
Orofacial findings and serial extraction procedure in Noonan syndrome

Maciej Iancu Potrubacz, Claudio Chimenti, Laura Marchione and Michele Tepedino

Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy

The case of an 8-year-old female affected by Noonan syndrome is presented. The orofacial findings comprised a skeletal Class III malocclusion, transverse maxillary deficiency, a long face and severe tooth size-arch length discrepancy. The interceptive orthodontic approach focused on addressing the patient's problems while keeping treatment as simple as possible. Management consisted of rapid maxillary expansion and serial extractions in the mandible. Treatment alternatives and results are discussed and a one-year follow-up is provided.

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Maciej Iancu Potrubacz: maciekip74@gmail.com; Claudio Chimenti: claudiochimenti@yahoo.it; Laura Marchione: marchione31@yahoo.it; Michele Tepedino: m.tepedino@hotmail.it

Introduction

Noonan syndrome (NS, OMIM 163950) is a relatively common, autosomal dominant, multisystem disorder with complete penetrance and variable expressivity, mainly characterised by a typical facial pattern, short stature and heart defects.¹ It was first described as a syndrome by Noonan and Ehmke in 1963.² It affects males and females with an incidence of 1:1000 to 1:2500³ for severe cases, but mild cases can be encountered more frequently.⁴ Although the syndrome is transmitted from parents to child in an autosomal dominant manner, sporadic cases have an incidence of approximately 60%.¹

The diagnosis of NS is mainly based on characteristic clinical findings, which include congenital cardiac defects (pulmonary stenosis 50–60%, hypertrophic cardiomyopathy 20%, secundum atrial septal defect 6–10%), thoracic deformities with superior pectus carinatum and inferior pectus excavatum, short stature and delayed pubertal growth spurt, short and webbed neck with redundant skin, a low posterior hairline, cryptorchidism, and bleeding diathesis caused mainly by coagulation defects. Also noted are feeding

difficulties (delayed gastrointestinal motor development, recurrent vomiting and gastrointestinal reflux), which can lead to a failure to thrive. Renal anomalies (10–11%), and lymphatic abnormalities (less than 20%) also occur. Intelligence is usually within a normal range but the prevalence of intellectual impairment is about 20%.^{5–8} Craniofacial findings include a high forehead, hypertelorism with downward sloping palpebral fissures, ptosis, epicanthal folds, strabismus and amblyopia, a short and broad nose with a depressed root, low-set and posteriorly rotated ears with an oval shape and thick helix, and a distinctive upper lip with a deeply grooved philtrum. Oral findings are recorded as a high-arched palate (50–100%), micrognathia (33–43%), dental malocclusions (50–67%) and dental anomalies. Some affected patients develop mandibular cysts characterised by multinucleated giant cells in a fibrous stroma that can mimic cherubism.^{5–10}

The aetiology of this syndrome has been associated with the molecular RAS-MAPK pathway, which is important for cell differentiation, growth and senescence.¹¹ In particular, mutations in the PTPN11 (protein tyrosine phosphatase non-receptor type 11) gene

are reported in 50% of cases of NS.³ The karyotype is normal, and this is one of the main differences between NS and Turner syndrome, which has similar clinical features. Other disorders with a significant phenotypic overlap with NS are cardiofaciocutaneous syndrome, Costello syndrome, LEOPARD (lentiginos, electrocardiographic anomalies, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, retardation of growth, deafness) syndrome, Aarskog syndrome, foetal alcohol syndrome, mosaic trisomy 22 and Baraitser-Winter syndrome.⁵ Genetic testing assists in the differential diagnosis and correct characterisation of each NS patient. Early and accurate diagnosis is necessary and important because NS can present with different characteristics, and therefore each patient has a different prognosis and needs an individual treatment and periodic supervision regimen. Management guidelines have been developed to help the clinician to fulfil the health care needs of these patients.⁵

Few cases have been reported regarding the dental management of young patients with NS.^{6,12-18} The management approach is often challenging because of the bleeding diathesis, risk of bacterial endocarditis and a strong gag reflex.

The aim of the present article is to describe the case of an 8-year-old female affected by NS, and discuss the orofacial findings and orthodontic treatment approach.

Case report

A female, eight years and four months of age, reported for an orthodontic examination.

The anamnestic investigation revealed NS caused by a PTPN11 gene mutation, a mild pulmonary stenosis, thrombocytopenia, scoliosis, short stature, and delayed bone ageing but with a normal response to growth hormone.

A full orthodontic evaluation was conducted, which comprised extra- and intraoral photographs, dental casts, panoramic radiograph and lateral cephalogram (Figure 1, 2). The records indicated the presence of a skeletal Class III malocclusion, a high-arched palate with a right lateral cross-bite, an anterior open bite, severe crowding (more than 9 mm) in both arches, and a mandibular dental midline shifted to the right as a consequence of the premature loss of the right lower deciduous canine.

Some of the typical facial characteristics associated with NS were present.

Bone ageing assessed through the cervical vertebral maturation method¹⁹ revealed a pre-pubertal stage (Cervical Stage 2).

Treatment objectives and alternatives

The treatment plan aimed to resolve the transverse maxillary deficiency and the unilateral cross-bite, establish a normal overbite and improve the crowding to allow unimpeded eruption of permanent teeth. An additional goal was to improve dental aesthetics and therefore the self-esteem and socialisation of the young patient, in as simple a way as possible, while recognising the general health status of the patient.

In a consideration of the skeletal nature of the malocclusion, there was a possible option of commencing early orthopaedic treatment to improve the skeletal Class III malocclusion and the mandibular high-angle pattern, or to wait for the end of growth and normalise the skeletal relationship through orthognathic surgery. In agreement with the parents and the referring general practitioner, the latter option was discarded because of the medical status of the patient.

The main alternatives for orthopaedic treatment were a chin cup or facemask protraction, while bone-plates and Class III elastics were also options.²⁰ The first two, however, are not best suited for high-angle patients, since one of their effects is a downward and backward rotation of the mandible.²¹ Bone-plates, on the other hand, were judged risky in a patient with valvulopathy because they can be a source of infection. Overall, the parents of the child required a treatment that was as simple as possible.

With all these considerations in mind, a camouflage treatment option was chosen.

The severity of the tooth size-arch length discrepancy, the mandibular high-angle pattern, the skeletal malocclusion and the impaired eruption of some permanent teeth were all factors that pointed to tooth extractions. The extraction of two premolars in the lower arch is a viable option for the camouflage treatment of a Class III malocclusion, and also from a long-term point of view.²² However, complementary extractions in the upper arch are required to obtain an Angle Class I molar relationship. The risk for bacterial endocarditis and the need for antibiotic prophylaxis



Figure 1. Pretreatment facial and intraoral photographs.

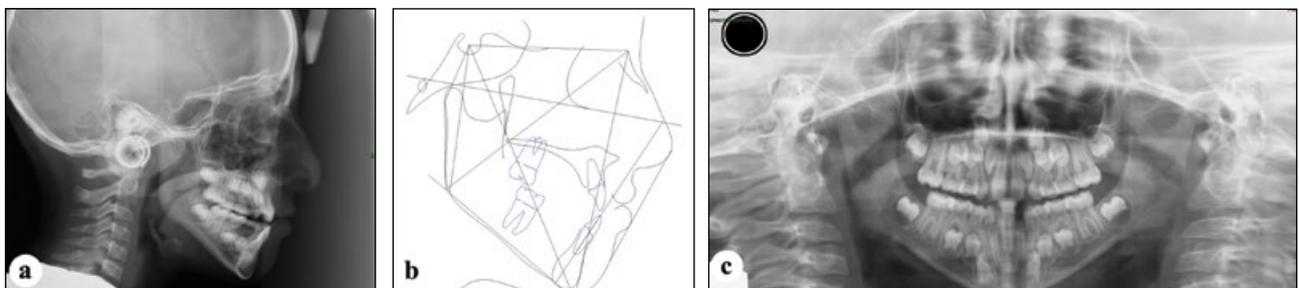


Figure 2. Pretreatment radiographic images. (a) Lateral cephalogram. (b) Tracing. (c) Panoramic radiograph.

makes surgical procedures more complicated in NS patients. Therefore, it was decided to perform extractions only of the lower first premolars.

The extractions could be deferred until the end of the mixed dentition, or performed early following a serial extraction approach. The presence of a maxillary cross-bite and the risk of permanent tooth impaction demanded early intervention, and so camouflage treatment comprising expansion of the maxillary

arch and serial extraction in the mandibular arch was decided upon.

Treatment progress

The position of the expansion screw into the palatal vault is of great importance to achieve a significant widening effect,²³ but the constricted palatal vault prevented fitting an expansion screw of the length required to manage the transverse maxillary deficiency.



Figure 3. Post-treatment facial and intraoral photographs.

Therefore, a two-band Hyrax expander with a 7 mm screw was bonded over the upper second deciduous molars and activated once a day. After achieving the transverse expansion allowed by the expander, the screw was blocked with composite resin and left in situ to act as a retainer. After eight months, a second rapid palatal expander was constructed, bonded and activated once a day until a corrected transverse maxillary dimension was achieved. A serial extraction protocol following Dewel’s method (CD4)²⁴ in the lower arch was started by the extraction of the lower left deciduous canine, followed several months later by the lower first deciduous molars. At this time, the dental midlines had considerably improved. When the tip of the cusp of each lower first premolar was visible, the extraction of these permanent teeth was performed. Each surgical procedure required an antibiotic prophylaxis, and so extractions were carefully planned. After the extraction of the lower teeth, the patient

underwent periodic review to monitor the eruption of the remaining permanent teeth.

Treatment results

An interceptive treatment programme requiring few appliances and minimal need for compliance was successful in achieving a corrected posterior overjet, and in improving the anterior overbite, dental midline, crowding, and dental aesthetics (Figure 3, 4). A diastema was still present between the lower left second premolar and the lower left canine, even though surgical procedures were performed with attention to maintain occlusal symmetry and function. Mesial migration of the posterior teeth into the extraction space occurred to a lesser extent on the side in which there was agenesis of the third molar.

Because two first premolars were extracted in the lower arch, it was not possible to obtain a molar and

Table I. Cephalometric analysis.

Measurement	Norm		Pretreatment	Post-treatment	Difference
	Mean	SD			
SNA (°)	82.0	3.5	80.1	80.1	0
SNB (°)	80.0	3.0	79.2	79.6	0.4
ANB (°)	2.0	2.4	0.9	0.5	-0.3
Wits appraisal (mm)	0.0	1.0	-4.0	-1.9	-2.1
FMA (°)	26.0	5.0	33.8	30.8	-3.0
U1-APo (mm)	6.0	2.2	1.9	4.6	2.7
L1-APo (mm)	2.0	2.3	2.8	0.5	-2.3
U1-PP (°)	110.0	5.0	108.3	113.4	5.1
IMPA (°)	95.0	7.0	81.9	76.6	-5.3

Abbreviations: S, sella; N, nasion; A, A point, B, B point; FMA, angle between the Frankfurt plane and mandibular plane; U1, upper central incisor, APo, the line connecting A point to pogonion; L1, lower central incisor; PP, palatal plane; IMPA, angle between mandibular plane and the long axis of the lower central incisor.

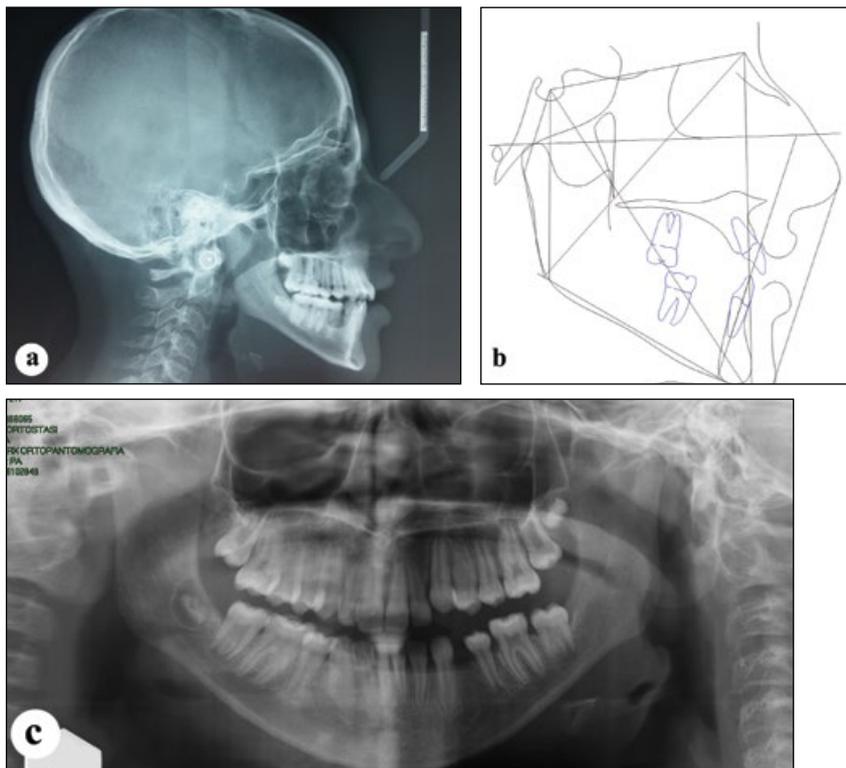


Figure 4. Post-treatment radiographic images. (a) Lateral cephalogram. (b)Tracing. (c) Panoramic radiograph.

canine Class I occlusion and an ideal intercuspation in the posterior segments.

A cephalometric improvement in the sagittal relationship between the maxilla and mandible (Wits appraisal) and a reduction of the Frankfort-mandibular plane angle (FMA) was observed, together with a slight worsening of the position of the upper and lower incisors (Figure 4, Table I).

The one-year follow-up showed stability of the achieved results (Figure 5).

Discussion

Considering the presence of NS and the health problems of the young patient, an ideal treatment plan involving orthognathic surgery was not considered



Figure 5. Intraoral photographs taken at one-year follow-up.

feasible, and so it was decided to adopt a simpler treatment option and camouflage the Class III malocclusion.

A variation of a serial extraction programme often begins with the removal of the deciduous canines, which helps to resolve incisor crowding. The extraction of the first deciduous molars follows to accelerate the eruption of the first premolars, which are subsequently extracted to allow the eruption of the permanent canines.²⁴ In rare cases, the premolars are enucleated in conjunction with the extraction of the deciduous molars. The aim of this procedure is to create sufficient space for the physiologic eruption of permanent teeth into more favourable positions and with healthy periodontal tissues. The advantages are an early correction of the malocclusion, a positive impact on the self-esteem of the young patient, and an easier second-phase of treatment with fixed appliances.^{25,26} The programme requires, however, a longer observation period, timely execution and a harmonious skeletal pattern because early extraction can affect facial development.^{27,28} Furthermore, there is no consensus that following a serial extraction programme the fixed appliance phase is shorter or simpler.²⁹

The presence of a skeletal Class III malocclusion is reported as a contraindication for serial extraction²³ because it is difficult to predict the outcome of future growth. Alternatively, a therapeutic value of serial

extractions has been described in the lower jaw in Class III malocclusions with crowding in the mandibular arch.²⁸ In the present case, serial extractions in the lower arch were effective, not only in relieving dental crowding and improving the midline, but also in improving the dental open bite and the FMA angle without damaging the patient's profile or worsening of the skeletal Class III malocclusion.

Due to the severe constriction of the palatal vault, it was not possible to gain sufficient space to resolve the crowding by means of the maxillary expansion. Bonding a rapid maxillary expander to the deciduous molars has an advantage, because the first permanent molars are not affected by the applied heavy forces or by the risk of tooth decay due to the presence of molar bands. Furthermore, the risk of creating an iatrogenic scissor-bite is significantly reduced.³⁰

Overall, the treatment programme was effective and easy to manage for the patient and family because a positive therapeutic result was obtained via two consecutive rapid palatal expanders and timely extractions in the lower jaw. The minimal orthodontic exposure was a great advantage for the young patient, who was simultaneously managed for her complex medical condition. Occlusal stability one-year post-treatment confirmed that the treatment was functionally effective.

The possibility of future orthodontic management

remains an option to finalise the case to an Angle Class I occlusion. This may be pursued by extractions of upper premolars and fixed appliances, or alternatively by the management of the skeletal disharmony by means of orthognathic surgery. Early appliance treatment would close the remaining diastema between the lower left canine and lower left premolar, which, in adult patients, may be followed by attachment loss if bone height has been reduced through remodelling.³¹ While mandibular spaces can be closed in adult patients with conventional mechanics,³² the use of orthodontic miniscrews or a corticotomy can be effective in reducing the risks related to the protraction of mandibular teeth into edentulous spaces.^{33,34}

Conclusions

- Noonan syndrome is a relatively common condition that clinicians may encounter.
- The management of these patients can be challenging and may require a multidisciplinary approach.
- The present case of an 8-year-old female described an interceptive orthodontic treatment programme comprising mandibular serial extraction, which was successful in improving the occlusion, the vertical and sagittal components of the skeletal malocclusion, and the patient's quality of life.
- The patient and her parents were satisfied with this result; however, the camouflage of the malocclusion may be improved with future extractions in the upper arch followed by appliance therapy.

Corresponding author

Dr. Michele Tepedino
 Research assistant
 Department of Biotechnological and Applied Clinical Sciences
 University of L'Aquila
 Viale S. Salvatore
 Edificio Delta 6
 67100
 L'Aquila (AQ)
 Italy
 Email: m.tepedino@hotmail.it

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