

Peer Review File

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Review Comments

The authors report a 15-year-old male adolescent with severe stenotic unicuspid aortic valve (gradient 67 mmHg) and progressive dilatation of the ascending aorta, who underwent Bentall surgical procedure with valve replacement by mechanical valve and ascending aorta replacement by prosthetic conduit.

Histology of the aortic wall showed disruption of the elastic lamellae with mucoid deposits. A variant mutation of Noonan syndrome gene was discovered by molecular investigations.

The authors question the current guidelines for indication of surgery (>4.5 cm), also for adolescents and children. They believe that also other factors should be taken into consideration.

Response: Thank you for summary of our case report. We are delighted by the consideration for publication decision with minor revisions. We have incorporated the following changes to the original manuscript.

Suggestions:

Comment 1: The loss of elastic fibers with wall stiffness may be diagnosed by echocardiography, regardless increased diameter of the aortic lumen (Nistri S, Grande-Allen J, Noale M, Basso C, Siviero P, Maggi S, Crepaldi G, Thiene G. Aortic elasticity and size in bicuspid aortic valve syndrome. *Eur Heart J*. 2008 Feb;29(4):472-9. doi: 10.1093/eurheartj/ehm528. Epub 2007 Dec 20. PMID: 18096569.);

Response 1: Thank you for this suggestion. This reference was added as Reference #6. A paragraph was added summarizing this study under Section 3.3 "Comparison with Similar Research." (page 6, line 135-142).

-Comment 2: The microscopic findings of the ascending aorta should be reported with illustrations. Please, as far as mucoid deposits, refer to the terminology of Erdheim cystic medial necrosis;

Response 2: Thank you for this suggestion. A pathology slide of the figure (Figure 4) was included along with the following explanation: *A representative slide of the aortic tissue demonstrates normal histology in terms of wall thickness and organization. (Figure 4) There is no evidence of myxoid degeneration or elastic fiber degradation.* (Section 2, Case Description, page 5).

Comment 3: The topics of aortopathy and familiarity should be discussed more in detail.

Response 3: Thank you for this suggestion. This is indeed an important factor to comment on for the reader to understand the multiple factors involved in BAV and Thoracic Aortic Aneurysm. We have chosen to focus on the genetic section moving Reference 8 to 5 (Elefeteriades and Farkas) with their discoveries on the hereditary aortic disease, which is an on-going area of research. A paragraph was added summarizing this study under Section 3.3 “Comparison with Similar Research.” (page 6, line 143-151).