Case report:

Noonan Syndrome with Multiple Lentigines: A rare Hereditary Multisystem Disorder

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Abstract

Noonan syndrome with multiple lentigines (NSML) is a rare hereditary disorder that was previously known as LEOPARD syndrome. We present a 24-year-old woman with hundreds of lentigines all over her body, wide-apart eyes, deafness, and an inability to talk since her childhood. Her hearing test revealed sensorineural deafness. She had a concentric type of cardiomyopathy in the echocardiographic report. Clinically she was labeled as Noonan syndrome with multiple lentigines. She had presented with greying of scalp hairs, which was a unique feature of such a case. Around 200 NSML cases were found worldwide. To the best of our knowledge, this is the first case of a patient with NSML presenting with grey hair.

Key words: Noonan syndrome with multiple lentigines, LEOPARD syndrome

Introduction

Noonan syndrome with multiple lentigines (NSML) previously known as LEOPARD syndrome (LS), is a rare autosomal condition with an unknown prevalence. LEOPARD is an acronym that stands for lentigines on the skin (L), electrocardiographic conduction defects (E), ocular hypertelorism (O), pulmonary stenosis (P), abnormal genitalia (A), retarded development (R), and deafness (D).[1,2] Mutations of the PTPN11 (90%), RAF1, BRAF, and MAP2K1 genes cause this syndrome. Noonan syndrome is an autosomal dominant condition similar to NSML.[3,4,5]

Several clinical findings of Noonan Syndrome overlap those of NSML, like facial anomalies, some congenital heart defects, sensorineural deafness, and growth retardation The leading causes of pediatric intracerebral haemorrhage (ICH) are arteriovenous malformations, hematologic abnormalities, and brain tumours.[6] NSML has no specific treatment option. Cardiovascular intervention and supportive measures can help the patients to continue a near-normal lifestyle.[7]

There is no single treatment for NSML. Some symptoms may require more regular follow up with different specialists than others. For example, hearing loss is usually followed closely and managed by an audiologist. Specific options for care may also depend on age. Regular follow-up can help inform appropriate screening and testing for health issues that may support a person with NSML.[8] Early intervention programs are useful to help the developmental differences in children with NSML. The life expectancy might differ among the people affected with NSML. Congenital heart defects can be a cause of shortened life span. Although some children may have more serious health complications, most children will meet almost all developmental milestones.[9]

Case report

A 24-year-old woman presented with hundreds of lentigines all over her body since early childhood. All of her dark spots were increasing in number, size, and pigmentation slowly day by day. The spots were asymptomatic and uniformly coloured. She had hearing loss and an inability to speak. Her hearing test revealed bilateral sensorineural deafness. Her eyes were wide apart (hypertelorism) but no visual

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impairment. Her parents noticed her shortness of breath and chest discomfort on vigorous exertion. There was a concentric type of cardiomyopathy in her echocardiographic report. All her family members were in good health. She comes from a non-consanguineous parent. Clinically she was labeled as Noonan syndrome with multiple lentigines. She had presented with greying of scalp hairs and that was a unique feature of such a case. She was visited at the Dermatology OPD of BSMMU in 2023. Consent was taken from the patient and her guardians for case report and photograph.

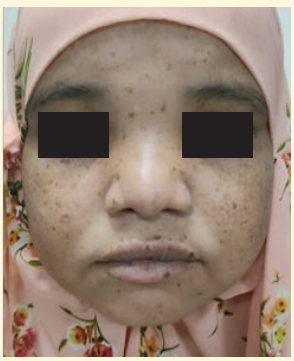

fig 1. Patients with multiple lentigines on the face with hypertelorism

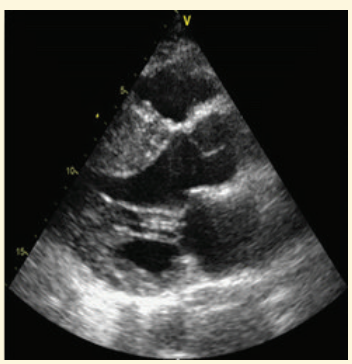

fig 2. Concentric cardiomyopathy on echocardiographic report

Discussion

There are various systemic presentations in NSML. Multiple dispersed flat, black-brown macules (lentigines), mostly on the face, neck, and upper part of the trunk sparing the mucosal surfaces. Lentigines usually appear at the age of four to five years and then increase up to thousands by puberty. Café au lait macules are observed in up to 70%-80% of affected individuals, usually preceding the appearance of lentigines. Skin hyperelasticity or lax skin has also been found in some cases. Neurofibromas have been observed in a few cases.[10] Approximately 85% of affected individuals have congenital heart defects similar to those observed in Noonan syndrome (NS). Hypertrophic cardiomyopathy is a common defect that is detected in 70% of individuals with heart disease. Pulmonary valve stenosis is described in approximately 25% of cases EKG abnormalities, with hypertrophic cardiomyopathy and conduction defects (23%).[11,12] In the present case a concentric type of cardiomyopathy was detected in echocardiography. Dysmorphic facial features are similar to those seen in Noonan syndrome. Inverted triangular-shaped faces, down-slanted palpebral fissures, widely spaced eyes (hypertelorism) and low-set and posteriorly rotated ears are the common presenting features of the face. A short neck with excess nuchal skin and a low-set posterior hairline is also described in some cases.[13,14] This patient has widely parted eyes but the ear and neck were normal. Sensorineural hearing loss is present in approximately 20% of persons with NSML.[15] Sensorineural deafness was detected in this case.

Pectus anomalies are present in 50% or more of affected individuals. Cryptorchidism, unilateral or bilateral, hypospadias, urinary tract defects, and ovarian abnormalities are observed infrequently.[16,17] Hypotonia is common in newborns and is associated with delayed psychomotor development.[18] But that feature was absent in the present case.

Gene mapping at least PTPNII was necessary to support the diagnosis but that was not possible for this case. Greying of hair is a new feature that was not listed before this case. There is no treatment option for NSML. We delivered details information about that syndrome to the patient attendance and suggested her to notice us about any discomfort or new features.

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