Clinical vignette

The LEOPARD syndrome: a rare condition associated with hypertrophic cardiomyopathy

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A 66-year-old woman, known for years with LEOPARD syndrome (LEOPARD stands for multiple Lentigines, Electrocardiographic conduc
tion defects; Ocular hypertelorism; Pulmonary stenosis; Abnormalities of the genitalia; Retardation of growth and sensorineural Deafness),
presented with complaints of progressive dyspnoea over the course of the last months. The physical examination revealed multiple lentigines, café-au-lait spots (Panel A), and pectus excavatum. The 12-lead ECG (Panel B) showed left-axis deviation, ST-segment abnormalities, and T-wave inversion. An echocardiographic analysis confirmed the diagnosis of hypertrophic obstructive cardiomyopathy (HOCM) with a maximal septal wall thickness of 19 mm, a left ventricular outflow tract (LVOT) dynamic gradient of 73 mmHg, and systolic anterior movement of the mitral valve (Panel C). A right and left ventricular catheterization was performed, confirming the diagnosis of HOCM (Brockenbrough sign positive) (Panel D).

Because of insufficient response to pharmacological therapy, we performed a TASH procedure (transcoronary alcohol septal ablation for hypertrophic cardiomyopathy). There was no pressure gradient in the LVOT left post-procedure, and the patient did clinically well without complaints of dyspnoea.

Multiple LEOPARD syndrome is an autosomal dominant multiple congenital anomaly syndrome, with high penetrance and markedly variable expression. It was originally described by Gorlin as multiple lentigines syndrome. It is also known as cardiocutaneous syndrome, Moynahan syndrome, lentiginosis profuse, and progressive cardiomyopathic lentiginosis. Apart from pulmonary valve stenosis, HOCM is a common feature of this syndrome and it may progress with age or present later in life than the other clinical findings. The most plausible explanation for the pathogenesis of the syndrome is an abnormality of the neural crest cell. The cells derived from the neural crest form spinal and autonomic ganglion cells, Schwann cells of peripheral nerves, as well as sympathetic terminations in the cardiac ventricles. Neural crest cells also give rise to melanocytes, thereby explaining the associated lentigines.

The underlying genetic defect associated with the development of the syndrome has been located on chromosome 12 (gene map locus 12q24.1), and the responsible gene is PTPN11 (protein tyrosine phosphatise non-receptor type 11), which codes for non-receptor protein tyrosine phosphatase, SHP2. Mutations in the same gene are known to lead to a number of congenital heart defects, among them Noonan syndrome, cardiomyopathic lentiginosis, and LEOPARD syndrome. Different heart defects correlate with different locations of mutations within the PTPN11 gene. The only son of our patient also demonstrated features of the LEOPARD syndrome, without documentation of cardiac involvement so far.

See supplementary movies available at European Heart Journal online.

Panel A. Multiple lentigines.
Panel B. Electrocardiogram showing left-axis deviation, left anterior hemiblock, ST-segment abnormalities, and T-wave inversions.
Panel C. Echocardiographic image of hypertrophic obstructive cardiomyopathy with thickened interventricular septum and systolic anterior motion of the mitral valve leaflets. The anterior mitral valve leaflet obstructing the left ventricular outflow tract is indicated with a white arrow.
Panel D. Haemodynamic tracings with intraventricular pressure gradient and positive Brockenbrough sign (post-extra systolic aggravation of obstruction with augmentation of the intraventricular pressure gradient and lowering of the aortic pressure), indicated in the figure with an asterisk.

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