th week.[1] Although it is well established that the parotid and minor salivary glands are derived from the ectoderm, it is thought that the epithelia of the submandibular and sublingual glands could potentially be derived from either the ectoderm or the endoderm.[1]

Developmental abnormalities of the major salivary glands, including agenesis and total lack of function, are rare.[2] Such abnormalities can involve any single gland or a group of glands, either unilaterally or bilaterally.[1] Aplasia of the salivary glands can occur either in isolation or in association with other developmental anomalies of the first branchial arch such as hemifacial microsomia, Treacher Collins syndrome, and multiple facial anomalies.[1] In a review of the literature, Matsuda et al.[3] mentioned 43 case reports of congenital salivary gland aplasia since the first reported case in 1885; 9 of the reported cases were classified as bilateral congenital aplasia of the parotid and submandibular glands.[3] As shown in Table 1, approximately 5 cases reporting bilateral congenital aplasia of both the parotid and submandibular glands have been reported since 1999.[4-8]

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An association between major salivary gland aplasia or hypofunction and other ectodermal defects—such as abnormalities of the lacrimal apparatus, skin conditions, dental hypodontia, and affected hair and nails—have also been noted in a number of case reports.[1,6,7,9-11] Salivary gland aplasia may also be a component of lacrimo-auriculo-dento-digital (LADD) syndrome, which is characterized by: hypoplasia; aplasia or atresia of the lacrimal system; deafness and ear malformations; and dental and digital anomalies.[12] The present authors have previously reported a case with congenital absence of salivary glands and lacrimal ducts, where congenital dysfunction of the major salivary glands resulted in severe tooth wear and dental erosion.[8]

Saliva plays a crucial role in regulating and maintaining the integrity of oral hard and soft tissues. The primary constituents of saliva are water, proline-rich glycoproteins, and electrolytes.[13] These components enhance taste, speech, and swallowing and facilitate irrigation, lubrication, and protection of the mucous membranes in the upper digestive tract.[14] Additional physiological functions of saliva, together with its various components such as mucin, histatins, lysozyme, and lactoferrin, provide antimicrobial and buffering activities protecting against dental caries and soft tissue infections.[13,15] Lack of function of salivary glands has the potential to disturb the homeostasis of the oral hard and soft tissues as well as the general health of the affected individual. Such effects include rampant caries, periodontal disease, mucosal infection, diminished mucosal wound healing, digestive disturbances, difficulty in speech and mastication, and an increase in opportunistic oral infections.[5,16,17] Furthermore, dental erosion is likely to be associated with xerostomia, although this complication has not been well recognized in the dental literature.[8]

Table 1. CASES OF SALIVARY GLAND APLASIA REPORTED FROM

Author	Year	Findings	Other associations
Ferreira et al.[24]	2000	• (Case 1) Bilateral aplasia of parotid glands • (Case 2) Bilateral aplasia of submandibular salivary glands • (Case 3) Bilateral aplasia of parotid glands	Aplasia of lacrimal puncta NA* NA
Young et al.[8]	2001	Bilateral aplasia of parotid and submandibular salivary glands	Absence of lacrimal ducts
Hodgson et al.[6]	2001	Bilateral aplasia of parotid and submandibular salivary glands	NA
Fracaro et al.[20]	2002	Absence of bilateral submandibular salivary glands and reduced functioning of parotid glands	Lack of sweat
Singh et al.[9]	2004	Bilateral aplasia of submandibular salivary glands and small parotid gland	Ectodermal dysplasia
Ferguson et al.[25]	2004	Bilateral aplasia of parotid salivary glands	Down syndrome
Martn-Granizo et al.[26]	2004	Unilateral agenesis of parotid salivary gland	NA
Inan et al.[23]	2006	Bilateral aplasia of parotid salivary glands	Lacrimo-auriculo-dento-digital syndrome
Antoniades et al.[27]	2006	Bilateral aplasia of parotid salivary glands	NA
Mandel[4]	2006	Bilateral aplasia of parotid and submandibular salivary glands	NA
Kwon et al.[7]	2006	Bilateral aplasia of parotid and submandibular salivary glands	Lacrimal gland agenesis
Srinviasan et al.[28]	2006	Unilateral submandibular gland aplasia and ipsilateral sublingual gland hypertrophy	NA
Heath et al.[5]	2006	Bilateral aplasia of parotid and submandibular salivary glands	NA
Güven et al.[16]	2007	Significant reduction in bilateral submandibular gland function	Rosai-Dorfman disease
Al-Talabani et al.[29]	2008	Bilateral agenesis of parotid salivary glands	NA
Mathison et al.[2]	2008	Bilateral submandibular gland aplasia and hypertrophy of sublingual glands	Previous Hodgkin lymphoma
Present study	2009	Bilateral aplasia of parotid and submandibular salivary glands	NA

* NA=no other association reported.

Patients with congenital xerostomia often do not complain of dry mouth or taste disturbances when compared to patients with acquired xerostomia.[18] Thus, many cases of congenital xerostomia may go unnoticed in children, even though the signs and symptoms have been present from birth. Hence, it is prudent to assess salivary function and xerostomia in suspected cases of salivary gland aplasia as early as possible. This allows appropriate preventive measures and advice to be implemented to avert significant damage to the dental soft and hard tissues.[18]

Investigations commonly utilized for salivary gland disease include radiography, sialography, ultrasonography, computerized tomography, and magnetic resonance imaging, which mainly demonstrate the anatomical structures of the major salivary glands.[6] Scintigraphy provides an accurate assessment of gland function and to a lesser degree salivary gland structure.[19]

The purpose of this report of a child with congenital absence of the salivary gland was to demonstrate the general and oral complications of the condition as well as the tests which helped in the diagnosis of the condition by pediatric dentists.

Case report

The patient, a 10-year-old male, was referred by his general medical practitioner for review of his persistent dry mouth since early childhood. He had not been previously diagnosed for any salivary gland disorders. His referring doctor indicated that he was otherwise healthy and was not taking any medications. The patient was the product of a normal pregnancy and was born 4 weeks premature, with a birth weight of 2,718 g (95.86 oz). There was no family history of xerostomia or extensive caries, and 2 older male siblings were unaffected.

At 4 years of age, the patient was referred to a major children's hospital for removal of all his severely carious primary teeth under general anaesthesia. Since dental treatment under general anaesthesia at 4 years of age, the patient had no further dental treatment until presentation to our facility.

His parents reported that he had a history of dry mouth since birth and a total absence of saliva and spitting. Additionally, severe dysphagia was present, and the child needed to drink water constantly. Although the patient appeared to have normal speech at the time of presentation, the parents reported that he had undergone many years of speech therapy. The patient's mother reported the presence of tears during crying and nasal discharge was present during upper respiratory tract infections. Sweating was reported as normal. The patient wore corrective glasses for reading. His mother also mentioned that he had a minor auditory deficit, was easily distracted, and had experienced some learning difficulties at school.

Examination. At 10-years-old, the patient had a height of 147 cm (60th percentile) and weight of 33 kg (25th percentile). An extraoral examination showed weeping eczema of the skin, which was most obvious behind both ears (Figure 1). The mother reported its occurrence on a regular basis around the elbow, knee, and groin regions. The hair and eyebrows were thin. There was frontal bossing, and a brachycephalic facial appearance was noted. The nails on his toes were dystrophic, presenting with ridging and splitting of the nail plates (Figure 2). On palpation, both the parotid and submandibular contours appeared normal and no obvious tissue deficit in these regions could be felt. Facial lymph nodes were palpable but unfixed. There was mild bilateral angular chelitis.

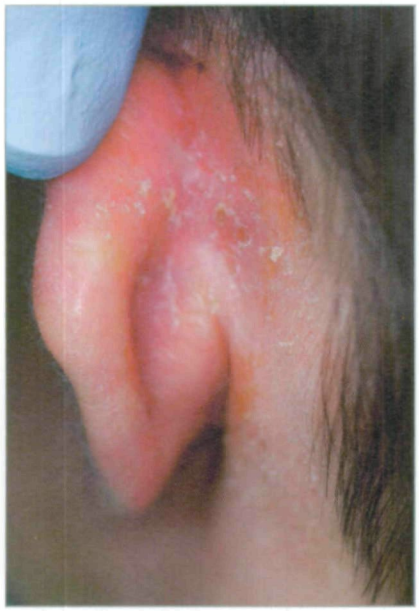


Figure 1. Severe weeping eczema of skin behind the left ear.

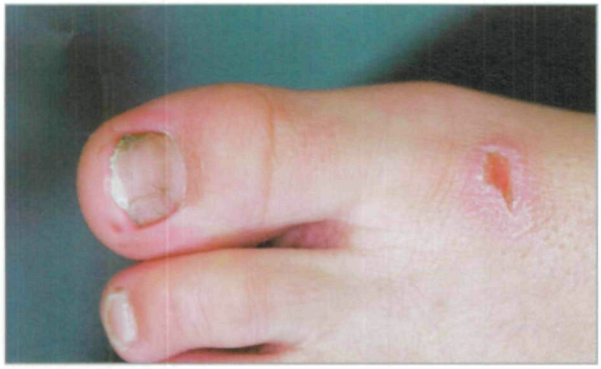


Figure 2. Toenail of the left foot showing dystrophic appearance with ridging and splitting.

Intraorally, there was profound lack of saliva. The patient presented with a low grade generalized mucosal atrophy, which extended to the filiform papillae on the dorsum of the lobulated and fissured tongue (Figures 3a and 3b). Mild marginal gingivitis was present around most of the erupted teeth.

At the time of initial consultation, the teeth present were the permanent maxillary and mandibular first molars, maxillary and mandibular central and lateral incisors, and the mandibular left permanent canine. The incisal and molar relationships were normal and Angle's Class I (Figure 4). As shown in Figure 4, there were enamel opacities as well as horizontal grooves of missing enamel on the labial surfaces of the maxillary central and all mandibular incisors. Caries were present on the permanent molars, the mandibular left permanent central and lateral incisors and the maxillary left permanent central incisor. A panoramic radiograph showed thirteen permanent teeth to be present, which were the 4 first permanent molars, 8 incisors and the left mandibular canine (Figure 5). There was evidence of tooth erosion such as the "cupping" defect seen on the mesiobuccal cusp of the maxillary right first permanent molar (Figure 6). Plaque deposits were noted on most surfaces of the teeth.

Further investigations. Based on the clinical history of xerostomia since birth, the authors recommended investigations for salivary gland disorders. He was referred to a radiology clinic for a sodium pertechnetate (Tc-99m) scintiscan, which was undertaken following IV administration of Tc-99m pertechnetate. A dynamic study over a 60-minute period was performed using an anterior projection. Lemon juice was given orally at 40 minutes to stimulate saliva secretion. Following the dynamic study, planar anterior, posterior, and lateral images were also exposed. Throughout the duration of the radiographic study, there was absence of detectable activity in the parotid or submandibular salivary glands, which was suggestive of aplasia of the salivary glands (Figure 7). By contrast, normal physiological activity was observed in the thyroid and blood pool activity in the structures

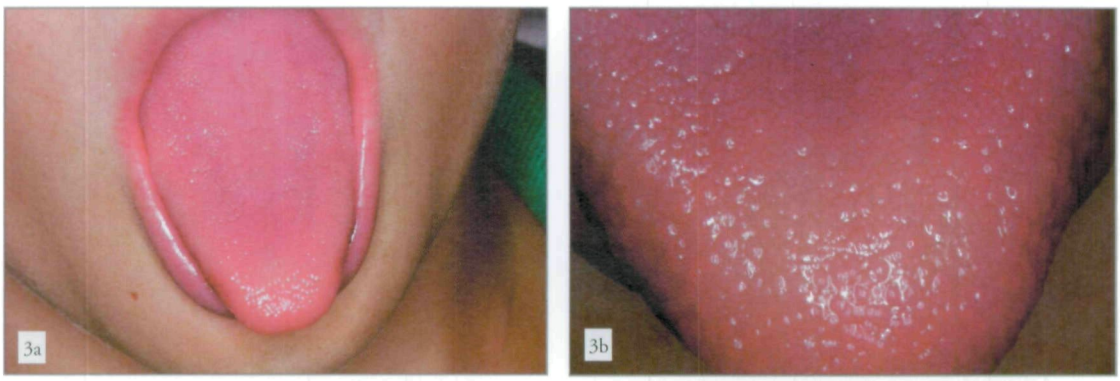
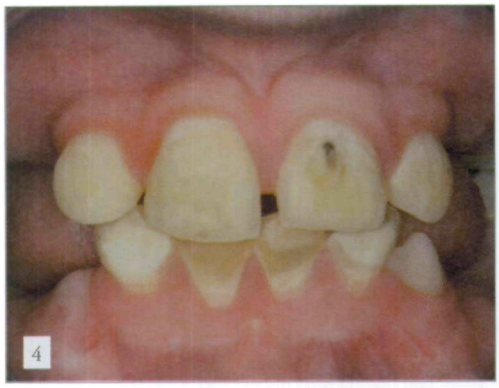
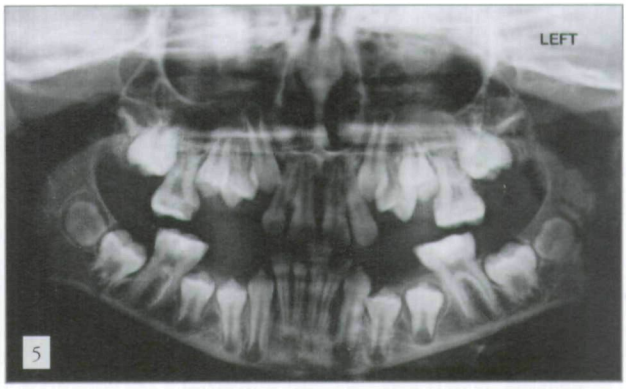
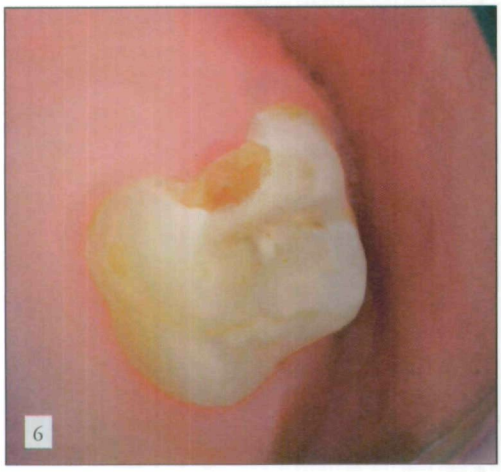


Figure 3. (a) Dorsal surface of the tongue, showing fissuring and lobulation of the mucosa; (b) Dorsum of the tongue showing low-grade generalized mucosal atrophy which extends to the filiform papillae.







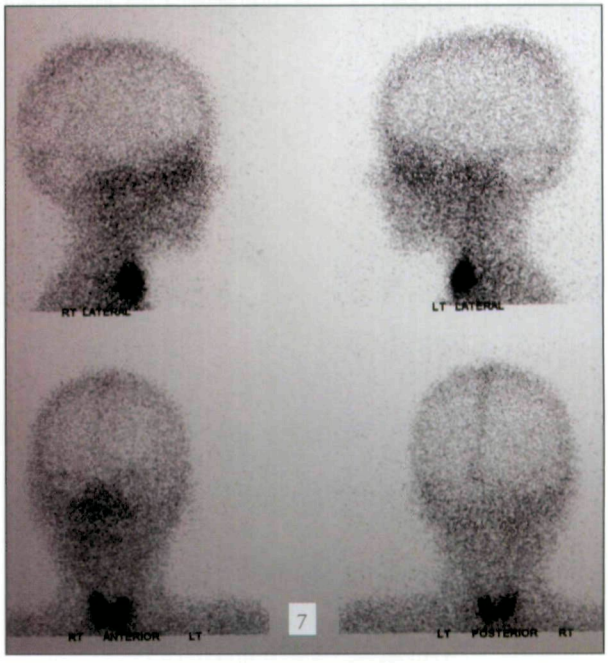


Figure 4. Anterior teeth of patient showing enamel with a hypomineralized and discolored appearance and horizontal bands of missing enamel and the presence of plaque and caries.
Figure 5. Orthopantomograph showing the presence of 32 permanent teeth.
Figure 6. Permanent maxillary right molar of the patient showing erosion in the mesiobuccal cusp area and caries on the mesial surface.
Figure 7. Dynamic radiographic images following intravenous injection of Tc-99m pertechnetate, showing absence of activity in the parotid and submandibular salivary glands, in contrast to the thyroid gland where marked activity was present (seen as dark patches).

of the head and neck. Referral to a medical geneticist for further follow-up was recommended but not undertaken as the parents did not wish to do so.

Management. An intensive preventive regime including oral hygiene, dietary evaluation and monitoring, nightly application of a casein phosphopeptide-containing product (CCP-ACP, Tooth Mousse, GC Corp, Tokyo, Japan), and daily 0.05% neutral sodium fluoride mouthrinse was recommended. In addition, professional 1.23% neutral sodium fluoride application was recommended. Daily use of sugar-free chewing gum was encouraged. A saliva substitute, Biotene Oralbalance gel (Biotene, Anglian, UK) with its main constituents being glycerate polymer base, lactoperoxidase, glucose oxidase and xylitol was recommended. The patient's present habit of continuous sipping of water was encouraged, and extensive oral hygiene reinforcement was implemented.

All carious lesions were restored using a glass ionomer base, followed by stainless steel crowns for the posterior teeth and composite resin for the anterior teeth. During the restorative procedure, the dentin was found to be very soft and suggestive of poor mineralization. Fissure sealants were placed on the occlusal surfaces of unrestored permanent molars. Following the completion of the restorative procedures, the patient was placed on 3-month recalls and annual radiographic examination.

An orthodontic consultation was sought regarding conservation of arch perimeter. Due to the patient's high caries risk status and inability to tolerate an intraoral appliance, orthodontic space maintainers were not recommended.

Discussion

Early identification of congenital absence of major salivary glands or salivary hypofunction is crucial for timely institution of preventive care and home regimes to prevent the onset of rampant caries in affected children. As the clinical presentations of salivary gland aplasia can vary depending on the

number of missing glands and their relative contribution to whole saliva, symptoms can range from negligible to profound and persistent dry mouth.[3]

Although patients with salivary gland aplasia are treated symptomatically, preventive strategies offer protection from rampant dental caries and early tooth loss. Artificial saliva sprays are useful for providing symptomatic relief for patients with salivary gland aplasia. Fluoride-containing sprays (eg, Saliva Orthana, Nycomed, Zurich, Switzerland) have been suggested as the preferred choice as most of the other preparations are acidic with a demineralizing effect on teeth.[18] The need for frequent administration of the salivary substitutes and their failure to mimic the physiological variation in salivary flow have been reported to cause long-term compliance problems and, thus, should be incorporated into the treatment plan with a degree of caution.[6]

Utilization of 0.05% neutral sodium fluoride mouthrinse nightly, oral hygiene instruction, and dietary evaluation are effective strategies to prevent caries associated with severe xerostomia.[5,17,20] Casein phosphopeptide-containing products, such as Tooth Mousse and chewing gum, are also promising for caries prevention.[21] Prevention of oral infections is another important consideration, as xerostomia predisposes the patient to increased risk to microbial infections. The patient should be given advice regarding prompt treatment of oral infections such as candidiasis.

Timely definitive diagnosis is crucial to ensure the institution of an effective treatment plan focused on preventive dentistry. Such an approach involves a thorough history-taking and examination of the patient, followed by referrals to other specialists for diagnostic tests. In the present case, radiographic imaging was fundamental in the detection of salivary gland hypofunction. Salivary gland scintigraphy with Tc-99m pertechnetate, first introduced by Börner et al. in 1965, is a useful technique for diagnosis of salivary gland disorders and dysfunction.[22] The test involves intravenous administration of a short-lived gamma-radiation-emitting isotope of Technetium (Tc-99m). Tc99m binds to the Na-K-Cl membrane transport system of the acinar cells of the salivary gland. This is followed by images taken with a gamma camera at appropriate intervals to carry out a dynamic study of the salivary glands, measuring the amount of radiation output from the tissue that directly correlates with the tissue uptake.[5,18] Regarding the salivary glands, no uptake correlates to absence of functional salivary tissue.[5] This technique provides valuable information on the functional and, to a lesser degree, the morphological and topographical status of the salivary glands.[16] In general, the patient's compliance, amount of radiation, and purpose of the investigation are important considerations in deciding the mode of investigation chosen.[5]

Computer searches employing the POSSUM database (Murdoch Children's Research Institute, Victoria, Australia) did not reveal a syndrome that can be fully matched with the clinical features seen in the present case. The patient's abnormalities of the salivary glands, skin, hair, and nails, however, resemble the clinical presentations of conditions associated with ectodermally derived tissue disorders. Of these, the closest matches are probably: LADD or Levy-Hollister syndrome of lacrimal system defects; "cup"-shaped ears; conductive or sensorineural deafness; enamel defects/hypodontia; radial and digital defects; and renal anomalies. Despite the lack of lacrimal, digital, and renal involvement, it is likely that this case is a variant of the LADD syndrome based on the presence of salivary gland aplasia, hearing impairment, and enamel defects.[23] The skin and nail defects suggest links with other ectodermally derived conditions although the presence of sweating excludes syndromes associated with hypohidriosis.[20] Acquired conditions such as the Rosai-Dorfman disease[16] are also excluded based on history and the radiological appearance of the salivary glands.

In conclusion, the present case report demonstrates the importance of early recognition of xerostomia and definitive diagnosis of hypofunction and/or aplasia of the major salivary glands. Patient education and an effective preventive oral regimen, together with regular professional monitoring, are crucial for maintaining the long-term oral health of affected individuals.

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