Cardiomyopathic Lentiginosis/ LEOPARD Syndrome Presenting as Sudden Cardiac Arrest*

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Hypertrophic cardiomyopathy occasionally is associated not only with sudden death and different congenital malformations, such as Noonan's syndrome, hereditary spinal (Friedreich's) ataxia, and dwarfism with cryptorchism,[1] but also with abnormalities of cutaneous pigmentation (cardiomyopathic lentiginosis[2] or lentigines [multiple], electrocardiographic abnormalities, ocular hypertelorism, pulmonary stenosis, abnormalities of the genitalia, retardation of growth, and deafness [sensorineural] syndrome [LEOPARD syndrome]).[3-5]

The case reported here is that of a young man with apical nonobstructive cardiomyopathy associated with lentiginosis and a variety of clinical disorders who was successfully resuscitated from ventricular fibrillation.

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Case Report

An apparently healthy 26-year-old man was admitted to the ICU after successful resuscitation from documented ventricular fibrillation sustained during dancing the polka. A comprehensive past medical history could be obtained from his mother: "moles" had erupted during childhood; a dermatologist had diagnosed nevi and had recommended surveillance. In 1980, an operation was performed for an undescended testicle; an aneurysm of the left femoral vein was excised in 1988. In 1991, ultrasound studies disclosed splenomegaly and a dystopic right kidney. He had repeatedly noted pitting edema and lost consciousness during exercise. The patient worked as a shop assistant; he had no children. His ancestors were of German and Eastern European origin; abnormal pigmentation, heart disease, syncope, and sudden death had not been reported among his family.

On examination, he was 1.92 m tall and weighed 86 kg. Hypertelorism, brevicollis, and pterygium colli were noted. Myriads of pinpoint to lentil-sized dark-brown macular lesions were present on the arms, legs, and back, whereas the abdomen and face were markedly spared (Fig 1).

The patient was found to have pectus excavatum and the apical beat was thrusting; first and second heart sounds were normal; a loud systolic murmur with midsystolic click was audible over the apex. Scoliosis, cubitus valgus, and brachydactyly were evident.

An ECG showed first-grade atrioventricular block, incomplete right bundle block with an rSr pattern, giant negative T waves in V_3-V_6, and left posterior hemiblock. QT, QT_c, JT, and JT_c intervals, respectively, were within normal limits. A chest radiograph showed enlargement of the left atrium and ventricle with a cardiothoracic ratio of 20:33. Echocardiography demonstrated hypertrophy of the interventricular septum to an end-systolic width of 16 mm and mitral valve prolapse with minimal regurgitation. Invasive studies ruled out coronary heart disease but left ventricular angiocardiography showed systolic mouse-tail phenomenon consistent with apical hypertrophic nonobstructive cardiomyopathy. The aortic cusp of the mitral valve was grossly enlarged and prolapsed with minimal mitral regurgitation. A long, gooseneck-like subaortic muscular tunnel without stenosis was present (Fig 2). The right atrium and ventricle were normal. There was no shunt, and hemodynamic parameters were within normal limits. Electrophysiologic testing disclosed no abnormalities. Punch biopsy of a skin lesion confirmed lentigo simplex. A CT scan revealed reduction in brain volume and a left frontal arachnoidal cyst with concomitant reduction in bone thickness. Audiometry disclosed mild unilateral sensorineural hearing loss. The patient made an uneventful recovery, a pacer-cardioverter-defibrillator device (Jewel 7221; Medtronic; Duesseldorf, Germany) was implanted, and he was discharged on metoprolol without sequelae of the incident.

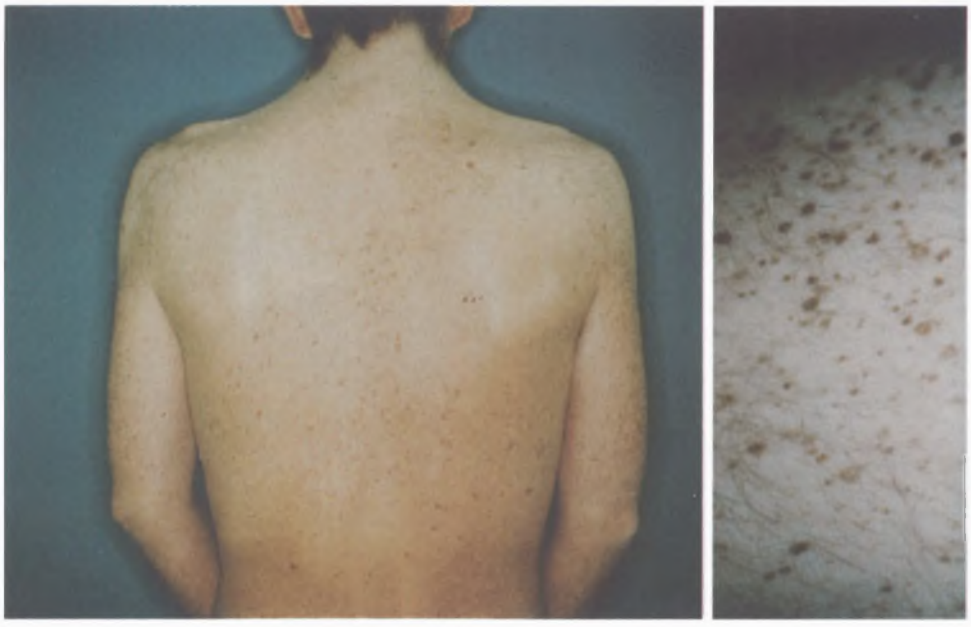

FIGURE 1. *Left*: On examination, myriads of pinpoint to lentil-sized dark-brown macular lesions are evident on the patient's trunk and extremities. *Right*: upper arm, close view (biopsy-proven lentigo simplex).

COMMENT

Sudden ventricular fibrillation is uncommon in young adults. Unlike in the elderly, coronary heart disease is rarely the cause. Instead, myocarditis, cardiomyopathy, right ventricular dysplasia, use of illicit drugs, and anomalies of the QT interval prevail. Hypertrophic cardiomyopathy is a key feature of cardiomyopathic lentiginosis.[6] Interestingly, sudden death has been mentioned in previous reports of the disorder.[7]

In this case, cardiomyopathy was revealed as the most

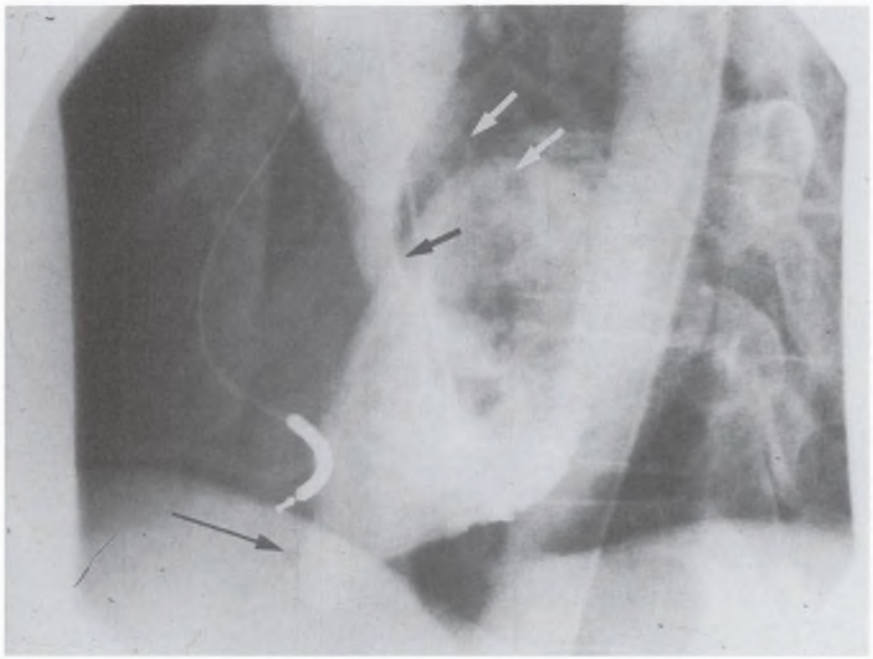

FIGURE 2. Left ventricular angiocardiography demonstrating subaortic muscular tunnel without stenosis (white arrows), flail mitral valve (small black arrow), apical hypertrophic nonobstructive cardiomyopathy (long black arrow) and pacer-cardioverter-defibrillator lead inside right ventricle (left anterior oblique view).

likely cause and concomitant lentiginosis prompted evaluation for a unifying diagnosis. Disorders of pigmentation have been reported in association with various cardiac abnormalities, but classification remains controversial. Features of both cardiomyopathic lentiginosis[2] and LEOPARD syndrome,[3-5] a mnemonic code for *l*entiginosis, *E*CG changes, *o*cular hypertelorism, *p*ulmonic stenosis, *a*bnormal genitalia, growth *r*etardation, and *d*eafness, were present. Pectus excavatum, skull defects, and other skeletal abnormalities as well as anomalies of the genitalia, such as undescended testicle, are frequently encountered whereas involvement of the urinary tract is believed to be rare. Somatic retardation is common. The presence of brain atrophy may indicate that mental impairment, one of the syndrome's key features, might ensue in the future. Finally, additional cases among the kindred of this patient were not detected; this suggests that a novel mutation may have occurred.

Both LEOPARD syndrome and cardiomyopathic lentiginosis, originally proposed to be distinct entities, have salient features in common, not the least of which is their mode of inheritance as an autosomal dominant trait and their preponderance to affect tissues of neural crest origin. It, therefore, seems intriguing to assume that both reflect variable penetrance and expression of the same genetic defect.[2] Among other features, atrial myxoma, mitral regurgitation, and, recently, recurrent arterial dissection have been reported in lentiginosis and may be variant forms of the disorder. The genetic basis of lentiginosis syndromes, however, remains entirely unknown, thus preventing proper classification and diagnosis.

Conclusion

Lentiginosis must prompt thorough evaluation since it may be part of a multifaceted syndrome that cannot only be associated with considerable morbidity but may even place patients at risk for sudden death. Although identification of patients in need of prophylactic treatment will remain difficult, pacer-cardioverter-defibrillator device therapy is believed to be indicated and beneficial in survivors of out-of-hospital ventricular fibrillation.

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