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Brief Report

Altered expression of dystrophin within the thoracic aorta in coarctation

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Abstract Although persisting endothelial dysfunction has been established in the vasculature of patients following surgical repair of coarctation, it is unknown whether there are alterations in the cytoskeleton of the aorta in such patients. We compared staining of N-terminus dystrophin in the smooth muscle of the aortic wall of a patient with coarctation to that in a patient without coarctation, the latter undergoing surgical treatment of a double aortic arch. There was a marked difference in the pattern of expression of dystrophin between the two, with the coarcted specimen demonstrating marked fragmentation but normal intensity of staining. As far as we are aware, ours is the first report to demonstrate the presence of dystrophin in the smooth muscle of the aorta. Alterations in the cytoskeletal structure may account for underlying aberrations in endothelial function in such patients, and is a topic that warrants further investigation.

Keywords: Aorta; cytoskeleton; endothelial function

ALTHOUGH PERSISTING ENDOTHELIAL dysfunction has been established in the vasculature of patients following surgical repair of coarctation, it is unknown whether there are alterations in the cytoskeleton of the aorta in such patients.[1] With this in mind, we compared staining of N-terminus dystrophin in the aortic wall of a patient with coarctation of the aorta to that in a patient without coarctation, who underwent surgical treatment of a double aortic arch. We discovered marked fragmentation in dystrophin within the vasculature of the aorta in the patient with coarctation.

Case report

The patient was a six-week-old infant with severe aortic valvar stenosis and severe preductal coarctation with normal left ventricular dimensions and mitral annular diameter. The aortic valve was bicuspid and thickened, with dysplastic leaflets. The child underwent surgical intervention, consisting of a Ross–Konno procedure, closure of an atrial septal defect within the oval fossa, and resection of the site of coarctation with advancement of the aortic arch. We compared the findings with those from an 11-year-old boy, who presented with dysphagia and was diagnosed with a double aortic arch after magnetic resonance imaging confirmed two aortic arches, both being widely patent with the posterior arch dominant.

At the time of surgery in the patient with coarctation, a segment of thoracic aorta of 4 millimetres length was resected just proximal to the abnormal segment, and immediately snap frozen in liquid nitrogen. Informed consent was obtained from the children's families, and the study was approved by the Internal Review Board of Baylor College of Medicine. The samples were stained with the DYS3 antibody against the amino (N-)terminus of dystrophin (Novocastra, Newcastle, United Kingdom). The primary antibody was diluted twentyfold in phosphate-buffered saline, and applied to each section for one hour at room temperature. After washing three times in phosphate-buffered saline, the slides were incubated for 30 minutes at room temperature with the secondary antibody, fluorescein-isothiocyanate-conjugated

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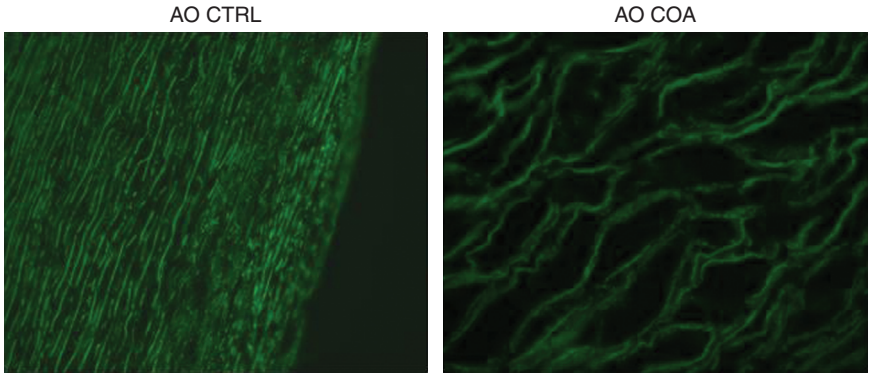

Figure 1.
Normal muscular morphology is detected by the antibody against the N-terminus of dystrophin in a section of transverse aortic arch in a patient with normal aorta (AO CTRL, left panel), in marked comparison to the fragmentation and fibre disarray found in the patient with coarctation of the aorta (AO COA, right panel). The level of staining for dystrophin itself, however, appeared comparable in the two settings.

anti-mouse immunoglobulinG (Novocastra, Newcastle upon Tyne, UK), diluted by 1 in 400, then washed and mounted, as previously described.[2]

There was a marked difference in the pattern of expression of dystrophin between the normal aorta and the segment of coarctation, with the latter demonstrating marked fragmentation but normal intensity of staining (Fig. 1).

Discussion

We have described the immunohistochemical demonstration of dystrophin in the smooth muscle of the human aorta, which we believe to be unique at this stage. We found that, while the smooth muscle in the normal aorta appeared compact and organized, the aorta in the patient with coarctation demonstrated abnormal morphology, with marked fragmentation compared to the control subject, although we were unable to detect any significant difference in expression of dystrophin. Such an altered cytoskeletal structure of the vessel may be a surrogate marker for abnormal endothelial function through a number of possible mechanisms. For example, the expression of C-type natriuretic peptide, an anti-inflammatory and antiproliferative mediator expressed by vascular endothelium, is crucial in regulating the neointimal fibroproliferative response within injured vasculature.[3,4] Further studies are now required to assess if such changes in cytosketal structure may be responsible for the known abnormalities in endothelial function in patients with coarctation.

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