Rare Complication of Saccular Aneurysm and Histological Dissection

An Autopsy Study of 5865 Elderly Cases.

Nobuto ORIGUCHI,^{1,2} MD, Shin-ichiro OHKAWA,³ MD, Yukiyoishi ESAKI,⁴ MD,
Yoji YOSHIDA,⁵ MD, and Hiroshi SHIGEMATSU,¹ MD

SUMMARY

The purpose of this study was to examine complicated lesions of saccular aneurysm and dissection. We investigated the ascending aortae in 5865 consecutive elderly autopsy cases, and 5 cases (0.085%) of aortic saccular aneurysms associated with dissection at the edges were selected. Their edges characteristically protruded like a shelf, which histologically consisted of an inner part of the dissected media. All patients were female and their mean age was 76.8 (67-89) years. The aneurysmal walls at the center showed severe fragmentation and disappearance of the elastic lamellae of the remaining outer media. Thus, partial sections of these lesions were not sufficient but cross-sections of the whole diseased regions including the edges were essential for diagnosis. One patient had 3 saccular aneurysms and an adjacent shallow depression, which we called "healed microscopic dissection". Histologically, it showed disappearance of the inner media and was replaced by fibrosis in continuation from the intima. This lesion showed no findings of intramural hemorrhage or thrombus, and thus it will differ from organized thrombi in the dissected false lumen. Another patient presented had an aneurysmal rupture which resulted in cardiac tamponade. This case implies the need for surgical treatment of this entity. (Jpn Heart J 2001; 42: 597-606)

Key words: Female, Ascending aorta, Saccular aneurysm, Shelf-like protrusion, Healed microscopic dissection, Atherosclerosis.

AORTIC dissection has been referred to as a dissecting aneurysm, since a false lumen disguises dilatation of the arterial diameter. However, dissection has recently been differentiated from aneurysm because dissection does not usually show actual dilatation of the arterial diameter. The pathogenesis of dissection and aneurysmal dilatation is still controversial, although atherosclerosis may affect both lesions. There have been only a few reports on the complication associated

From ¹ Department of Vascular Surgery, the University of Tokyo, ² Department of Surgery, Tokyo Senbai Hospital, ³ Division of Cardiology, Tokyo Metropolitan Geriatric Hospital, ⁴ Department of Pathology, Tokyo Metropolitan Geriatric Hospital, Tokyo, ⁵ First Department of Pathology, Yamanashi Medical University, Yamanashi, Japan.

Address for correspondence: Nobuto Origuchi, MD, Department of Surgery, Tokyo Senbai Hospital, 1-4-3 Mita, Minato-ku, Tokyo 108-8329, Japan.

Received for publication January 12, 2001.

Revised and accepted April 19, 2001.

with both diseases.¹⁻⁴⁾ The purpose of this study was to examine such lesions with their initial changes in the ascending aortae of elderly autopsy cases.

METHOD

We examined ascending aortae in 5865 consecutive elderly autopsy cases at Tokyo Metropolitan Geriatric Hospital between September 1972 and August 1995. Criteria for the entity "complicated lesions of saccular aneurysm and histological dissection" were as follows: (1) grossly, a saccular aneurysm with a shelf-like protrusion at the edge (Figure 1), and (2) histologically, severe fragmentation and disappearance of elastic lamellae of the remaining outer media at the center of aneurysmal walls and fibrosis of the medial dissection at the edge (Figures 2 & 3a).

Formalin-fixed, paraffin-embedded specimens were stained with hematoxylin and eosin, elastic van Gieson, Azan and iron stainings.

Figure 1. **a:** Gross appearance of the aneurysms (A) and (B). Lesion (C) was concealed. **b:** Longitudinal aspect of Lesion (A). The aortic wall protrudes like a shelf at the proximal edge (arrow). **c:** Longitudinal aspect of Lesion (B). Shelf-like protrusions are observed at both the proximal and distal edges (arrows). Lesion (C) is a small ulceration adjacent to Lesion (A) (arrowhead) and Lesion (D) is a shallow depression adjacent to Lesion (C) (asterisk).

Figure 2. Histological view of Lesions (A) and (B) (Elastic van Gieson, original magnification x1). The shelf-like protrusions histologically showed fibrous dissection (arrows).

Figure 3. a: Histological findings at the center of the aneurysmal wall of Lesion (A) (Elastic van Gieson, original magnification x 10). The media was severely atrophic and damaged, as in an ordinary atherosclerotic aneurysm. **b:** The center of the aneurysmal wall of Lesion (C). The medial elastic layer was atrophic but preserved compared to Lesion (A) (Elastic van Gieson, original magnification x 5). (I=intima; M=media; A=adventitia)

Deparaffinized sections, 4 μ m thick, were incubated in methanol containing 0.3% H₂O₂ for 30 minutes at room temperature to quench endogenous peroxidase activity. After blocking non-specific staining with 5% skimmed milk (Snow Brand Milk Products, Sapporo, Japan) for 30 minutes, the sections were stained with monoclonal antibody HHF35 against muscle-specific actin⁵⁾ and HAM56 against monocyte/macrophage,⁶⁾ both of which were generously supplied by Dr.

Toyohiro Tsukada of Sanraku Hospital (Tokyo). After biotinylated anti-mouse immunoglobulin and peroxidase-labeled streptavidin (DAKO LSAB™ Kit, Peroxidase; Dako Japan, Kyoto, Japan) were both applied for 10 minutes, 3,3'-diaminobenzidine (DAB, Wako Pure Chemical Industries, Osaka, Japan) was applied for 10 minutes. The sections were then counterstained with methyl green.

RESULTS

We encountered 5 cases (0.085%) with this entity (Table I). All 5 patients were female. Their mean age was 76.8 years (range 67 to 89). One patient died of cardiac tamponade due to aneurysmal rupture. Their ascending aortae were moderately to severely atherosclerotic. All 5 patients were negative for syphilis. Aortic regurgitation was confirmed only in Case 1. With regard to systemic atherosclerotic diseases, acute myocardial infarction was a direct cause of death in Cases 1 and 5. Old myocardial infarction was observed in Case 3. Arteriosclerosis obliterans of the left femoral artery was observed in Case 5. Small cerebral and/or cerebellar vascular diseases were observed in 4 cases.

We describe Cases 1 and 4 in detail below.

CASE REPORTS

Case 1: An 86-year-old Japanese woman died of acute myocardial infarction. Autopsy findings showed 3 saccular aneurysms, measuring 5 x 5 x 4 cm (A), 4 x 3 x 3 cm (B), and 2 x 1 x 1 cm (C), in the ascending aorta 3.5 cm distal from

Table I. Summary of Patients

Case (Age/Sex)	Cause of death	Aortic atherosclerosis	ASO	CVD	Smoking (/day)
86/F	Acute myocardial infarction	Severe	—	Small cerebral infarcts and cerebellar hemorrhages	Several
89/F	Asphyxia	Severe	—	Small cerebral and cerebellar infarcts	20
71/F	Cholangiocellular carcinoma	Severe	—	Small cerebral infarcts and hemorrhages	No
67/F	Cardiac tamponade	Moderate to Severe	—	—	No
71/F	Acute myocardial infarction	Severe	+	Small cerebral infarcts	Unknown

Avg 76.8

the aortic valves (Figure 1). Jet lesions,⁷⁾ which are areas of endothelial roughening and reactive fibrosis at sites where a swift and turbulent regurgitant stream of blood strikes the endothelium, were confirmed on the left ventricular surface. Lesions (A) and (B) compressed the left atrium. Lesion (A) was filled with thrombus and Lesion (B) had a thrombus in the proximal part of the lumen. Their most characteristic gross appearances were shelf-like protrusions at the proximal edge of Lesion (A) (Figure 1b, arrow) and at both the proximal and distal edges of Lesion (B) (Figure 1c, arrows). Histological examinations showed that the shelf-like protrusion comprised the inner wall of dissection to form aneurysmal orifices (Figure 2, arrows) and that the dissected middle-third of the media in the neighboring segments was densely fibrous. The centers of the aneurysmal walls of Lesions (A) and (B) showed severe fragmentation and disappearance of the elastic lamellae in the remaining outer media (Figure 3a). Immunohistochemical examinations showed that the dense fibrosis had cells positive for HHF35 and there were few infiltrates of HAM56-positive cells. In Lesion (C), both edges showed dense fibrosis without atherosclerotic changes such as atheroma or foam cells (Figure 4a), while the medial elastic lamellae were relatively preserved at the center of the aneurysmal wall (Figure 3b). Immunohistochemical examinations showed that the fibrosis had cells positive for HHF35 and that the edge was infiltrated by HAM56-positive macrophages. Lesion (D), a shallow depression without gross dilatation or dissection, was adjacent to Lesion (C). Histologically, a zonal and fine fibrosis extended throughout the middle-third of the aortic media without atherosclerotic changes such as atheroma or foam cells. At the shallow depression of Lesion (D), fine fibrosis continued from the intima to the media (Figure 4b). A mild proliferation of capillaries was observed. There were no findings of hemorrhage or thrombus in the fibrous tissue and iron staining showed no hemosiderosis in the lesion. Immunohistochemical findings were similar to those of Lesions (A) and (B).

Dissection was localized within two-thirds of the circumference of the ascending aorta, and did not extend to the aortic valves or the arch. Cystic medial necrosis was observed in the non-dissecting segment of the aorta.

Case 4: A 67-year-old Japanese woman complained of back pain and was referred to Tokyo Metropolitan Geriatric Hospital. On admission, she presented with cardiomegaly (cardiothoracic ratio; 70%). She died suddenly on the 25th hospital day. Autopsy findings showed a saccular aneurysm, 3.5 cm in diameter, in the ascending aorta, which ruptured and resulted in cardiac tamponade (Figure 5). The proximal edge of the aneurysm protruded like a shelf and histologically showed dissection with dense fibrosis. Immunohistochemically, the fibrosis had cells positive for HHF35. The distal edge was connected to the macroscopic complete dissection with a false lumen filled with thrombus.

Figure 4. **a:** Histological view of Lesion (C) (Elastic van Gieson, original magnification x 2.5). Here we show an edge and the other edge had similar fibrosis. **b:** Histological view of Lesion (D) (Elastic van Gieson, original magnification x 2.5). Fibrous dissection extended from the intima to the medial layer (arrow).

Figure 5. Gross appearance of the aneurysm in Case 4. Rupture resulted in a cardiac tamponade. Macroscopic dissection developed distal to the aneurysm and a false lumen was filled with thrombus (arrow).

DISCUSSION

Saccular aneurysms developed in “healed microscopic dissection”, as shown in Case 1 in our study. In the initial stage, fibrosis was observed from the intima to the middle-third of the media, which was accompanied by disappearance of the medial elastic fibers. Zonal fibrosis extended throughout the middle-third of the media without any gross dilatation of the aortic lumen, which we refer to as “healed microscopic dissection” (Figure 6a). The aorta in this stage did not dilate at all and there were no findings of hemorrhage in the wall. Thus, this lesion will be different from fibrosis of an organized thrombus in the dissected false lumen (Figure 6d). The prototype of this lesion may be an ulcer-like lesion.⁸⁻¹¹⁾ Cystic medial necrosis was observed in the non-dissecting segment of

Figure 6. a-c: Schemata of this entity at different stages. a: first stage: degeneration and fibrosis of the intima and a part of the media. b: Second stage: ulceration of the intima. There were macrophages in the aneurysmal wall, and neutrophils in the thrombus. c: Final stage: aneurysm formation. Macrophages had disappeared. d: Schema of an ordinary dissection with re-entry. An increase in diameter results from blood invasion into a false lumen. Medial elastin and smooth muscle cells are relatively preserved. (I=intima; M=media; A=adventitia; F=false lumen) (Oblique lines and dots show the distribution of fibrosis and the medial elastic layers, respectively.)

the aorta of Case 1 and this degeneration might be the underlying abnormality of these lesions, although its significance in dissection is controversial.¹²⁻¹⁸⁾ Marsalese, *et al*¹⁹⁾ reported that 53% of patients with cystic medial necrosis died of aortic dissection or rupture. Hartman and Eftychiadis²⁰⁾ reported that medial hemorrhage, proliferation with fibrosis of smooth muscle cells, vacuolar degeneration and coagulation necrosis of smooth muscle cells, elastin fragmentation, and collagen degeneration were prototypes for dissection.

The second stage of dilatation showed ulceration of the intima (Figure 6b). Macrophages may play a role in the destruction of the wall. Another possibility is that a jet-like stream of the blood at the ascending aorta in the systole could peel the inner layers of the wall from the dissection by shear stress, if the dissection occurred relatively closely to the lumen. In this stage, the medial elastic fibers were still preserved in the outer-third of the media.

In the final stage of aneurysm formation, a gross characteristic was a shelf-like protrusion at the edge. At the center of the aneurysmal wall, the media became thin and the medial elastic fibers almost disappeared (Figure 6c). Thus, partial sections at the periphery of the discussed region are not sufficient for diagnosis; cross-sections of the whole region which include the edges of the aneurysm are necessary for diagnosis. One patient died of cardiac tamponade due to rupture in our study. Since the likely result of a fragile aneurysmal wall is rupture, this lesion should be treated surgically if possible.

Macroscopic dissection was complicated in Case 4. Cassidy and Pinniger¹⁾ reported a similar autopsy case of a 45-year-old man. His saccular aneurysm in the ascending aorta had a characteristic "rest" which appears to be similar to what we referred to as a "shelf-like protrusion", but histological findings of this rest are not available.

To the best of our knowledge, there have been only a few previous reports on this entity. Saito, *et al*²⁾ reported two types of saccular aneurysms caused by "healed medial dissection". Type I developed at the site where the inner wall of the dissection blew out and type II developed in the full-layered aorta. Our cases can be classified as their type I. They reported 3 autopsy cases with type I aneurysm; two aortic aneurysms and one subclavian artery aneurysm at the ages of 60, 37, and 62, respectively. Two cases were female and one was male. They suggested that this type of aneurysm was formed by enlargement of the ulcer-like projection. They also stated that hemorrhage of the vasa vasorum in the media would be the initial lesion in dissection for 2 reasons. First, saccular aneurysm was considered to be formed after rupture of a partly organized intramural hematoma into the arterial lumen. This meant that medial dissection preceded intimal tearing. Second, their cases did not rupture despite a thin medial layer. This indicated that intimal laceration followed organization of the hematoma,

strengthening the arterial wall. With regard to the pathogenesis, they speculated that cystic medial degeneration, which was observed in two cases, might induce a dissection.

Murray, *et al*³⁾ reported this type of dissection as “incomplete dissection”, which accounts for intramural dissection; following laceration of the intima and subjacent media without complete laceration, the edges would retract and the “bare area” would be filled in with a neointima composed primarily of fibrous tissue which would become covered by endothelium. They reported that 8 of 12 patients (75%) with “incomplete dissection” manifested aortic regurgitation, although only one patient (25%) showed this symptom in our study.

In conclusion, we have reported 5 cases of saccular aneurysms in the ascending aorta associated with histological dissection. Partial sections were not sufficient for diagnosis; cross-sections which included the edges were necessary. The incidence was 0.085% among elderly autopsy cases. All 5 cases were female. The initial lesion showed histological fibrosis of the intima and the media without gross dilatation or dissection. This “healed microscopic dissection” is not the same with fibrosis of an organized thrombus in the dissected false lumen. In one case, rupture of the aneurysmal wall resulted in a cardiac tamponade. Surgical treatment is advisable, as with an ordinary atherosclerotic aneurysm.

This material was originally reported at the 36th Annual Meeting of the Japanese College of Angiology, Okinawa, Japan in 1995.

ACKNOWLEDGEMENTS

We thank Professor Y. Hosoda (Keio University) and K. Saito (Jichi Medical School) for their valuable advice regarding Case 1. We also thank Ms. A. Toku and Mr. K. Nakamura (Department of Clinical Pathology, Tokyo Metropolitan Institute of Gerontology) for their technical assistance with the pathology sections.

REFERENCES

1. Cassidy M, Pinniger J. Healed dissecting aneurysm. *Br Heart J* 1946; 8: 130-40.
2. Saito K, Shimizu H, Kawai T, Yamada S, Furuse M, Fukushima K. Pathology and morphogenesis of the saccular aneurysm of the aorta and large elastic artery with healed medical dissection (in Japanese with an English abstract). *Jpn J Chest Dis* 1994; 53: 1-10.
3. Murray CA, Edwards JE. Spontaneous laceration of ascending aorta. *Circulation* 1973; 47: 848-58.
4. Stehbens WE. Aneurysms. In: Stehbens WE, Lie JT, eds. *Vascular Pathology*. Oxford: Chapman & Hall, 1995; 357-62.
5. Tsukada T, Tipples D, Gordon D, Ross R, Gown AM. HHF35, a muscle-actin-specific monoclonal antibody. I. Immunocytochemical and biochemical characterization. *Am J Pathol* 1987; 126: 51-60.
6. Gown AM, Tsukada T, Ross R. Human atherosclerosis. II. Immunocytochemical analysis of the cellular composition of human atherosclerotic lesion. *Am J Pathol* 1986; 125: 191-207.

7. Edwards JE Jr, Burchell HB. Endocardial and intimal lesions (jet impact) as possible sites of origin of murmurs. *Circulation* 1958; 18: 946-60.
8. Stanson AW, Kazmier FJ, Hollier LH, *et al*. Penetrating atherosclerotic ulcers of the thoracic aorta: natural history and clinicopathologic correlations. *Ann Vasc Surg* 1986; 1: 15-23.
9. Cooke JP, Kazmier FJ, Orszulak TA. The penetrating aortic ulcer: pathologic manifestations, diagnosis, and management. *Mayo Clin Proc* 1988; 63: 718-25.
10. Harris JA, Bis KG, Glover JL, Bendick PJ, Shetty A, Brown OW. Penetrating atherosclerotic ulcers of the aorta. *J Vasc Surg* 1994; 19: 90-9.
11. Origuchi N, Shigematsu H, Nunokawa M, Yasuhara H, Muto T. Spontaneous perforation of a non-aneurysmal atherosclerotic abdominal aorta or femoral artery. *Cardiovasc Surg* 1996; 4: 351-5.
12. Rottino A. Medial degeneration of the aorta as seen in twelve cases of dissecting aneurysm. *Arch Pathol Lab Med* 1939; 28: 1-10.
13. Gore I, Hirst AE Jr. Dissecting aneurysm of the aorta. *Cardiovasc Clin* 1973; 5: 239-60.
14. Hirst AE, Gore I. Is cystic medionecrosis the cause of dissecting aortic aneurysm? *Circulation* 1976; 53: 915-6.
15. Becker AE. Medionecrosis aortae. *Pathol Microbiol Basel* 1975; 43: 124-8.
16. Schlatmann TJM, Becker AE. Histologic changes in the normal aging aorta: Implications for dissecting aortic aneurysm. *Am J Cardiol* 1977; 39: 13-20.
17. Schlatmann TJM, Becker AE. Pathogenesis of dissecting aneurysm of aorta: Comparative study of significance of medial change. *Am J Cardiol* 1977; 39: 21-6.
18. Larson EW, Edwards WD. Risk factors for aortic dissection: A necropsy study of 161 cases. *Am J Cardiol* 1984; 53: 849-55.
19. Marsalese DL, Moodie DS, Lytle BW, *et al*. Cystic medial necrosis of the aorta in patients without Marfan's syndrome: Surgical outcome and long-term follow-up. *J Am Coll Cardiol* 1990; 16: 68-73.
20. Hartman JD, Eftychiadis AS. Medial smooth-muscle cell lesions and dissection of the aorta and muscular arteries. *Arch Pathol Lab Med* 1990; 114: 50-61.