Case Reports

Two Cases of Aortitis Syndrome with Aneurysm Formation

Hideo UEDA, M.D.,* Kyoko OHNO, M.D., Iwao ITŌ, M.D., Tadanao TAKEDA, M.D., Yoshimi SAITO, M.D., and Akira UENO, M.D.

SUMMARY

Clinical pictures of aortitis syndrome are remarkably manifold. Depending on the site of lesions, many signs and symptoms can grow such as Takayasu’s ocular change, pulseless disease, atypical coarctation of the aorta, renovascular hypertension and aortic regurgitation, with several combination in a case. Moreover, occurrence of dilative and aneurysmal changes of the aorta and its main branches in aortitis syndrome has recently been recognized. Two cases of aneurysms in the main branches of the aorta are presented with review of literature. The authors regard them as one of various important manifestations of aortitis syndrome, especially from prognostic and therapeutic standpoints.

Additional Indexing Words:

Pulseless disease Atypical coarctation of the aorta Renovascular hypertension Aortic regurgitation Chronic panaortitis Dilatation of the aorta Nonspecific aortitis

Since the first presentation by Takayasu,1 a number of cases whose clinical pictures are due to chronic panarteritis of the aorta and great vessels of unknown etiology have been reported.

Variable symptoms have been noted according to the localization of vascular lesions. The authors have advocated to summarize them under the term of aortitis syndrome.

It has been generally appreciated that manifestations of aortitis syndrome are mainly attributable to occlusive lesions of the aorta and/or its main branches, but it should be emphasized that dilative changes of arteries could grow in this syndrome.

The authors reported8) previously that aortitis syndrome was not in-
frequently accompanied by aortic insufficiency which could occur as a result of dilatation of the ascending aorta.

In this paper, 2 cases of aortitis syndrome with aneurysms of main branches are presented.

**Case Reports**

*Case 1.* K. T., a 29-year-old housewife, was admitted to the Second Department of Internal Medicine, University of Tokyo on October 5, 1966, with the chief complaint of weak pulsation on her right radial artery. Her family history was not contributory. She had been frequently troubled by tonsillitis from her childhood and at times had suffered from arthralgia since 1959. She began feeling tired in 1961, when albuminuria was pointed out. Vertigo by a sudden change of position, easy fatigability, slight fever and loss of weight appeared in 1963 and albuminuria was also noted at that time.

It was noticed in 1965 that her right radial pulse was weak and the blood pressure of the right upper extremity was lower than that of the left.

Physical examination on admission revealed well developed, moderately obese woman in no apparent discomfort. The skin was fine and pale. Temperature was 36.9°C, pulse rate 60/min., and blood pressure was 102/80 mm.Hg in the right arm, 136/72 in the left arm, 162/80 in the right leg and 164/88 in the left leg.

The right radial pulse was very feeble and the right carotid pulse was a little weak. The cardiac dullness was not enlarged. On auscultation the second heart sound was accentuated and a grade 2 ejection systolic murmur and a grade 1 diastolic blowing murmur were heard best in the Erb's area. Moreover, continuous murmurs which were composed of a grade 3 harsh diamond-shaped systolic murmur and a grade 2 decrescendo short diastolic murmur were audible over the right carotid artery. A grade 1 to 2 ejection systolic murmur of short duration was heard over the left supraclavicular fossa. On the epigastrium, a faint but long systolic murmur of grade 1 was also audible.

Laboratory findings on admission were as follows: Examination of the blood disclosed hemoglobin content of 68% (Sahli), 312×10^4 red blood cells and 7,100 white blood cells with a normal differential count. Thrombocyte count was 13×10^4, reticulocytes 13%, coagulation time 7.5 min., bleeding time 3 min. and prothrombin concentration was 115% of normal.

Erythrocyte sedimentation rate was 50 mm. in 1 hour.

Urinalysis revealed trace of albumin, no sugar and the sediment was unremarkable on several occasions. The serologic test for syphilis, RA-test, Waaler-Rose test, Coombs' test and cold agglutination test were all negative. L-E cell was not found. Tuberculin test was questionable (induration 8×9 mm.). CRP was negative or one plus on several occasions and the titer of ASL-O was 250 units.

The chest X-ray film and ECG revealed no abnormality. Serum total protein was 8.8 Gm./100 ml. of which 50.5% was albumin, 9.7% Α₁, 12.9% Α₂, 9.7% Β, and 17.2% γ-globulin. Blood urea nitrogen and serum sodium, potassium, chloride and cholesterol levels were all within normal range. Liver function tests were not remarkable. The phenolsulfophthalein test showed 25% excretion of injected dye in 15 min. and 60% in 2 hours. The maximum urine concentration by Fishberg's method was
Renal clearance test revealed RBF of 1,178 ml./min., RPF of 778 ml./min., GFR of 140 ml./min. and FF of 0.18. BMR was +18% and serum Fe content was 75 μg/100 ml. The titer of anti-aorta antibody in serum by complement fixation test was 1:5. Aschner and Czermak maneuvers were both negative. EEG revealed no abnormality. Visual acuity was 0.2 in the right eye and 0.9 in the left.

The blood pressure in the retinal artery was 77/14 mm.Hg in the right side and 65/15 mm.Hg in the left. Funduscopic findings were normal.

Aortogram was as follows (Fig. 1 and 2): The ascending aorta was generally dilated and a portion of projection to the right was found near its origin. The wall of the innominate artery was irregular and a spherical aneurysm of 3.1 × 3.5 cm. in diameter was located just distal to the short stenotic segment of the right subclavian artery at its origin. There was obstruction of the right subclavian artery at the distal portion of the aneurysm and several anastomoses were developed between the right axillary artery and internal thoracic artery.

The right carotid artery had narrowing and irregularity of the wall, slight winding starting at the orifice and poststenotic dilatation at the portion of bifurcation. The left carotid, subclavian and vertebral arteries were grossly normal. The wall of lower portion of the descending aorta also had irregular appearance to some extent. The diameter was wide from the lower thoracic to the upper abdominal aorta and the inner outline was uneven. There was partial stenosis of the right and left main renal arteries, particularly of the former, accompanied by poststenotic dilatation.

An intravenous pyelogram showed delayed hyperconcentration on the right side, though appearance time of contrast medium and nephrograms were equal on the right and the left. There was no significant difference in renogram between both sides.

The result of split renal function studies was interpreted as technically inadequate because of some bladder leakage of the urine specimen.
The renin activity of the renal venous blood obtained by a catheter was 31 ng. angiotensin equivalent per ml. of plasma on the right side and 22 ng. on the left (normal value is 0.9–4.5). The latter value was almost the same as that of peripheral venous blood. Renal biopsy performed on the right side revealed no specific findings.

Treatment and clinical course: With administration of prednisolone 30 mg. per day, ESR lowered to 10–20 mm. per hour, CRP became persistently negative and ASLO lowered below 100 units. After diminution of the steroid to 5 mg. per day, she was discharged and has been followed at the out-patient clinic.

Case 2. M.K., a 32-year-old man, was admitted to the Second Department of Internal Medicine, University of Tokyo on February 19, 1962, with the complaints of right-sided migraine and easy-fatigue of right upper and lower extremities. The patient suffered from rheumatoid arthritis and pulmonary tuberculosis at age 31. One of his sisters and two sisters of his mother had cardiac disease.

At the age of 31, the patient had two occasions of syncopal attack, the duration of which was few minutes. One month before his admission, he felt dizzy on walking, followed by transient unconsciousness with resultant left hemiplegia, paresthesia, speech disturbance and facial palsy.

On physical examination, the positive findings were limited to the nervous and vascular system. The blood pressure was 120/80 mm.Hg in the right arm, but was often unobtainable in the left. The patient was well developed. A pulsatile non-tender, elastic soft mass with a harsh systolic murmur was noted in the right carotid area.

The lungs were clear to percussion and auscultation. The heart was not enlarged, sounds were normal and no murmurs were detected. The liver and the kidney were not palpable. No pretibial or pedal edema was present. There was paralysis of the left upper and lower extremities with hemiparesis involving the face.

Laboratory data: The urine was normal. Examination of the blood revealed the hemoglobin content of 110% (Sahli), the red cell count of 525 x 10⁴ and the white cell count of 8,800, with 69% neutrophils, 2% band forms, 1% eosinophils and 17% lymphocytes. The serologic tests for syphilis were negative. The blood urea nitrogen was 20.5 mg., the serum total protein 8.7 Gm. (A/G ratio 1.34) and cholesterol 220 mg. per 100 ml. The serum sodium was 142 mEq./L., potassium 4.3 mEq./L., and chloride 102 mEq./L. The erythrocyte sedimentation rate was 18 mm. in 1 hour. CRP was negative. The thymol turbidity test was 4.1 units, and the zinc sulfate test was 10.0 units.

The chest X-ray film and ECG were almost normal. Funduscopic examination revealed no abnormalities.

The clinical diagnosis was cerebral embolism and probably cervical aneurysm. On March 13, 1962, he was referred to the Second Department of Surgery of Tokyo University. A retrograde aortogram failed to visualize the both carotid and subclavian arteries. After discharge the aneurysm gradually enlarged, and in the middle of August it was egg-sized with fluctuation in the central area. On October 8, he was readmitted to the same Department of Surgery because of abrupt attack of dyspnea, coarseness of voice and throat pain.

On the second admission, the patient was poorly nourished. Blood pressure was 120/90 mm.Hg in the right arm, and was unmeasurable in the left. Pulse was regular with a rate of 120 per min. Radial pulses were difficult to feel in the left arm.
The mass in the right neck was about 16 by 25 cm. with a systolic murmur heard over it.

The patient was operated upon on October 9, 1962, under the profound hypothermia by means of extracorporeal circulation. The orifice of aneurysmal rupture was noted on the level of the right common carotid artery, 3 cm. distal to the innominate artery. An arterio-venous fistula was found to have been formed between the right common carotid artery and the cervical vein, each of which was ligated at the both ends.

After operation consciousness was not restored and blood pressure fell down to 60 mm.Hg systolic. The patient expired on October 10, 1962.

Postmortem examination revealed the followings.

Gross findings: The right internal carotid artery and the left subclavian artery were markedly narrowed, the former being filled with a thrombus. A post-operative state of resection and ligation of aneurysm-like dilatation of the right common carotid artery, which was performed against hemorrhagic necrotic abscess formation with rupture of dilated region, was noted.

The aortic arch was coarse-walled and revealed coarctation. No remarkable sclerotic change was found in the whole vascular system.

There was old cerebral softening in the right hemisphere, involving the posterolateral part of the frontal lobe, whole structure of basal ganglia with internal and external capsules, insula and anterior half of the temporal lobe.

Microscopic findings: In the aortic arch, there was progressive separation of the elastica by increasing amounts of fibrosis around the vasa vasorum in the outer part of media, accompanied by focal intimal thickening (Fig. 3). Beyond the junction of the right common carotid artery, a wide spectrum of changes were seen, becoming progressively more severe distally, and resulting in the formation of aneurysm near the bifurcation. The change affected all layers but the intensity of the inflammatory reaction was invariably more pronounced in the media, accompanied by hemorrhagic necrosis, granuloma formation and dearrangement of elastic fibers (Fig. 4).

In close proximity to the above-mentioned aneurysm, the right common carotid artery showed intimal thickening, the degree of which corresponded to the severity

Fig. 3. Aortic arch (H-E). Note fibrosis around vasa vasorum in the outer layer of the media.

Fig. 4. Aneurysm of right common carotid artery (Elastica van Gieson). Note hemorrhagic necrosis, granulation tissue and dearrangement of the elastic layer.
Fig. 5. Right common carotid artery proximally to the aneurysm (H-E). Note intimal thickening, medial damage and granulation tissue in the adventitia.

Fig. 6. Right internal carotid artery (H-E). Note complete occlusion and recanalization.

Fig. 7. Left subclavian artery (Elastica van Gieson). Note disorganization of the elastic layer and recanalization.

of medial damage, and granulation tissue in the adventitia (Fig. 5). The right internal carotid artery was completely occluded with associated recanalization (Fig. 6). There was moderate disorganization of elastic layers and recanalization in the left subclavian artery (Fig. 7).

DISCUSSION

Under the term of aortitis syndrome, a certain group of diseases are summarized which are characterized pathologically as nonspecific inflammation of the aorta and its main branches, and epidemiologically as high incidence among young women in the Orient. Aortitis syndrome may have a great variety of clinical pictures, depending on the site of arterial lesions.

Historically, peculiar vascular abnormalities of the retiae were first noted by Takayasu\(^1\) in 1908. Ohnishi and Kagoshima added the opinion that the same ocular changes were associated with non-palpable radial pulse. Shimizu
and Sano reviewed 25 cases in 1948 and summarized them as 'pulseless disease', proposing occlusive thromboarteritis of subclavian and carotid arteries as its pathogenesis. After that, a certain disease named 'atypical coarctation of the aorta' whose lesion was present mainly in the descending aorta was reported by Inada in 1961, and its pathogenesis was considered to be essentially the same as that of the pulseless disease.

Danaraj illustrated several cases of renovascular hypertension due to extension of aortitis to the renal arteries and Ueda reported that aortitis syndrome occupied a large etiological portion of renovascular hypertension in Japan, indicating the incidence of about 30% of the cases.

Aortitis syndrome was formerly considered to produce only stenotic or obstructive changes on which manifestations above-described were all based. Recently, attention has been payed to the presence of dilative and aneurysmal changes.

As reported previously, aortic insufficiency secondary to dilatation of the ascending aorta was not infrequently found in aortitis syndrome.

The authors have experienced 2 cases of aortitis syndrome with aneurysms, one on the right subclavian and the other on the right common carotid artery. One was diagnosed by history, physical examination, laboratory data and aortogram, and because of having a mild activity steroid therapy was given. The other case developed spontaneous rupture of the aneurysm and postmortem examination was performed.

It may be emphasized that symptoms due to aneurysmal change should be recognized to be one of various manifestations of this syndrome.

Maekawa reported previously 3 cases of aortic aneurysm due to unknown etiology, suspecting cystic medionecrosis as its pathogenesis. However, these 3 cases were all young females and they revealed discrepancy in the pulses and blood pressure between the right and left arms, evidence of systemic inflammation such as elevated ESR, positive CRP, leukocytosis and slight fever. Therefore, the aneurysms in these cases are reasonably attributed to aortitis syndrome rather than to cystic medionecrosis.

Kimoto presented 4 cases with aneurysms of main branches and 5 cases with abdominal aneurysms due to aortitis and he stressed the necessity of surgery in early stage because those inflammatory aneurysms were liable to rupture even if they were small.

Nakao and associates collected 84 cases of aortitis syndrome, including one case with irregular saccular aneurysm, 3 cases with dilatation of the descending or abdominal aorta, 4 cases with dilatation of the ascending aorta and 1 case with aneurysm of a certain aortic branch.

Recently, Vinijchaikul reported that aneurysms of the aorta, often
multiple, were discovered in 7 of 8 cases of aortitis syndrome ascertained with postmortem examination. Seven saccular aneurysms ranging from 0.5 to 4 cm. in diameter were found at the root of the ascending aorta in 5 cases. As to the abdominal aorta, 5 saccular aneurysms in 3 cases and 2 fusiform in a case were present. Then he illustrated that abdominal aneurysms were in general larger than those at the root of ascending aorta and that the formers could be visualized by aortogram, though the latters were found only at autopsy.

Prior to these reports, there had been sporadically similar reports of aneurysm and localized dilatation associated with nonspecific aortitis by Maycock\textsuperscript{13}, Isaacson\textsuperscript{14}, Danaraj\textsuperscript{5} and others.\textsuperscript{15--17}

The exact cause of aortitis syndrome is still obscure. Main pathological findings are destruction of elastic fibers in the media, cellular infiltration of the adventitia and media, and fibrosis and hyperplasia of the intima without cellular infiltration. When changes of intima are marked compared with those of media and adventitia, stenotic or occlusive lesions may occur, and when destruction of the medial elastic fibers proceeds against the protection of the affected adventitia, dilatation or aneurysm may be formed.

Dilative or aneurysmal change in aortitis syndrome seems to be apt to occur in the right major branches and upper abdominal aorta, in contrast to the fact that stenosis or occlusion is common in the left. It is the general view that the most commonly affected artery to stenosis is the left subclavian artery.\textsuperscript{18}

The reason for this laterality is not clear, but it is speculated that local change of hemodynamic action or congenital arterial change may provoke the development of aneurysm under the destruction of medial elastic fibers. As rupture of the aneurysms may occasionally occur and it may be the cause of death, surgical intervention should be considered whenever possible.

\textbf{References}