Aortic Arch Syndrome with Special Reference to Pulseless Disease and Its Variants

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Analyses were made on the records of 14 patients with aortic arch syndrome and 6 with atypical coarctation of the aorta. A diagnosis of pulseless disease (Shimizu and Sano) was made in 13 of 14 cases of aortic arch syndrome.

The pathogenesis of atypical coarctation was interpreted to be essentially the same as that of pulseless disease, based on the comparison of sex and age distribution, laboratory data and autopsy findings between the both conditions. It was therefore recommended that these conditions be described under a single term (panaortitis syndrome, for example) and be divided into subtypes such as aortic arch type, abdominal type and extensive type according to the localization of the lesions.

The prognosis of the patients with this entity seemed in general to be relatively good, although they were found to suffer from long-persisting disability of varying degrees.

PULSELESS disease represents a distinct entity characterized by the absence or diminution of arterial pulsation in the arms and neck, often associated with peculiar vascular abnormalities of the retinæ. These manifestations are due to a peculiar form of chronic panarteritis of the great vessels arising from the aortic arch which usually occurs in young women. In the original case report presented by Takayasu before the 12th Congress of the Japanese Ophthalmologic Society, only the eye findings were noted, although in the following discussion Onishi mentioned that he had encountered the similar ocular changes in a patient who had no pulses in the upper part of body. Later, Shimizu and Sano described the condition more completely. However, any occlusive lesions of the aortic arch can produce a similar picture of absent arterial pulsation of the arms and neck. Ross and McKusick used the term “aortic arch syndromes” to describe the clinical manifestations caused by these lesions, and found syphilitic aortitis to be the common cause of these syndromes.

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According to Ross and McKusick, pulseless disease is classified as “young female arteritis” variety of the aortic arch syndrome.

The purpose of this paper is to describe the observations on our patients with aortic arch syndrome and relating conditions with special reference to pulseless disease and its variants and to discuss the adequacy of the term “pulseless disease”.

**Materials**

The records of 14 patients with aortic arch syndrome who were admitted to the Second Department of Internal Medicine, Faculty of Medicine, University of Tokyo during the period from April, 1951 to June, 1962 were reviewed. Additional 6 cases which were diagnosed to have atypical coarctation of the aorta were also analysed.

**Results**

*Incidence of Pulseless Disease among the Patients with Aortic Arch Syndrome:*

Etiologic analysis of our 14 cases of aortic arch syndrome demonstrated that 13 of them were diagnosed to have pulseless disease as described by Shimizu and Sano (Table I). The remaining one case was a 40-year-old woman with familial hypercholesterolemia and multiple xanthomas of the skin, and the obstructive lesions of the great vessels in this case were attributed to atheromatous changes of the arterial wall. During the same period of observation, 10 cases of syphilitic aortitis or aneurysm of the aorta, 2 of dissecting aneurysm of the aorta, 4 of aneurysm of the aorta of other origin and 25 of mediastinal tumor of various natures have been seen, but none of them revealed evidences of aortic arch syndrome.

**Table I. Etiologic Classification of 14 Patients with Aortic Arch Syndrome**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulseless disease</td>
<td>13</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>1</td>
</tr>
<tr>
<td>Syphilitic aortitis or aneurysm of the aorta</td>
<td>0</td>
</tr>
<tr>
<td>Dissecting aneurysm of the aorta</td>
<td>0</td>
</tr>
<tr>
<td>Aneurysm of the aorta of other origin</td>
<td>0</td>
</tr>
<tr>
<td>Mediastinal tumor</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
</tr>
</tbody>
</table>

Sex and Age Distribution of Pulseless Disease:

As illustrated in Fig. 1, 10 of 13 patients with pulseless disease were
female and most of them aged 20 to 29 years old.

Clinical Manifestations of Pulseless Disease:

The frequency of various clinical manifestations in the 13 patients with pulseless disease is shown in Table II. The pulsation of the radial artery was absent or diminished in all of the 13 cases. Murmurs were audible on the anterior chest wall in 11 cases and on the neck in 9 cases. Headache, dizziness and general fatigue were complained in 10 cases. Other common symptoms and signs were syncopal attack, diminished or absent pulsation of the carotid artery, numbness of the fingers and cerebral symptoms including electroencephalographic abnormalities. Hypersensitivity of the carotid sinus and peculiar vascular abnormalities of the retinae were less frequent, though these were described by Shimizu and Sano to be one of the cardinal symptoms of pulseless disease. Laboratory examinations revealed positive tuberculin reaction in 11 cases, increased erythrocyte sedimentation rate in 10, elevated C-reactive protein in 6 and electrocardiographic abnormalities including the changes in ST-segment
and T-wave in 6. In none of 13 cases, the serologic reaction for syphilis was positive.

Successful aortography was performed in 8 cases. In 2 of them, marked narrowing or obstruction was disclosed in the brachiocephalic artery, left common carotid artery and left subclavian artery, though the changes in aortic arch were mild. In 4 cases, stenosis was present in one or 2 major branches of the aortic arch. In another case, stenotic lesions were found not only in the aortic arch and its major branches but also in the abdominal aorta. Narrowing of the all 3 major branches of the aortic arch associated with marked calcification was demonstrated in the remaining case. Of 5 cases in which aortography was not performed or unsuccessful, one was found to have stenotic lesions of the left common carotid artery and subclavian artery at operation, and another case, which was reported elsewhere, was confirmed at autopsy after death by an accident to have panarteritis with marked secondary calcification involving the entire aortic segments as well as the brachiocephalic and left common carotid arteries.

**Analysis of Cases of Atypical Coarctation of the Aorta:**

During the period mentioned above, the authors experienced 2 patients with typical congenital coarctation of the aorta and 6 patients with atypical coarctation of the aorta. Both of the cases of typical coarctation were males aging 14 and 25 years old, respectively. In contrast, the sex and age distribution of the cases of atypical coarctation was quite similar to that of the cases of pulseless disease, revealing a high incidence in the young females (Fig. 2).

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 - 29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 - 39</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>40 - 49</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Fig. 2. Sex and age distribution of the patients with atypical coarctation of the aorta.

The diagnosis of atypical coarctation of the aorta was made by aortography in 5 of 6 cases and by autopsy in the remaining one. In one of them, obliteration of the left subclavian artery was also demonstrated by aortography. An elevated blood pressure of the arms was found in all of the 6 cases and there was a significant difference between the blood pressures of the both arms in 2 of them. The blood pressure of the lower
extremities was obviously lower than that of the arms in 5 cases. Evidence suggesting the presence of inflammatory process such as increased erythrocyte sedimentation rate, elevated C-reactive protein and leukocytosis were noted in 4 cases.

The following report of an autopsy case offers an interesting suggestion regarding the relationship between pulseless disease and atypical coarctation of the aorta.

Case: A 23-year-old female was hospitalized with a diagnosis of juvenile hypertension. Three years prior to admission, the patient began to complain of headache, nausea and visual disturbance. At the time of admission, the blood pressure was 260/98 mm Hg on the right arm and 260/126 mm Hg on the left. Ophthalmoscopic findings exhibited marked arteriosclerosis of the retinal and right retinal hemorrhage. White blood cell count was 14,200 and C-reactive protein was negative. In the evening on the day of admission, the patient developed numbness of the upper and lower extremities of the right side, headache and nausea followed by loss of consciousness, and died in early morning on the next day.

Postmortem examination revealed that the cause of death was massive bleeding in the pons. The prominent feature was thickening of the arterial wall with fine wrinkle formation on its inner surface which involved the entire segments of the aorta. Such changes were especially marked in the abdominal aorta, resulting in strongly stenotic or obstructive lesions of the orifices of bilateral renal arteries and celiac artery. Necrosis of the right kidney and ischemic degenerative changes in the left kidney were noted.

Histologically, the changes of the aortic wall consisted of fragmentation of elastic fibers of the media (Fig. 3), periarteriolar round cell infiltration accompanied by appearance of giant cells between the media and adventitia (Fig. 4), and marked intimal thickening due presumably to secondary fibrous hyperplasia.

Fig. 3. Fragmentation of medial elastic fibers of the aorta. Elastica-van Gieson stain, ×40.
Fig. 4. Round cell infiltration between the adventitia and the media of the aorta accompanied by appearance of giant cells. Fragments of elastic fibers are seen on the right to the giant cells.

It is of special interest that these histological findings are identical to those which are known characteristic of pulseless disease.

The hypertension in this patient was interpreted to be of renal origin due to renal arterial obstruction.

Results of Follow-up Study:

As will be discussed in the following part of this paper, the authors are of opinion that the pathogenesis of atypical coarctation of the aorta is, probably in most instances, identical to that of pulseless disease, although the clinical manifestations are entirely different between these two conditions. Accordingly, the follow-up studies were made on our series including both the patients with pulseless disease and those with atypical coarctation.

Three of these patients were treated surgically with some improvements. The other patients were treated with various drugs such as steroid hormones, antituberculous drugs, anticoagulants and vasodilator drugs. In some cases, especially those in the early stage of the disease, steroid hormone gave subjective as well as objective improvements, but the effects of other drugs were obscure.

During the observation period, a patient with pulseless disease died of an accident and another patient with severe hypertension died of pons bleeding on the day of admission as described above. Eleven patients, who were discharged from the hospital 2 to 7 years before, were reexamined by communication or at the outpatient clinic and informations were obtained in 7 of them. These patients were found to have persistent disability of varying degrees, but in no patient the data of reexamination indicated a deterioration of the disease, suggesting that the prognosis of
these patients are generally not unfavorable.*

**DISCUSSION**

Pulseless disease, a particular form of aortic arch syndrome, has been known to be much more frequently encountered in the Orient than in the other areas of the world. In the analysis of our 14 patients with aortic arch syndrome, 13 of them were diagnosed as having pulseless disease and in only one case the changes in the aorta and its major branches were considered to be of atheromatous nature. As has been pointed out, the incidence of pulseless disease was conspicuously high among the young women.

It has also been recognized that in Japan reports of typical congenital coarctation of the aorta are exceedingly rare, while cases of atypical acquired coarctation of the aorta are relatively common. During our observation period, there have been 6 cases in which coarctation of the aorta was found in atypical portions by aortography or autopsy, whereas only 2 cases of typical coarctation were seen.

The autopsy findings in 2 cases lead us to speculate an intimate relationship between the pulseless disease and the atypical coarctation of the aorta. One case was diagnosed as pulseless disease clinically and was found at autopsy to have panarteritis with marked secondary calcification involving not only the aortic arch and its major branches but also the entire segments of the aorta. The other case was diagnosed as juvenile hypertension clinically but postmortem examination revealed panarteritis of the aorta which was especially marked in the abdominal aorta causing obstructive changes of the bilateral renal arteries and ischemic degeneration and necrosis of the kidneys. The histological findings of the aorta in the second case were identical to those of pulseless disease.

The fact that most of our patients with atypical coarctation of the aorta had evidences such as increased erythrocyte sedimentation rate, elevated C-reactive protein and leukocytosis suggests that the lesions of the aorta in these patients may also be of inflammatory nature. Moreover, their sex and age distribution was quite similar to that of the cases of pulseless disease.

From these observations, the authors think that the pathogenesis of atypical coarctation of the aorta is, probably in most instances, essentially the same as that of pulseless disease, although the clinical manifestations

* After the manuscript of this paper was completed, the authors experienced a 63-year-old female patient with aortic arch syndrome. The initial symptoms in this patient were tinnitus and impaired hearing which occurred 26 years prior to admission. During the subsequent course, the patient developed weakness and numbness of the extremities, visual symptoms and diminished arterial pulsation in the arms. Extensive examinations indicated that this is a case of long-standing pulseless disease.
are entirely different between these two conditions depending upon the localization of the main pathological changes. It is therefore recommended to describe these conditions under a single term, panaortitis syndrome for example, and to divide them into subtypes such as aortic arch type (so called puseless disease), abdominal aorta type and extensive type according to the localization of the lesions.

There have been considerable confusions in the nomenclature of pulseless disease. Different terms have been given to the identical entity from different viewpoints. They are: thrombotic obliteration of the branches of the aortic arch,\(^7\) obliterative brachiocephalic arteritis,\(^8\) chronic subclavian carotid artery obstruction,\(^9\) segmental thrombo-obliterative disease of branches of aortic arch,\(^10\) and young female arteritis variety of the aortic arch syndrome.\(^4\) Although the etiology of this clinical entity is still obscure, it is general agreement that its pathological finding consists of panarteritis characterized by round cell infiltration and giant cells appearing between the media and the adventitia of the aorta.\(^11\) The report which reviewed 16 autopsy cases of pulseless disease described that the changes in the aortic arch extended over the thoracic aorta in 12 of them and over the abdominal aorta in 10.\(^5\) Two cases of aortitis which mainly involved the abdominal aorta as in one of our autopsy cases were also reported.\(^12\) In addition, Inada and coworkers\(^13\) recently pointed out that both pulseless disease and atypical coarctation of the aorta are caused by acquired arteritis and that the differences between the clinical pictures of these two conditions are attributed to the distribution of the lesion. Our data support their opinion.

The clinical diagnosis is usually not difficult in the cases of aortic arch type of arteritis presenting the well recognized manifestation of pulseless disease as described by Shimizu and Sano, however in those of abdominal aorta type or extensive type symptoms are more complicated, sometimes making the diagnosis confused. Aortography is the definitive method for demonstrating the localization and distribution of the lesion. Blood pressure measurements in the upper and lower extremities, erythrocyte sedimentation rate, C-reactive protein and white blood cell count may give additional diagnostic clue. It should be kept in mind that calcification of the aortic wall does not necessarily indicate primary atherosclerotic changes but may occur secondarily to chronic inflammatory process or traumatic lesions.

Based on the follow-up study of our patients with chronic arteritis of the aorta including those with pulseless disease and atypical coarctation of the aorta, the prognosis of these patients seems to be in general relatively good in spite of the persistence of disability of varying degrees. However,
further long-term observations are required to elucidate the more exact picture.

Steroid hormones give sometimes definite subjective and objective improvements, especially in patients in the early stage of the disease. Surgical intervention may be indicated in severely disabled patients.

**SUMMARY**

(1) Out of 14 cases of aortic arch syndrome experienced during the last 11 years, 13 were diagnosed as pulseless disease described by Shimizu and Sano, reflecting the high frequency of this disease in Japan.

(2) Six cases of atypical coarctation of the aorta seen during the same period of time were also analysed. The pathogenesis of atypical coarctation was interpreted to be identical to that of pulseless disease, based on the comparison of sex and age distribution, several laboratory data and autopsy findings between the both conditions.

(3) It was recommended to describe these apparently different conditions under a single term, for example panaortitis syndrome, and to divide them into subtypes such as aortic arch type, abdominal aorta type and extensive type according to the localization of the lesions.

(4) The prognosis of these patients seemed in general to be not unfavorable despite the persistence of disability of varying degrees.

**REFERENCES**