Clinical Manifestations and Oral Findings in Fraser Syndrome

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ABSTRACT

This article is the first known case report of Fraser syndrome in the dental literature. Its purpose was to present the clinical manifestations, oral findings, and dental treatment of a 14-year, 10-month-old female patient. Fraser syndrome is a rare recessive autosomal genetic disorder characterized by multisystemic malformation, usually comprising cryptophthalmos, syndactyly, and renal defects. The child presented with: (1) hydrocephaly; (2) face asymmetry; (3) low-inserted ears; (4) flat nose bridge; (5) cryptophthalmos; (6) bilateral absence of eyeballs; (7) hypertelorism; (8) syndactyly on the left fingers and toes; (9) skeletal defects; and (10) lower limb asymmetry. The intraoral examination revealed: (1) complete primary denture; (2) malocclusion; (3) tooth crowding; (4) ogival palate; (5) normal labial frena; (6) absence of lingual frenum (not compromising the tongue movements); (7) parched lips; (8) supragingival calculus adhered to all tooth surfaces; and (9) moderate gingivitis. The dental treatment consisted of periodic monitoring of the patient's oral health status and supragingival scaling associated with topical applications of 0.12% chlorhexidine digluconate gel at 2-week intervals to reduce gingivitis. (J Dent Child 2007;74:231-5)

KEYWORDS: FRASER SYNDROME, ORAL FINDINGS, TOOTH ANOMALIES

Fraser syndrome is a rare genetic disorder with a recessive autosomal pattern of inheritance with a reported incidence of consanguinity ranging from 15%[1] to 25%.[2] It was first reported in 1962 by George Fraser,[3] who identified 2 siblings bearing cryptophthalmos associated with multiple anomalies. The primary manifestations of Fraser syndrome are: cryptophthalmos (congenital partial or total absence of the eyelids), hand and foot syndactyly, and genital anomalies.

Secondary manifestations may also occur, specifically: (1) congenital nose; (2) ear; (3) larynx malformations; (4) cleft lip/palate; (5) skeletal defects; (6) umbilical hernia; (7) renal agenesis; and (8) mental retardation.[1,2,10] The diagnosis is based on the presence of at least 2 primary and 1 secondary characteristic or, alternatively, 1 primary and at least 4 secondary characteristics.[1]

Two new genes, Fras1 and Frem2, have been recently identified as causing Fraser syndrome in humans. Fras1, Frem2, Grip1, and Qbrick/Fren1, respectively, have been identified as the mutative genes in bl (blebbed), my (myelencephalic blebs), eb (eye blebs), and heb (head blebs) of rats.[4-9]

Cryptophthalmos is encountered in 85% of Fraser syndrome patients. In 72% of these cases, there is bilateral involvement.[1] Cryptophthalmos was first noted by Pliny the Elder in the first century A.D., who described a family of 3 children born with a membrane over the eye. In more modern times, the first report of cryptophthalmos with additional malformations was attributed to Zehender.[11]

Oral manifestations associated with this syndrome are ankyloglossia[10,12-14], tooth crowding[13], fusion of primary teeth[15,16], malocclusion[13,17], hypoplastic teeth[13,17], ogival palate[2], and cleft lip/palate.[2,18] A previous clinical paper[19] reported other manifestations associated with Fraser syndrome, including: delayed dental development; overretention of primary teeth; agenesis of second premolars;

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microdontia of primary molars; and formation of a wide fibrous band in the vestibular mucosa.

This article is the first known case report of Fraser syndrome in the dental literature. Its purpose was to present the clinical manifestations, oral findings, and dental treatment in a young girl diagnosed with Fraser syndrome.

CASE REPORT

A 4-year, 10-month-old female was brought to the pediatric dentistry clinic at the School of Dentistry of Araraquara, Brazil for dental treatment in December, 2004 with the chief complaint of halitosis and difficulty in performing oral hygiene. During the clinical interview, the mother reported that the girl had Fraser syndrome and was under medical, speech therapy and physical treatment. The mother's grandparents were consanguineously related, and there is a history of Moebius syndrome in the family.

The patient had been subjected to several surgical procedures on the right leg because of skeletal malformations and also in the eyes for implantation of an ocular expanding device. She was not under any systemic drug therapy and, according to her mother, had no involvement of vital organs, but presented with a certain level of mental deficiency.

The child used pacifiers up to the age of 3 and was fed using nursing bottles exclusively. According to the mother, the child had masticatory problems and her diet consisted basically of cow's milk-based infant formulas and honey or yogurts, seldom including legumes and vegetables.

In the first clinical evaluation, the child's height was 96 cm (<third percentile; 50th percentile for 3-years, 2-months-old) and her weight was 13.7 kg (third percentile; 50th percentile for 2-years, 11-months-old), according to the World Health Organization.[20] Physical examination revealed hydrocephaly, face asymmetry, low-inserted ears, flat nose bridge, cryptophthalmos, bilateral absence of eyeballs, hypertelorism, syndactyly on the left fingers and toes, skeletal defects, and lower limb asymmetry (Figures 1 and 2). It was also observed that the child had mental, auditory, visual, communication, and locomotion problems. Nevertheless, her mother reported that no specific assessment for these alterations had been performed. Also observed were mouth-breathing, parafunctional habit of occluding the arches repeatedly, hypertrophy, and tension on the masseter muscle.

The intraoral examination showed:

1. complete primary denture;
2. malocclusion;
3. tooth crowding;
4. ogival palate;
5. normal labial frena;
6. absence of lingual frenum (not compromising the tongue movements);
7. parched lips;
8. supragingival calculus adhered to all tooth surfaces; and
9. moderate gingivitis.

The aspect of macroglossia was due to the narrowing of the maxillary and mandibular dental arches (Figures 3 and 4).

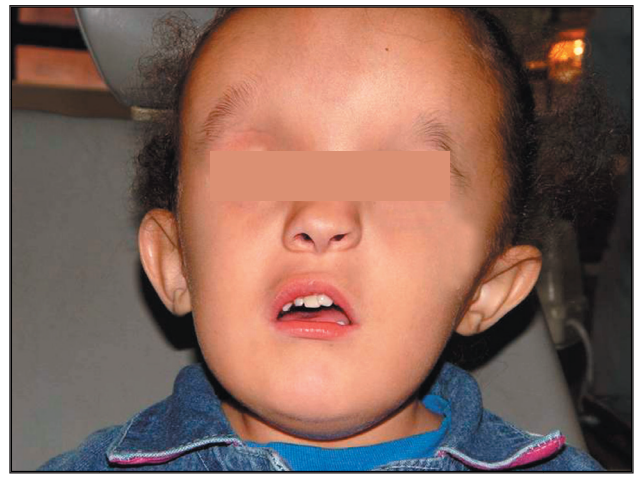

Figure 1. Facial characteristics of Fraser syndrome: hydrocephaly, asymmetrical face, low-inserted ears, flat nose bridge, cryptophtalmos, bilateral absence of eyeballs and hypertelorism.

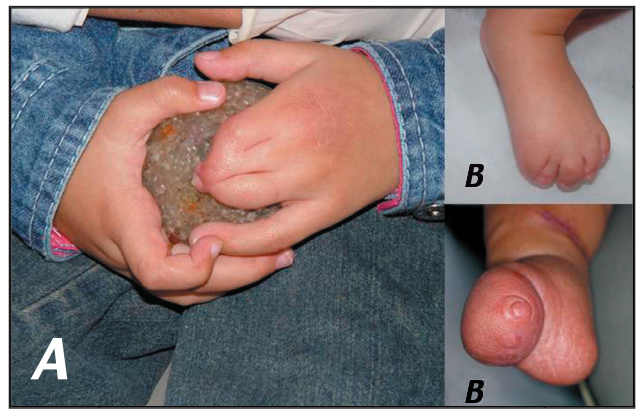

Figure 2. Syndactyly on the left fingers (A) and toes (B).

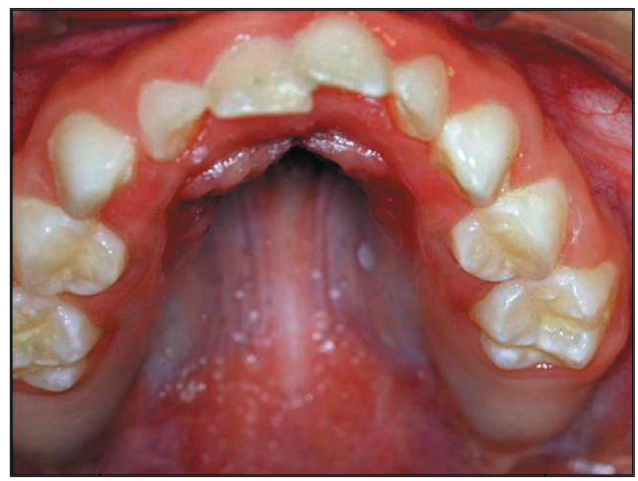

Figure 3. Tooth crowding, ogival palate, supragingival calculus and moderate gingivitis.

A periapical radiograph was taken from the area suspected to be decayed, but no carious lesions were observed. The radiograph revealed the presence of the permanent tooth germs in this area (Figure 5). The permanent right mandibular first molar had two thirds of its crown completed, while the crown of the second premolar was in its initial stage of calcification. This indicated a delay in the

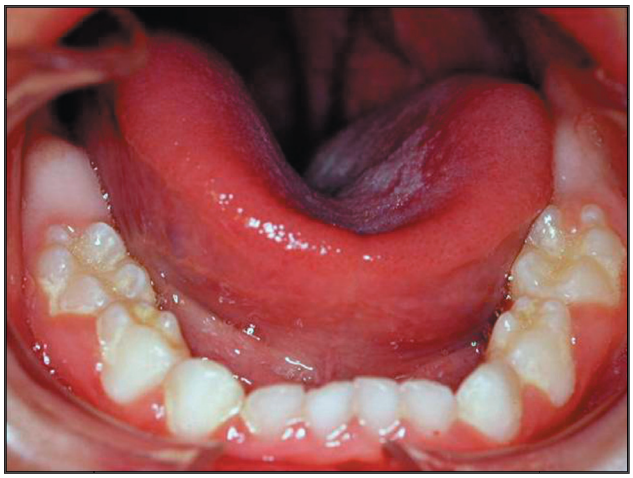

Figure 4. Absence of lingual frenum, supragingival calculus and moderate gingivitis.

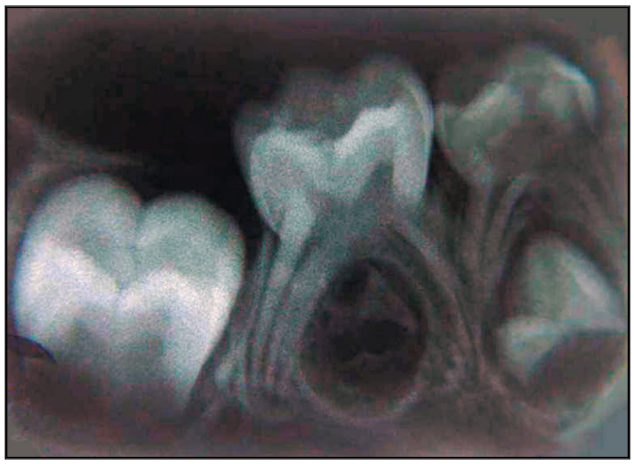

Figure 5. Radiograph showing the presence of the permanent tooth germs.

dental development, since the enamel of the permanent right mandibular first molar should be complete between 2.5 and 3 years, according to the table of human dentition chronology proposed by Logan and Kronfeld (1933).[21] Apart from this, periodontal health was observed without localized bone loss.

Before the dental treatment started, the patient's attending physicians were consulted for a medical opinion about her general health but did not make any specific recommendations. Instructions on oral hygiene (tooth-brushing with a fluoride-containing dentifrice and use of dental floss) and feeding habits were given, with emphasis on the need to discontinue bottle-feeding. Treatment strategies included supragingival scaling and topical applications of 0.12% chlorhexidine gluconate gel on both arches. On the following visits, which occurred at 15-day intervals, however, new supragingival calculus deposits were observed on the same previously scaled areas. Therefore, the patient was enrolled in a preventive treatment plan that included: scaling by quadrants, professional prophylaxis, and 0.12% chlorhexidine application once a month. In July 2005, during the course of the dental treatment, the patient was subjected to a new surgical interventions on the eyes for the insertion of an ocular spreader, opening of the lachrymal canal, and separation of the fingers on the left hand.

In the first 6 months, the preventive treatment plan was followed at 15-day intervals and, thereafter, at 1-month intervals.

DISCUSSION

Fraser syndrome is a genetic disorder that presents multiple malformations with a wide range of expressions. Even though new genetic mutations have been reported in Fraser syndrome patients, including genetic-model studies in animals using specific genes, it is still not possible to establish a genotype-phenotype relationship. There is, however, evidence of genetic heterogeneity.[22]

Cryptophthalmos is a remarkable characteristic of this syndrome, although it is not always present.[23] The findings of 2 papers that reviewed 185 cases of Fraser syndrome[2,10] showed that the craniofacial anomalies associated with this disorder were encountered in the following percentages:

1. cryptophthalmos was present in 88% to 93% of the cases and syndactyly in 54% to 62%.
2. Ear, nose, genital, and renal anomalies are reported in 44% to 54%, 21% to 37%, 32% to 49%, and 23% to 37% of the cases, respectively.
3. Facial asymmetry was found in 10% of the cases,[4] skeletal defects in 7%,[2] and hypertelorism in 21%.[2]

The present case report is within the criteria described in the literature, although the patient also presented with hydrocephaly, which is an alteration reported in only 4 cases.[2,10]

Despite the ear and eye anomalies, which are common manifestations in Fraser syndrome, hearing is usually normal. The visual function, however, has a poor prognosis because it is impossible to be recovered.[10] Regarding mental development, little is known. Among 37 children described in the literature who survived beyond the first year of life,[10,24,25] mental retardation was reported in 7 cases and normal intelligence in 5 cases. No report of mental involvement was issued for the patient of the present case. During the clinical sessions, however, the child demonstrated only little understanding and receptiveness.

The prevalence of Fraser syndrome has been estimated in about 0.43 per 100,000 liveborn infants and 11.06 per 100,000 stillbirths,[26] affecting both genders equally.[27] The life expectancy of patients who survive the first year of life is still uncertain.[10] Among the born infants, approximately: 25% are stillborn and 25% usually die within the first week[28] due to renal and laryngeal malformations.[2,10,14] 50% survive 1 year or more.

Despite the low survival rate described in the literature, this patient was 4 years old, and surpassed several life expectancy reports of Fraser syndrome patients. According to the literature, the oldest Fraser syndrome patients were between 35 and 40 years.[29,30]

The relationship of the phenotypic expression of Fraser syndrome with the parents' consanguinity has been described.[1,2,31,32] In the present case, it was confirmed by the consanguineous marriage of the child's maternal grandparents.

Because this syndrome has not been reported in the dental literature, it is difficult to relate the oral clinical findings described in this paper as typical manifestations of this syndrome. Oral manifestations of Fraser syndrome are rare and dental anomalies have been noticed in only 7% of the 68 cases reported in literature.[10] Some of the oral findings described in the present case, such as tooth crowding, malocclusion, and ogival palate, have also been reported in other cases.[2,13,17] There has been, however, no report of supragingival calculus, moderate gingivitis, and absence of lingual frenum. It may be speculated that the presence of supragingival calculus and gingivitis are related to the difficulty of removing the bacterial biofilm associated with a feeding regimen based on soft-consistence and fermentable foods.

The dental treatment consisted of periodic monitoring of the patient's oral health status and supragingival scaling associated with topical applications of 0.12% chlorhexidine digluconate gel at 2-week intervals.

Although the patient had no severe oral involvement, there were difficulties in conducting the dental treatment due to lack of understanding and cooperation on the part of the patient's family. This is because the child required continuous medical care and was totally dependent on the parents. Furthermore, the child's lack of interactivity hampered the performance of specific tests for assessment of speech, hearing, and intelligence alterations by other professionals. Nevertheless, along the repeated preventive care sessions, the mother's compliance increased and the child's oral hygiene improved but there was no change in her feeding habits.

CONCLUSIONS

The lack of knowledge about the clinical manifestations and oral findings of Fraser syndrome patients may cause apprehension and insecurity on dentists treating these patients for the first time. Therefore, the publication of case reports is important to enlighten and support both the dental professionals and the families while looking for a better quality of life for these patients.

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