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CASE REPORT

Supernumeraries in Nicolaides–Baraitser Syndrome

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Background. Nicolaides–Baraitser Syndrome(NCBRS) is an extremely rare condition which has been reported in only a few cases. NCBRS is a distinct clinical condition with typical clinical features of pre- and post-natal global developmental delay, impaired speech, and seizures. Microcephaly, sparse hair, anteverted alae nasi, undefined philtrum, prominence of distal phalanges and interphalangeal joints, and short metacarpals are also typical of NCBRS.

Case Report. There are no reported cases in the literature of patients with NCBRS presenting with multiple dental impactions, and to the authors' knowledge, this is the 28th fully documented case of NCBRS and only 75 cases identified as potentially having NCBRS. The clinical features, diagnosis, and course of management are also described.

Conclusion. Although NCBRS is very rare, it is important to assess dental development in view of the possibility of multiple supernumerary teeth which can have detrimental effects on the occlusion.

Introduction

Nicolaides–Baraitser Syndrome (NCBRS; OMIM #601358, (http://www.omim.org/, 23/01/2016) is a very rare syndrome with 75 cases identified as of 2017 (https://ghr.nlm.nih.gov/condition/nicolaides-baraitser-syndrome#statistics, 14/03/2017). It is caused by a heterozygous missense mutation in *SMARCA2* on chromosome 9p24.[1] The syndrome was originally described by Nicolaides and Baraitser in 1993.[2] The main characteristics include epilepsy, short stature, intellectual disability, severely impaired speech, brachydactyly, and interphalangeal joint swellings.[1,3] With regard to the facial morphology, the following have been noted: microcephaly, sparse hair, long/broad philtrum, large mouth with thick vermillion.[4,5] The dental features have not previously been described, and all the published reports focus on extraoral and digital abnormalities. In addition, all the reports were published in genetic, dermatological, and clinical dysmorphological journals possibly allowing total unawareness of this syndrome amongst specialists in paediatrics, orthodontics, and other clinicians treating patients with craniofacial syndromes. This case report concerns a 12-year-old male with a confirmed diagnosis of NCBRS who was referred to the Maxillofacial and Dental department at Great Ormond Street Hospital for Children NHS Foundation Trust for an orthodontic assessment and treatment. The presenting features are described including that of multiple dental impactions, which could redefine the phenotypic features that characterise patients with NCBRS. The course of management is also outlined.

Case report

The patient was 12 years old at the time of presentation and the first child of non-consanguineous parents. Foetal ultrasound scans demonstrated mild intrauterine growth retardation without additional foetal and/or placental abnormalities. The patient was born at term (40 weeks) by normal delivery. His weight was 2150 g (0.5th percentile), length

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was 50 cm (2nd centile), and head circumference was 40 cm (9th centile). He was bottle-fed for the first week to gain weight speedily; however, due to problems complying with feeding regimen, feeding aids had to be used to encourage an increase in body weight. Sparse hair was noted in the first 6 months, and he was able to walk at 20 months and babble at 15 months.

At the time of examination, his weight was 43.6 kg (10th percentile), height was 148.4 cm (5th percentile), and a head circumference was 50 cm (0.5th centile). He had severe mental delay with major difficulties in articulating words and constructing sentences. He was capable of repeating a few words by mimicking. His motor development was acceptable, however, he was always accompanied and physically aided by both parents. He attended a specialised school that caters for children with special needs.

He had an overall pleasant personality with bouts of non cooperation, stubborn behaviour, and sporadic episodes of bad temper which were difficult to control.

Figures 1 and 2 show the facial and dental features at the initial assessment. The facial appearance is in keeping with previous descriptions, that is, sparse hair, slightly broad philtrum, and a broad mouth. In profile, the lower facial third is convex with his lips just about in contact at rest. His skeletal pattern was class II. His lower anterior face height was slightly reduced and no transverse facial asymmetry noted. The naso-labial angle was obtuse. Intraorally, he presented in the mixed dentition with extrinsic food staining. Of note was the failure of eruption of the upper right central incisor, lower left canine, and lower right second premolar. The incisor classification was class I, overjet measured at 2 millimetres, overbite was average and complete to tooth, and the lower centre line was shifted to the left by 3 mm due to the impacted lower left canine. Subsequent radiographic examination (Fig. 3 DPT, USO, and CBCT) revealed the presence of six supernumerary teeth. In the maxilla, two supernumerary teeth were located palatal to each central incisor and a mesiodens was also identified. In the mandible, supernumerary teeth

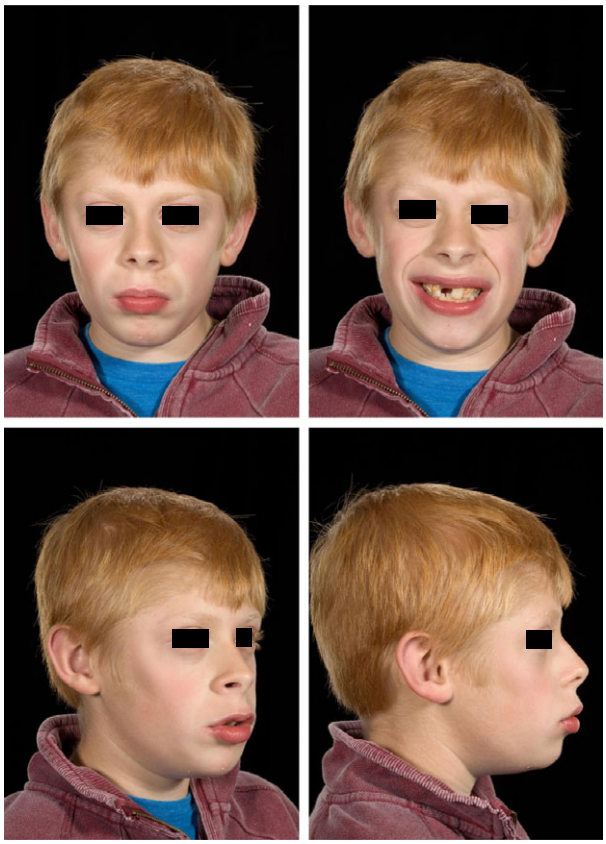


Fig. 1. Pre-operative extraoral appearance at 12 years of age.

are present lingual to LR2,3 and LL3,4 and between LL2,C.

Under general anaesthesia, all remaining primary teeth and the six supernumerary teeth were removed. The upper right central incisor was successfully aligned using an upper arch fixed appliance.

Discussion

The surprise finding in this case was the presence of six supernumerary teeth. Supernumerary teeth are those present in addition to the normal complement within the dentition and can occur singularly or in multiples, unilaterally or bilaterally and in the maxilla or mandible[6,7]. In the permanent dentition, supernumeraries are seen in 0.1% to 3.2% of the population and are more common in males with a relative frequency of around 2:1 in Caucasians[2]. Multiple supernumeraries tend to occur in patients with syndromes such as cleidocranial dysostosis and ectodermal dysplasia.

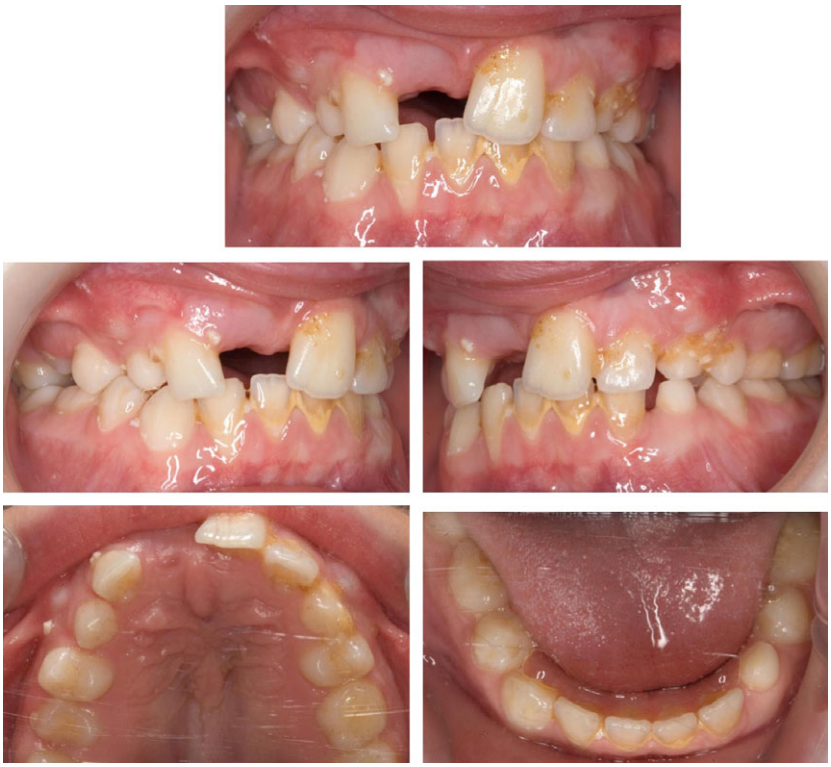


Fig. 2. Pre-operative intraoral features at 12 years of age. Note the number and site of unerupted teeth.

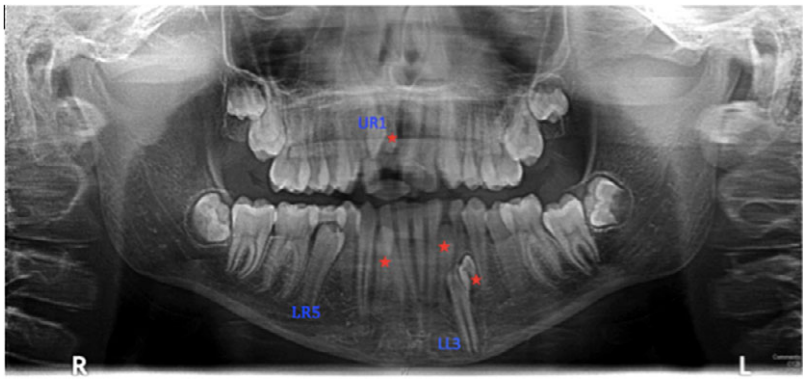
Little is known about the initiation of tooth formation, the genetic control of successional teeth, and the mechanisms underlying supernumerary tooth formation[6]. Multiple supernumeraries are a common feature in many genetic disorders, which suggests that supernumerary teeth may have genetic components in their aetiology[6]. Our current knowledge regarding tooth development is based on mouse models, which has provided insight on how tooth number is controlled at the molecular level[6]. Evidence from mutant mouse models suggests that inappropriate regulation of Sonic Hedgehog (Shh) activity may play a key role in the formation of supernumerary teeth[8]. Other molecular signalling pathways known to be involved in normal development of the tooth germ can also give rise to additional teeth if inappropriately regulated[6]. These include components of the fibroblast growth factor (FGF)[9], Wnt[10], tumour necrosis factor (TNF)[11], and bone morphogenetic protein (BMP)[12] families, which provide fundamental insights into the molecular genetics of supernumerary teeth and may help identify the genes responsible for supernumerary tooth formation.

The authors recommend including delayed dental eruption and multiple dental impactions as part of the major features constituting NCBRS. The presence of supernumerary teeth can disrupt the eruption of teeth as occurred in this case with the failure of UR1 and LL3 to erupt. In addition, supernumerary teeth can occasionally cause the displacement of permanent teeth, dentigerous cyst formation, and the resorption of roots adjacent to the supernumerary.

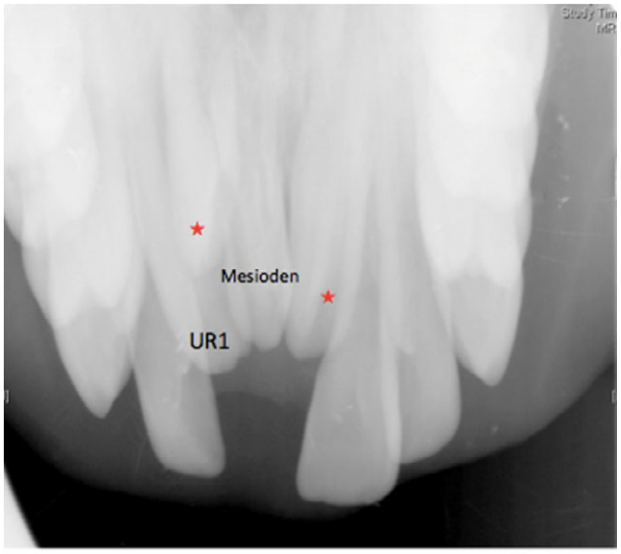
Conclusion

The main clinical features of NCBRS are severe mental impairment with speech delay, seizures, short stature, sparse hair, and brachydactyly. The dental examination of the patient provides precious data for our understanding of the oral features of this rare condition. Multiple dental impactions caused by supernumerary teeth could redefine the phenotypic features that characterise patients

(a) Dental panoramic tomogram



(b) Upper standard occlusal



(c) CBCT

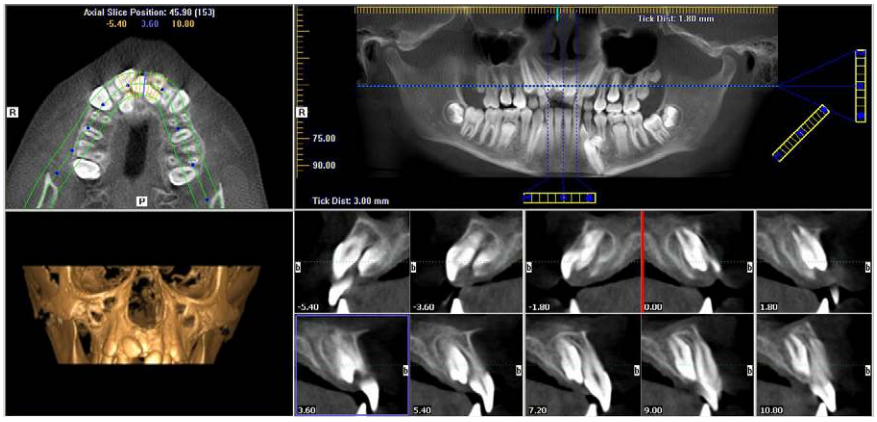


Fig. 3. Radiographic findings. The dental panoramic tomogram (DPT) (a) clearly reveals the presence of three supernumeraries (★) in the mandible and an impacted UR1, LL3, and LR5. The two supernumeraries palatal to the central incisors and the mesiodens are not clearly visible on the DPT due to the focal trough however, are visible on the upper standard occlusal (b). Cone beam computed tomography (c) confirming the presence and position of all six supernumeraries.

with NCBRS. Whether or not the heterozygous missense mutation in SMARCA2 is in any way responsible for the development of multiple supernumerary teeth is currently unknown.

Why this study is important to paediatric dentists

- Although NCBRS is very rare, it is important to assess dental development in view of the possibility of multiple supernumerary teeth and the potential detrimental effect this can have on the occlusion.

Disclosure of interest

The authors report no conflict of interests.

Authors contributions

Bouthayna Al-Tamimi wrote the article. Stefan Abela advised and edited the manuscript. Huw G Jeremiah treated the patient. Robert D Evans supervised the treatment.

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