

# Multiple Lentiginos Syndrome: A Rare Case of Noonan Related Syndrome

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**Abstract:** We report a rare case of an 8 - year - old male with features of short stature, hypertelorism, low set ears, hypertrophic cardiomyopathy suggestive of Noonan syndrome. Noonan syndrome is an autosomal dominant disorder resulting in mutations in genes involved in the RAS - MAPK pathway. On examination of our patient, he was found to have multiple lentiginos throughout the body along with features such as ECG abnormalities, cryptorchidism and sensorineural deafness. These features are found in LEOPARD syndrome which is a Noonan related syndrome, which are characterised by overlapping phenotypes with Noonan syndrome. LEOPARD syndrome is now known as Multiple lentiginos syndrome.

**Keywords:** Lentiginos, Noonan syndrome, Hypertrophic cardiomyopathy, LEOPARD syndrome, ECG abnormalities, Hearing loss

## 1. Case Presentation

An 8 - year - old male had come with complaints of lethargy for 2 days. On examination, he had anirregular heart rate from 54 to 102bpm with normal blood pressure and GCS 15/15. Electrocardiographic changes were present.

Child was born at full term by C - section with birth weight: 4.5kg to a mother with gestational diabetes mellitus. On day of life 5, 2Decho was done which was suggestive of interventricular septal hypertrophic cardiomyopathy. Hence child was started on beta blocker, propranolol which was continued till date.

At 3 years of age, child underwent right orchidopexy in view of undescended testis which was detected on ultrasonographic examination.

Developmental milestones were achieved appropriately in all domains except language. Evaluation for failure to develop language milestones was done including hearing assessment. It revealed 100% hearing loss of right and left ear. He underwent a cochlear implant surgery at 6 years of age. Gradually his speech improved.

On physical examination and anthropometric evaluation, child had short stature. Multiple lentiginos were found with generalised symmetrical distribution. Facial dysmorphism was present in the form of triangular facies, tall forehead, epicanthal folds, ocular hypertelorism, downward slanting palpebral fissure and low set ears. All routine blood investigation were reported to be normal.

2DECHO was repeated and reports were suggestive of hypertrophic cardiomyopathy with asymmetric septal hypertrophy of thickness 10 mm. All cardiac valves were reported to be normal.



Figure 1: Clinical photo of face of patient



Figure 2: Multiple lentiginos

## 2. Discussion

Multiple lentiginos syndrome is a rare multiple congenital anomaly syndrome formerly known as LEOPARD syndrome characterised by Lentiginos, Electrocardiographic abnormalities, Ocular hypertelorism, pulmonary stenosis, abnormalities of genitalia, retardation of growth, deafness (1). It is an autosomal dominant with variable penetrance and expressivity. Only few patients possess all the features and no single feature is pathognomic. Most commonly associated mutations are found in PTPN11 and RAF1 gene. (2)

Noonan syndrome is an entity, clinical features of which closely resembles Turner's syndrome. It is an autosomal dominant disorder resulting from mutation in several genes involved in RAS - MAPK (mitogen activated protein kinase) pathway. Signs associated with Noonan syndrome include

short stature, failure to thrive, tall forehead, epicanthal folds, ptosis, blue - green irises, hypertelorism, low nasal bridge, upturned nose, downward - slanting palpebral fissures, myopia, nystagmus, low - set and posteriorly rotated auricles, dental malocclusion, low posterior hairline, short webbed neck (excessive nuchal skin), cystic hygroma, shieldchest, pectus carinatum, scoliosis, pigmented villonodular synovitis, cubitus valgus, pulmonary valve stenosis, hypertrophic cardiomyopathy, atrial septal defect, ventricular septal defect. lymphedema, nevi, lentigines, café au lait spots, cryptorchidism, small penis, delayed puberty, bleeding disorders, including thrombocytopenia and coagulation factor deficiencies, leukaemia, myeloproliferative disorders, cognitive delay. Syndromes with overlapping phenotypes with Noonan syndrome are known as Noonan - related syndrome. These comprise of LEOPARD syndrome, cardiofaciocutaneous syndrome and Costello syndrome. (2)

Our patient had following features of Noonan syndrome - short stature, tall forehead, epicanthal folds, hypertelorism, downward slanting palpebral fissures, low set ears, hypertrophic cardiomyopathy, lentigines and cryptorchidism. Overlapping features of multiple lentigines syndrome found in our patient were lentigines, ECG changes, ocular hypertelorism, abnormalities of genitalia, growth retardation, deafness with no evidence of pulmonary stenosis.

A Sarkozy et al in 2004, studied the phenotypic spectrum of patients with mutations concluded that it is associated with a marked clinical variation in the absence of any pathognomonic feature. Hypertrophic cardiomyopathy should be suspected and screened for in patients with multiple lentigines, LEOPARD syndrome who do not harbour PTPN11 mutations, and careful cardiac evaluation and follow up also should be performed in asymptomatic people. (3)

Voron DA et al stated that there is markedly variable expressivity of this syndrome making establishment of diagnostic criteria difficult. However, based on analysis of the data that was collected, a minimum criteria for diagnosis was proposed (4)

A Sarkozy et al in 2003 also concluded that pulmonary stenosis and hypertrophic cardiomyopathy are the prevailing congenital heart defects in Noonan syndrome and multiple lentigines syndrome associated with PTPN11 mutations. Different heart defects show correlations with the location of mutations within the PTPN11 gene, with statistically significant associations for pulmonary stenosis, hypertrophic cardiomyopathy, and ASD, which appear to cluster to distinct gene domains. (5)

### 3. Conclusion

Children presenting with hypertrophic cardiomyopathy must be evaluated for multiple lentigines syndrome and Noonan syndrome in the presence of any characteristic phenotypic features, if not all. In the presence of lentigines, cardiac evaluation should be done even if children are asymptomatic.

### References

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