www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i5.82

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Case Report

Noonan Syndrome – A Case Report

Authors
Pritesh B. Ruparelia, Bharvi A. Shukla*
Department of Oral Medicine and Radiology, College of Dental Sciences & Research Centre, Ahmedabad, Gujarat, India
Corresponding Author
Dr Bharvi A. Shukla
Block E-1/6, "Vikramnagar", ISRO Colony, Behind Iskon temple, Ambli-Bopal Road, Ahmedabad Gujarat, India

Abstract
Noonan syndrome is an autosomal dominant multisystem disorder, associated with cardiac anomalies and a distinctive facial appearance, characterized by genetic heterogeneity. Noonan syndrome affects both females and males, and has an estimated incidence of 1 per 1,000-2,500 live births. The present report aims at presenting the oro-facial findings in a case of Noonan syndrome in a 16 year-old male.
Keywords: *Noonan Syndrome (NS), Webbed neck, Short stature, Pectus excavatum.*

Introduction

Noonan syndrome (NS) is an autosomal dominant, variably expressed, multisystem disorder.[1] It's first description was made in 1883 by Kobylinski.[2] However studies on the NS had been first conducted in 1963 by Jaqueline Noonan and Ehmke.[2,3,4]

NS is also called Webbed neck syndrome, Pseudo-Ullrich Turner syndrome, Female Pseudo-Turner syndrome or Turner-like syndrome.[5]

The incidence is one in 1,000 to 2,500 live births for severe phenotype, but mild cases may be as common as one in 100 live births. Familial recurrence is consistent with an autosomal dominant mode of inheritance, but de novo mutations are more common, accounting for 60% of cases.[6]

Tartaglia et al. in 2001 reported the molecular basis of this syndrome: mutation in the PTPN11 (protein tyrosine phosphatase non-receptor type 11) gene on chromosome number 12, in about 50% of the individuals with NS.[5]

To date, many cases have been reported, but there have been few descriptions of the cranio-dento-facial features. Therefore, the present paper is intended to describe the oro-facial findings in a case of NS.

Case Report

A16-years old male patient came to the department of Oral Medicine & Radiology with chief complain of unaesthetic appearance of teeth.

There was no relevant medical or family history. Patient had slurred speech and showed poor school records i.e. he had failed thrice in the 7th grade and so was dropped out from school.

On general examination, patient was of short stature i.e., 4 feet and 8 inches and showed facial

dimorphism, with facial shape of an inverted triangle (Figure 1). Physical examination revealed webbing of neck/ ptergium colli (this was the most dominant feature), pectus excavatum and wide spaced nipples which appeared to be low-set (Figure 2 and 3). Also features like thickly hooded prominent eyes with mild hypertelorism, multiple lentigines on nose, epicanthic folds and deeply grooved philtrum were present (Figure 1). Moreover he had a tendency for lip incompetence and he reported the habit of mouth breathing.

On intra oral examination multiple retained deciduous teeth and multiple missing permanent teeth was found.

On panoramic radiograph multiple over retained deciduous teeth in relation to 55, 63, 73, 75 & 83 and multiple unerupted permanent teeth in relation to 15, 23, 33, 35 and 43 were seen (Figure 4).

Based on clinical and radiographic features observed a provisional diagnosis of Noonan's syndrome was established. Comprehensive treatment was planned which included extraction of retained deciduous teeth and orthodontic treatment.

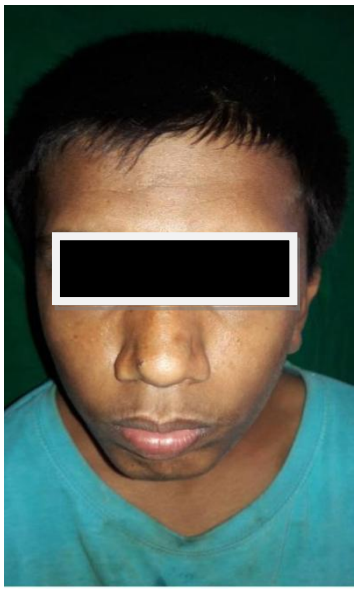

Figure 1: Extraoral features showing facial dimorphism, facial shape of an inverted triangle, multiple lentigines on nose, epicanthic folds and deeply grooved philtrum.

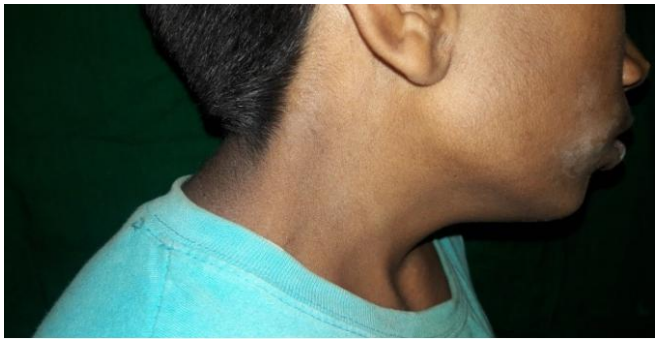

Figure 2: Webbing of neck

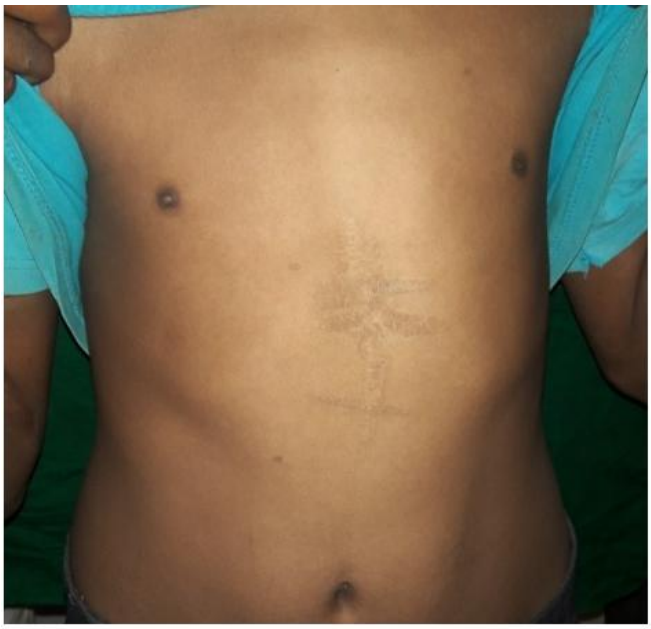

Figure 3: Pectus excavatum with wide spaced nipples.

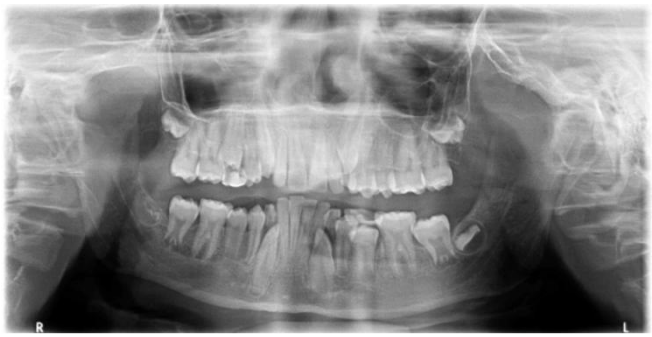

Figure 4: Panoramic radiograph showing: multiple retained deciduous teeth in relation to 55, 63, 73, 75, 83 and multiple unerupted permanent teeth in relation to 15, 23, 33, 35, 43.

Table 1:

DIAGNOSTIC CRITERIA FOR NOONAN SYNDROME		
FEATURES	**A-MAJOR**	**B-MINOR**
1. Facial	Typical facial dysmorphology*	Suggestive facial dysmorphology
2. Cardiac	Pulmonary valve stenosis, hypertrophic cardiomyopathy, and/or electrocardiographic results typical of Noonan syndrome	Other defect
3. Height	<3rd percentile	<10th percentile*
4. Chest wall	Pectus carinatum/excavatum*	Broad thorax
5. Family history	First-degree relative with definite Noonan syndrome	First-degree relative with suggestive Noonan syndrome
6. Other features	All of the following: intellectual disability, cryptochoridism, and lymphatic vessel dysplasia	One of the following: intellectual disability*, cryptochoridism, and lymphatic vessel dysplasia
NOTE: Noonan syndrome is considered present if the patient has typical facial dysmorphology plus one feature from categories 2A through 6A or two categories from features 2B through 6B, or has suggestive facial dysmorphology plus two features from categories 2A through 6A or three features from categories 2B through 6B.		

* : Features present in our case.

Table 2:

Features of NS		
	Expected	In Present Case
Cardiovascular	Pulmonary valvular stenosis Hypertrophic cardiomyopathy Patent ductus arteriosus Arterial septal defect Ventricular septal defect Mitral insufficiency	No abnormality was detected on clinical examination and on reported by physician.
Growth	Short stature Birth weight and length normal	Short stature
Skeletal	Sternal deformity: Pectus carinatum, Pectus excavatum Spinal abnormality Cubitus valgus	Pectus excavatum
Dysmorphic facial features (changes with age)	• Newborn: Hypertelorism, downward slant of palpabral fissure, Short neck, Low set posteriorly rotated ears with thick helix, Short broad nose, Large head compared to face, Swollen edematous dorsum of hands and feet • Infant: Wispy hair, Thickly hooded prominent eyes, Wide-based, depressed nose, Cupid bow appearance of upper lip • Adolescent: Inverted triangle shaped head, Neck skin webbing, Pectus sternal deformity, Small chin, Widely spaced nipples, Curly / wooly hair, Nose has a pinched root and a thin high bridge • Adult: Prominent naso-labial folds, High anterior hair line, Transparent and wrinkled skin	NA NA Inverted triangle shaped head Neck skin webbing Pectus sterna deformity Prominent naso labial folds Deeply grooved philtrum Widely spaced nipples NA
Neurologic	Learning difficulties	Learning difficulties

	Mild intellectual disability Speech difficulties	Mild intellectual disability Speech difficulties
Skin and Hairs	Lentigines Café-au-lait spots Pigmented nevi Thick curly or thin sparse hairs	Lentigines
Genitourinary	Cryptorchidism Males can have fertility issues Puberty can be delayed in both genders	No relevant history
Eyes	Hypertelorism Ptosis of eyelids Epicanthic folds Down slanting palpabrael fissures	Mild hypertelorism
Ears	Low set posteriorly rotated Hearing loss	Not present
Gastrointestinal	Feeding difficulties	NA
Hematologic	Increased bleeding tendency: Factor deficiency, Platelet defect	No relevant history
Intra oral	High arched palate Delayed eruption Malocclusion Articulation difficulty Micrognathia	High arched palate Delayed eruption Malocclusion Retained deciduous teeth

Discussion

NS is a multisystem disease with a wide spectrum of heterogeneity regarding the genetic and clinical characteristics.[7] The eponym "Noonan syndrome" was adopted in recognition of Dr Noonan, because she was the first to indicate that this condition occurred in both genders, was associated with normal chromosomes, included congenital heart defects, and could be familial.[8]

The characteristic abnormalities resemble those in Turner syndrome, which only affects females and so NS was used to be called as "Male Turner syndrome". This term is no longer used because NS can affect females also. The observation that patients with NS have normal karyotypes (46XY) was important in allowing the distinction to be made between the Turner and Noonan syndromes.[5]

Autosomal dominant abnormalities are the results of germline mutations in the intracellular retrovirus associated DNA sequences (RAS) / mitogen-activated protein kinase (MAPK) pathway which can lead to NS and the associated abnormalities.[8] NS has been linked to the chromosomal band 12q24.1. Also studies suggest that 50% of cases of NS are caused by missense, gain-of-function mutations in PTPN11.[1]

As it is an autosomal dominant anomaly, any person affected has up to a 50% chance of transmitting it to their children.[3] However in the present case there was no such family history, makes it more likely to be of mutation possibility.

A scoring system given in Table - 1 by van der Burgt et al in 1994 has been devised to help diagnose patients with the condition.[6]

Thus it confirms with the diagnosis of NS.

Cardiovascular abnormalities are common in patient with NS and it includes pulmonary valvular stenosis, hypertrophic cardiomyopathy, patent ductus arteriosus, arterial septal defect, ventricular septal defect and mitral insufficiency.[5,6,7] Though birth weight and length are normal, they generally have short stature.[6]

Pectus excavatum is commonly seen though other skeletal deformities like pectus carinatum, spinal abnormality and cubitus valgus can occur.[6]

Facial features often changes with age. In newborns large head compared to face, hypertelorism, downward slant of palpabral fissure, short neck, low set posteriorly rotated ears with thick helix, short broad nose, Swollen edematous dorsum of hands and feet are seen. In Infants features like wispy hair, thickly hooded prominent eyes, wide-based depressed nose and

cupid bow appearance of upper lip occurs. Adolescents presents typically with inverted triangle shaped head, small chin, neck skin webbing, pectus sternal deformity, widely spaced nipples and curly / wooly hairs. Adults with NS have prominent naso-labial folds, high anterior hair line and transparent and wrinkled skin.[6]

Patient may have learning and speech difficulties and may present with mild intellectual disability.[6] Lentigines, café-au-lait spots and pigmented nevi can be the skin manifestations of NS.[5] Males can have fertility issues and cryptorchidism but puberty can be delayed in both genders. Patient may have feeding difficulties.[6] Intra oral manifestations of NS includes high arched palate, delayed eruption, malocclusion, articulation difficulty and micrognathia.[5,6] Moreover these patients may have increased bleeding tendency due to factor deficiency and platelet defects.[6]

Details regarding expected features in this syndrome and that which were present in our case are listed in Table – 2.[5,6,7]

The syndromes that should be differentiated with NS includes LEOPARD syndrome (acronym stands for lentigines, electrocardiogram abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, retardation of growth, and deafness), Cardiofaciocutaneous syndrome, Costello syndrome, Turner syndrome, Fetal alcohol syndrome, Aarskog syndrome, Baraitser-Winter syndrome and Neurofibromatosis type 1.[1,8]

All individuals with NS require detailed and regular follow up for ongoing developmental, audiologic, ophthalmologic, cardiac, neurologic and other associated problems. Because bleeding anomalies and blood clotting disorders have been reported, a full hematologic workup must be performed before any dental surgery.[9]

Conclusion

With a prevalence of one in 1000–2500, NS is a disorder that dentist may encounter during their career. Because presentation can be mild and the typical facial features recede with age, the diagnosis might be overlooked. No confirmatory testing for NS is available. This entity remains a strictly clinical diagnosis because of characteristic dental and skeletal structures and dentists can play a major role in the diagnosis of this syndrome. Regular detailed follow-up with a multidisciplinary approach is often needed to address the medical and developmental complications of NS.

Acknowledgments: Nil
Support of Sources: Nil
Conflicts of Interest: There are no conflicts of interest

References

1. Roberts AE, Allanson JE, Tartaglia M, Gelb BD. Noonan syndrome. Lancet. 2013;381:333–342.
2. Ierardo G, Luzzi V, Panetta F, Sfasciotti GL, Polimeni A. Noonan Syndrome: A case report. Europian journal of Paediatric Dentistry. 2010;11(2):97-100.
3. Emral ME, Akcam MO. Noonan syndrome: a case report. Journal of Oral Science. 2009;51(2):301-306.
4. Digilio MC, Marino B. Clinical manifestations of Noonan syndrome. Images Paediatr Cardiol. 2001;3(2):19-30.
5. Asokan S, Muthu M, Rathna PV. Noonan syndrome: A case report. J Indian Soc Pedod Prevent Dent. 2007 Sept;144-147.
6. Bhambhani V, Muenke M. Noonan Syndrome. Am Fam Physician. 2014;89(1):37-43.
7. Tafazoli A, Eshraghi P, Koleti ZK, Abbaszadegan M. Noonan syndrome – a new survey. Arch Med Sci. 2017;13(1):215-222
8. Romano AA, Allanson JE, Dahlgren J, Gelb BD, Hall B, Pierpont ME, Roberts AE, Robinson W, Takemoto CM, Noonan JA. Noonan Syndrome: Clinical Features, Diagnosis and Management Guidelines.

Journal of the American Academy of Pediatrics. 2010;126:746-759.

9. Kumar M, Chandar VV, Koduri S, Sankireddy S. Noonan Syndrome with cleft palate: A rare case report. J Indian Acad Oral Med Radiol. 2016;28:207-210.