Congenital nephrotic syndrome: Oral manifestations and dental implications

Winey Wan*/ Richard Widmer**/ Neeta Prabhu***

Children with congenital nephrotic syndrome (CNS) can present with oro-dental complications secondary to the disease or from the treatment of the condition. This case report describes the multidisciplinary management of a 12-year-old male patient with CNS. It highlights the importance for pediatricians and nephrologists to be aware of the dentists' role in the general health and well-being of children with chronic renal disease.

Keywords: *Nephrotic, Oral manifestation, Renal, Dental, Enamel hypoplasia*

INTRODUCTION

Congenital nephrotic syndrome (CNS) is a rare, heterogeneous group of disorders with an estimated incidence of 0.5:100,000 live births[1]. CNS affects the glomerular filtration barrier (GFB) of the kidneys and is characterized by severe proteinuria and oedema and manifests in utero or during the first three months of life[2]. Most CNS presentations are autosomal recessive disorders caused by genetic aberrations in podocytes, most commonly affecting the *NPHS1* gene encoding nephrin and *NPHS2* gene encoding podocin[3]. The incidence of CNS with mutations in the *NPHS1* gene, is reported to be as high as 1:8200 live births in Finland[2].

The clinical course of CNS is progressive, and the majority of cases will proceed to end-stage renal failure (ESRF) by two to three years of age[4]. In most CNS cases, early life kidney transplantation (KTx) is the only curative treatment, and the outcome is generally excellent with low recurrence rates[2]. The advent of KTx has seen an improved survival of children with CNS from a life expectancy of two to three years to an overall 5-year survival of over 90%[5].

Chronological enamel hypoplasia (CEH) is a developmental defect that presents with distinct characteristic banding around the crowns of teeth. The location of the defective enamel is a permanent chronological record of past disturbances, corresponding with the age of disease onset[6]. Enamel hypoplasia (EH) is a well-known phenomenon in children with chronic renal failure (CRF)[7]. While there are various studies reporting EH in patients with CRF and nephrotic syndrome (NS)[8,9], there are no published reports specific to the oral manifestations of CNS.

CASE REPORT

A 12-year-old male presented to the Dental Department at the Children's Hospital at Westmead for a routine dental review. The patient was born prematurely at 36.5 weeks gestation in Alice Springs, Australia. His medical history included

*Winey Wan, BOH, BDSc, Postgraduate Registrar, Department of Paediatric Dentistry, Children's Hospital at Westmead Hospital, School of Dentistry, University of Sydney, New South Wales, Australia.
**Richard Widmer, BDS, MDS, Senior Staff Specialist, Head of Department, Department of Paediatric Dentistry, Children's Hospital at Westmead, Clinical Associate Professor, School of Dentistry, University of Sydney, New South Wales, Australia.
***Neeta Prabhu, BDS, MDS, MPhil, Staff Specialist, Paediatric Dentistry, Westmead Hospital, Head of Discipline, School of Dentistry, University of Sydney, New South Wales, Australia.

Corresponding Author:
Neeta Prabhu
Westmead Hospital and The University of Sydney,
Westmead, New South Wales, Australia.
Phone: +61-298457537
Fax: +61-298458306
E-mail: Neeta.Prabhu@health.nsw.gov.au

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developmental delay, autism spectrum disorder, and CNS involving genetic mutations in *NPHS1* and *NPHS2*. The patient had received treatment for ESRF secondary to CNS between the age of four to five years. His treatment involved hemodialysis over a three-month period and KTx. Three years post-KTx, the patient was diagnosed with recurrent focal segmental glomerulosclerosis. He was treated with plasmapheresis and two doses of rituximab infusion over two weeks. At this dental review, the patient's renal function was normal, and his medications included tacrolimus, mycophenolate mofetil, prednisone, amlodipine and irbesartan.

The primary concerns expressed by the patient's mother were the poor aesthetics and pain from the hypoplastic teeth. The patient's true symptoms were difficult to assess due to his limited cognition. A clinical and radiographic examination (Fig. 1) revealed a mixed dentition with multiple dental anomalies and dental caries. Other findings included mouth breathing tendencies and a developing malocclusion from a narrow palate and an anterior crossbite. CEH with associated post-eruptive breakdown (PEB) was noted on multiple anterior and posterior permanent teeth (Fig. 2).

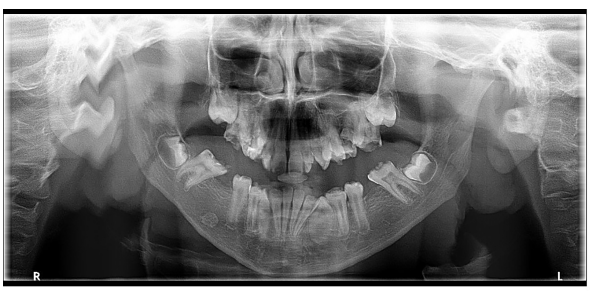

Figure 1: Orthopantomogram (OPG) at 12-years of age.

Previous dental records revealed the patient's first dental visit was at the age of five years, one month prior to KTx. At that visit, hypoplasia of his primary dentition with mild PEB was identified, however the specific affected teeth were not recorded. The child subsequently had a general anesthetic procedure (GA) at seven years of age for the placement of multiple composite restorations on his primary molars and extraction of all permanent first molars due to extensive dental caries.

In view of the child's extensive treatment needs at the recent visit, a GA was arranged for in consultation with the orthodontic, anesthetic, and pediatric nephrology teams. The treatment completed included extraction of the over-retained primary teeth and the permanent maxillary second molars, and restoration of the permanent molars, premolars, and maxillary central incisors. On recommendation from the nephrologist, antibiotic prophylaxis was administered intraoperatively due to the child's immunosuppressed status and invasive nature of the dental treatment.

The child was reviewed seven months post-operatively. He presented with newly erupted maxillary second premolars with severe CEH (Fig. 3) and dental caries on the premolar teeth. The father reported that the child appeared much settled since his last treatment and demonstrated less fussy eating habits. The child's previous adverse behaviours suggestive of oral discomfort had also ceased. However, a further GA was necessary for the restoration of the newly affected teeth.

DISCUSSION

Children presenting with NS are more likely to develop EH compared to healthy controls. Earlier observations of CEH affecting the primary and permanent dentition in children with NS have been reported, with incidences ranging from 19%–36%[8,9]. CNS differs in its clinical course and management to childhood NS as most CNS cases will inevitably progress to ESRF by two to three years of age[4]. KTx in the early years of life is often the only curative treatment for children with CNS[2].

Although the underlying mechanisms are not clear, disturbances in calcium homeostasis and vitamin D deficiencies that can occur in NS[2], in particular during dental development, have been associated with the development of EH[6]. A correlation between an early age of onset of the NS and the prevalence of CEH has been reported[8]. This is significant for children with CNS as they will often develop ESRF with associated metabolic disturbances, in their first few years of life, when the development of the primary and permanent dentitions are most active[2]. Our patient suffered from ESRF from four to five years of age, and this is reflected in the location of the EH defects on the occlusal half to third of the tooth crowns of his permanent premolars and second molars. Following KTx, this child's renal function returned to normal and this is reflected by healthy sound enamel located on the gingival half to two-thirds of the tooth crowns affected by EH.

CEH can result in poor aesthetics, tooth sensitivity and dental caries, especially when the defects are plaque retentive[10]. Treatment of EH depends on the severity of the defects and can involve conservative aesthetic techniques such as enamel microabrasion and direct composite restorations, to the more invasive full coverage restorative options for more severe defects[11]. CNS represents a unique cohort of patients due to the early onset of metabolic disturbances associated with this condition. Although there are currently no studies investigating the development of CEH in this cohort, one could speculate that theoretically, most children with CNS would develop CEH in their primary and permanent dentition due to the early onset and progressive nature of the condition.

CNS differs to other forms of childhood NS in that most children will undergo KTx in early life[2]. Following KTx, immunosuppressant therapy is required to prevent the rejection of allogenic renal transplants. This generally consists of a triple therapy including a combination of corticosteroids, calcineurin inhibitors like cyclosporine or tacrolimus, or lymphocyte-proliferation inhibitors like mycophenolate mofetil[12]. Gingival enlargement in response to cyclosporine A has been reported in children[13]. The unpleasant appearance of such gingival enlargement can have negative psychological impacts on the young patient, interfere with normal oral function, speech and oral hygiene, and can cause delayed or ectopic eruption of teeth[7]. Gingival overgrowth may be further exacerbated in children with NS as they often have poor

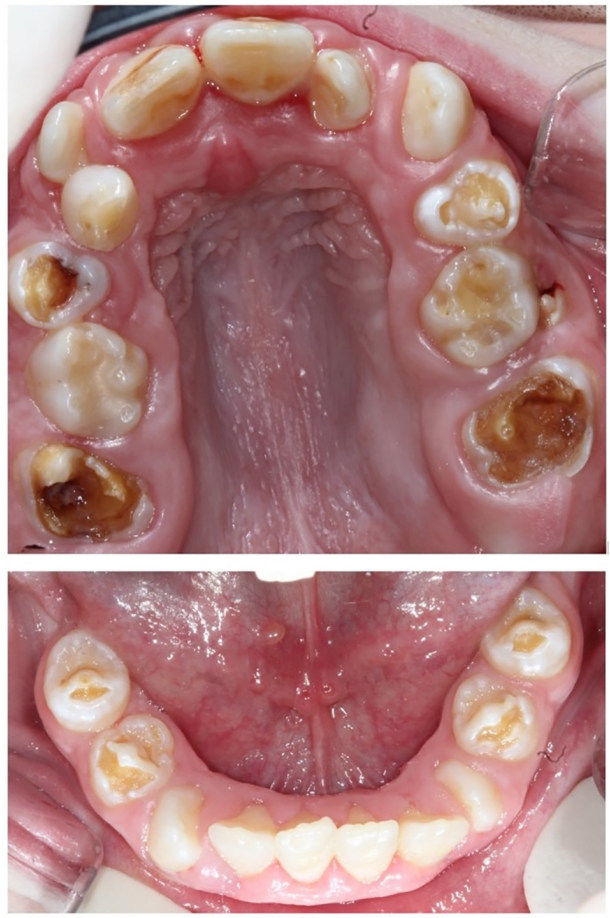

Figure 2: Chronological enamel hypoplasia. Distinct characteristic banding around the crowns of premolar and molar teeth.

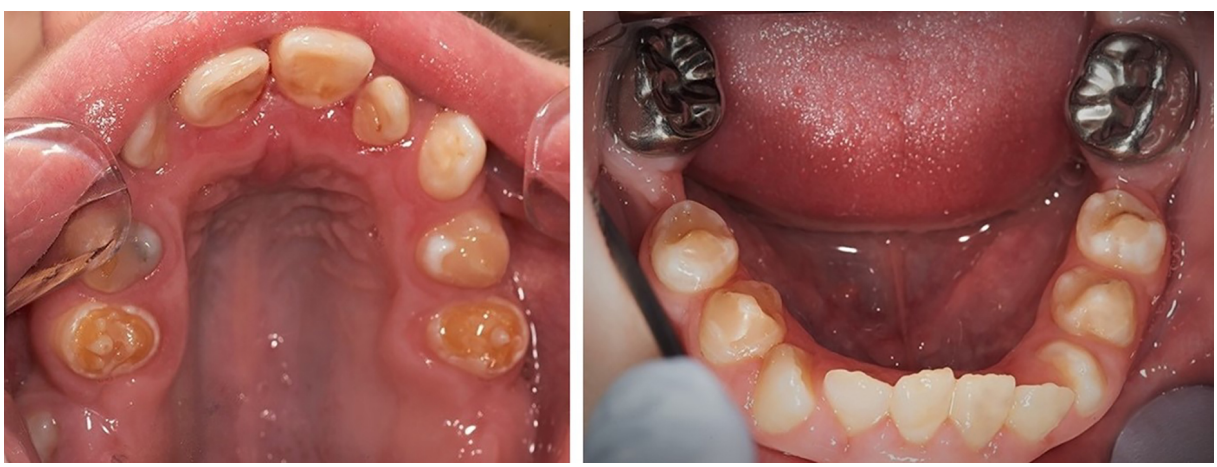

Figure 3: Seven-month follow-up showing newly erupted permanent maxillary second premolars with chronological enamel hypoplasia.

plaque control and more gingivitis when compared to healthy controls[9]. Tacrolimus has been marketed as an effective alternative to cyclosporin A and is less associated with gingival overgrowth in children[14]. Our patient who is treated with tacrolimus demonstrated a mild degree of gingival hyperplasia.

Routine dental treatment during the remission period can be carried out without special considerations in children with CNS. However, long-term medication induced immunosuppression in children with CNS post KTx, may warrant antibiotic prophylaxis for invasive dental procedures due to the increased risk of infection[7]. Long-term use of corticosteroids in children after KTx may necessitate corticosteroid cover for invasive procedures to minimize the risk of adrenal crisis[7]. Consultation with the patient's nephrologist is therefore essential.

CONCLUSIONS

Children with CNS are at risk of developing oro-dental problems that can be of functional and aesthetic concern. This can result in significant dental treatment burden throughout childhood and adolescent years and have negative psychosocial impacts on the child and the family. It is therefore paramount that a timely referral to the dentist is made from the time the first primary tooth erupts. This will enhance opportunities for anticipatory guidance for families, early detection and intervention of dental defects, and long-term dental surveillance. CNS is a rare disease; however, the improved survival of these patients means that they will become increasingly prevalent in dental practice. Therefore, it is important for all involved in the care of patients with CNS—nephrologists, pediatricians, pediatric and general dentists, to work collaboratively in optimizing oral health and ultimately the well-being of these patients.

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CONSENT TO PARTICIPATE

Consent for images was obtained from the parent of the patient.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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