Pulseless Disease due to Branchial Arteritis

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REPEATED reports from Japan and from north European countries have brought attention to a new clinical syndrome called "pulseless, or Takayasu disease." The condition is found in young women and is characterized by thrombosis of the vessels deriving from the arch of the aorta associated with cerebral, ocular, and upper extremity symptoms. Its etiology is obscure. We are presenting a case of this disease observed in a young Negro woman and studies carried out to clarify the pathogenesis of the disorder and its differentiation from the other known arterial diseases.

CASE REPORT

The patient was first seen on our service in October 1954. She complained of generalized weakness and experienced several episodes of dizziness and palpitation. The attacks were related to exertion and were relieved in a few minutes by lying down. On 2 occasions the patient lost consciousness for a short period of time, but had no convulsions. In March 1953 she was hospitalized elsewhere, where a diagnosis of congenital heart disease was entertained. Thoracotomy revealed partial occlusion of the great vessels of the aortic arch in their proximal portions, and more completely distally. As surgical correction was impossible, nothing further was done. The past history was negative for colds or upper respiratory infections. There was no personal or family history of syphilis.

Physical examination revealed a well developed 13-year-old Negro girl. There were no trophic changes in nose or mouth. The pupillary reflexes and ocular fundi were normal. There was marked tenderness in the left supraclavicular area. The chest was clear, and there were no palpable pulsations or bruit over the intercostal arteries. The heart was not enlarged. There was a grade I soft systolic murmur in the aortic and right cervical areas. A loud, high pitched, systolic murmur was heard in the left supraclavicular area. The murmur was not transmitted to the carotid arteries and did not change in character with pressure of the stethoscope bell. Venous pressure and circulation times with ether and dehydrocholic acid were normal. Radial, brachial, and temporal arteries were not palpable. Carotid pulsation was absent on the left and was slight on the right. Compression of the carotid sinuses caused dizziness but no loss of consciousness or pulse changes. Femoral, popliteal, and pedal pulses were strong and symmetrical. Except for the left hand being 2 degrees cooler than the right, there were no skin temperature changes between the 2 sides. On oscillometry, oscillations were absent in the arms, but in the thighs and calves they were strong and symmetrical. The left hand showed pallor on elevation. Blood pressure was not obtainable in the arms. It was 150/90 mm. Hg in the right leg and 160/95 mm. Hg in the left. The abdominal aorta pulsated freely. The liver and spleen were not enlarged. There was no clubbing of the fingers. Neurologic examination revealed hyperactive tendon reflexes, but no other abnormalities. The intelligence quotient was low with an index of 58 by the Stanford-Binet method, but the patient seemed to be well adjusted.

Pertinent laboratory data were as follows: Urine showed 15 to 25 leukocytes per high-power field, staphylococci, and coliform bacilli. Urea clearance was 106 per cent of normal. Blood counts revealed hemoglobin, 10 Gm. per cent; erythrocytes 3,560,000, leukocytes 5,050, and platelets, 267,000 per mm.³. The differential count was normal, the bleeding time was 1 minute, coagulation time 7 minutes and reticulocytes were 0.4 per cent. There was no sickling of erythrocytes. Coombs test, cold agglutinins, and LE-crot test were negative. Sedimentation rate was 60 mm./hr. (Westergren). Blood serologic tests, as well as treponema immobilization test, were negative. Antistreptolysin-O titer was 166 units. Repeated blood cultures were negative. Blood chemistry was as follows: serum protein, 7.65 Gm. per cent; albumin-globulin ratio, 4.2/3.45; nonprotein nitrogen, 22 mg. per cent; cholesterol, 165 mg. per cent; prothrombin, 58 per cent; bilirubin, 0.45 mg. per cent; serum iron, 195 µg. per cent; total iron-binding capacity 395 µg. per cent. Electrophoresis of plasma proteins showed a slight increase in gamma globulins. The basal metabolic rate was minus 10 per cent. Excretion of 17-ketosteroids in urine was normal. An electrocardiogram was normal. Electroencephalogram showed paroxysmal bursts of 4 to 5 per second, high voltage waves occurring from all leads. No alteration was present with sedatives or photic stimulation. X-rays of chest, spine, skull, kidneys, and gallbladder were essentially negative.

Clinical Course. The patient showed slight fever that persisted even after the urinary infection was cleared with oxytetracycline. Treatment with vasodilators brought no improvement, and the dizzy spells persisted without change. In order to assess

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the possibility of surgical correction of the obstruction, the right common carotid artery was explored. The vessel was markedly thickened and edematous. A small biopsy was taken from the arterial wall. On histologic examination there was marked fibrosis and a nonspecific acute inflammatory reaction in the periarterial tissue and neighboring muscles. The infiltrates consisted predominantly of polymorphonuclear cells with a few lymphocytes and monocytes (fig. 1). The small arteries and veins visible in the specimen were patent and presented a normal wall.

Arteriography showed dye passing retrograde through the common carotid into the innominate artery and apparently normal aorta. The filling of the subclavian artery was good on both sides up to the region where the axillary artery begins. At this point there was apparently an occlusion, and the further course of the artery could be outlined for only a short distance through the filling of the vasa vasorum. None of the dye went into the internal carotid artery. The thyrocervical trunk was well visualized and there was good filling of the vertebral artery on both sides. Marked collateral circulation was evident about the scapula (fig. 2).

During the procedure the patient had a generalized convulsion. Her immediate recovery was prolonged because she developed a transient paralysis of both legs. Weakness in the right leg persisted for 2 months. Postoperatively a depression of the S-T segments and negativity of T waves were also evident in the electrocardiogram. These changes regressed spontaneously during a period of 3 weeks.

Following the arteriography the patient was placed on anticoagulants for a period of 4 weeks. Because of the evidence of inflammatory periarteritis, it was decided to use long-term steroid therapy. After a 3-month course of 100 mg. of cortisone daily, the patient felt greatly improved. She had no fainting spells and her neurologic symptoms disappeared completely. Her body weight increased from 108 to 133 pounds. Auscultatory blood pressure was still not obtainable in the arms; the flush method showed it to be 55 mm. Hg. The values in the legs were 180/80 mm. Hg. Oscillometric excursions were strong in the legs, but still absent in the arms. Sedimentation rate was only 4 mm./hr., antistreptolysin-O titer was 50 units, C-reactive protein test was negative. Cortisone treatment had seemed to arrest the progressing vascular disease and another arterial biopsy was performed from the right elbow. The artery showed no pulsations, but the wall was not thickened and there were no periarterial adhesions. On incision the intima was smooth and a small amount of blood was oozing slowly out of the vessel. Microscopic examination revealed a normal arterial wall with no sign of infiltration or fibrosis.

The cortisone treatment was maintained through the following 2 years with decreasing doses. The patient continued to feel well and was completely free of symptoms. Her sedimentation rate remained low, and there was no evidence of fever or anemia. A complicating tubo-ovarian abscess was treated successfully with oxytetracycline in 1955. In 1956 the patient became pregnant and delivered spontaneously a full-term healthy girl.

**Discussion**

The symptoms and clinical findings in this case are quite typical of “pulseless disease” of the “young female arteritis” type. The primary pathologic lesion apparently consisted of an acute, almost phlegmonous, periarteritis. The process was strictly segmental as only the large elastic arteries of the aortic arch were involved, while the arteries distal to the diseased area were free from inflammation or thrombosis. In the 12 autopsies reported in the literature the arterial disease was also limited to this region. The thoracic aorta was quite often involved, but only in its proximal parts. The restriction of the arteritis to the originally branchial branches is very characteristic and deserves more attention in future etiologic and pathogenetic studies (congenital branchial arteritis?).

Histologic examination in these cases re-
PULSELESS DISEASE

FIG. 2. Photomicrograph of biopsy from the right common carotid artery. Adventitia is thickened and contains many hypertrophic nerves. In the internal layers there is a dense infiltration of polymorphonuclear and mononuclear leukocytes.

revealed the fibrosis to be the result of a panarteritis. All 3 layers of the arteries were involved with most evidence pointing to a primary periarteritis. In Harbitz's case the round-cell infiltration in the aortic adventitia was very pronounced. Similar inflammatory changes were present in the carotid and subclavian arteries. There were no giant cells in the media so characteristic of temporal arteritis and no fibroinoid degeneration in the intima as occurs in thromboangiitis obliterans. Beneke also described primary periarteritis of the aorta with necrosis of the media and sclerosis of the intima. Oota reported marked fibrosis of the adventitia of the aortic arch and its branches and atrophy of the media. The granulation tissue showed lymphocytic and plasmacellular infiltrations. In Frovig's case the aorta and its branches revealed massive inflammatory foci in the media and adventitia. The medial coat showed a fibroblastic proliferation with numerous giant cells. However, the importance of these findings should not be overestimated as giant cells are a common finding in atrophy of muscular or elastic tissue. Primary periarteritis with secondary thrombosis may also be suspected in the cases of Marinescu and Kreindler, Gilmour, and Maspetiolo and Taptas, although in these cases fibrosis and degenerative changes were predominant.

The pathologic changes are characteristic enough to regard the condition as an independent syndrome that can be differentiated from other inflammatory and degenerative arterial disorders. As shown in our case, the primary lesion apparently consists of an acute neutrophilic periarteritis that progresses to panarteritis and causes arterial thrombosis. Later stages are characterized by fibroblastic hypertrophy of adventitia and chronic inflammatory changes.

In view of these findings the report of the Committee on Nomenclature of the American Society for the Study of Arteriosclerosis that the "aortic arch arteritis" is a proliferative disorder involving the intimal and medial coats needs a revision. The definition was possibly influenced by the case report of Barker and Edwards of arteritis of the aortic arch in a 62-year-old woman. However, the patient was not a typical example of "pulseless disease;" and the clinical and pathologic findings show a
far greater similarity to the central form of temporal arteritis, as reported previously by Sproul and Hawthorne,20 and Gilmour.9

Prognostically, “pulseless disease” or “branchial arteritis,” as we would call it, is a serious condition as most cases died before the fourth decade with death usually resulting from cerebral ischemia or coronary insufficiency.7 The course of the disease is chronic and progressive but with variable remissions. Spontaneous regression appears possible as some cases showed only minimal inflammatory changes at the time of the autopsy.8, 10, 11

The treatment has in most cases had little effect on the course of the disease. Surgical measures such as thrombectomy, sympathetic denervation, and grafting of the carotid artery have not been successful.21 Excision of the carotid sinus ameliorated the symptoms caused by the sensitive carotid sinus,22 but did not arrest the progressive course of the arteritis.13 Experience in this case with the use of steroids and anticoagulants is encouraging but does not allow any conclusions. Antibiotics and steroids had no apparent effect in other reported cases,12, 13 but in no instance was the treatment of significant duration.

Summary

A case of pulseless disease or branchial arteritis is described and findings of arteriography and arterial biopsy are observed. The primary lesion seems to consist of an acute neutrophilic periarteritis progressing to panarteritis, causing arterial thrombosis. Later stages are characterized by fibroblastic hypertrophy of adventitia with lymphocytic and plasmacellular infiltrations.

The anatomic changes are characteristic enough to regard the condition as an independent syndrome that can usually be well differentiated from other inflammatory and degenerative arterial diseases.

The arteritis in this case seemed to respond to combined steroid and anticoagulant therapy.

Summario in Interlingua

Es describite un caso de morbo apulsatile o arteritis branchial. Constataiones de arteriographia e de biopsia arterial es presentate. Il pare que le lesion primari es un acute periarteritis neutrophilique progredente a panarteritis e causante thrombosis arterial. Stadios plus avante es characterisate per hypertrophia fibroblastic del adventitia e del media con infiltraciones lymphocytic e plasmacellular.

Le alterationes es satis characteristic pro establir le condition como un syndrome independente e usualmente ben differentiabile ab altere morbos arterial inflammatiori e degenerative.

In le presente caso, le arteritis pareva responder a un therapia steroide e anticoagulante combinate.

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A dose of hydergine or priscol was injected down the catheter into the main stem of the pulmonary artery of 9 patients with mitral stenosis, 1 with mitral stenosis and regurgitation, 1 with mitral stenosis and aortic stenosis, 1 with pulmonary heart disease and 1 with pulmonary stenosis. Hydergine produced no constant effect on cardiac output, pulmonary arterial pressure, or pulmonary resistance. There was no evidence that it was a pulmonary vasodilator. Priscol had a variable effect except for an invariable increase in heart rate. Priscol also occasionally raised pulmonary artery pressure, perhaps by a direct effect upon arterial smooth muscle. It is therefore potentially dangerous in persons with pulmonary hypertension.
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