

Do you know this syndrome?*

*Você conhece esta síndrome?**

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CASE REPORT

The case of a white 15-year-old female patient born in and coming from Minas Gerais is hereby reported. She presented syndromic face, with hypertelorism and convergent strabismus (Figure 1), growth and pubertal retardation, associated to dozens of well-delimited brownish maculae, measuring few millimeters in diameter, affecting the skin diffusely, which developed after her first year of life (Figure 2). Moreover, two other darker, larger and isolated lesions were evidenced on the thigh and dorsum.

Systemic manifestations included an electrocardiogram with diffuse alterations in repolarization, subaortic stenosis and hypertrophic cardiomyopathy. Pelvic ultrasonography revealed absence of left ovary, with no other alterations. Intellectual development was normal. She denied parent consanguinity and had a dizygotic twin sister, whose clinical examination and imaging studies had no alterations. She denied the existence of similar cases in the family. Histopathological examination of the dorsal lesion

(publication with written consent by patient / guardian)



FIGURA 1: CHARACTERISTIC FACE OF LEOPARD SYNDROME



FIGURE 2: Multiple dorsal lentiginous lesions

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revealed alterations consistent with simple lentigo.

WHAT IS THIS SYNDROME?

Leopard syndrome

Multiple lentiginous syndrome is characterized by multiple lentiginous stains, associated to specific systemic alterations. The term Leopard was coined by Golin, Anderson and Blaw in 1969, and serves as a mnemonic rule for the syndrome characterized by multiple lentiginous lesions, ECG conduction abnormalities, ocular hypertelorism, pulmonic stenosis, abnormal genitalia, retardation of growth, and sensorineural deafness.¹

Since systemic alterations may not be all present simultaneously, Voron et al. suggested a minimal set of characteristics for the diagnosis of this syndrome: besides lentiginous, at least two other systemic alterations should be present, or simply three non-lentiginous alterations.²

Lentiginosis is the most marking characteristic of this syndrome. It is manifested by means of multiple well-delineated brownish maculae, measuring approximately 5mm in diameter, concentrated mainly on the neck, trunk, upper extremities and below the knees. They may also affect face, scalp, palms and soles, genitals, but the mucosa is invariably spared. Lentiginous are present ever since birth, or may have their onset during infancy, becoming progressively larger and darker with age. Occasionally, larger and darker maculae with geometrical contours can be associated.^{2,5}

An abnormal electrocardiogram is common in this syndrome, being pulmonary stenosis the most common structural defect. Axis deviation is the most reported abnormality. Other frequent alterations include P-R interval prolongation, isolated ectopic ventricular beat, widening of the QRS complex, abnormal P wave, T wave inversion, left anterior branch block and total ventricular block.⁵ Prognosis

of the syndrome depends essentially on cardiac alterations.

Hypertelorism is not as common as the other features of the syndrome. However, strabismus and nistagmus have been reported with some frequency.² Genitourinary alterations are more common among males, cryptorchidia being the most commonly reported manifestation.⁵ In women, ovary hypoplasia is usually found, or, if there is a single ovary, early puberty and late menopause occur. Growth retardation is a common characteristic, most patients being classified below the 25 percentile for both weight and height.

The patient whose case is reported here presented multiple lentiginous lesions, electrocardiogram repolarization abnormalities, hypertelorism and ocular strabismus, pubertal retardation with absence of left ovary, growth retardation and, up to the present date, absence of neurosensory hearing loss.³ Of all characteristics of the syndrome, hearing loss is the least often found. It is classically of the neurosensory type, and usually diagnosed during childhood, albeit it can develop later.

Leopard syndrome is manifested in a dominant autosomal pattern, with high penetrance and variable expressivity. It is rare, with approximately 100 cases described up to 2006. It affects both genders alike. Pathogenesis is still unknown, although a gene PTPN11 (Shp2) mutation occurs in 90% of the cases.^{4,6}

Although rare, leopard syndrome should always be remembered in patients with multiple lentiginous lesions and cardiac alterations. Thorough physical examination and systemic investigation are crucial. Neurosensory hearing alterations may develop late in the course of the disease, but should be periodically monitored during childhood and adolescence, for a late diagnosis can harm the child's neuropsychomotor development and thus learning. □

Abstract: LEOPARD syndrome is a dominant autosomal anomaly, with high penetrance and markedly variable expression. The acronym LEOPARD was coined in 1969 as a mnemonic rule, highlighting the major features of this syndrome: lentigines, ECG conduction abnormalities, ocular hypertelorism, pulmonic stenosis, abnormal genitalia, retardation of growth, and sensorineural deafness. We report the case of a 15-year-old girl with characteristics of LEOPARD syndrome and further discuss the main clinical and genetical features of the disorder.

Keywords: Esotropia; Genitalia; Genitalia/ abnormalities; Hearing loss; Lentigo; Leopard syndrome; Pulmonary valve stenosis

Resumo: A síndrome Leopard é distúrbio autossômico dominante de forte penetrância e expressividade variável. O epônimo Leopard foi criado em 1969 como regra mnemônica, ressaltando as características mais marcantes da síndrome: lentiginose, distúrbios de condução no ECG, hipertelorismo ocular, estenose pulmonar, anormalidade genital, retardo do crescimento e déficit auditivo sensorial. Relata-se o caso de uma menina de 15 anos com características da síndrome Leopard e discutem-se suas principais manifestações clínicas e genéticas.

Palavras-chave: Esotropia; Estenose da valva pulmonar; Genitália; Genitália/anormalidades; Lentigo; Perda auditiva; Síndrome Leopard

REFERENCES

- Pickering D, Laski B, Macmillan DC, Rose V. "Little Leopard" syndrome. Description of 3 cases and review of 24. *Arch Dis Child.* 1971;46:85-90.
- Agha A, Hashimoto K. Multiple lentigines (LEOPARD) syndrome with Chiara I malformation. *J Dermatol.* 1995;22:520-3.
- Ribeiro AP, Romiti R, Machado MCR, Belda W, Oliveira ZNP. Leopard syndrome. *Eur J Pediatr Dermatol.* 1997;7:163-6.
- 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;41:68.
- David A, Voron MD, Hayes H, Hatfield MD, Ronald K, Kalkhoff MD. Multiple lentigines Syndrome: case report and review of the literature. *Am J Med.* 1976;60:447-55.
- Kontaridis MI, Swanson KD, David FS, Barford D, Neel BG. PTPN11 (Shp2) mutations in LEOPARD syndrome have dominant negative, not activating, effects. *J Biol Chem.* 2006;281:6785-92.

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