A seven-year-old boy was referred for cardiac evaluation due to decreased exercise tolerance. The patient had a systolic heart murmur heard best at the upper left sternal border which was present since birth, and was thought to have been contributing to his fatigue. His resting electrocardiogram is shown below (Fig 1).

On examination of his skin, the patient was found to have numerous brownish-black macular lesions distributed over his entire body but sparing his lips and oral mucous membranes (Fig 2). According to the patient’s parents, these skin lesions appeared shortly after birth and continued to increase in number with age.

There was no history of melanoma in the patient or other family members.

What is the likely diagnosis?

A) Peutz-Jeghers syndrome
B) Albright’s syndrome
C) Dysplastic nevus syndrome
D) Leopard syndrome
E) Neurofibromatosis
**The answer is: D) Leopard syndrome**

The leopard syndrome, also known as the multiple lentigines syndrome, is one of the many cardiocutaneous syndromes associated with heart anomalies and pigmented lesions of the skin. The "leopard" acronym was suggested in 1969 by Gorlin et al. to distinguish this syndrome from the other syndromes because of its distinctive features. The complex of abnormalities with variable penetrance may include lentigines, electrocardiographic conduction defects, ocular hypertelorism, pulmonary stenosis, abnormalities of the genitalia, retardation of growth, and deafness. This syndrome is inherited in an autosomal dominant fashion. These manifestations can best be explained by a defect of neural crest origin.

Lentigines are light tan to brownish-black flat lesions that are commonly found on skin examination. However, when a myriad of these lesions are present, one should consider a possible association with a cardiac abnormality. Numerous reports describe lentigines associated with the following cardiac defects: electrocardiographic axis deviation, conduction defects (prolonged PR interval), bundle branch blocks, atrial myxomas, pulmonary stenosis, and idiopathic hypertrophic subaortic stenosis.

This patient was admitted to the Kansas University Medical Center for evaluation of fatigue. Physical examination revealed a seven-year-old boy who was below the third percentile in height and weight. His skin was covered with thousands of lentigines (1-5 mm in diameter) which spared his mucous membranes. He had no eye or hearing abnormalities. Cardiovascular examination was remarkable for a mid-systolic thrill at the upper left sternal border. A grade 4/6 systolic ejection murmur was heard best along the upper left sternal border, with transmission to the suprasternal notch and the carotid arteries. The heart sounds were normal and no systolic ejection click was audible. His abdomen was supple and without masses or organ enlargement. The genitalia demonstrated an undescended left testicle.

His electrocardiogram showed normal sinus rhythm with right axis deviation of 150° with a suggestion of right ventricular hypertrophy. The patient underwent cardiac catheterization which was consistent with minimal pulmonary stenosis and idiopathic hypertrophic subaortic stenosis. He was followed annually for six years with little cardiac or cutaneous change.

Peutz-Jeghers syndrome is an autosomal dominant disorder also characterized by lentigines which usually involve the skin but more often the mucous membranes of the lips and oral mucosa. It may be associated with intestinal polyps, melena, and intussusception, but there is no association with cardiac disease.

Albright's syndrome includes *cafe-au-lait* marks which are asymmetrical and found mainly on the trunk, buttocks, and thighs. Polyostotic fibrous dysplasia, endocrine dysfunction, and precocious puberty in females and occasionally in males are features of this syndrome.

The dysplastic nevus syndrome is manifested by pigmented skin nevi which are considered precursors to malignant melanoma. Members of melanoma-prone families with these lesions are at high risk to develop melanoma during their lifetimes. There are no cardiovascular findings with this syndrome.

Neurofibromatosis is manifested by six or more *cafe-au-lait* spots which are greater than 1.5 cm in diameter. Freckle-like pigmentation of the axilla and multiple cutaneous neurofibromas are other diagnostic criteria. Cardiac involvement may occur on rare occasion.

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**REFERENCES**