TAKAYASU'S ARTERITIS

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Absent or diminished pulses in the limbs and neck are an elementary, albeit dramatic physical finding; the interpretation, however, is often complex and difficult. A considerable amount of confusion is occasioned by nosologic diversities and prolixity.

The term, 'pulseless disease', has been applied to this general type of abnormality.[1] For those cases in which there is obliteration or stenosis of the great vessels arising from the arch of the aorta, Frovig[2] coined the term 'aortic arch syndrome'. This designated a clinico-anatomic complex and did not initially include those instances in which the arterial pathology was located at a distance from the arch. However, the current concept of the aortic arch syndrome (perhaps more appropriately described as 'large vessel occlusive syndromes') is of narrowing or occlusion of the arteries arising from the aortic arch and in which involvement of the aorta itself along the whole or part of its length, together with its associated branches, may be a concomitant.

Such a picture may be produced by any of a number of pathologic processes. One form of the syndrome is an obliterative disorder of uncertain aetiology, common in young females and known as Takayasu's arteritis, 2 cases of which are presented in this paper.

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CASE REPORTS

Case 1

History. A 19-year-old, unmarried, White female was referred from the Cardiac Clinic to the Nursing Home Unit of the Johannesburg General Hospital for further investigation.

For about 1 year her right arm had become 'lame' while she was writing or sewing, but this feeling passed off when she rested. There was, in addition, a generalized feeling of tiredness accompanied by substernal discomfort on exercise. There was no claudication in the limbs. Severe occipital headaches had been present for many months and her vision was blurred at times. In the month before admission there had been several vertiginous attacks and episodes of fainting. Neither seems to have been related to postural change.

She had been well previously and there was no family history of either occlusive vascular disease or of collagenosis.

Examination showed a healthy-looking young female who was apyrexial. The heart rate was 86/min. Marked slowing of the rate, accompanied by a feeling of faintness, was produced by carotid pressure. Blood pressure was 130/80 mm. Hg in the left arm and 200/110 mm.Hg in the left leg. Several pulses were absent or diminished: The left carotid pulsation was weak. The right subclavian, axillary and brachial pulses were impalpable, while the radial pulse on that side was felt with difficulty. The left upper limb pulses were all present but a marked systolic thrill was felt over the left subclavian artery. The femoral, popliteal and pedal pulses on both sides were barely palpable.

There was a loud systolic bruit in the left supraclavicular fossa, a soft systolic murmur over the left carotid artery and loud systolic bruits over both femoral arteries. There were no renal artery bruits.

No trophic changes were present in the upper or lower limbs, and overt collateral vessels were absent. The heart, lungs and other organ systems were clinically normal. A few cytoid bodies, probably related to early ischaemia, were noted in the left fundus. The visual fields were normal.

Further investigations. (1) There was a mild normochromic, normocytic anaemia of 12 G/100 ml. and the erythrocyte sedimentation rate by the Westergren method was persistently elevated in the region of 30 mm. in one hour. White blood count was normal. (2) The mucoproteins, c-reactive protein (CRP) and fibrinogen were not elevated. (3) Several examinations for LE cells in peripheral blood were negative. (4) The blood urea was 35 mg./100 ml.; the urine was normal. (5) Protein electrophoresis showed a total protein of 7·6 G/100 ml., albumin 3·8 G/100 ml. and globulins 3·8 G/100 ml., of which gamma globulin was raised to 1·95 G/100 ml. (6) The blood lipids were normal. (7) The blood serology was negative. (8) An effort electrocardiogram (ECG) showed mild ischaemic changes in the chest leads. (9) A retrograde aortogram was performed and showed the following (Figs. 1, 2):

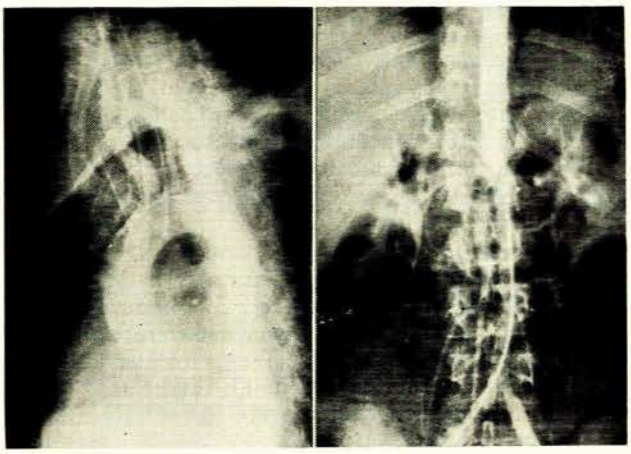

Fig. 1 *Fig. 2*

Fig. 1. The left subclavian artery is narrowed near its origin while the right is not shown at all. There is irregular narrowing of the aortic arch.
Fig. 2. The abdominal aorta is narrowed and there is stenosis at the origins of the iliac arteries.

Obliteration of the right subclavian artery just distal to its origin.

Proximal narrowing of the left subclavian artery.

Apparently normal carotid and vertebral arteries.

Narrowing of the arch of the aorta and the whole aorta down to the bifurcation.

The renal arteries did not show up well but the nephrogram phase was normal.

Aorto-iliac narrowing was present on both sides.

The patient, therefore, had clinical evidence of the aortic arch syndrome with symptoms referable to cerebral and upper limb ischaemia. In addition there was involvement of the aortic and iliac vessels (possibly also the renal artery in view of the hypertension). The mild myocardial ischaemia may portend coronary ostial narrowing by the pathologic process in the aorta. The presence of occlusive arterial disease in a young female in whom no definitive aetio-pathology can be demonstrated and in whom persistent elevation of the ESR and gamma globulins was found, places her in the category of Takayasu's arteritis.

She has been treated with anticoagulants.

Case 2

History. A 24-year-old White housewife was admitted to the Nursing Home Unit of the Johannesburg General Hospital for investigation of pulselessness in the right arm. For about a year the patient had suffered from vague abdominal pains unrelated to meals or menstruation. For 6 months she had noticed that her right arm became lame after minimal exercise. There were no symptoms referable to the central nervous system, the cardiac organ or the lower limbs. She had previously been perfectly well and the family history was non-contributory.

On examination she appeared well and was apyrexial. The heart rate was 65/min. The right subclavian, axillary, brachial and radial pulses could not be felt. The left subclavian and axillary pulses were not palpable although the brachial and radial pulses were weakly present. Blood pressure in the left arm was 105/80 mm.Hg.

In the lower limbs, both femoral pulses were palpable but reduced in intensity. The popliteal pulses were weak and the pedal pulses could not be detected. Blood pressure in the left leg was 130/75 mm.Hg.

A fairly loud systolic bruit was present just below the umbilicus and radiated to both femoral arteries. There were no other murmurs. There were no trophic changes in the limbs. The rest of the physical examination was normal.

Further investigations. (1) Full blood count showed an eosinophilia of 7%. ESR (Westergren) was elevated to 27 mm. in one hour. (2) Mucoproteins, CRP and fibrinogen were normal. (3) Protein electrophoresis was normal. (4) The lipogram was normal. (5) Blood urea was 28 mg./100 ml. and the urine was clear. (6) The serology was negative. (7) No cause for the eosinophilia was found; stool was negative for helminths and parasites, rectal biopsy showed no bilharzial ova and the bilharzial complement-fixation test was negative. (8) LE cells were not found in peripheral blood. (9) Chest X-ray examination was normal. (10) Aortogram could not be completed since fairly severe abdominal pain supervened during retrograde passage of the aortic catheter. It seemed possible that this represented mesenteric angina.

The finding of occlusive arterial disease involving the major vessels coming off the aortic arch, the major vessels in the legs and possibly the abdominal aorta itself, in a young woman with no evidence of other disease process and with elevation of the ESR, is strongly in favour of Takayasu's arteritis. The eosinophilia may well represent an allergic manifestation of the disease in this patient.

No specific therapy has been given and she will be followed up as an outpatient.

DISCUSSION

From the historical point of view, a number of milestones merit consideration. The first is the original report in 1839 by the Englishman, John Davy,[3] of pulselessness in the neck and upper extremities. Secondly, the Japanese ophthalmologist, Takayasu,[4] achieved eponymization with his outline in 1908 of the peculiar fundal changes, later shown to be associated with the ocular ischaemia of the aortic arch syndrome. Finally credit is due to Martorell and Fabré[5] for the first adequate description of the complete syndrome.

The causes of the aortic arch syndrome (of which Takayasu's arteritis is but one) are numerous and diverse (Table I). The extravascular occlusive syndromes which

occur at the thoracic outlet or with superior mediastinal space-occupying lesions, should be differentiated and excluded from this group.

TABLE I. CAUSES OF AORTIC ARCH SYNDROME*

1. Atherosclerosis
2. Syphilitic aortitis with or without aneurysm
3. Trauma with or without aneurysm
4. Congenital (anomalous branches, coarctation, certain cases of patent ductus)
5. Chronic dissection of the aorta
6. Various forms of arteritis
   - Takayasu
   - Collagen diseases
   - Giant cell arteritis
7. Obscure causes including calcific aortitis due to
   - Medial necrosis
   - Syphilis
   - Hypoplastic aorta
8. Embolism
9. Idiopathic thrombosis (as in thrombophilia or homocystinuria)
10. Connective tissue disorders
    - Pseudoxanthoma elasticum
    - Marman syndrome
    - Lathyrism
11. Infective—tuberculous aortitis

*After Ross and McKusick (1953)[6]

Features of Takayasu's Arteritis

Almost all the cases reported have been females under the age of 20 years. This is such a striking feature that Ross and McKusick[6] in their comprehensive review designated this entity as the 'young female arteritis type of aortic arch syndrome'. Males are not immune but are only rarely affected.[7] The disease appears to be much more frequent in the Orient than in the Occident.[8]

Systemic manifestations. Evidence that the disorder is a generalized one and not solely confined to the major arteries, is suggested by elevation of the ESR, mild leucocytosis and hypergammaglobulinaemia. Eosinophilia has not previously been reported and this is an unusual feature of the second case. Other manifestations have been pyrexia, polyarthritis and anaemia.[9,25] In several cases a false biologic positive test for syphilis has been observed.[8]

Aetiology and pathology. The aetiology remains cryptogenic. Some of the features point to an autoimmune disorder or connective tissue disease.[8-10,25] There is nothing to support a genetic mechanism. There is sex limitation, however, and 'femaleness' appears to exert a permissive effect. The stress factor seems to be important inasmuch as the areas subjected to greatest haemodynamic forces are earliest and most severely affected.

On gross morphology, there is involvement of the aorta (mainly the thoracic part) and the proximal segments of its large branches with sparing of the more distal parts of these vessels. Histologically, a mesarteritis is found with granulomatous or diffuse productive inflammation of the media and adventitia. Medial necrosis and disruption of the elastic layer ensue. Giant cells have been observed during this phase as part of a non-specific organizing process. Sclerosis, thickening and superimposed thrombosis follow and result in occlusion. In the main, there is a histologic resemblance to syphilitic endarteritis.[11]

Clinical features. The most remarkable features of the disease are ascribable to chronic hypoxia of the head and arms consequent on severe bilateral stenosis or occlusion of the primary and secondary branches of the aorta. The clinical picture is protean and the various components, ocular, cerebral, upper-limb, hypertensive and cardiovascular have been delineated and well discussed previously.[9,12]

Vertigo, syncope and headaches are most frequently complained of. Presentation may be with unconsciousness, fits or as a cerebrovascular accident. Visual disturbances such as flashes of light, amaurosis fugax and field defects are classically most prominent on upturning of the head.[5] Weakness, coldness or paraesthesia in an arm are common symptoms.

The cerebral picture is explicable on the basis of (a) carotid or vertebral artery involvement, (b) an abnormally sensitive carotid sinus (which is a feature in these cases and was demonstrated in our first patient) or (c) the brachio-basilar[13] or subclavian 'steal' syndromes,[14] where blood is diverted from the brain to supply an ischaemic upper limb.

Any combination of absent or diminished pulses in the neck or upper limbs is found. There are several eye signs which have recently been reviewed by Hodges.[15] Characteristically, neo-vascularization is seen in the eye in association with ischaemic and atrophic changes. More rarely, but strikingly, atrophy of the facial tissues such as skin and hair, muscle, bone or cartilage occurs.

There is little or no trophic change in affected limbs. Onset of arterial occlusion before adolescence, however, may result in deficient growth of the involved limb.[8] Overt collateral circulation is sometimes extensive and arteriovenous aneurysms may be observed in the fingertips. Thrills or bruits occur over collaterals or stenotic vessels. In severe instances of stenosis, the murmur is frequently continuous because of the high pressure gradient generated at the two ends of the narrow segment throughout the cardiac cycle.[16]

Involvement of the aorta, not only at the arch but along its whole length, has now been well documented.[8,17,20] The disease process may produce uniform narrowing of the aorta or a segmental constriction as in coarctation.[8] The abdominal branches of the aorta, the renal arteries and the ileo-femoral vessels may all be involved. Calcification of the aorta is not rare.[8,20,21]

The blood pressure is usually low in the upper limbs and may be high in the legs—the so-called reversed coarctation effect. The causes of the hypertension are diminished pressure in the carotid sinuses[8] and renal artery obstruction.[22,23] There may be tachycardia and cardiomegaly[20] and aortic regurgitation[8] and coronary artery narrowing have been observed.

Diagnosis and Therapy

The diagnosis is established by excluding the other causes of the aortic arch syndrome, together with the causes of the extravascular compression syndromes. Angiography is invaluable in demonstrating the localization, nature and extent of the obliterative process. An elevated ESR, leucocytosis and protein electrophoretic derangement provide helpful positive evidence.

There is no specific therapy for Takayasu's arteritis. Anticoagulants and corticosteroids have been employed with variable and varied results. Corticosteroids are probably most useful when there are prominent systemic manifestations in fulminant forms of the disease, or where early diagnosis can be made.[9] The majority of patients present with established obstructive arteriopathy necessitating surgical management. Local resection with grafting would appear to offer better results than simple endarterectomy.[24]

Prognosis has been difficult to assess in view of the fact that the total number of cases reported has been small, presentation is often late and follow-up observation inadequate. However, survival of up to 20 years is not unknown.[5]

SUMMARY

Two young White females with Takayasu's arteritis are presented.

Nosology is dealt with and it is stressed that the term aortic arch syndrome should be used to describe the general clinico-anatomic complex regardless of cause, whereas Takayasu's arteritis should be restricted to the idiopathic obliterative arteritis usually seen in young females. Furthermore, it is pointed out that the whole or part of the aorta with its primary and secondary branches may be affected in this disease.

Aetio-pathology, clinical features and diagnosis and therapy are briefly outlined.

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