

ABSTRACT

Infantile Refsum disease (IRD) is a peroxisome biogenesis disorder (PBD), and is part of a larger group of diseases called leukodystrophies, which are inherited conditions that damage the white matter of the brain and affect motor movements. Multiple signs and symptoms of IRD begin in infancy and progress through early childhood, including hearing and visual impairment, intellectual and growth impairment, seizures, liver involvement, and orofacial and dental abnormalities. This paper presents a case history of a 12-year-old female patient with IRD who underwent dental rehabilitation in the operating room under general anesthesia and includes a 2-year follow-up. Medical, dental, and management considerations in the care of this child's condition are presented. This paper also discusses the importance of a multidisciplinary approach in the management of children with special needs.

KEY WORDS: infantile Refsum disease, leukodystrophy, enamel hypoplasia, composite strip crowns, general anesthesia

Medical—dental findings and management of a child with infantile Refsum disease: a case report

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Introduction

Infantile Refsum disease (IRD) is one of a small group of genetic autosomal recessive diseases called peroxisome biogenesis disorders (PBD).¹ PBDs are part of a larger group of diseases called leukodystrophies, which are inherited conditions that damage the white matter of the brain and affect motor movements.¹ IRD is the mildest form of PBD; Zellweger syndrome, neonatal adrenoleukodystrophy, and rhizomelic chondrodysplasia have symptoms that are similar but more severe.¹ PBDs are caused by defects in the genes that are associated with the breakdown of phytanic acid (a substance commonly found in foods such as dairy products, beef, lamb, and fatty fish). As a result, toxic levels of phytanic acid build up in the brain, blood, and other tissues.¹

Initially, only an accumulation of phytanic acid was thought to be present in patients with IRD.² More recent research showed a biochemical profile very similar to that found in classical Zellweger syndrome or neonatal adrenoleukodystrophy.² It also involves the metabolism of very-long-chain fatty acids (VLCFA), pipecolic acid and bile acids and the biosynthesis of plasmalogens.² All three disorders are associated with multiple peroxisomal dysfunctions.²

The clinical course of IRD is variable and may include developmental delays, hearing loss, vision impairment, liver dysfunction, episodes of hemorrhage, and intracranial bleeding.³ Other symptoms include nystagmus, hypotonia, ataxia (mild tremors or seizures), mental

and growth retardation, failure to thrive, minor facial dysmorphism, hepatomegaly, hypocholesterolemia, and mild facial abnormalities.^{1,2}

In a study by Poll-The *et al.*,⁴ a cohort of 31 patients with IRD was examined to assess the most commonly occurring signs and symptoms. All 31 patients had severe vision and hearing loss and 27 patients wore hearing aids. Liver enlargement was seen in 21 of the 31 patients and seven patients were identified with seizures. Facial dysmorphic features noted were a high forehead in 18 patients and abnormally attached ear lobes in 20 patients. Several children (33%) had delayed tooth eruption, malpositioned teeth, and enamel hypoplasia.

The primary treatment of IRD is to avoid foods containing phytanic acid, which include dairy products, beef, lamb, and fatty fish like tuna, cod, and haddock.¹ Sometimes, children with IRD may have to be fed via a gastrostomy tube.³ Some infants and children require plasmapheresis (blood drawn, filtered, and reinfused back into the body to control build-up of phytanic acid).¹ Sensorineural hearing loss is the most common manifestation in children with IRD and hearing should be evaluated annually.^{3,4} Many children may have had early cataract removal in infancy and most wear eyeglasses to correct refractive errors.³ Due to liver involvement, vitamin K and other fat-soluble vitamin supplementation may be necessary and coagulation factors and liver function need periodic monitoring.³ Seizures have been reported in some children with IRD, but are more common in other PBDs.²

IRD is a fatal disease, but medical advances have helped some children survive into their teens and 20s and possibly beyond.⁴

Dental findings in children with IRD have not been studied adequately, and appropriate management has not been documented. Bader *et al.*⁶ studied the facial and dental findings in IRD among four Amish siblings. They found large anterior fontanelles and distinct dental abnormalities. Prominent forehead and facial asymmetry have been mentioned in several case reports.^{5,6} The eyes were noted to have ptosis, underdeveloped discs, strabismus, and incompletely out-folded scapha-helix. Teeth were small, poorly formed, and yellow-orange in color with a central diastema.^{5,6}

Case report

A 12-year-old white female patient was brought by her mother to the Special Children's Dental Clinic at the Children's Hospital in New Orleans, Louisiana. She had a medical diagnosis of IRD. She was diagnosed with IRD in 2005 at 9 years of age and had severe hearing and vision loss. She wore hearing aids in both ears and had eyeglasses.

She also had a severe intellectual disability and had a history of spinal meningitis at 18 months of age. The patient did not have a history of seizures and her only medication was a daily multivitamin. The patient's mother reported that her child had an allergy to amoxicillin, which had produced a rash.

As stated by the mother, the patient's chief complaint was pain associated with the maxillary left lateral incisor and that her front teeth were yellow had a rough appearance. Due to the patient's intellectual disability, she was unable to cooperate for in-office treatment. She cried hysterically at the mere sight of strangers and had to be restrained by the mother in her lap to be examined in the dental clinic. A limited in-office examination supported the decision to complete the patient's comprehensive evaluation and treatment in the operating room. The patient's oral hygiene was poor, as the mother had difficulty brushing her teeth at least once a day. The brief oral examination showed that she had several unerupted permanent teeth; a panoramic radiograph was attempted with no success. It was decided that full mouth periapical radiographs would be made in the operating room to help develop a comprehensive treatment plan.

Several consultations were obtained with her primary care physician, geneticist, and neurologist to get clearance for the patient to be treated under general anesthesia. No one physician was solely able to clear the patient for surgery without further tests. A preoperative evaluation was completed by a physician at Children's Hospital in New Orleans. Based on the patient's diagnosis and the findings associated with IRD, appropriate tests were ordered which included a complete blood count (CBC) with differential, liver function tests (LFT), and Prothrombin Time/International Normalized Ratio (PT-INR). All the tests were within normal range as evaluated by the physician and anesthesiologist at Children's Hospital and the patient was cleared for treatment under general anesthesia.

On the day of the procedure, the patient was brought into the operating

Table 1. Teeth clinically visible in a child with infantile refsum disease.

A	5	7	8	9	10	I	J
T		26	25	24	23		K

room, induced with sevoflurane and propofol, and intubated using a nasotracheal tube by the anesthesiologist. A complete extra-oral and intra-oral examination was performed in the operating room. The patient did not present all the distinct facial features characteristic of IRD but did have a large forehead and mild facial dysmorphism. The intra-oral examination revealed over-retained primary molars (A, I, J, K, and T) and their unerupted permanent counterparts.

Table 1 shows the teeth that were clinically visible intra-orally. The maxillary right lateral and central incisors and the left central incisor were yellow in color and poorly formed. Although the incisal edges were intact, the facial surface of the maxillary central incisors showed irregular and deficient tooth structure (Figure 1). The maxillary left lateral incisor had severe attrition with pulpal involvement, Grade II mobility, and a periapical abscess. The mandibular incisors, though yellow in appearance, were smooth and intact with no missing tooth structure. The patient had pre-existing stainless steel crowns on teeth I and K. Her anterior occlusion was evaluated in the operating room prior to treatment of the anterior teeth to select the appropriate full coverage restorations. Posteriorly, teeth A and T and teeth J and K were in crossbite.

The radiographic examination (Figure 2) included six periapical films and a mandibular occlusal film which, when evaluated, revealed that although the root formation on almost all of the posterior permanent teeth was more than two-third complete, they were still clinically unerupted. Only nine permanent teeth were clinically erupted, including the maxillary and mandibular incisors and the maxillary right first premolar.



Figure 1. Clinical photographs of the patient's occlusion and dentition prior to treatment, showing the occlusal wear.

The following treatment was completed under general anesthesia: all remaining primary teeth (A, I, J, K, and T) were extracted to allow for eruption of the permanent successors. The maxillary left permanent lateral incisor was extracted, because the mobility and the abscess suggested a very guarded

endodontic prognosis and the breakdown below the gingival margin would have made it impossible to obtain a good crown margin without crown lengthening. Surgical exposure of the permanent teeth to expedite eruption was considered, but ruled out due to the fact that the teeth may be more susceptible to

caries or breakdown due to hypocalcification. Due to the parent's inability to maintain the child's oral hygiene at an appropriate level, especially in the posterior region of the mouth, it was decided to monitor the eruption of the teeth. The mandibular teeth were clinically intact, so no treatment was planned for them.

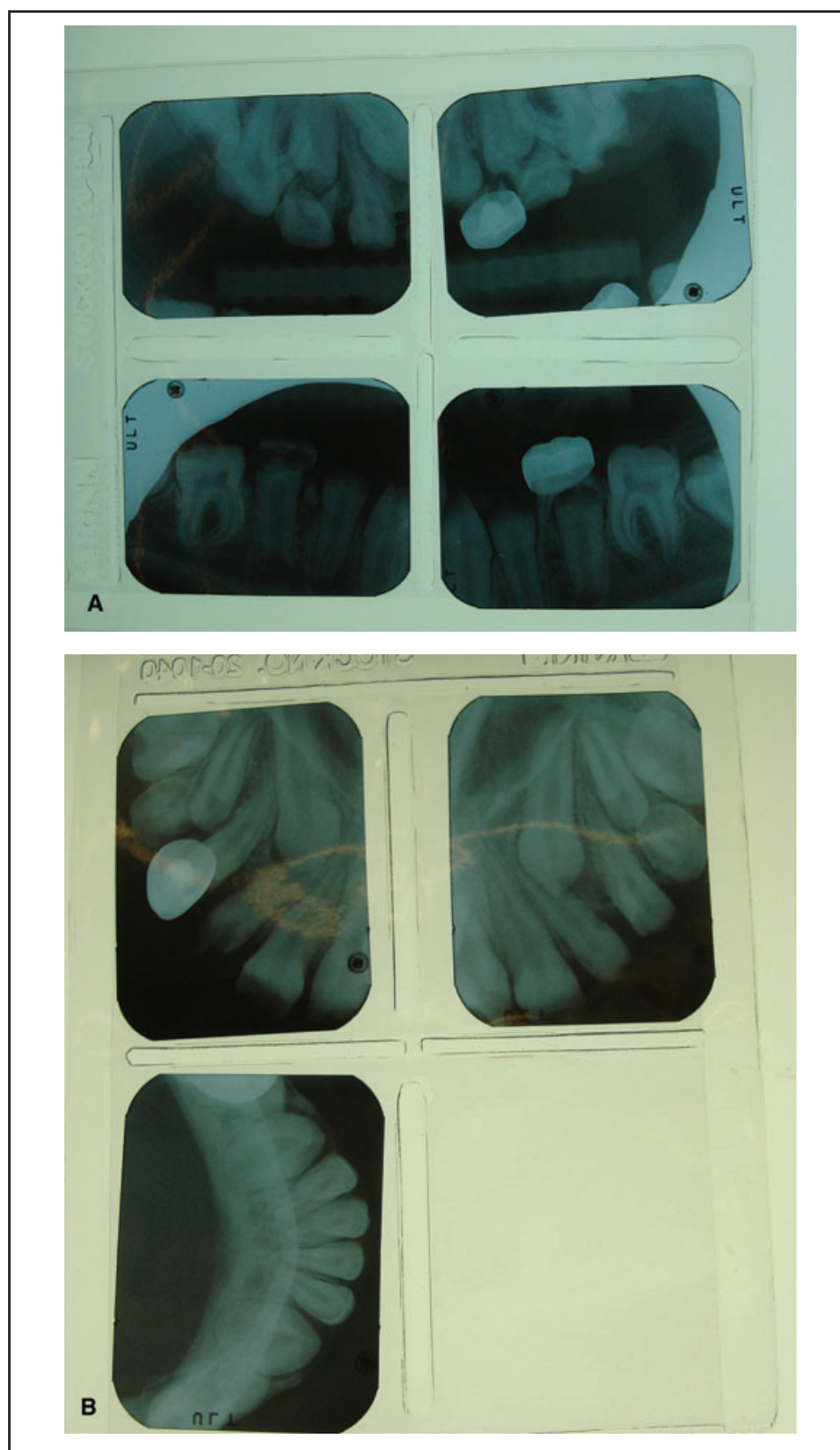


Figure 2. Photographs of the patient's periapical radiographs, showing that the root formation of most of the posterior teeth was about two-third completed. The mandibular occlusal radiograph shows that the mandibular teeth were fully erupted.

Because esthetics of the maxillary anterior teeth was a chief complaint, a tooth-colored restoration was the treatment of choice. Although some concern was raised regarding the bond strength of composites to hypomineralized enamel, a decision was made to do full coverage composite restorations to improve overall strength and improve bonding; the surface area to be etched was increased. Therefore, teeth 7, 8, and 9 received bonded composite resin strip crowns (Unitek 3M Strip Crown Forms). The appropriate crown forms were selected and trimmed to size; a vent was made on the disto-incisal line angle to let the excess composite flow out. The teeth were prepared with a 169-L bur using a high-speed handpiece. The teeth were etched with 37% phosphoric acid, dried, bonded using 3M ESPE adhesive (Nowak Dental Supplies, Chalmette, LA, USA), light-cured for 20 seconds, and restored with Z-250 shade A3 composite (Filtek™ Supreme Ultra, 3M, St. Paul, MN, USA). The composite material was placed into the crown forms and the crown forms were placed firmly onto the teeth. The excess composite that came out through the vent was removed using a plastic instrument and the material was then light-cured for 40 seconds on the buccal and 40 seconds on the lingual side. All three crown forms were seated and light-cured one at a time (Figure 3).

At her two-week follow-up, the patient was very happy with the appearance of her teeth and came in smiling. She was again examined in her mother's lap. The composite margins were checked and were within normal limits and the gingiva around the crowns appeared healthy. Oral hygiene had significantly improved and extraction sites were healing well. At this point, it was decided to do a follow-up visit in 3–6 months for adequacy of oral hygiene as well as to evaluate the eruption of the permanent teeth.

The patient missed several recall appointments and was again seen in January 2010, almost 2 years from the date of treatment. The restorations were still functional and well maintained, and the premolars had begun to erupt but

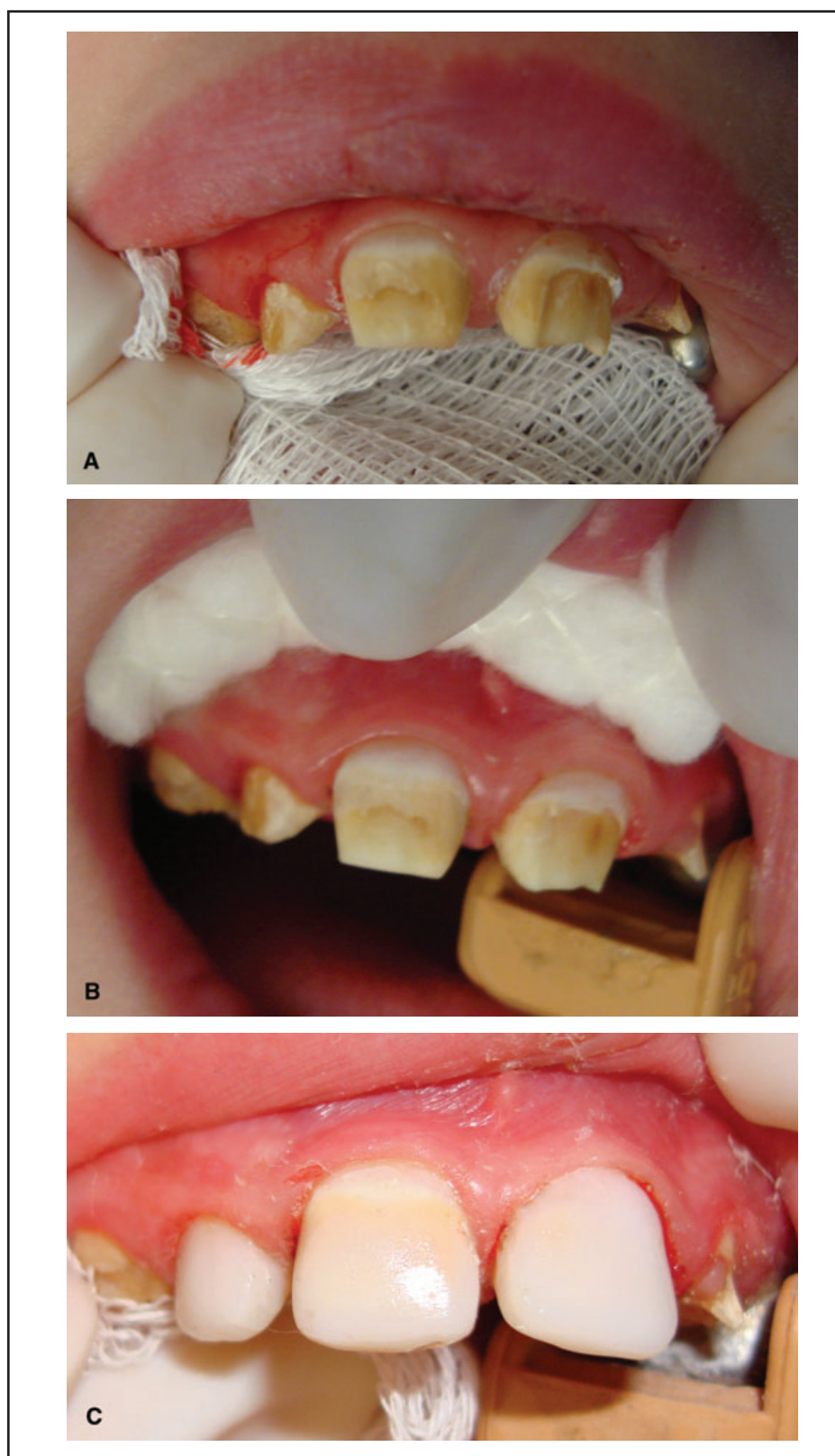


Figure 3. Shows teeth #7, 8, and 9 prior to treatment. (A) Shows the teeth prepared for composite crowns. (B) Shows the cemented composite crowns.

had the same yellowish appearance (Figure 4).

Discussion

Management of young permanent teeth with developmental defects in children depends on the type and severity of the defect. With anterior teeth, esthetics becomes an important factor in treatment decisions; therefore, composite resins seem to be the restoration of choice for these permanent teeth. The shear bond strength of resin composite bonded to hypomineralized enamel is significantly lower than bonding to normal enamel.⁷ Treatment options can range from the most conservative treatment, which consists of bonding a tooth-colored material to the tooth to protect it from further wear or sensitivity, to less conservative treatment like the use of stainless steel crowns, permanent cast crowns, or extraction of affected teeth and replacement with a fixed partial denture or with implants, if the patient can afford this treatment.⁸ In a study by Seow and Amaratunge⁹ on treatment of hypocalcified enamel affected by amelogenesis imperfecta, the authors found it was possible to obtain an etched surface after use of 37% phosphoric acid for all types of amelogenesis imperfecta.

In our patient, we used 37% phosphoric acid and full coverage in the form of bonded composite resin strip crowns. In our opinion, this improved the overall strength and bonding by increasing the surface area that was etched and bonded. Also, it was thought that the pressure from placing the composite with a crown form would improve retention. However, in young permanent teeth, the ultimate treatment option depends on the remaining growth and development of the alveolar bone. It is important to also keep in mind that no matter what restoration is chosen, it may need replacement or modification as the child grows to adulthood to accommodate alveolar changes related to growth and eruption of surrounding teeth.

When treating children with special needs in a hospital setting, the treatment of choice should be one that is durable



Figure 4. Shows the anterior teeth at the 2-year follow-up.

but at the same time provides an esthetic and functional result. When treating severe cases of enamel hypoplasia involving proximal surfaces, bonded composite resin strip crowns offer reasonable esthetics and retention. In hypoplastic teeth, pretreatment with 5% sodium hypochlorite to remove the protein encasing the hydroxyapatite is suggested (deproteinization), followed by a self-etching, primer-bonding system.⁹ However, a recent study¹⁰ showed that deproteinization had no significant effect on the success of adhesive restorations.

Although the literature^{4,6} may refer to the teeth in children with IRD as being hypoplastic or poorly formed, in retrospect it may have been beneficial to send these teeth to pathology to understand the exact enamel/dentin defect. Nevertheless, for our patient, at the 2-year follow-up, there was a good result in terms of retention and intact restoration margins. Also, she did not report any pain or sensitivity of the treated teeth.

Composite resin strip crowns can offer a good transitional treatment out-

come for the management of young permanent anterior teeth with enamel hypoplasia in children with IRD or other similar special healthcare needs.

Conclusion

With advances in medical diagnoses and treatments, many children with complex medical conditions are surviving beyond their life expectancy. Many children are also being born with rare syndromes and conditions that require multiple medical specialties to coordinate care and to improve their quality of life. A multidisciplinary team approach has been suggested to treat these children to accurately assess the risks versus the benefits and possible complications associated with elective surgical procedures.

In obtaining medical clearance for these children, it is important to keep in mind that the physician may not be familiar with the risks associated with dental procedures. It is important for the dentist to be an advocate

for his/her patients in coordinating their medical information and obtaining the appropriate consultations and referrals.

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