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Case Report

Ultrastructural Features of the Aortic Wall in a Patient with Kommerell Diverticulum

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Abstract: We report on the ultrastructural features of the aortic wall in a patient with Kommerell diverticulum. A 70-year-old woman with a right aortic arch, aberrant left subclavian artery, and Kommerell diverticulum underwent a successful total arch replacement plus the frozen elephant trunk procedure with anatomical left subclavian artery reconstruction. Small pieces of the ascending aorta, distal arch, right common carotid artery, and left subclavian artery were investigated ultrastructurally. In the ascending aortic wall, multiple cystic cavities were observed in the subintimal region of the media by scanning electron microscopy. Changes in organelles, including mild dilation of rough-surfaced endoplasmic reticulum and mitochondrial swelling and degrading, were also observed in all specimens by transmission electron microscopy. These ultrastructural features may indicate the fragility or stress of the aortic wall and are useful when considering the early surgical intervention of a patient with Kommerell diverticulum.

Kommerell diverticulum (KD) is a developmental error that involves a remnant of the fourth dorsal aortic arch. Cystic medial necrosis is usually present in the diverticulum wall, which explains the high rates of aortic dissection and rupture associated with the diverticulum.[1] To prevent catastrophic events, early surgical intervention that includes open and endovascular repair is recommended, although the optimal operative timing remains under debate.[1–3] In general, the operative indication is acceptable for symptomatic KD or when the diameter of the diverticulum orifice exceeds 30 mm or when the diameter of the descending aorta adjacent to the diverticulum exceeds 50 mm.[4] The features of the aortic wall other than those in KD have not yet been examined and remain unclear. Here, we investigated the ultrastructural features of the aortic wall in a patient with KD and considered the operative timing.

CASE REPORT

A 70-year-old woman with a history of hypertension and hyperlipidemia presented with dysphagia and respiratory symptoms. Computed tomography (CT) revealed the right aortic arch, aberrant left subclavian artery (ALSA), and KD. The diameter of the ascending aorta was 28 mm and the orifice diameter of the KD was 27 mm. The diameter of the descending aorta adjacent to the diverticulum was 27 mm. The patient had experienced increasing swallowing difficulties over the past 3 years. KD had been identified 2 years previously, and the KD orifice had expanded 2 mm per year. Surgical treatment was planned because of the diverticulum growth and pressure on the

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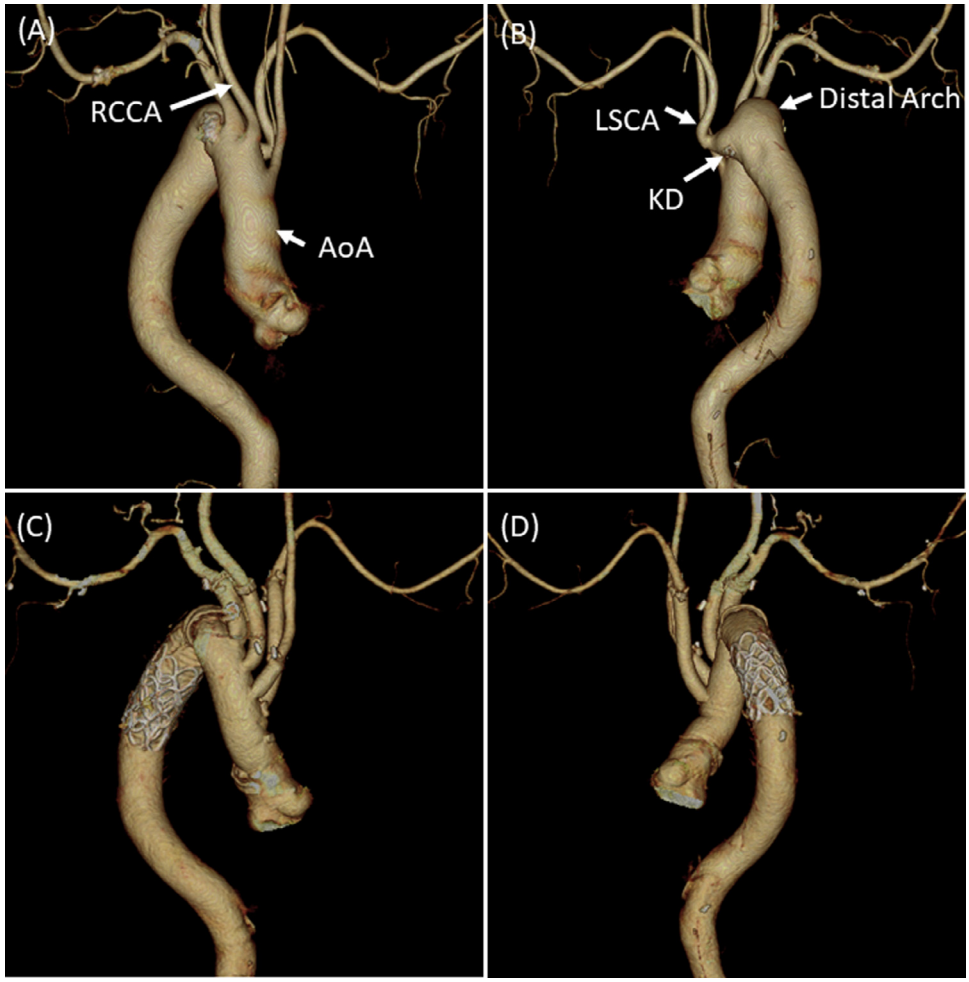

Fig. 1. Volume-rendering CT image of the thoracic aorta. Preoperative (A) frontal view and (B) rear view with the collected locations of each sample, including the AoA, distal arch, RCCA, and LSCA. Postoperative (C) frontal view and (D) rear view. CT, computed tomography; AoA, ascending aorta; RCCA, right common carotid artery; LSCA, left subclavian artery; KD, Kommerell diverticulum

esophagus and possibly the trachea, not because of the diameter of the aorta or KD.

ALSA transection and left subclavian artery (LSCA) reconstruction (8 mm Gelweave graft®, Vascutek Terumo, Renfrewshire, Scotland, UK) was opted for in order to release the compressed esophagus, and was accompanied by total arch replacement (Gelweave $22 \times 10 \times 8 \times 8$ mm graft, Vascutek Terumo) plus the frozen elephant trunk procedure (J Graft FROZENIX 25×60 mm®, Japan Lifeline, Tokyo, Japan) for KD occlusion. During the operation, small pieces of the ascending aorta (AoA), distal arch, right common carotid artery (RCCA), and LSCA were collected (Fig. 1). A piece of the wall of the KD was unable to be collected because of the location over the distal anastomosis. The extracted specimens were immediately immersed in 10% formalin solution and kept at 4°C. Each sample was processed and examined by a field emission scanning electron microscope (SEM; Regulus8100; Hitachi High Technologies, Tokyo, Japan) and a transmission electron microscope (TEM; H-7500; Hitachi High Technologies).

To assess the suitability for ultrastructural analysis of the operatively extracted specimens for ordinary pathological diagnosis, the toluidine blue–stained semithin sections from the AoA, distal arch, RCCA, and LSCA samples were observed. All 4 tissue sections exhibited fine blood vessel morphology (Fig. 2A–D).

As the AoA tissue was large in size, the SEM was utilized to observe the whole image of the AoA tissue. At low magnification, loose and spongy

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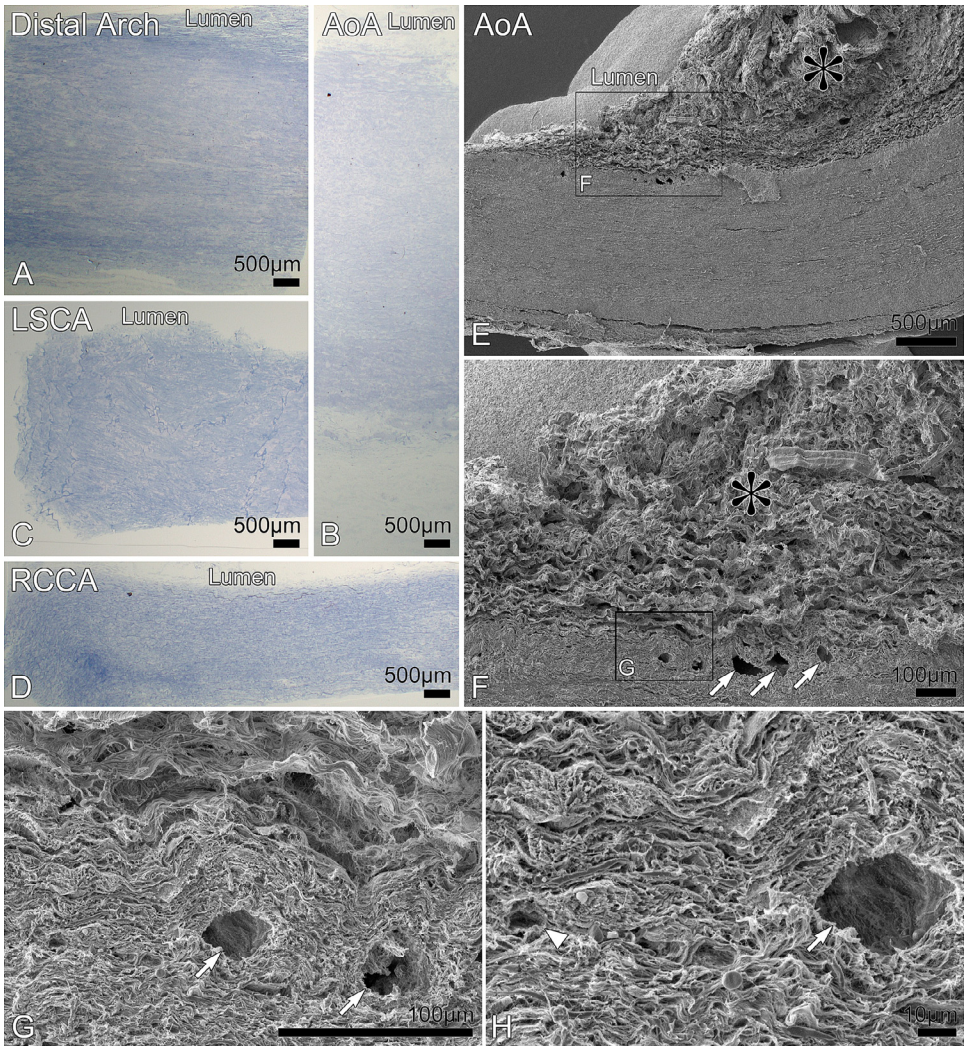

Fig. 2. Optical microscopy and SEM findings. (A–D) Overall picture of an Epon-embedded tissue semithin section of the distal arch (A), AoA (B), LSCA (C), and RCCA (D). Scale bars = 500 μm. (E–H) SEM observation of the AoA tissue. Overall picture of the AoA wall (E, scale bar = 500 μm). The partial area indicated in E was further photographed at higher magnification (F, scale bar = 100 μm), and the partial area indicated in F was further photographed at higher magnification (G and H, scale bars = 100 and 10 μm, respectively).
SEM, scanning electron microscope; AoA, ascending aorta; RCCA, right common carotid artery; LSCA, left subclavian artery

tissue attached to the intimal border of the luminal side was visible (Fig. 2E and F, asterisk). In addition, multiple cystic cavities were observed in the subintimal region of the media (Fig. 2F–H, arrows). At high magnification, these cystic cavities clearly differed from the small vessels because of a lack of endothelium (Fig. 2H, arrowhead).

To clarify the intracellular ultrastructural characteristics of each component of the artery tissue with KD, tissue samples of the AoA, distal arch, RCCA, and LSCA were observed using the TEM. In all 4 arterial tissues, fibroblasts exhibited viable nuclear morphology (Fig. 3), however, there was also mild dilation of rough-surfaced endoplasmic reticulum (rER) (Fig. 3, arrowheads), swelling and degrading mitochondria (Fig. 3, arrows), and vacuolation (Fig. 3, asterisk).

The patient had a stable postoperative course without any complications. Her dysphagia and respiratory symptoms completely disappeared. She was discharged on the 14th postoperative day.

COMMENT

Here, we presented the ultrastructural features of the aortic wall features beyond the diverticulum

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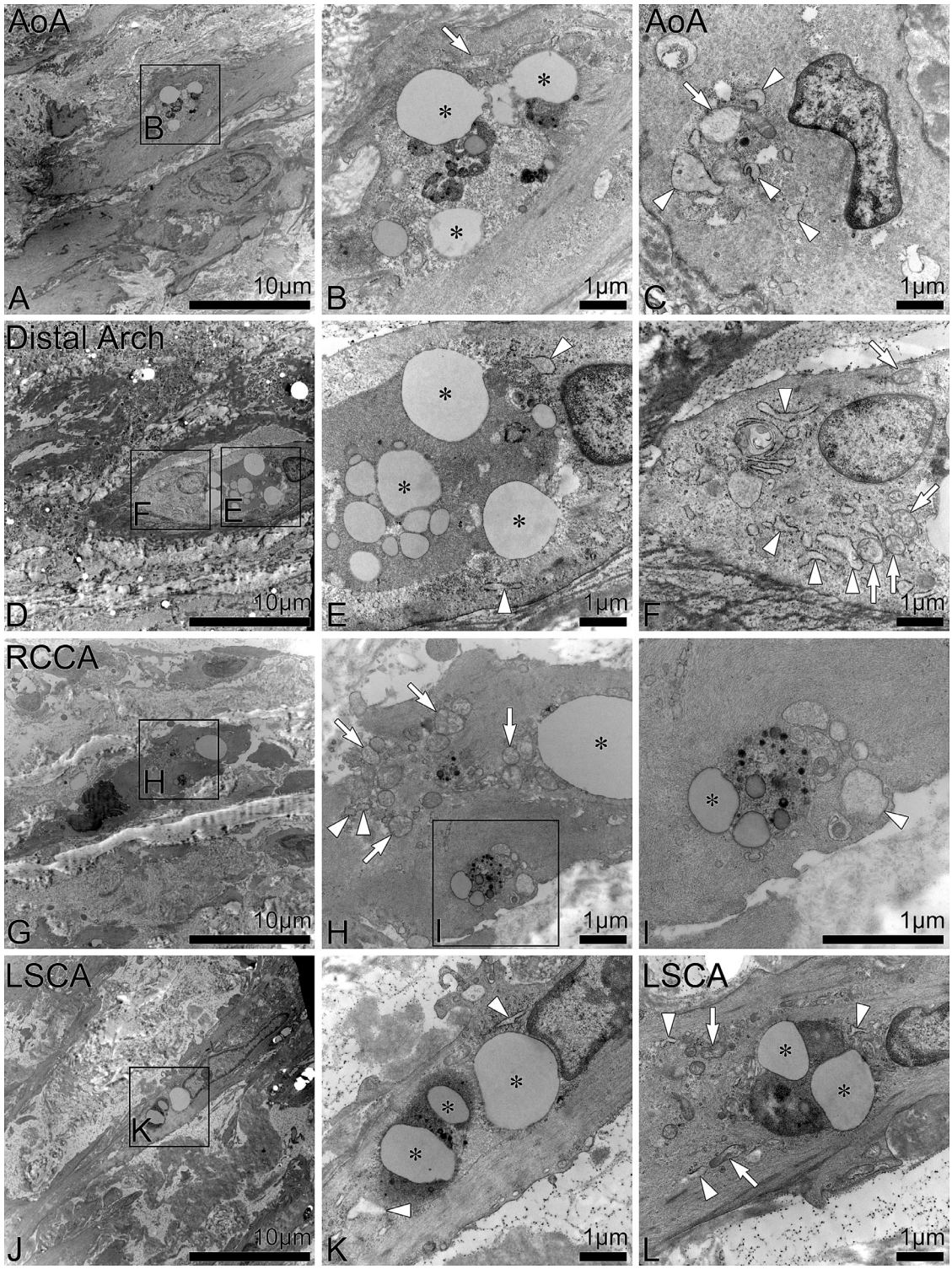

Fig. 3. TEM findings. TEM observation of the tissues of the AoA (A–C), distal arch (D–F), RCCA (G–I), and LSCA (J–L). A, D, G, and J are low-magnification images. Scale bars = 10 μm. The partial areas indicated in A, D, G, and J were further photographed at higher magnification (B, E, F, H, and K, scale bars = 1 μm), and the partial area indicated in H was further photographed at higher magnification (I, scale bar = 1 μm). C and L were observed in an independent location from panel A and J, respectively. Scale bars = 1 μm

TEM, transmission electron microscope; AoA, ascending aorta; RCCA, right common carotid artery; LSCA, left subclavian artery

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in a patient with KD. In the ascending aortic wall, multiple cystic cavities were observed in the subintimal region of the media by SEM. In previous studies, multiple cystic cavities were found in the ascending aortic dilatation and type A aortic dissection.[5,6] This case exhibited multiple cystic cavities in the aortic wall regardless of aortic dilatation. This feature might indicate potential aortic degeneration in patients with KD.

Cystic medial necrosis is associated with the internal part of KD, and causes aortic dissection and rupture.[7] The specimen in this report did not exhibit rough spaces between the media as cystic medial necrosis. There were some cavities in the subintimal region of the media, however. These features suggest that the aortic wall could easily dilate or dissect in areas other than the diverticulum associated with the KD.

Changes in organelles, including mild dilation of rough-surfaced endoplasmic reticulum and mitochondrial swelling and degrading, were also found by TEM. These features demonstrated the possibility of mechanical stress, including body pressure and shear stress, production of reactive oxygen species, and apoptosis by signal pathway.[8] For example, shear stress is affected by the anatomical form. KD is often accompanied by a steep right aortic arch. The aortic arch or bifurcation to the cervical branches is likely affected by shear stress.

The LSCA in patients with KD is embryologically aberrant because it follows the KD which is the remnant of the fourth dorsal arch and loses arch continuity.[1] TEM samples demonstrate that the aortic wall of the LSCA was not particularly damaged in this case. In contrast, it was reported that patients with aberrant LSCA demonstrated a trend toward association with aneurysmal degeneration and dissection.[9] Embryological features similar to KD may have some influence on the aortic wall.

Regarding the operative strategy in this case, as we described in our previous report[10], we selected the anatomical LSCA reconstruction and total arch replacement plus the frozen elephant trunk procedure. The standard operation for KD is a resection of the KD and descending aorta replacement at the origin of the KD with a lateral thoracotomy.[11] This operation is, however, invasive for elderly patients. Thoracic endovascular aortic repair (TEVAR) for asymptomatic KD has favorable outcomes, and is a good option in anatomically suitable cases.[1,2] For symptomatic KD, however, although TEVAR is expected to have a decompressing effect due to simple occlusion of the KD and the aberrant subclavian artery, the rate of symptom improvement by TEVAR is lower than that of resection cases.[2] In this case, it was considered that the abnormal subclavian artery was the main cause of her symptoms. Therefore, transection of the subclavian artery was performed instead of diverticulum resection and descending aorta replacement.

To reduce residual diverticulum pressure and ensure preventive treatment for expanding the diverticulum, total arch replacement with the frozen elephant trunk procedure was performed. TEVAR was deemed inappropriate because of the steep transition from the arch to the descending aorta with the right aortic arch. This operative strategy was considered acceptable as there were no postoperative complications or remaining symptoms.

In conclusion, in the present case, we found that the aortic wall was negatively affected and appeared fragile and/or stressed in areas beyond the diverticulum associated with KD. The ultrastructural findings of this case may indicate the fragility or stress of the aortic wall and are useful when considering early surgical intervention in patients with KD. Further research is necessary to identify the exact etiology of the ultrastructural features of the aortic wall in patients with KD.

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REFERENCES

1. Tanaka A, Milner R, Ota T. Kommerell's diverticulum in the current era: a comprehensive review. Gen Thorac Cardiovasc Surg 2015;63:245–59.
2. Vinnakota A, Idrees JJ, Rosinski BF, et al. Outcomes of repair of Kommerell diverticulum. Ann Thorac Surg 2019;108:1745–50.
3. Ikeno Y, Koda Y, Yokawa K, et al. Graft replacement of Kommerell diverticulum and in situ aberrant subclavian artery reconstruction. Ann Thorac Surg 2019;107:770–9.
4. Erben Y, Brownstein AJ, Velasquez CA, et al. Natural history and management of Kommerell's diverticulum in a single tertiary referral center. J Vasc Surg 2020;71:2004–11.
5. Schmitto JD, Popov AF, Coskun KO, et al. Morphological investigations of type A aortic dissection. Ann Thorac Cardiovasc Surg 2010;16:331–4.
6. Ferraraccio F, Esposito S, Santé P, et al. Scanning electron microscopy of aortic medial changes in aortic ascending dilatation. Ultrastruct Pathol 2004;28:137–40.
7. Luciano D, Mitchell J, Fraisse A, et al. Kommerell diverticulum should be removed in children with vascular ring and aberrant left subclavian artery. Ann Thorac Surg 2015;100:2293–7.

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8. Zorov DB, Juhaszova M, Sollott SJ. Mitochondrial reactive oxygen species (ROS) and ROS-induced ROS release. Physiol Rev 2014;94:909–50.
9. Plotkin A, Ng B, Han SM, et al. Association of aberrant subclavian arteries with aortic pathology and proposed classification system. J Vasc Surg 2020;72:1534–43.
10. Tsukagoshi J, Iba Y, Kurimoto Y, et al. Hybrid repair of Kommerell diverticulum and aberrant subclavian artery with compressive symptoms and a new strategy: case report. Ann Vasc Dis 2021;14:60–3.
11. Kouchoukos NT, Masetti P. Aberrant subclavian artery and Kommerell aneurysm: Surgical treatment with a standard approach. J Thorac Cardiovasc Surg 2007;133:888–92.

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