Cardiovascular risk factors and genetic predisposition: an unusual case of aortic regurgitation and LVOT obstruction

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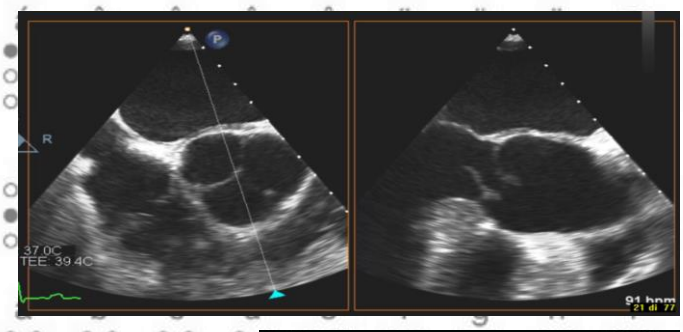
CLINICAL CASE

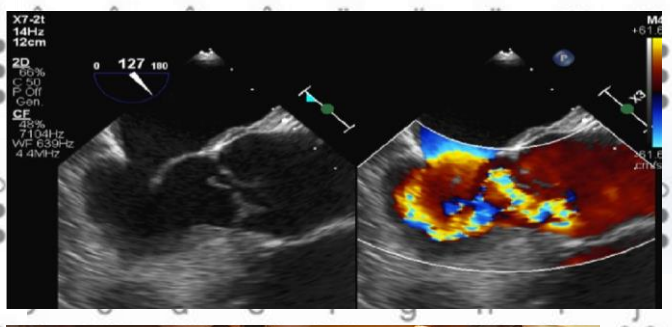
A 38-year-old obese man presented to our outpatients' clinic for progressive dyspnea and chest pain during exertion.

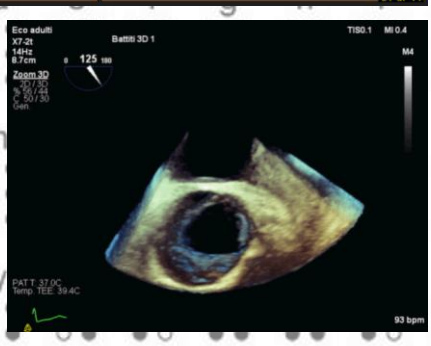
* ***Patient history:*** PFO closure, uncontrolled hypertension, congenital blindness in bilateral cataract.
* ***Clinical evaluation:*** Blood pressure 170/75 mmHg, the other vital signs were normal. A new ejective systolic murmur on the aortic area at the auscultation was revealed, no signs of heart failure.
* ***ECG:*** first-degree atrio-ventricular block, signs of left ventricular hypertrophy.
* ***Transthoracic echocardiography****:* slightly reduced left ventricular ejection fraction, severe left ventricle dilatation and mild left atrial dilatation, severe aortic regurgitation and a mobile ill-defined subaortic structure prolapsing into the LVOT producing a severe obstruction.
* ***Transesophageal echocardiography****:* an abnormal movement of the aortic right coronary cusp, losing the coaptation point and everting totally in the LVOT was revealed and confirmed on 3D reconstruction.

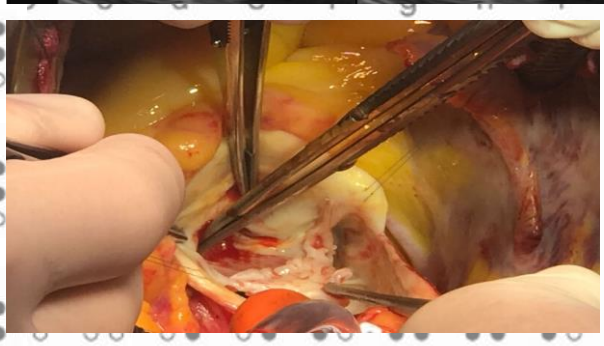
This finding was first interpreted as a right coronary cusp flail, which was consistent with the severe aortic regurgitation but not with the LVOT systolic gradient.
Patient's symptoms together with the echocardiographic findings made the surgical solution recommended: the native aortic valve was removed and a mechanical prostheses was implanted.

* ***Intraoperative inspection****: the* aortic valve was tricuspid with fibromuscular metaplasia of the cusps structure and delamination of the right coronary cusp, which was split in two layers: one layer adherent to the valve annulus and the other protruding into the LVOT.









DISCUSSION

In human and animal models, valve integrity is actively maintained in a homeostatic balance by paracrine interactions between valve interstitial cells (VIC) and valve endothelial cells (VEC), which inhibit endothelial-to-mesenchymal transition. The exposure to different types of stress entails a valve change in dimension, shape and stiffness secondary to the interaction between cells and extracellular matrix.
Several studies demonstrated the role of TGFβ overexpression in the development of lens opacity in patients with congenital cataract. TGFβ can activate mesenchymal signaling programs and in canine valve cultures the combination of TGFβ1 overexposure and cyclic strain induced myofibroblastic differentiation in VIC.
Uncontrolled hypertension is a cause of excessive shear stress and together with an anomalous signaling pathway involving TGFβ cascade may result in valve metaplasia and disruption.
These mechanisms could explain the peculiar finding of a cusp delamination causing severe valve regurgitation and the presence of valve muscular metaplasia projecting through the LVOT.

CONCLUSION

Valve tissue remodeling is a complex process, where genes and environment act together to produce the valve phenotype. The genetic predisposition in an adult with a congenital eye disease associated with the mechanical stress of arterial hypertension led to a peculiar fibromuscular degeneration of the aortic valve with the need of surgical replacement. Echocardiography played an important role for working diagnosis, but surgical evaluation was essential to characterize this unusual condition.