Can general histopathology distinguish bicuspid aortopathy?

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EDITORIAL

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Surgical ascending aortic wall specimens are often obtained during thoracic aortic aneurysm or dissection repair. Several conditions ranging from connective tissue disorders to degenerative aging predispose patients to the development of thoracic aortopathy. Postoperative general histopathological analysis of surgical specimens often informs the surgeon of the likeability of an underlying genetic disorder and thereby the need for further counseling. Across the spectrum of diseases that could lead to aortopathy, there is an array of overlapping histopathologic changes to the aorta. Over the years, these collections of typical histopathology findings are considered characteristic of a certain syndromic condition. Marfan syndrome and Ehlers Danlos for instance typically demonstrate overall medial degeneration (MD), mucoid extracellular matrix accumulation (MEMA), smooth muscle cell nuclei loss (SMCNL), and elastic fiber fragmentation/loss (EFF/L) and degeneration (EFD).[1]

A bicuspid aortic valve is the most common congenital cardiac malformation. Patients with a bicuspid aortic valve carry an increased risk to develop thoracic aortopathy during their lifetime. Histopathological analysis of bicuspid aortopathy is, however, complicated due to lack of the abovementioned typical medial pathological features.[2] Several studies have highlighted pathological mechanisms in BAV such as vascular smooth muscle cell defects which can be identified with specific immunohistochemistry.[3,4] It is, however, time-consuming and highly costly to perform these studies on the ascending aortic wall which is sent in for pathological analysis. In this paper, we, therefore, summarize important typical general histopathological findings which can aid pathologists, cardiologists, and cardiac surgeons in the diagnosis of bicuspid aortopathy.

We illustrate this approach using experience from our departments. Bicuspid and tricuspid aortic wall (TAV) specimens are traditionally approached by the classical histopathological staining hematoxylin-eosin, resorcin fuchsin, and Movat pentachrome procedure, staining protocol as described in our previous publication.[5] In our case, specimens were obtained from non- and dilated BAV ($n = 36$) and TAV ($n = 23$) individuals. Dilatation was defined as a diameter of ≥45 mm. Specimens from non- and dilated BAV and dilated TAV patients were obtained during elective repair, and nondilated TAV specimens were obtained postmortem. Sample collection and handling were carried out according to the official guidelines of the Medical Ethical Committee of Leiden University Medical Center, Leiden, and the code of conduct of the Dutch Federation of Biomedical Scientific Societies.

Histopathological analysis revealed a significantly thinner intimal layer in all BAV patients as compared to the TAV patients ($p < .001$). In all BAV patients, the medial layer was characterized by elastic fiber thinning and MEMA between the lamellae. Medial pathologic features including overall MD, SMCNL, EFF/L, and EFD were significantly less apparent in the dilated BAV as compared to the dilated TAV ($p < .001$, $p < .001$, $p < .0001$, $p < .01$, respectively).

Many syndromic and degenerative thoracic aortopathy conditions can be characterized by general histopathological features. BAV aortopathy is not often diagnosed on basis of general histopathological features.

In conclusion, the typical histopathological appearance of a bicuspid ascending aortic wall are the following: a thin intima, elastic fiber thinning, and profound interlamellar MEMA (Figure 1). Degenerative medial pathological features are rarely seen in BAV. We assume that this summary will assist in scientific reporting and diagnoses of bicuspid aortopathy.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Nimrat Grewal and Robert Poelmann. The first draft of the manuscript was written by Nimrat Grewal and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Abbreviations: HE, hematoxylin-eosin; RF, resorcin fuchsin.

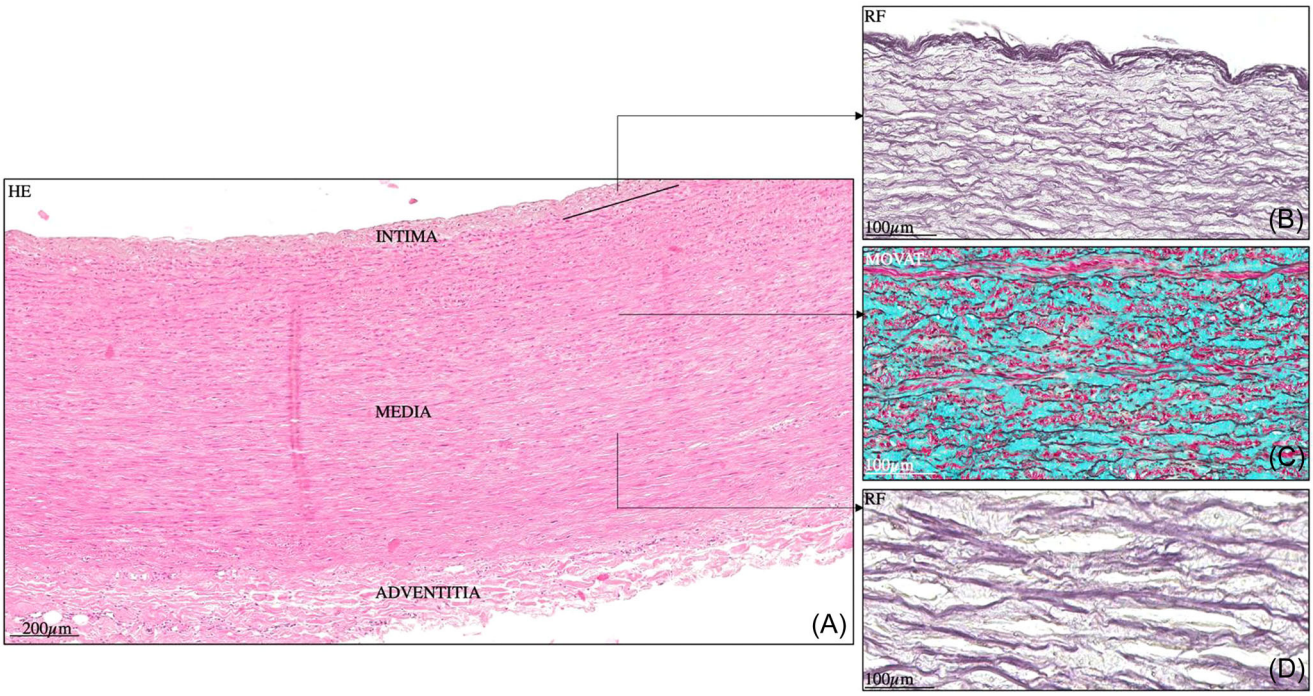

FIGURE 1 Transverse histological sections (5 μm) of a dilated ascending aortic wall in a bicuspid aortic valve patient, stained for hematoxylin-eosin (A), resorcin fuchsin (B,D) and MOVAT (C). The intima, media, and adventitia are shown in the overview of the ascending aortic wall (A). The intima is thin-layered, as shown in detail in (B). (C) A detailed overview of the medial layer stained for MOVAT, the vascular smooth muscle cells are seen in red and the elastic fibers in black, an abundance of extracellular matrix can be appreciated in blue. The medial layer is further characterized by fine elastic lamellae (D).

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