Editöre Mektup — Letter to the Editor

Acute myocardial infarction in a young patient with bicuspid aortic valve

Acute myocardial infarction and bicuspid aortic valve

Dear Editor,

In the October 2009 issue of this journal, Dr. Demir presented a very interesting case of congenital bicuspid aortic valve (BAV) in an 18-year-old man who suffered an acute myocardial infarction.[1] I would like to comment on the pathophysiological aspects of arterial complications of BAV disease as well as how this disease process could potentially involve the coronary arteries and lead to complications, specifically spontaneous dissection.

It is well known that BAV can be associated with progressive dilation of the aortic root, aneurysm of the ascending aorta, and even aortic rupture or dissection. The diameters of the aortic root and ascending aorta are significantly greater in subjects with a bicuspid than a tricuspid aortic valve irrespective of valve function while aortic dilation in patients with a stenotic or regurgitant BAV is out of proportion to the severity of valvular dysfunction.[2] These observations have led to the establishment of a primary aortopathy with the histopathological phenotype of cystic medial degeneration as an inherent feature of this disease. The aorta is rendered weak, with abnormal elastic properties and increased stiffness, hence vulnerable to the aforementioned complications. The fact that BAV is strongly associated with congenital anomalies of the aorta such as coarctation and hypoplasia supports the concept of a common underlying developmental defect.[2,3] The latter originates in the neural crest cells (NCCs) from which the aortic valve cusps and musculoconnective tissue of the ascending aorta and aortic arch system derive. Vascular smooth muscle cells (VSMCs) play a key role in the remodeling of the aortic media; they produce the bulk of the complex arterial extracellular matrix. In aortas with a BAV, the VSMCs are defective and accumulate extracellular matrix proteins that accelerate their apoptosis.[2] The resulting decreased extracellular matrix protein distribution and increased degradation secondary to the release of matrix metalloproteinases from the apoptotic cells help in setting the picture of medial degeneration. In mice, VSMCs of NCC origin have been shown to be present not only in the media of the ascending aorta and arch, but also in the media of the innominate, right subclavian, and right and left common carotid arteries.[4] While there is uncertainty regarding the exact boundaries of these cells, the media of the descending thoracic and abdominal aorta, coronary arteries, pulmonary arteries, left subclavian artery, and distal portions of the internal carotid arteries have been shown to be devoid of NCC-derived VSMCs. Hence, the former arterial sites may serve as targets for cystic medial degeneration and dissection. Indeed, familial aorto-cervicocephalic arterial dissections have been described in conjunction with BAV disease.[5]

The NCCs contribute directly to the formation of the VSMCs of the ostial regions of the coronary arteries.[2,4] Beyond this site, the VSMCs arise from proepicardially-derived epicardial cells that undergo epithelial-mesenchymal transformation.[6] However, the NCCs do play a regulatory role in coronary artery development. They ensure the survival of the definite coronary arteries by laying down the parasympathetic ganglia at the base of the heart while those involved in the peripheral innervation of the heart may help pattern coronary arteries through paracrine signaling that modulates proepicardial cell migration. Coronary artery patterning is also facilitated by gap junctions-mediated NCCs-proepicardial cells interactions; mice lacking the a1 connexin-43 gap junction gene exhibited defective gap junctions-mediated cell-cell interactions that led to improper deployment of the NCCs and proepicardial cells and coronary artery patterning defects. Furthermore, although VSMC differentiation is not altered in such settings, VSMC myosin expression in the coronary arteries has been found reduced, exhibiting a patchy pattern suggesting that coronary artery media may be somewhat deficient of VSMCs.[6] Provided the defective NCCs in BAV disease, a defective regulation of coronary artery development/patterning could be proposed. Indeed, an association of BAV with single coronary artery has been reported.[2] The reported association of BAV with an immediate bifurcation of the left main stem, a short left main stem (<10 mm) and left coronary artery dominance

may also mirror the somewhat altered but not necessarily pathological regulatory role of the NCCs.[7] Furthermore, the potentially decreased abundance of VSMCs may result in a decreased maintenance of the extracellular matrix and loss of the structural support of the coronary artery media. Whether such changes exist or underlie a pathological remodeling process that can progress to cystic medial degeneration similar to that seen in the aortas of BAV patients remains to be shown. However, such a process is possible and may provide a pathophysiological link with spontaneous coronary artery dissection (SCAD).

Labombarda et al.[8] reported a 53-year-old man with a normally functioning BAV and a dilated ascending aorta, who suffered ST-segment elevation myocardial infarction secondary to dissection of the distal left anterior descending coronary artery. In the absence of atherosclerotic coronary artery disease or other risk factors for SCAD, the authors raised the possible linkage between SCAD and BAV. In the case presented by Demir, the electrocardiogram is typical of a distal left anterior descending artery occlusion; the ST deviation vector points in an apical direction producing ST-segment elevation in V5-V6, and lead II greater than in III signifying an inferoapical ischemic area. Consequently, the segment just beyond the major diagonal branch was likely to be the culprit site. An angiogram in the acute phase could have revealed a dissection flap, but unfortunately it was not carried out due to patient refusal. However, such a typical picture for SCAD might have not been revealed if a dissecting intramural hematoma lacking a flap and producing a smooth stenosis had been the case, raising the importance of maintaining a high index of suspicion. Even though the angiogram does not show frank abnormalities, it does not exclude SCAD which might have healed during the two weeks time elapsed from the index event.

In conclusion, a coronary arteriopathy that predisposes to SCAD may be a feature of BAV disease. Acute myocardial infarction in a patient with BAV should raise the suspicion for SCAD particularly if the patient is young or free of risk factors for atherosclerosis. Accordingly, implementation of immediate coronary angiography may be preferable to thrombolysis because the latter may cause extension of the dissection and deterioration of the patient's status.

Sincerely,

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