Do you know this syndrome? Leopard syndrome*

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CASE REPORT

A 12-year-old dark-skinned male patient was admitted at the dermatology service with the following characteristics: hypertelorism, macroglossia, lentigines, hypospadias, cryptorchidism, subaortic stenosis, growth retardation, and about 50% of his hearing compromised (Figure 1). Electrocardiogram showed a prolonged PR interval. The patient had a severe anterior open bite (no contact of the upper and lower front teeth) due to macroglossia (Figure 2). His legal guardian reported that he had been treated for patent ductus arteriosus and for cryptorchidism, hypospadias, subaortic stenosis, and blue nevus on his arm and back. He had also undergone tonsillectomy and adenoidectomy. Regarding family background, the patient was the second child of a healthy, nonconsanguineous young couple. He had a sister and a brother without symptoms.

DISCUSSION

Multiple lentigines syndrome is a genetic disorder caused by a mutation. It is characterized by multiple lentiginous spots associated with specific systemic changes. The term Leopard was originally used by Golin, Anderson, and Blaw in 1971, and works as a mnemonic rule for the syndrome characterized by multiple lentiginous lesions, abnormal electrocardiogram, ocular hypertelorism, pulmonary stenosis, genital and reproductive abnormalities, growth

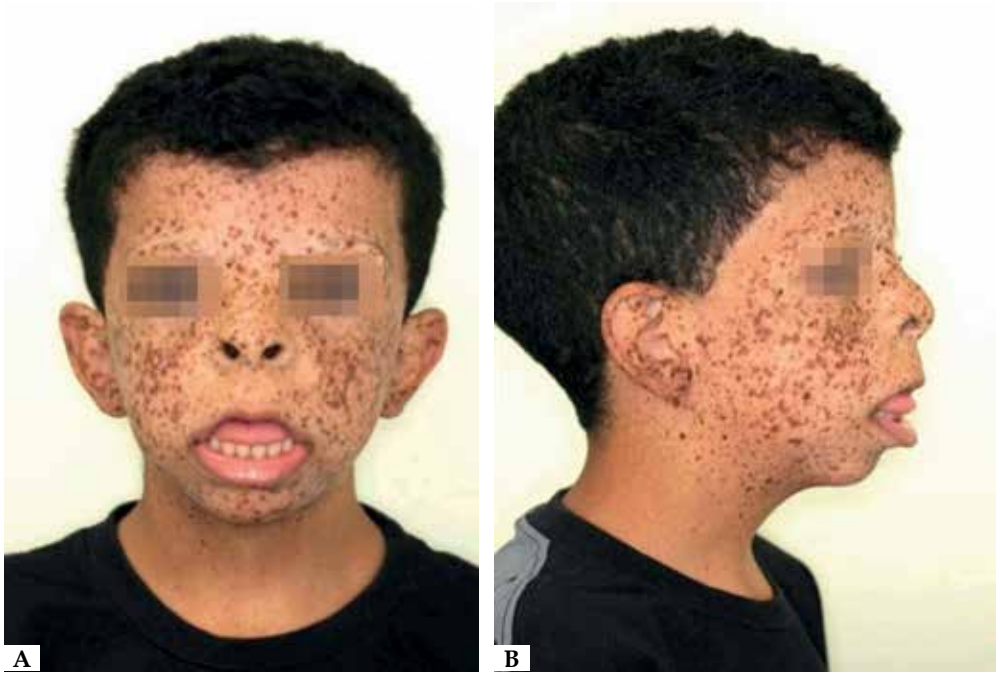

Figure 1:
A. Patient's face (front view), showing lentigines, hypertelorism, and tongue protrusion. **B.** Patient's face (profile view), showing lentigines, hypertelorism, and tongue protrusion

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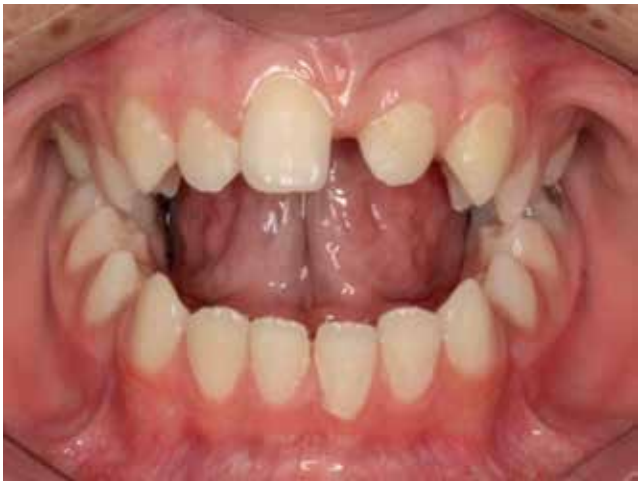

Figure 2: Intraoral photograph showing severe anterior open bite due to macroglossia

retardation, and deafness.[1]

Mutations in PTPN11, RAF1, or BRAF genes are related to multiple lentigines syndrome. Approximately 90% of individuals with this syndrome show mutations in the *PTPN11* gene.[2]

The Leopard syndrome (LS) and Noonan syndrome are part of the "rasopathies" group, a new family of autosomal dominant syndrome caused by mutations in the germline.[3] A rather current synonym is called NSL, or Noonan syndrome with lentigines, that shows the spectrum of rasopathies.[4]

As not all systemic changes develop simultaneously, Rizun *et al*.[5] suggested a minimal set of characteristics to diagnose this syndrome: apart from lentigines, at least two other systemic changes must be present, or just three non-lentigine characteristics. The patient of this case showed, in addition to lentiginous lesions, abnormal electrocardiogram, cryptorchidism, subaortic stenosis, ocular hypertelorism, growth retardation, and hearing impairment. They all led to the diagnosis of LS.

Lentigines is the most significant characteristic of this syndrome.[6] It develops as multiple well-defined brownish blotches of approximately 5 mm in diameter, mostly on the neck, upper extremities, trunk, and below the knees._ENREF_6 Face, scalp, palms, plants, and genitals are also affected, but the mucosa is invariably preserved.[7,8]

Cardiac exam is one of the most relevant tools to assess LS patients and to control the disorder, and should always be taken into account. LS usually appears in early childhood; if the cardiopathy occurs, disease requires monitoring, as it can be progressive, and might vary in patients in need of treatment with antibiotic prophylaxis before any invasive procedure, in order to decrease the risk of developing bacterial endocarditis.[9,10]

Although rare, LS should always be taken into account in patients with multiple lentiginous lesions and cardiac abnormalities. Physical examination and thorough systemic research are essential. Sensorineural hearing loss may occur later, but should be periodically monitored during childhood and adolescence, as late diagnosis may hinder the child's psychomotor development and learning. ❑

Abstract: Hypertrophic cardiomyopathy is known as Leopard syndrome, which is a mnemonic rule for multiple lentigines (L), electrocardiographic conduction abnormalities (E), ocular hypertelorism (O), pulmonary stenosis (P), abnormalities of genitalia (A), retardation of growth (R), and deafness (D). We report the case of a 12-year-old patient with some of the above-mentioned characteristics: hypertelorism, macroglossia, lentigines, hypospadias, cryptorchidism, subaortic stenosis, growth retardation, and hearing impairment. Due to this set of symptoms, we diagnosed Leopard syndrome.
Keywords: Hearing loss; Hypertelorism; Leopard syndrome

REFERENCES

1. Gorlin RJ, Anderson RC, Moller JH. The leopard (multiple lentigines) syndrome revisited. Birth Defects Orig Artic Ser. 1971;07:110-5.
2. Ahlbom BE, Dahl N, Zetterqvist P, Annerén G. Noonan syndrome with cafe-au-lait spots and multiple lentigines syndrome are not linked to the neurofibromatosis type 1 locus. Clin Genet. 1995;48:85-9.
3. Lauriol J, Kontaridis MI. PTPN11-associated mutations in the heart: has LEOPARD changed Its RASpots? Trends Cardiovasc Med. 2011;21:97-104.
4. Gelb BD, Tartaglia M. Noonan Syndrome with Multiple Lentigines. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, et al., editors. GeneReviews(R). Seattle (WA): University of Washington; 1993.
5. Rizun LI, Voronina TS, Frolova IuV, Raskin VV, Rumiantseva VA, Zakliaz'minskaia EV, et al. Progressive cardiomyopathy by the LEOPARD syndrome. Khirurgiia (Mosk). 2012;12:56-61.
6. Cerqueira RS, Belda Jr W, Machado MCR, Romiti AR, Oliveira ZNP, Romiti R. Você conhece esta síndrome? An Bras Dermatol. 2006;81:599-601.
7. Ramos-Geldres TT, Davila-Seijo P, Duat-Rodriguez A, Noguera-Morel L, Ezquieta-Zubicaray B, Roson-Lopez E, et al. LEOPARD Syndrome Without Hearing Loss or Pulmonary Stenosis: A Report of 2 Cases. Actas Dermosifiliogr. 2014;106:e-19-e-22.
8. Wang Y, Chen C, Wang DW. Leopard syndrome caused by heterozygous missense mutation of Tyr 279 Cys in the PTPN11 gene in a sporadic case of Chinese Han. Int J Cardiol. 2014;174:e101-4.
9. Kalev I, Muru K, Teek R, Zordania R, Reimand T, Köbas K, et al. LEOPARD syndrome with recurrent PTPN11 mutation Y279C and different cutaneous manifestations: two case reports and a review of the literature. Eur J Pediatr. 2010;169:469-73.
10. Sarkozy A, Digilio MC, Dallapiccola B. Leopard syndrome. Orphanet J Rare Dis. 2008;3:13.

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