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Leopard syndrome: A rare case report

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Abstract
Multiple lentigines (LEOPARD) syndrome is an inherited autosomal dominant disorder which presents with multiple lentigines and wide range of multisystem developmental defects. We here report a case of 6 year old male child, who presented with multiple scattered brownish pigmented lesions predominantly over trunk. Patient was deaf and mute since birth. Mother and elder sister had similar cutaneous lesions over body but no systemic complaints. On systemic examination, mild growth retardation was present. Hypertelorism was observed. On genital palpation it was found that the testes were very well in the sac but they were retractile. ECG showed conduction abnormalities. 2D Echo was normal with no pulmonary stenosis. Patient was referred to ENT department for deafness. Audiometry revealed bilateral sensorineural hearing loss.

Keywords: Lentigines, Café-au-lait macule (CLM), Deafness, Conduction abnormality, Leopard syndrome (LS).

Introduction
Leopard syndrome is a rare autosomal dominant genetic disorder. Gorlin *et al* introduced the acronym LEOPARD as the name of syndrome in 1969 to recall the main features of the disorder: Lentigines, ECG abnormalities, Ocular hypertelorism, Pulmonary stenosis, Abnormal Genitalia, Retarded growth and Deafness. It is also called as Noonan Syndrome with Multiple Lentigines or Cardiocutaneous Syndrome. It is a condition characterized by abnormality of the skin, heart, inner ears, genitalia. It is caused by mutation in the PTPN11 and RAF1 genes.

Case report
A 6 year old male child born from a non-consanguineous marriage presented to dermatology department with complaints of multiple, brownish pigmented lesions over body. His birth was at full-term from uneventful pregnancy. On detailed history child was deaf and mute since birth. Mother [Figure 3 & 4] and elder sister had similar cutaneous lesions over body but no systemic complaints.
Cutaneous examination showed multiple, discrete, lentigines on trunk, face [Figure 1], extremities, palms and soles. Patient also had Café-au-lait macule present over right forearm [Figure 2]. Mucosa, nails, teeth and hair were normal.
On systemic examination hypertelorism was observed. On genital palpation it was found that the testes were very well in the sac but they were retractile. Mild growth retardation was present (height – 98cm).
ECG showed conduction abnormalities. 2D Echo was normal with no evidence of pulmonary stenosis. Patient was referred to ENT department for deafness. Audiometry revealed bilateral sensorineural hearing loss.

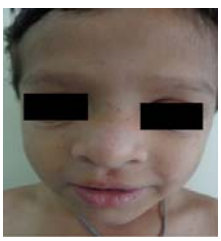

Fig 1: Lentigines over face and hypertelorism

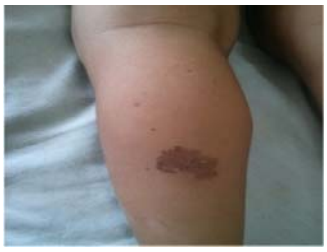

Fig 2: Café-au-lait macule over right forearm

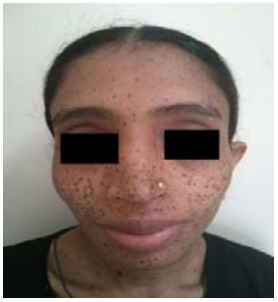

Fig 3: Lentigines over face and neck in mother

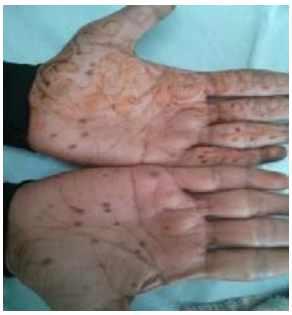

Fig 4: Lentigines over palms in mother

Discussion

The syndrome is also known as Multiple Lentigines syndrome, Cardio-cutaneous syndrome, Moynahan syndrome, Lentiginosis profusa, Progressive Cardiomyopathic Lentiginosis.

LS was first reported by Zeisler and Becker in 1936, in a 24-year-old woman presenting with multiple lentigines, increasing in number from birth to puberty, pectus carinatum, hypertelorism and prognathism. A few decades later, Gorlin *et al*. reviewed this disorder and coined the LEOPARD acronym supporting the concept of a more generalised condition.

LS is a rare condition, but the exact birth prevalence is unknown. Not less than 200 patients have been reported and two reviews published.

Within the group of the so called 'neuro-cardio-facial-cutaneous' (NCFC) syndromes, LS is probably the second most common disorder after Noonan syndrome (NS).

However, LS is likely underdiagnosed or misdiagnosed as many of its features are mild and the correct diagnosis might be missed in the absence of lentiginosis.

LS may be sporadic or inherited as an autosomal dominant fully penetrant trait with variable expressivity.

In approximately 85% of the patients with a definite diagnosis of LS, a missense mutation is found in the PTPN11 gene, located on chromosome 12q24.1. RAF1 gene mutations are found in PTNP11 mutation negative LS patients.

Facial features like facial dysmorphism, hypertelorism, dysmorphic ears are present.

In cardiovascular system ECG anomalies (75%) and progressive conduction anomalies (23%) are the most common heart defects. Previous reports suggested that pulmonary valve stenosis. (PVS), with or without dysplasia, is the most common defect (40%). Hypertrophic cardiomyopathy (HCM) is the most frequent anomaly and represents the only life-threatening problem in these patients. Mitral valve prolapse, clefting or other morphological abnormalities have been found in up to 42% of cases.

In skin multiple lentigines are a distinct feature of LS. The cafè-au-lait spots (CLS), occurring in about half of the patients.

LS patients show retardation of growth, with 25% of cases below the 3rd centile in height and 85% of adults below the 25th centile.

In skeletal anomalies thorax anomalies, including broad chest, pectus carinatum or excavatum are found in up to 75% of the newborns. Mandibular prognathism, winging of the scapulae, scoliosis, joint hypermobility and other findings are less common.

In genital anomalies bilateral cryptorchidism occurs in about 50% of males. Delayed puberty and hypoplastic ovary have been reported in females.

Sensorineural deafness occurs in about 15–25% of patient.

Hypotonia is common in the newborn and can result in delayed psychomotor development. Mild learning difficulties are reported in about 30% of the cases, while mental retardation is rare.

Haematological complications, such as myelodysplasia, acute myelogenous leukaemia and neuroblastoma, have been described in a few patients.

Thus cardinal features of LS are short stature, facial dysmorphisms, cardiac anomalies and hyperpigmented skin lesions, specifically multiple lentigines and CLS.

According to Voron *et al*., clinical diagnosis of LS may be suspected

1. Presence of multiple lentigines + two cardinal features.
2. In the absence of lentiginosis, three features in the patient + the presence of an affected first degree relative.

- Since some features manifest with advancing age, the diagnosis may be problematic in very young patients with only partial phenotypes.
- However, molecular testing for the PTPN11 gene and the RAF1 is supportive in this difficult task.

Digilio *et al*. suggested that diagnosis of LS in the first months of age can be clinically suspected in the presence of three main features, including HCM, distinct facial dysmorphisms and CLS.

Close differential diagnosis of LS are Neurofibromatosis type 1, Costello syndrome, Cardiofaciocutaneous syndrome

The management of LS is directed toward the specific symptoms that are present in each individual. It may require the coordinated efforts of a team of specialists. Genetic counselling is also an important part of management.

References

1. Jean L Bolognia, Joseph Jorizzo L, Julie Schaffer V. third edition, publisher Elsevier, 2012; II:1855-1857.
2. Coppin BD, Temple IK. Multiple lentigines syndrome

(LEOPARD syndrome or progressive cardiomyopathic lentiginosis). J Med Genet. 1997; 34:582-6.
3. Limongelli G, Sarkozy A, Pacileo G, Calabrò P, Digilio MC, Maddaloni V *et al*. Genotype-phenotype analysis and natural history of left ventricular hypertrophy in LEOPARD syndrome. Am J Med Genet A. 2008; 460:620-8.
4. Digilio MC, Sarkozy A, de Zorzi A, Pacileo G, Limongelli G, Mingarelli R *et al*. LEOPARD syndrome: clinical diagnosis in the first year of life. Am J Med Genet A. 2006; 140:740-6.
5. Voron DA, Hatfield HH, Kalkhoff RK. Multiple lentigines syndrome. Case report and review of the literature. Am J Med. 1976; 60:447-56.
6. Sarkozy A, Conti E, Digilio MC, Marino B, Morini E, Pacileo G *et al*. Clinical and molecular analysis of 30 patients with multiple lentigines LEOPARD syndrome. J Med Genet. 2004; 41:e68.