Case Report

Aortic Arch Syndrome with Cardiomegaly and Aortic Calcification

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THE aortic arch syndrome is resulted from syphilis, atheromatosis, trauma, thrombophilia, tuberculosis, idiopathic arteritis, and other conditions which cause stenosis or obliteration of the branches of the aortic arch.^{1),2)} Its clinical picture is said to be various. According to Shimizu, pulseless disease, one of the aortic arch syndrome, has a triad^{3),4)} and it is also named Takayasu⁵⁾-Onishi⁶⁾-Kagoshima⁷⁾ disease after the first reporters of the retinal change characteristic of pulseless disease. Up to the date, more than 130 cases of pulseless disease have been reported in Japan and many in abroad.

We observed 3 cases of the aortic arch syndrome without eye symptoms, but with cardiomegaly and aortic calcification as cardinal symptoms. These cases seemed to be caused by generalized arteritis, one of which was ascertained by postmortem examination.

CASE REPORTS

Case 1, M. T., a 46-year-old house wife entered the Tokyo University Hospital on May 20, 1960 because of the absence of the radial pulse. Family history non-contributory. Birth and childhood normal. Menstruated at 17, regular till 44. At the age of 27, her first pregnancy, she was found to have a heart murmur and diminished pulsations in both radial arteries. But she had been rather well till August, 1959, when she had fever over 38.5°C followed by dizziness, headache, nausea, palpitation and dyspnea. The swelling and painful annular erythemas of the right ankle appeared frequently. These symptoms with fever lasted for about 6 weeks. In November of the same year, fever and the above symptoms reappeared. She continued to have the symptoms and she visited the out-patient clinic of Tokyo University Hospital complaining of palpitation and edema over the feet and was admitted on May 20.

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On admission, physical examination was not remarkable except in the cardiovascular system. The blood pressure was 110/90 mm. Hg in the right arm but often unmeasurable in the left, and 170/110 mm. Hg in the left leg. Both right and left radial pulsations were very feeble. The right carotid artery was strongly palpable with systolic thrill and murmur. The left carotid pulse was absent. The cardiac rhythm was regular with a rate of 97. The cardiac dullness was extended to the both sides and the apical impulse was palpable in the 6th interspace on nearly anterior axillary line. Auscultation revealed a systolic (not continuous) murmur (grade V) with thrill maximal at the right neck, indicating stenosis of right carotid artery. This murmur was transmitted to the base of heart, where both abnormal loud aortic ejection sound and paradoxical splitting of second sound were noted. Loud presystolic gallop rhythm was heard at the apex, indicating myocardial damage (Fig. 1). In the

Fig. 1. Phonocardiogram of case 1.

abdomen the liver was palpable with 3 fingers-breadth below the costal margin and was hard but not tender. The spleen was also palpable.

Laboratory examination: Blood study was normal except mild hypochromic anemia (Sahli 68%). Serum protein was normal (8.0 Gm./100 ml.), but A/G ratio was markedly decreased (0.47), with hypergammaglobulinemia (32.5%). Liver function tests revealed normal results except zinc sulfate turbidity test (22.5). Serum cholesterol was within normal range (182 mg./100 ml.). Tuberculin skin test was positive, serological tests for syphilis was negative and C-reactive protein was 3 (+) positive. Albuminuria and markedly increased erythrocyte sedimentation rate (60 mm./hr.) were noticed. L. E. cells were negative. Ophthalmoscopic examination revealed mild arteriolar sclerosis. There was difference of the retinal arterial pressure between the left (102/55 mm. Hg) and the right (130/50 mm. Hg).

Pressing or massage on the region of the carotid sinus with the fingers on either side produced slight prolongation of the respiration intervals and mild bradycardia. Pressing on the right carotid sinus, arterial pressure decreased from 180 mm. Hg to 120 mm. Hg in systole. Chest X-ray (Fig. 2) demonstrated marked generalized

Fig. 2. Chest X-ray of case 1.

cardiac enlargement and remarkable calcification of the aorta, from the arch to the abdominal aorta. Aortogram showed the string-like left carotid artery with obliteration of the subclavian arteries of both sides and irregular arterial wall. There was well developed collateral circulation to the arms (Fig. 3). The

Fig. 3. Aortogram of case 1.

electrocardiogram (Fig. 4) showed the left ventricular hypertrophy.

Needle biopsy specimen of the kidney revealed thickening of the intima and the media of the arterioles. There were few atrophied or fibrinized glomeruli (3/20) and a swollen glomerulus with thickened capillary wall. Patient was dis-

Fig. 4. Electrocardiogram of case 1.

charged from the hospital with good effect of prednisolone and was followed at out-patient clinic. The blood pressure in the arms became recordable by the administration of prednisolone, but, the blood pressure became unmeasurable again without the medication.

Case 2, T. O., a 48-year-old woman was admitted to the Tokyo University Hospital on January 20, 1961, complaining of dull pain on the right temple, attacks of palpitation, shortness of breath and tachycardia, for about one and a half years. These symptoms appeared on exertion and were relieved by rest. There was neither history of syphilis nor other general inflammatory disease like a rheumatic fever in the past. At the age of 33, she had an operation for retroverted uterus, and her radial pulse was noticed to be very feeble. She had never experienced intermittent claudication, except an episode that about a year ago, her right leg suddenly became dark red without pain for a few hours. She had never complained of decrease in visual acuity.

Outstanding physical findings on admission were as follows. The blood pressure was 240/50 mm.Hg in the right arm, 130/70 mm.Hg in the left and 180/70 mm.Hg in the lower limbs. Both carotid arteries were strongly palpable, with systolic thrill and bruit. The cardiac dullness was enlarged and loud systolic murmur was heard over the manubrium sterni. Atrial gallop and paradoxical splitting of second sound were also noted. Faint aortic diastolic murmur was noted at the Erb's area. A harsh systolic bruit with slight thrill was present around the umbilicus, and also on the back of the thorax.

Laboratory examination: White blood cell count 12,000 with neutrophilia, E. S. R. 63 mm./hr., C-reactive protein 6(+) and tuberculin test strongly positive, while Sahli was 80%, platelets count was 230,000 and serological tests for syphilis were negative. There was hyperglobulinemia (A/G ratio 1.08) without impairment of liver function. Renal blood flow by PAH method was 664 ml./min., glomerular filtration rate was 53.1 ml./min. No functional difference was detected between the both kidneys. An electrocardiogram showed marked left ventricular hypertrophy and strain. Phonocardiogram showed a typical ejection

murmur (grade V), which was most marked on the left and right subclavian fossa and moderately intense at the epigastric region. Chest X-ray showed enlargement of the left ventricle and extensive calcification of the aorta, extending from the arch to the diaphragm. Retrograde aortography revealed a marked stenosis of the left subclavian artery at its origin, narrowing of the mid portion of the right carotid artery and many collateral vessels from the right subclavian artery. During the withdrawal of catheter from the arch, blood pressure dropped suddenly at the point of the diaphragm. This evidence, together with the systolic bruit heard about the umbilicus, suggested the narrowing of the abdominal aorta.

Case 3, Y.Y., a 28-year-old man. On April 11, 1956, he was admitted to the Tokyo University Hospital, complaining of nausea, vomiting, palpitation and edema. Family history; father and grandfather of the father side died of apoplexia, mother died from syphilis and one of sisters from lung tuberculosis. Birth and childhood were normal. At the age of 16, dyspnea on exertion, general malaise, diarrhea and edema appeared. At 17 years old, tuberculin intracutaneous reaction became positive. At 18, the patient developed right coxalgia and myalgia of the feet, with recurrence in the winter. In 1954, when he was 26 years old, he developed congestive heart failure. At that time vertigo provoked by turning the head backward was noticed. In February, 1956, he had frequent attacks of nocturnal dyspnea.

Physical examination revealed an average sized man with the puffy face and edema on the lower extremities. The dilatation of the jugular vein was noticed. The pulsation of the radial arteries was weak in both sides. Cardiac beats were regular with a rate of 104. The systolic blood pressure was 108 mm.Hg in the right arm and 104 mm.Hg in the left by the tactile method. The heart was enlarged to the both left and right on percussion and the apical impulse was seen on the anterior axillary line. On auscultation, besides vessel murmur of the neck, there was systolic murmur at pulmonic area, and apical rumbling and basal blowing diastolic murmurs were noted. On the abdomen, the liver with the hard margin and tenderness was palpable about 2 fingers-breadth below the costal margin.

Laboratory examination revealed albuminuria, elevated venous pressure (405 mm. H₂O) and prolongation of the circulation time (33 sec.). Liver function test had abnormal results (icterus index 24, B. S. P. 22.5% at 45 min., cobalt reaction R₈₍₇₎). Serum cholesterol was 225 mg./100 ml. CRP was positive, while there was no increase in the erythrocyte sedimentation rate. Chest X-ray revealed cardiac enlargement and marked calcification of the aortic arch. The electrocardiogram showed left ventricular hypertrophy pattern with regular rhythm.

The patient was treated with digitalis, but he expired by an accident on May 10, 1956.

Postmortem examination: The heart weighed 890 Gm., showing marked left ventricular hypertrophy with a mild dilatation. No coronary sclerosis was ascertained. Mitral valves were hard and thick, and was contracted. Aortic valves were also thickened and hardened. There was no fresh inflammatory change in neither the endocardium nor the valves.

Findings of the arterial system were characterized by marked juvenile

sclerosis, probably secondary to generalized chronic arteritis, chiefly involving the aorta and the middle-sized arteries. The aorta presented thickening of the intima, atheromatosis and deposits of calcium as illustrated in Fig. 5. The left common carotid artery was obliterated with its thickened wall (Fig. 6).

Fig. 5.

Fig. 6. Obliterated left common carotid artery

The left subclavian, brachiocephalic, renal and coeliac arteries were much narrowed. The iliac artery was normal on both sides from the bifurcation.

Histology: The thoracic aorta revealed marked fibrosis involving all layers, that is, the intima, media and adventitia. Disappearance of the elastica in the media was most conspicuous feature (Fig. 7). There was also mild infiltration of lymphocytes, monocytes, fibroblasts and other cells around the vasa vasorum in the media and at the border between the media and adventitia (Fig. 8). In the wall of the coeliac artery, there were also fibrosis and fragmentation of the elastica in the media. These lesions had the same character as in the thoracic

Fig. 7. Marked fibrosis involving all layers of the thoracic aorta.

Fig. 8. Vasa vasorum at the border between the media and adventitia (thoracic aorta).

Fig. 9. Diffuse fibrosis of the myocardium.

aorta, but was less pronounced. The wall of the heart showed diffuse and marked fibrosis, which was especially marked around the blood vessels (Fig. 9). This fact suggests that an angitis in the heart muscle caused such a fibrosis.

Summarizing these necropsy findings, it may be said that this lesion was caused by the generalized chronic arteritis of the unknown origin.

DISCUSSION

The peculiar retinal change, anastomosis peripapillaris, was reported by Takayasu in 1908.⁵⁾ At the same time, Kagoshima and Onishi reported separately the similar cases, whose radial pulses were non-palpable.^{6), 7)} Pulseless disease was established in 1948 by Shimizu as a new clinical entity with a triad, that is, no radial pulsation, characteristic eye change (hypotensive ophthalmopathy), and hyperactive

carotid sinus reflex.^{3),4)} Pulseless disease is also called as Takayasu's disease, idiopathic arteritis, young female arteritis,²⁾ primary arteritis,^{8),9),10)} branchial arteritis,¹¹⁾ aortic arch arteritis,¹¹⁾ and Martorell's syndrome.¹²⁾ Pathologically, tuberculosis has been said to be most suggestive as the cause of pulseless disease.^{3),4)} Others suspect on rheumatic arteritis,¹³⁾ allergic arteritis,¹⁴⁾ and collagen disease¹⁵⁾ as the cause. Recently, atherosclerosis has been said to be important as the cause of aortic arch syndrome.^{13),16)} But there have been not so many necropsy cases to confirm the hypothesis, and we were able to review only 15 autopsy cases in Japan.

We analyzed reports of so called "pulseless disease," that is, the aortic arch syndrome without any proved cause, such as syphilis, primary atherosclerosis, thrombophilia etc. The heart involvement of aortic arch syndrome has been a matter of little concern up to the present except in a few reports. Abnormal heart findings were reported in 20 of 85 cases of so called pulseless disease outside of Japan.^{1),2),8)-11),13),17)-29)} In these cases the cardiac symptoms dominated the entire clinical pictures. The blood pressure was recorded in the legs in 49 patients and in 33 cases of these the systolic pressure was higher than 160 mm. Hg. The calcification of the aorta was registered in 8 cases clinically or by the postmortem examination. In Japan, Shimizu reported 5 cases with heart involvement. Of 139 clinical cases in Japan which we could study by literature, only 14 cases were described to have abnormal heart findings, one of which was diagnosed as having a valvular disease. The systolic blood pressure in the legs was registered in 13 of 35 cases to be greater than 160 mm. Hg.

In autopsy series (Table I),^{14),30)-42)} hypertrophy of the heart was found in 7 of 16 cases and valvular involvement was noticed in 3 cases, one of which was described as fibrous endocarditis. Considering the

Table I. Autopsy Findings of 16 Cases of So-Called "Pulseless Disease"

1. Heart	
Hypertrophy with or without dilatation	7 cases
Dilatation only	2 cases
Valvular involvement	3 cases
2. Sites of lesion in vascular system	
Aortic arch	16 cases
Thoracic aorta	12 cases
Abdominal aorta	10 cases
Arteries other than aortic arch branches	9 cases
Deposits of calcium in the aorta	3 cases
3. Etiological consideration	
Angitis	13 cases
Suspected angitis	3 cases

(Case 3 of the present report is included in this table.)

relationship between etiological factor of vascular lesion and cardiac involvement, 6 of 8 cases suspected to be primary or idiopathic arteritis, had hypertrophy of the heart or valvular lesion. But only one case was described to have cardiac hypertrophy among 7 cases which were suspected of the etiological relation to tuberculosis or allergic disease. Necropsy series also revealed that the vascular involvement of pulseless disease is not limited to the aortic arch and its branches, but descending aorta, abdominal aorta and middle sized arteries other than aortic arch branches were affected.²⁴⁾ Deposits of calcium in the aorta were ascertained in 3 cases.

Summary of the symptoms and laboratory findings of 3 cases in the present report is as follows (Table II). Diminished or absent pulses, cardiomegaly, aortic calcification, positive C.R.P. reaction were recognized in all cases, while albuminuria and arthralgia were present in case 1 and 3. In case 1 and 2, marked increase in erythrocyte sedimentation rate was noticed.

Table II.

	Case 1	Case 2	Case 3
Age, Sex	46, female	48, female	28, male
History or initial symptoms	at 27, diminished radial pulsation, heart murmur; at 45, fever, dyspnea palpitation, giddiness	at 33, diminished left radial pulsation; at 47, palpitation, tachycardia, pain on the left temple	at 16, dyspnea, edema, palpitation; since 18, right coxalgia, and myalgia of the feet; at 26, vertigo
Heart murmur	vessel murmur, gallop	vessel murmur, gallop, aortic diast. m.	(vessel murmur), aortic diast. m., apical rumble
Cardiomegaly	+	+	+
E. C. G.	left ventricular hypertrophy	left ventricular hypertrophy	left ventricular hypertrophy
Aortic calcification (thoracic and abdominal aorta)	+	thoracic +	+
E. S. R.	very increased	very increased	normal
C. R. P.	3 (+)	6 (+)	+
Leukocyte count	normal	12,000~7,200	normal
Eye ground	arteriolosclerotic change of K-W II	K-W I	normal
Carotid sinus reflex	mild	?	suggestive
Hypertension in the legs	+	+, but lower than B.P. in right arm	
Arthralgia	+	?	+
Erythema	+	-	-
Tuberculin skin test	positive	positive	positive since 17 years old
Albuminuria	+	-	+

Ophthalmoscopic examination revealed no retinal changes characteristic of pulseless disease. The response of carotid sinus reflex was moderate in case 1 and suggestive in case 3.

Third case of this paper showed a marked hypertrophy of the heart, weighed 890 Gm. In this case, involvement of aortic valve was not anatomically remarkable. But from the clinical point of view, especially from heart murmur, aortic regurgitation was present at least functionally. The aortic insufficiency and heart failure played one of parts of causing marked hypertrophy of the heart and intense fibrosis of myocardium. But the fact that diffuse fibrosis of the cardiac wall is most conspicuous around the blood vessels, is suggestive of the heart lesion partly produced by the same cause as the generalized idiopathic arteritis. The other 2 cases are suspected to have the same pathological changes as the third case from the similar clinical picture of these 3 cases.

These cases suggest that there is a heart disease, that is, cardiomegaly and aortic calcification with aortic arch syndrome produced by the same cause as the generalized idiopathic arteritis. Though the etiology of this disease is unknown as yet, such a condition can be separated from the pulseless disease as a specific clinical entity.

SUMMARY

Three cases of the aortic arch syndrome with cardiomegaly and aortic calcification as cardinal symptoms were reported. Fifteen necropsy cases of pulseless disease in Japan were reviewed chiefly about heart involvement, sites of lesion in vascular system and etiological consideration.

These reported cases suggest that there is a heart lesion produced by the same cause as the generalized idiopathic arteritis.

(The essential point of this paper with presentation of case 1 and 3 was reported at the first congress of Japanese College of Angiology (September 20, 1960))

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