Thrombotic Obliteration of the Branches of the Aortic Arch

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This report presents the sixth case of thrombotic obliteration of the branches of the aortic arch to be documented in this country. The world's literature on this subject is reviewed and analyzed from the standpoints of clinical characteristics, etiology, and pathology.

PULSELESS disease, or Takayashu's disease, is an unusual syndrome characterized by the obliteration of the major branches of the arch of the aorta. The name, pulseless disease, does not appear to be adequate, for it fails to indicate the peculiar localization of the disease and the clinical variants with diminished, but present pulses. The name Takayashu's disease is subject to the criticism usually voiced against eponyms; further, Takayashu described only the ocular manifestations of this condition. In addition, this syndrome was adequately documented by Broadbent3 33 years prior to Takayashu's description. The most appropriate nomenclature is considered to be thrombotic obliteration or thromboangiitis obliterans of the branches of the aortic arch because of the consistent demonstration of intravascular clot formation (thrombus), of inflammation of the vessel wall (angiitis), and of the peculiar anatomic localization (aortic arch). Furthermore, this name implies an appropriate lack of knowledge of specific etiology.

Although 90 cases have been reported of this condition to the present time,1, 2-7 only 5 reports have originated in the United States.3, 5-7 This report presents the sixth case to be documented in this country and a comprehensive review on this subject.

CASE REPORT

M.B., a 41-year-old white woman, was first seen on November 5, 1955, with the chief complaint of dizziness of 10 years' duration.

Present Illness. The patient stated that she was apparently well until about 1945, when she noted the onset of dizziness; this sensation consisted of subjective vertigo and occurred chiefly on change of position or on walking along the street at a moderate pace. The symptom was slowly progressive in frequency and duration. During the 3 months prior to entry, she had 2 episodes of loss of consciousness while walking, without aura, vomiting, convulsions, or tongue biting. For about 6 months she noted weakness of all her extremities with fatigue that necessitated complete rest of the involved extremities. Over this same time cramps in the shoulders and hands occurred, particularly when knitting or writing, severe enough to make her discontinue these activities.

She was troubled with almost constant tingling and numbness of the fingers and toes for about 3 years, more pronounced on the right. For the same time she was aware of some thinning of the facial muscles and easy fatigue of the muscles of mastication; accordingly, she learned to eat slower and to eliminate gum chewing. The patient was unaware of any ocular or mental abnormalities.

Past History. The patient had the usual childhood diseases, an appendectomy in 1922, and a kidney suspension in 1945. At that time she was first told that the blood pressure could not be obtained in the upper extremities. A hysterectomy was performed for uterine fibroids in 1945. There was no history of unexplained fevers, venereal disease, or other illnesses other than respiratory illnesses.

She smoked 10 cigarettes a day, but denied any intake of alcoholic beverages. The system history was noncontributory.

Physical Examination. The patient was asthenic but in no apparent discomfort. There was marked atrophy of all the facial muscles, and forced mastication resulted in fatigue with claudication. There was no nystagmus, strabismus, or corneal opacity; the arteriolar light reflex was increased and there were no hemorrhages, exudates, papilledema, or vascular anastomoses. There were no other abnormalities of the eyes, ears, nose, or throat. No goiter was palpated. The lungs were clear. The heart rate was 84 and regular and the left heart border was at the midclavicular line in the fifth interspace. The sounds were audible without murmurs, gallops, or rubs; A2 was greater than P2. The abdomen was not remark-
able, the reflexes were physiologic, and no lymph nodes were palpated. Rectal and pelvic examination were normal except for mild cervicitis.

Pulses were not palpated in the radial, ulnar, brachial, subclavian, innominate, right common carotid, or right and left temporal arteries. There was a weak pulsation in the left common carotid artery and minimal pressure over it resulted in syncope. There were no thrills, murmurs, or bruits in the neck. All the pulses in the lower extremities were palpable, but weak; the abdominal aorta was also weakly palpable. The blood pressure in the legs was 150/90. As would be expected, there were no oscillometric deflections in the upper extremities and less than a 1-point deflection in the neck. The skin and appendages of the extremities were not atrophied and skin temperature felt normal.

Laboratory Examination. The erythrocyte sedimentation rate was 8 mm. per hour (Wintrobe). The white blood count was 10,050 and 19,800 per mm.; the differential count was 39 per cent polymorphonuclear leukocytes, 43 per cent lymphocytes, 2 per cent eosinophils, and 5 per cent monocytes. The hemoglobin was 10.5 Gm. per cent. Serologic test for syphilis was negative. Urinalysis showed a specific gravity of 1.015 and negative albumin, sugar, and microscopic examinations. The lupus erythematosus preparation was negative and a biopsy of the gastrocnemius muscle was normal.

Agglutinations for typhoid, paratyphoid, proteus OX 19, and Brucella abortus were negative. The total protein was 5.8 Gm. per cent with 4.5 Gm. of albumin. An electrocardiogram showed incomplete right bundle-branch block. A ballistocardiogram* displayed cut-off K waves. Skin tests were negative for histoplasmin and P.P.D. no. 1 and positive for P.P.D. no. 2 and coccidioidin 1/100.

The patient was referred back to her family physician with the advice that she be maintained on anticoagulant therapy.

Historical Aspects

Although there have been many case reports of absent pulses in the upper extremities due to syphilitic aneurysms,8-11 these cases do not logically belong within the scope of this paper because of their different etiology. In 1875, Broadbent8 described a 50-year-old man with absent radial pulses and a history of syphilis in whom no aneurysm was found at postmortem examination. The patient did have extensive atheromata with calcification and complete obliteration of the great vessels; endarteritis obliterans was present histologically. No subsequent description of this condition was forthcoming until the much quoted report by Takayasu, a Japanese ophthalmologist, in 1908.1 He described the ocular manifestations, particularly emphasizing the peripapillary anastomoses. He had no postmortem confirmation, but correctly hypothesized occlusion of the great vessels of the arch of the aorta. In the following years, several cases of this condition were reported in the Japanese literature almost exclusively by ophthalmologists without pathologic confirmation.1,12,13 Case reports also appeared outside of Japan under various titles.14,15 Interest in this disease received its biggest impetus when Shimizu reviewed the literature in 1951 and coined the catchy phrase “pulseless disease”; Shimizu’s account received wide recognition and was abstracted in the J. A. M. A. in 1951.16

The first account of this condition to appear in the American literature was by Giffin and associates of the Mayo Clinic in 1939.7 He correctly alluded to this condition as a reversed coarctation with symptoms of a brain tumor. His patient was a 19-year-old white girl. The second case report from the United States was in 1954 by Caccamise and White,4 also of a 19-year-old white girl. Two additional cases were reported from the United States in 1953 in a complete review of the aortic arch syndrome: one in a 33-year-old Indian woman, the other, in a 45-year-old white man. The etiology was obscure in both patients.5 In 1955, a second case of aortic arch syndrome was reported from the Mayo Clinic,6 in a 64-year-old white woman; this patient died of a subendocardial myocardial infarction. At postmortem examination the entire thoracic aorta, as well as the branches of the arch of the aorta were involved with a chronic inflammatory reaction; the coronary arteries were patent, but the ostia were narrowed by a nonatheromatous deposition of connective tissue in the intima of the aorta. Although this patient’s age was unusual for this condition, her pulses may have been absent for many years without clinical recognition. The pertinent data of the cases reported until this time in the American literature are summarized in table 1.

* Ballistocardiograph (Photoelectric), Sanborn Company, Cambridge, Mass.
In 1954 Erik Ask-Upmark\textsuperscript{3} reviewed the world's literature, excluding Japan, of 28 recorded cases, including 2 of his own. Of necessity we have drawn heavily on the material presented in this paper.

**Clinical Description**

_Age_. The age at onset in those cases reported outside of Japan varied from 11 to 64, with an average of 19; the diagnosis was usually made about the age of 31. The first knowledge of absent pulses in our patient was at the age of 29.

_Sex_. As has been noted by others,\textsuperscript{1,3,4} this disease tends to affect young women. In the Japanese series 45 out of 50 cases where sex was mentioned were female; in the cases reported outside of Japan, all but 2 have been female, one exception being a case report from Great Britain by Skipper and Flint in 1953,\textsuperscript{18} and the second, a 45-year-old white man from the United States.\textsuperscript{5} This strong predilection for the female sex has been a factor in helping to eliminate such diseases as arteriosclerosis and thromboangiitis obliterans. The reason for this preponderance has not been elucidated; there has been no evidence of endocrine disease in those instances in which it has been looked for.\textsuperscript{3}

_Incidence_. The frequency of this disease is difficult to estimate; 90 cases have been documented in the world's literature. However, it is doubtful that only 6 cases have existed in this country, 5 of which were recorded in the last 4 years. Since the preparation of this paper, I have been told of another case in the United States that was not published. It is hoped that the present review will increase clinical awareness of this condition.

**Geographic Distribution.** As already indicated, 58 cases have been reported from Japan; the 32 cases outside of Japan have the following geographic distribution: Sweden 10, United States 6, Great Britain 5, Norway 3, Hungary 2, and 1 case each from Germany, France, Roumania, Greece, Switzerland, and Spain. We think that these figures do not reflect the true geographic incidence of the disease.

_Symptoms and Signs_. The symptoms and signs of this disease may be conveniently classified into 3 categories: (1) symptoms and signs due to inadequate circulation, (2) symptoms and signs due to collateral circulation, (3) associated symptoms and signs.

1. Symptoms and signs due to inadequate circulation (table 2).

   (A.) Inadequate cerebral circulation.

Most of the patients complained of dizziness or vertigo at some stage of their illness.\textsuperscript{3,4} Our patient had objective vertigo that was progressive in nature. These symptoms were often precipitated or aggravated by physical exertion, which apparently increased the discrepancy between supply and demand. Syncope as a symptom was first described by Lewis and Stokes,\textsuperscript{14} from information in the literature as well as clinical analysis of our case, it would appear that any of the following mechanisms might be responsible for the syncope associated with this disease: 1. Hyper-
sensitive carotid sinus, (a) due to bradycardia, (b) due to hypotension, (c) due to cerebral ischemia; 2. cerebral ischemia; 3. orthostatic hypotension. In the literature the frequency of the hypersensitive carotid sinus syndrome in patients with pulseless disease has been emphasized, this association being noted in at least 7 cases. The increased sensitivity has been thought to be due to scar tissue in the area of the sinus causing traction on movement of the head. It is difficult for us to understand how pressure over the carotid sinus with resultant syncope can be ascribed even partially to hypersensitivity in a patient in whom this pressure removes the sole source of cerebral circulation. In our patient, very minimal pressure over the left carotid sinus caused syncope; since this vessel was the only pulsatile one remaining in the neck, we assumed the syncope was due to cerebral ischemia per se rather than a hypersensitive carotid sinus. However, there is 1 case reported of hypersensitive carotid sinus occurring after ipsilateral ligation of the common carotid and internal carotid arteries that responded favorably to removal of the carotid bifurcation.

(B.) Inadequate circulation to the face.

The ocular manifestations were emphasized in the Japanese literature by the ophthalmologists and have been considered by some as essential to the diagnosis; as might be anticipated, however, there are all degrees of ocular anemia. Our patient had no subjective or objective evidence of eye involvement.

Lewis and Stokes have described the only instance of optic atrophy; the type of involvement most commonly emphasized has been the striking peripapillary anastomoses. The interesting observation has been made that all of the ocular signs are exaggerated in the sitting or standing position, further, the retinal pathology usually precedes the corneal pathology, and the right eye was involved earlier and more severely than the left eye.

In many cases the ocular complaints dominated the clinical picture.

(C.) Inadequate circulation to the face. Our patient demonstrated advanced facial atrophy with a bird-like facies, atrophic pigmentation, and a thinned skin. The adverse cosmetic effects are self evident.

(D.) Inadequate circulation to the upper extremities. Manifestations in the upper extremities have been surprisingly mild, apparently due to the gradual onset of the disease, the development of collateral circulation, and the probable utilization of preformed collateral channels. Although trophic changes may be present in the upper extremities, only 2 patients have complained of claudication in the arms.
2. Symptoms and signs due to collateral circulation.

Palpable superficial arteries on the outer chest wall have been frequently noted. Crenations of the ribs have also been described and should be diligently sought. Machinery murmurs with systolic accentuations may be audible over the areas of the collateral vessels. No evidence of collateral circulation was found in our patient. The term reversed coarctation has been used for this syndrome because the collateral blood flows in a cephalad direction instead of a caudal direction, as in a true coarctation of the aorta. In 1 patient the diagnosis of patent ductus arteriosus was suspected because of a continuous murmur, probably due to dilated and tortuous arterial collateral channels.

3. Associated symptoms and signs.

Changed auditory perception in this condition has been mentioned. Some patients have tachycardia at rest. Arterial hypertension in the lower extremities has been described and many explanations have been offered for it. However, this finding has been observed in only a minority of cases and the opposite condition prevailed in our patient, namely, relative hypotension in the lower extremities. Cardiovascular manifestations have been reported, including 4 instances of angina pectoris. The pathogenesis of the coronary artery disease may well be involvement of the coronary ostia with chronic inflammatory disease. The only laboratory findings of significance are an elevated erythrocyte sedimentation rate and a leukocytosis in the great majority of cases; the absence of these findings in any given case may reflect the duration of the disease with the stage of active inflammation having passed.

Pathology

Although different terms have been given to this entity, the anatomic descriptions are very similar. The condition has been called thromboangiitis obliterans, periarteritis nodosa, periarteritis of the major arteries, tuberculosis, and syphilis. The involved vessels show a panarteritis involving all the layers of the wall with a resultant obliteration of the lumen; in some cases attempts at recanalization have been noted. Important is the absence of fibrinoid necrosis. The inflammatory infiltrate consists chiefly of lymphocytes and plasma cells with predominant involvement of the media and the vasa vasorum. There is usually a proliferation of the intima and a fibroblastic proliferation of the media with occasional, inconstant giant cells in the media; round cells may be present between the adventitia and the media. The giant cells may resemble those seen in tuberculosis; however, no organisms have been found even with the presence of acid-fast stains.

The pathologic process appears to be localized to the innominate, subclavian, and carotid arteries; however, the condition may extend to just below the base of the skull. In the few postmortem examinations reported, the carotid artery and, by adventitial spread, the carotid sinus have usually been involved. There has not been any involvement of the intracranial vessels. Despite the universal involvement of the branches of the arch of the aorta and the absence of involvement of other vessels in the clinical material, there have been a few case reports of histologic involvement of visceral vessels. Harbitz described an infiltrative lesion of the abdominal aorta with cartilaginous consistency; Frovig described involvement of the superior mesenteric artery; involvement of the orifices of the coronary arteries and the pulmonary arteries has also been described. Ask-Upmark reported a patient with renal hypoplasia supposedly due to involvement of the renal artery. As already mentioned, the entire thoracic aorta was involved in a case reported from the Mayo Clinic. It must be emphasized that no case has been reported, to the authors' knowledge, with complete obliteration of the aortic lumen; this disease state primarily involves the branches of the aorta. The additional anatomic changes result from the collateral circulation, chiefly from the intercostal branches of the descending aorta communicating with the subclavian arteries. Crenation of the lower borders of the ribs and prominent superficial arteries on the abdominal wall and dorsal thorax have been seen.
Etiology

Up to the present time the etiology of this condition has been obscure. Although pathologic findings have been reported occasionally consistent with well-known disease states, these have not been uniform or consistent in the material available.\(^2\)\(^-\)\(^4\) Furthermore, it must be recognized that most diseases, at one time or another, may have bizarre manifestations that overlap other well-defined disease states; examples of this overlapping are particularly common in the collagen vascular diseases and in the group of malignant lymphomas and leukemias. The presence of the bizarre atypical cases, however, should not detract from our attempt to categorize the typical case in an orderly way. We believe that such reasoning is particularly pertinent in this disease. Since the majority of the pathologic findings have indicated a nonspecific arteritis, the few case reports of apparent specific but atypical etiologies should not lead us astray. The various etiologies that have been mentioned will be considered individually.

Syphilis has been mentioned because of the predilection of the syphilitic aneurysms for the ascending arch of the aorta; however, none of the case reports accepted in this review had evidence of aneurysm. All 22 patients in whom serologic tests were determined had negative results. No evidence of syphilis has been found pathologically.

The pathologic lesion closely resembles that seen in tuberculosis, including the occasional mention of Langerhans' cells.\(^4\) One patient in the Japanese series had evidence of active pulmonary tuberculosis;\(^4\) however, the almost universal absence of tuberculosis elsewhere, the absence of tubercle formation and caseation necrosis, the peculiar anatomic localization, and the vascular involvement that is rarely encountered in tuberculosis are points that strongly militate against the diagnosis of tuberculosis.

The chief point of similarity between lupus erythematosus and thrombotic obliteration of the branches of the aortic arch is the predilection for young women. However, the peculiar anatomic localization, the absence of systemic symptoms or signs, the absence of leukopenia with a tendency toward leukocytosis, the absence of skin rashes, and the negative peripheral blood preparation for lupus erythematosus tend to eliminate this condition from consideration. The negative lupus erythematosus preparation in our patient is thought to be the first instance in which this diagnostic test was used in a patient with thrombotic obliteration of the branches of the aortic arch.

Periarteritis nodosa should be discarded as a possibility because of its tendency to affect men with pathologic involvement of smaller vessels and striking fibrinoid necrosis. There is no evidence in the literature of involvement of large-sized arteries in periarteritis nodosa. Furthermore, the absence of hypertension, cardiomegaly, fever, albuminuria, neuritis, and allergic manifestations in thrombotic obliteration of the branches of the aortic arch seems to eliminate periarteritis nodosa from consideration.

Cranial arteritis also has a peculiar localization, which, however, differs from the condition under question. Biopsies of affected vessels show a panarteritis with giant cells that closely simulates that found in thrombotic obliteration of the branches of the aortic arch. There have been reports of involvement of occipital, radial, facial, carotid, brachial, and cerebral arteries in temporal arteritis.\(^2\)\(^3\) However, the latter condition usually involves the 55 to 80 age group, shows no preference for the female sex, and exhibits a different anatomic localization. Although a relationship between these conditions cannot be denied, it would appear wiser, for the present time, to consider them as separate entities.

It is pertinent to mention that necrotizing angiitis has been offered as a convenient generic term for the group of vascular diseases, including hypersensitivity angiitis, allergic granulomatosis, rheumatic arteritis, periarteritis nodosa, and cranial arteritis;\(^2\) however, the pathologic \textit{sina qua non} for the diagnosis of this group is fibrinoid necrosis plus a panarteritis; since the disease under discussion has in no case demonstrated fibrinoid necrosis, it would by definition be excluded from the category of necrotizing angiitis.

Thromboangiitis obliterans (Buerger's dis-
ease) differs from thrombotic obliteration of
the branches of the aortic arch by virtue of
differences in age and sex predilection, different
anatomic localization, and the commonly
associated thrombophlebitis. However, the
pathologic picture, the end result in the
arteries, and the size of arteries attacked, are
similar in these 2 conditions. Accordingly, the
term thrombotic obliteration of the branches
of the aortic arch was thought to be an ap-
propriate designation, as it reflects the close
relationship to Buerger's disease, while, at the
same time, emphasizing the different anatomic
localization.

In the reported cases of pulseless disease,
there has been no instance of clinical involve-
ment of the extremities; in the few postmortem
examinations reported, there has been no
mention of involvement of peripheral vessels.
Thus, from a purely pathologic standpoint, we
cannot completely eliminate Buerger's disease
as a diagnostic possibility. The smoking habits
of patients with pulseless disease have gen-
erally not been commented upon. Our patient
smoked an average of 10 cigarettes per day.

The following conditions, which at first
sight might appear to be related to the con-
dition under question, cannot be incriminated
because of obvious clinical and pathologic
differences: Wegener's granulomatosis, sar
coidosis, the mycoses, brucellosis, giant-cell
arteritis, leprosy, arteriosclerosis, and con-
genital malformations. To the authors' knowl-
dge, there has been no case of congenital
malformations that resulted in absence of
pulses in both upper extremities. It should be
re-emphasized that 1 or 2 cases may demon-
strate some of the histologic characteristics of
1 of the above diseases, but the failure to
demonstrate these characteristics consistently
in all, or even in the majority, of the cases
casts a great deal of doubt on the pathogenetic
relationship.

Prognosis

Because of the paucity of clinical material,
no clear-cut statement can be made con-
cerning prognosis. The time that has elapsed
in cases cited in the literature from the ap-
parent onset of the condition to death varies
from 1.5 years to 14 years; the usual cause of
death is cerebral ischemia in some form. Ob-
viously, accurate statistics on longevity are
difficult to obtain, as it is difficult to date the
onset in any individual case. One might con-
servatively conclude that this disease sig-
nificantly reduces the life span of an affected
individual.

Treatment

Because the etiology of this condition is
unknown, it might be anticipated that there is
no specific treatment. The following methods
of treatment have been advised: change of
climate, minimizing the recumbent position,
exercise short of claudication, Buerger's exer-
cises of the upper part of the body, antibiotic,
anticoagulant, and vasodilator agents, steroid
therapy, androgen therapy, cervical sympa-
thectomy, and symptomatic treatment. The
number of therapeutic procedures advocated
indicate the lack of specificity of any given one.
Certain general measures seem to be in order:
All smoking should be eliminated, because of
the close relationship to Buerger's disease;
digitalis should be used cautiously because of
its known ability to increase the sensitivity of
the carotid sinus; prophylactic atropine therapy
in patients with syncope should be adminis-
tered cautiously, if at all, because of the
danger of precipitating or aggravating glau-
coma; long-term anticoagulant therapy ap-
pears to be rational because of the relation of
the arterial occlusions to the symptoms.
More definitive therapy may be forthcoming
with recent surgical technics of endarterectomy,
local resection, and homotransplantation.

Summary

The sixth case of so-called "pulseless disease"
was presented. The use of the more descriptive
term "thrombotic obliteration of the branches
of the aortic arch" has been suggested. The
world's literature has been reviewed and the
clinical material presented. Therapeutic recom-
mandations and admonitions have been made

Addendum

Subsequent to the preparation of this paper, an
additional case of this condition has been reported

SUMMARIO IN INTERLINGUA


REFERENCES


What is spoken of as a “clinical picture” is not just a photograph of a man sick in bed; it is an impressionistic painting of the patient surrounded by his home, his work, his relations, his friends, his joys, sorrows, hopes, and fears.—Francis Weld Peabody. The Care of the Patient. Harvard University Press, 1927.
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