ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 8 | August - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

NOONAN SYNDROME: A CLINICAL STRATEGY FOR DENTAL MANAGEMENT

Dental Science

Asha J* Assistant Professor, Department of Dentistry, Trichy SRM Medical college Hospital and Research Centre*Corresponding Author

Vijayalakshmi D Professor, Department of Dentistry, Trichy SRM Medical college Hospital and Research Centre

Senthilkumaran M Assistant Professor, Department of Dentistry, Dhanalakshmi Srinivasan Medical College

JaysimhaRaj U Professor and Head, Department of Dentistry, Trichy SRM Medical college Hospital and Research Centre

ABSTRACT

Noonan syndrome is an autosomal dominant genetic disorder with multisystem involvement inclusive of distinctive facial features that rather go unnoticed. The possible correlation of the oral manifestations with the various other systemic findings will enable a multidisciplinary approach and timely management. We describe an exceptional case of Noonan syndrome with typical facial characteristics, skin and oral manifestations with Keratocystic odontogenic tumor of mandible and predilection to Neurofibromatosis. The article also aims to put forth our clinical strategy of management of a patient diagnosed with this syndrome.

KEYWORDS

Noonan, Keratocystic odontogenic tumor, Neurofibromatosis

INTRODUCTION:

Noonan syndrome (NS) is a relatively common, clinically variable and genetically heterogeneous developmental disorder characterized by reduced postnatal growth, distinctive facial dysmorphism, cardiac defects and variable cognitive deficits. Other associated features include ectodermal and skeletal defects, cryptorchidism, lymphatic dysplasias, bleeding tendency, and rarely, predisposition to hematologic malignancies during childhood1. Its frequency has been estimated as 1 in 1,000 to 1 in 2,500[2,12].

The distinctive facial features of a patient with Noonan syndrome are found to vary with age3. Though only facial dysmorphism has been predominantly mentioned in the literature, there have been various other dental and maxillofacial manifestations associated with the syndrome. Yazdizadeh M et al (2004) has described the major diagnostic features of Noonan syndrome as given in table 14. However, the universally accepted diagnostic criteria for Noonan syndrome was by van der Burgt 1997 (table 2)[5,6].

We henceforth report a case of Noonan syndrome with the emphasis on establishing a clinical strategy of multi-disciplinary approach and management.

TABLE 1. MAJOR DIAGNOSTIC FEATURES OF NOONAN SYNDROME[4]

Diagnostic features
1. Short stature (50%)
2. Mild mental retardation (33%)
3. Epicanthic folds, ptosis of eyelids, hypertelorism, down slanting palpebral fissures
4. Low nasal bridge
5. Ears: Low set posteriorly rotated with thick helix &/or abnormal auricles (90%)
6. Short/webbed neck
7. Excess nuchal skin with low posterior hair-line (55%)
8. Thorax: shied chest, pectus excavatum or carinatum or both(70%)
9. Skeletal abnormalities: Cubitus Valgus (50%), vertebral anomalies
10. Cardiac Anomalies: pulmonary valve stenosis(50%), atrial septal defects (10%), patent ductus arteriosus, left axis deviation (33%)
11. Skin: Café-au-lait spots (10%), lentingines(2%), pigment nevi (25%)
12. Genital: cryptorchidism (60%), small penis
13. Oral manifestations: deeply grooved philtrum with high wide peaks of vermillion border of upper lip (95%), moderate retrognathia, high arch palate (45%)

Table 2 . Diagnostic criteria of Noonan Syndrome6

FEATURE	A=MAJOR	B=MINOR
1. FACIAL	Typical face dysmorphology	Suggestive face dysmorphology
2. cardiac	Pulmonary valve stenosis, HOCM and/or ECG typical of NS	Other defect
3. Height	<P3*	<P10*
4. chest wall	Pectus carinatum/excavatum	Broad thorax
5. family history	First degree relative with definitive NS	First degree relative with suggestive NS
6. other	Mental retardation, cryptorchidism and lymphatic dysplasia	One of Mental retardation, cryptorchidism and lymphatic dysplasia

HOCM- Hypertrophic Obstructive Cardiac Myopathy

*P3 and *P10 refer to percentile lines of height according to age.

Definitive NS: 1 "A" plus one other major sign or two minor signs; 1 "B" plus two major signs or three minor signs

Case Report:

A 16 year old female reported to our department of dentistry with complaints of pain in the right lower back tooth region since one month. She was apparently normal one month ago when she started developing intermittent, non-radiating pain in the right angle of the mandible region which was followed by a intraoral swelling of 3x1cm in the right lower vestibule. Her past medical history was relatively insignificant but for a family history of Neurofibromatosis apparent in her father who accompanied the patient to the dental office. Patient's father also presented with features suggestive of Noonan syndrome (Figure 5). The age of menarche was found to be 15 years denoting a slight delay in puberty.

On examination, patient was of short stature (height: 138cm) with a normal gait. She was thin built (weight: 40kgs) and was conscious and well oriented to time and place. Facial examination of the patient was suggestive of triangular face form with a pointed chin. The patient also presented with hypertelorism, broad nasal bridge, down slanting palpebral fissures, low set ears with posterior angulation (Figure 1) and a short neck with webbing of trapezius (Figure 2).

Figure 1: Typical facial Dysmorphism

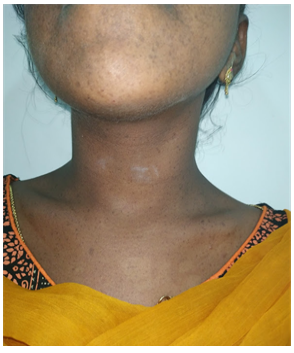

Figure 2: Webbing of neck

The philtrum of upper lip was marked by high wide peaks of vermillion border (Figure 3). The facial skin had multiple hyperpigmented pin-point lesions (Figure 4).

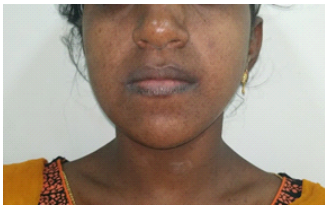

Figure 3: High Peaks of Vermillion Border

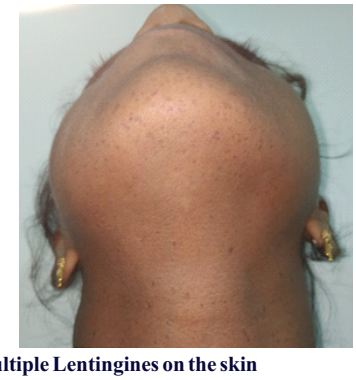

Figure 4: Multiple Lentingines on the skin

There were two large cutaneous macules present in the right forearm and left leg (Figure 6). There was also a cutaneous nodule palpable over the bridge of the nose.

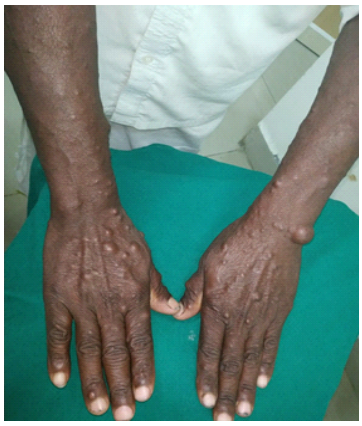

Figure 5: First degree relative with suggestive Noonan Syndrome and definitive Neurofibromatosis

Intraoral examination revealed a tender cystic swelling in the right buccal vestibular region in relation to 46, 47 region, obliterating the sulcus. The swelling was fluctuant in relation to 46 regions. She had a high arched palate. The periodontal status of the patient was good.

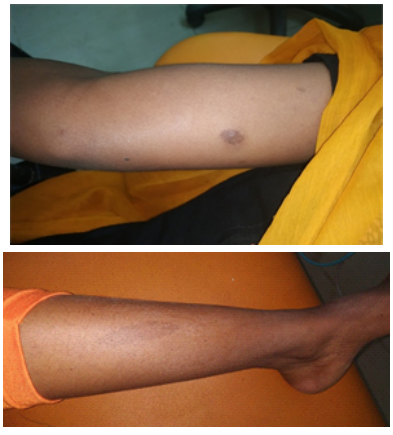

Figure 6: cutaneous macules over the right forearm and left leg

A panaromic radiograph revealed a well-defined unilocular radiolucency in the right body of the mandible involving the roots of 46, 47 (Figure 7).

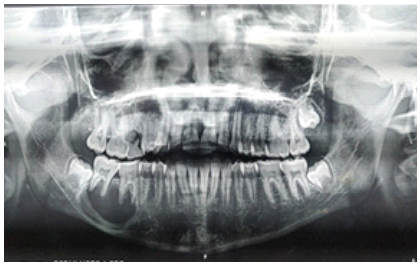

Figure 7: OPG revealing unilocular well circumscribed radiolucency in the right body of the mandible

Pulp vitality testing found 46 and 47 to be vital. Routine blood investigation inclusive of PT, APTT, INR were carried out to rule out any form of blood diathesis. Cardiologist opinion was sought and she was found to be fit without any cardiac complications.

Based on the features and the diagnostic criteria, a definitive clinical diagnosis of Noonan syndrome with jaw cyst was made.

After running through the routine blood investigations to rule out any blood dyscrasias, decompression of the cystic cavity was carried out where the cyst content was found to be white and cheesy in consistency. The cyst wall lining was sent for histopathological examination. A custom made stent was placed in the decompressed cyst cavity (Figure 8).

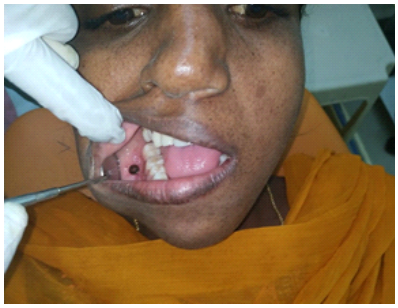

Figure 8: Decompression of the cystic cavity with the custom-made stent in situ

The histopathology of the given section showed a cystic lumen with scattered keratinaceous debris. The lining epithelium was parakeratinized stratified squamous type, exhibiting surface corrugation in some areas and 5-10 cells thickness. The basal cells were tall columnar with hyperchromatic & palisaded nuclei. The underlying connective tissue wall was fibrocellular in nature with mild chronic inflammatory infiltrate. Based on the features mentioned a diagnosis of keratocystic odontogenic tumor was made.

DISCUSSION:

Noonan syndrome though finds its place in the database of the rare diseases. It is found to be a relatively common congenital condition with no obvious sex predilection. Study of "the Noonan" syndrome (NS) began at least 100 years ago when Kobylinski (1883), a medical student at the Russian/Estonian University of Dorpat, described a tubercular 20-year-old Jewish man with several remarkable clinical manifestations[7].

The syndrome is predominantly reported in the literature with short stature, typical face dysmorphology and congenital heart defects. The characteristic facial features are the most important key for early diagnosis and intervention. Thus, age of the patient plays a significant role in the diagnostic process as the characteristic facial features are found to change with age. The facial features can be subtle, especially at old age6. In our case report, patient has been diagnosed as late as 16 years of age though an early diagnosis at birth could have ensured an early education, counseling and multi-system interception for growth and development.

It is characterized by a wide array of clinical symptoms thus making the necessity of a specific diagnostic criterion very useful. Based on the internationally accepted scoring criteria by van der Burgt 1997, our patient presented with one major signs (typical face dysmorphology 1A) and two minor sign (height less than 10% growth percentile + first degree relative with suggestive NS) contributing to a definitive diagnosis of Noonan syndrome.

There is also a predilection to Neurofibromatosis1 in our patient considering the two macular lesions and a cutaneous nodule not to forget the evident family history. Though based on the diagnostic criteria of neurofibromatosis4,13, a definitive diagnosis of neurofibromatosis cannot be made in our patient. Several cases with features of Neurofibromatosis and Noonan syndrome (NFNS) have been reported in the past. There have been various cases of multiple giant cell lesions reported along with Noonan syndrome. But, there are very few reports mentioning the association of Odontogenic keratocysts along with Noonan syndrome 9. Our patient is one such rare case presenting with keratocystic odontogenic tumor in the right body of the mandible. Risk of developing multiple jaw cysts in Neurofibromatosis-Noonan syndrome (NFNS) should be taken into consideration and periodic follow up is therefore mandatory.

Another striking dermatological feature is the presence of multiple lentigines which could be associated with LEOPARD syndrome, confirmation of which requires hearing deficits. But association of the features of Noonan and LEOPARD syndrome (genetic allelic disorders10) is attributed to the genetic alterations occurring on the same long arm of the chromosome.

The proposed strategy of management for such a patient would be based on the age at which the diagnosis is made. The guidelines5 have been divided into 4 age groups- 1.neonatal and infancy (0-1years); 2. Childhood (1-11years); 3. Adolescence: 11—18 years old; 4. Adulthood: above 18 years. Our patient falling into the adolescence group requires a thorough cardiac evaluation and screening for delayed puberty, scoliosis, neurological deficits, thyroid dysfunction and bleeding disorders. Further dental treatment should be carried out only after complete evaluation of the systemic condition. Once the dental treatment is carried out and adequately managed, it should be followed by adulthood management that includes genetic counselling, mutation testing and discussion of risks to children and options in pregnancy. Counseling about the syndrome and the need for regular follow ups also plays a crucial role in early intervention and management of the syndrome.

CONCLUSION:

We have described a rare case of Noonan syndrome with the possible predilection for Neurofibromatosis1, associated with keratocystic odontogenic tumor. An appropriate diagnosis of the syndrome associated with the odontogenic tumor would aid in comprehensive early intervention and multi-system management of the underlying condition.

REFERENCES:

1. Tartaglia M., Zampino G., Gelb B.D. Noonan Syndrome: Clinical Aspects and Molecular Pathogenesis Mol Syndromol 2010;1:2–26.
2. Tullu M S, Muranjan M N, Kantharia V C, Parmar R C, Sahu D R, Bavdekar S B, Bharucha B A. Neurofibromatosis-Noonan syndrome or LEOPARD Syndrome? A clinical dilemma. J Postgrad Med 2000;46:98-100
3. Roberts AE. Allanson JE. Tartaglia M. Gelb BD. Noonan syndrome.The Lancet.2013
4. Yazdizadeh M et al. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004;98:316-20
5. Dyscerne. Management of Noonan Syndrome: A Clinical Guideline.2010
6. van der Burgt I. Noonan syndrome. Orphanet J Rare Dis. 2007;2:4. Published 2007 Jan 14. doi:10.1186/1750-1172-2-4
7. Mendez HM., Opitz JM., Noonan syndrome: A Review. American Journal of Medical Genetics 1985; 21:493-506.
8. Jorge AL., Malaquias AC., Arnhold JP., Mendonca BB., Noonan Syndrome and Related Disorders: A Review of Clinical Features and Mutations in Genes of the RAS/MAPK Pathway. Horm Res 2009;71:185–193
9. Yamashita H., Fujita S., Ikeda T., Asahina I., Multiple Odontogenic cysts in patient with Neurofibromatosis-Noonan syndrome.
10. Allanson JE., Roberts AE., Noonan Syndrome. Gene Reviews University of Washington, Seattle; 1993–2020.
11. Gelb BD., Tartglia M., Noonan Syndrome With Multiple Lentigines. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2020.
12. Narayanan DL et al., Hotspots in PTPN11 Gene Among Indian Children With Noonan Syndrome. Indian Pediatrics 2017; 54: 638-641.
13. Boyd KP, Korf BR, Theos A. Neurofibromatosis type 1. J Am Acad Dermatol. 2009;61(1):1-16.