A CASE OF IDIOPATHIC CENTRAL ARTERITIS

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In searching for the cause of severe hypertensive disease in young persons, arteriography sometimes reveals lesions of the renal arteries which are part of a more widespread process affecting the aorta and its large branches. While the aetiology of the arterial lesions is sometimes obvious—atherosclerosis, syphilis, rheumatic fever—its nature is obscure in many cases. Savory (1856)[1] is credited with the first account of this obscure condition; another historically important contribution is that of the Japanese ophthalmologist, Takayashu (1908).[2] Recently there has been an increase in the reports of this condition from many parts of the world. Notable among these are the papers by Isaacson and his colleagues at the Baragwanath Hospital which have drawn attention to cases in this country.[3-5] The purpose of our paper is to report another case and to discuss it in the light of the published experience of others.

CASE REPORT

In May 1962 C.L., a Cape Coloured female, was referred to the Groote Schuur Hospital from the Windermere Clinic of the Students' Health and Welfare Centres Organization of the University of Cape Town. She was then 14 years old and complained of palpitations and dyspnoea on effort which had been present for 1 year. She did not complain of headaches, swelling of the legs or intermittent claudication and she had no urinary symptoms. She had not recently had a sore throat. Poor vision had been present all her life. She had previously been in the Karl Bremer Hospital where an arteriogram had been performed through the left brachial artery.

She was small and thin; there was no pallor or oedema. Vigorous arterial pulsation in the neck was a striking feature. Bilateral keratitis was present; this prevented adequate examination of the fundus but it was occasionally possible to catch fleeting glimpses of a normal disc and rather narrow irregular arteries; haemorrhages and exudates were not seen.

The peripheral pulses were all palpable but unequal. The blood pressure in the left arm (the site of the previous arteriogram) was 260/165, in the right arm 300/180, and in the legs 260/135 mm.Hg. There was considerable cardiac enlargement with a heaving, hypertrophied left ventricular apex in the sixth left intercostal space beyond the midclavicular line. A loud ejection systolic murmur was heard all over the praecordium, at the back of the chest, down the lumbar spine and up into the neck. A presystolic gallop was audible between the apex of the heart and the left sternal border. No bruit was heard over the renal arteries. The abdominal aorta was not palpable and its pulsations could not be felt. The kidneys were not palpably abnormal.

Investigations

The urine was normal. Hb. was 14·5 G per 100 ml.; WBC 6,000 per cu.mm.; and ESR was on several occasions raised to about 35 mm. per hour (Westergen). Blood urea 24 mg. per 100 ml., creatinine clearance test normal. On 2 occasions the Wassermann test was non-reactive. LE cells could not be demonstrated. The anti-streptolysin-O titre 100 Todd units; Mantoux test (1 in 1,000) positive. Serum albumin 5·1 G per 100 ml.; serum globulin 3·8 G per 100 ml., with a relative increase in the gamma-globins demonstrated by electrophoresis.

Chest X-ray showed cardiac enlargement mainly resulting from an enlarged left ventricle (cardio-thoracic ratio 58%); the ascending aorta was prominent and the aortic knuckle was rather small; there were no bony abnormalities or parenchymal lung lesions. ECG showed considerable left ventricular hypertrophy.

An *intravenous pyelogram* showed normal function and structure of the left kidney but there was very little excretion of the dye by the right kidney.

Retrograde pyelography revealed no abnormality on either side.

Arteriography. Dr. Ronald Kottler performed two arteriograms. The first was through the left femoral artery. This showed normal iliac arteries and a normal aorta up to the origin of the renal arteries; the left renal artery was also normal but there was narrowing of the first part of the right renal artery with post-stenotic dilation. A fusiform aneurysm was present on the first part of the superior mesenteric artery (Figs. 1 and 4). The second arteriogram was through the right brachial artery; it showed an apparently normal aortic arch but there was diffuse, irregular narrowing and multiple saccular aneurysms of the descending aorta (Figs. 2 - 4).

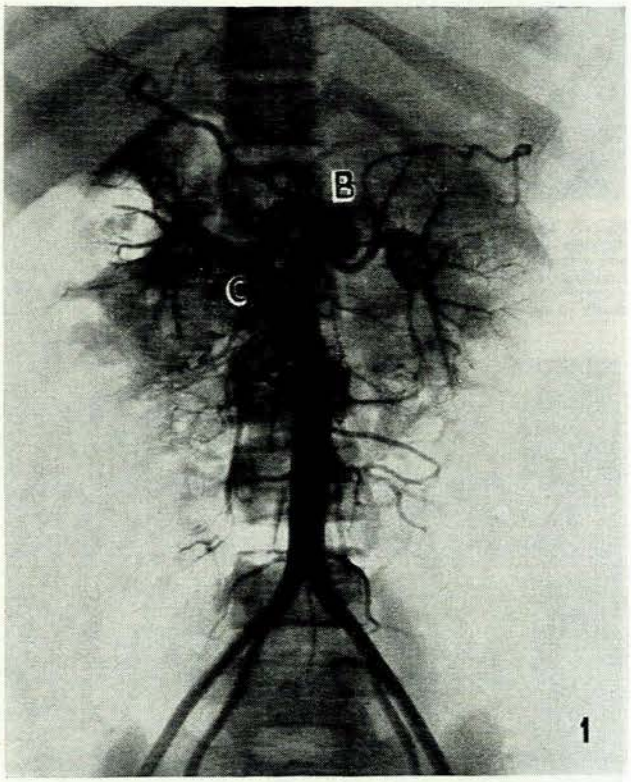


Fig. 1. Left femoral arteriogram, showing an aneurysm at the beginning of the superior mesenteric artery (B) and the irregular narrowing of the right renal artery (C).

Course

The extent of the arterial lesions excluded the possibility of operative treatment. The medical regime aimed at lowering the blood pressure and returning the patient to moderate activity. To start with, 0·25 mg. of reserpine and 50 mg. of hydrochlorthiazide were each given twice daily, while the patient was up and about in the ward. Since there was no fall in the standing blood pressure after a week, guanethedine was introduced, starting with 25 mg. and increasing step-wise to 100 mg. daily. The standing blood pressure was still not affected, so the guanethedine was withdrawn and mecamylamine substituted in doses of 10 mg. twice daily. This pro-

duced a prompt and sustained fall in the standing blood pressure in the right arm from about 280/180 to about 160/120 mm.Hg. This reduction of the blood pressure was not accompanied by any discomfort to the patient nor by impairment of her renal function.

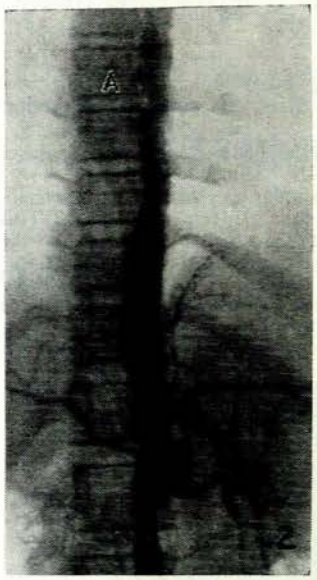
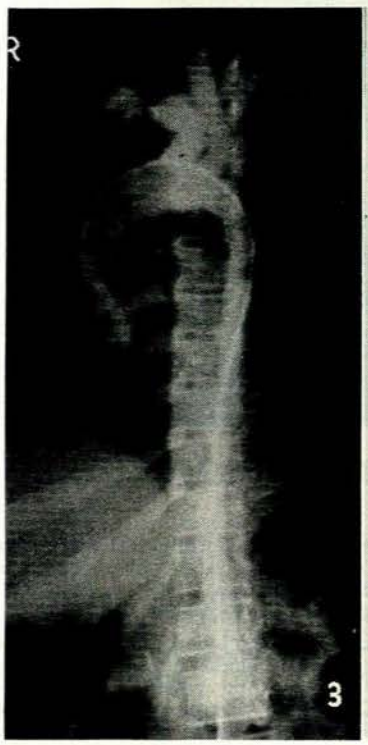


Fig. 2. Right brachial arteriogram showing multiple saccular aneurysms and irregular narrowing of the descending thoracic aorta. (A) The aneurysm of the superior mesenteric artery is again demonstrated.

In August 1962 she was discharged, first to the Bonnytoun Place of Safety, and then to the care of her mother who is a labourer on a fruit farm in Franschhoek. She was seen regularly at the Comprehensive Care Clinic where fair control of the blood pressure was maintained. It became necessary from time to time to increase the dose of mecamylamine to a maximum of 80 mg. daily. After about 6 months, she became depressed and often cried. The reserpine was replaced by phenobarbitone gr. ¼ twice daily and her sunny disposition returned and she began to do light work on the farm.

In January 1963 and again in March 1963 she had to be admitted to this hospital because of severe anaemia owing to menorrhagia. On each occasion, blood transfusions were necessary. Vaginal examination revealed no abnormality. Eventually, in consultation with the late Prof. J. T. Louw, it was decided that there was no possibility of this patient ever achieving a successful pregnancy and that a hysterectomy was necessary to stop the repeated and dangerous attacks of menorrhagia. Professor Louw performed a total abdominal hysterectomy, during the course of which the attending physicians were given an opportunity to palpate the abdominal aorta directly. The aorta was hard, rigid and irregular but no definite aneurysms were palpable. The other abdominal and pelvic arteries which were seen or felt were apparently normal. *There was no microscopic abnormality of any sort in the blood vessels of the uterus.*

Since the operation, the patient has been generally well apart from minor intercurrent illnesses. Control of her blood pressure has been less satisfactory partly owing to the fact that she lives a long way from the hospital and cannot attend as often as we would like her to. It is expected that she will soon have to be admitted again for stabilization of the blood pressure (see addendum).



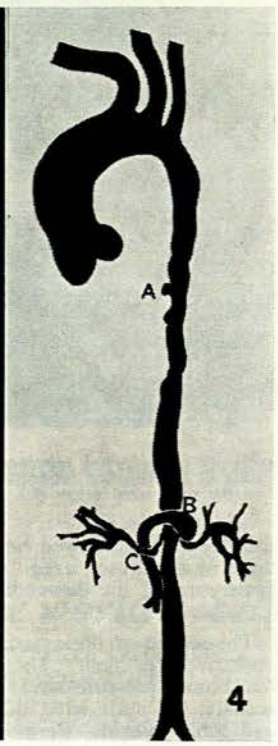


Fig. 3. Arteriogram showing normal aortic arch and the vessels arising from it (right oblique).

Fig. 4. Composite diagram of the patient's aorta and its main branches. A=aneurysms and indentations of the descending thoracic aorta, B=aneurysm of superior mesenteric artery, C=narrowing of right renal artery. Compare with Figs. 1 - 3.

DISCUSSION

This patient presents evidence of disease in three of her large arteries: the aorta, the superior mesenteric artery and the right renal artery. Of these, the stenosis of the first part of the right renal artery, by producing renal ischaemia, is responsible for the severe hypertension which is her most striking clinical feature and the most immediately dangerous.

The cause of the arterial disease is not obvious: atherosclerosis is unlikely in view of her age, sex, socio-economic position and the absence of an inborn error of lipid metabolism; she does not have the signs of congenital syphilis; and there is no reason to suspect rheumatic fever. Diagnostically, this case belongs to the 'idiopathic arteritis' group of diseases.

The clinical manifestations of this group of diseases are varied but can be grouped into a number of fairly constant syndromes depending on the main site of the disease process. If the aortic arch is predominantly affected, the patient presents with the clinical picture of 'brachio-cephalic arteritis', and the signs include absent pulses in the neck and arms, headaches, dizziness, fainting spells or strokes, and ocular lesions such as cataract, retinal atrophy and iritis.[6,7] Many examples of this syndrome have been reported from Japan and it is sometimes known as Takayashu's disease or 'Japanese pulseless disease'. However, many patients are not Japanese and it is probable that Takayashu's description was not the first. Our patient has bilateral keratitis which has been reported occasionally in this syndrome, but she has none of the cerebral manifestations and the pulses in her arms and neck are bounding rather than absent. The arteriograms do not show any abnormality of her aortic arch or its branches.

When the brunt of the disease affects the root of the aorta, there may be symptoms and signs of coronary ischaemia or of aortic incompetence.[7,8] When the descending thoracic aorta is mainly involved there may be hypertension in the arms and a relatively low blood pressure in the legs simulating a coarctation of the aorta.[3] When the lesion predominates in the mesenteric arteries there may be constipation and abdominal pain.[9] If the lower abdominal aorta is diseased, there may be intermittent claudication and absent pulses in the legs.[9] Although there is radiological evidence in our patient of widespread involvement of the descending aorta and of the superior mesenteric

artery, she has none of these clinical manifestations. The widely conducted systolic murmur is the only clinical sign of her aortic disease.

Finally, when the disease causes narrowing of one or both renal vessels, the clinical equivalent of the Goldblatt experiment is produced: the patient suffers from severe hypertension and may develop heart failure or retinopathy and is exposed to the risk of a cerebral haemorrhage. In our young patient, the untreated blood pressure (300/180 mm.Hg) was very high indeed, but this is not exceptional: one of Isaacson's cases was an 8-year-old African girl, who presented as a case of malignant hypertension with a blood pressure of 235/185 mm.Hg.[4] Although not a feature of the early reports of 'idiopathic arteritis', hypertension owing to narrowing of the renal artery is now well-recognized in this condition.[9] Generally, the hypertension is difficult to control with available medicaments. An unexplained feature of our case was the prompt response to mecamylamine after guanethedine had proved to be ineffective. In a few cases, unilateral nephrectomy has been performed but without benefit to the patient: either the primary arterial disease had been too extensive before the nephrectomy or it continued to progress after the operation.[9]

Despite the protean clinical manifestations of the disease, the pathological changes are usually similar and non-specific in most of the cases which have come to necropsy. The intima of the affected arteries is thickened mainly by an excess of connective tissue; sometimes there is intimal calcification and sometimes the arterial lumen is further obstructed by endothelial thrombosis. In the media, the elastic fibres are usually fragmented and the defects may be the site of aneurysm formation. In the adventitia, there is an excess of connective tissue and striking endothelial proliferation of the vasa vasorum. Sometimes there are 'infarcts' in the adventitia which appear as areas of coagulative necrosis.[4,9]

The pathogenesis of these changes can be regarded most plausibly to be initiated by a primary endarteritis of the vasa vasorum. This produces a local inflammatory reaction in the adventitia and areas of infarction; there is ischaemic damage to the elastica and secondary hyperplasia of the intima, on top of which thrombi may be deposited.

Although the cellular reaction in the adventitia may vary from case to case and may consist predominantly of lymphocytes, neutrophils, eosinophils or giant cells, the pathological changes are essentially non-specific and provide no clue to establishing the cause of the disease. It has therefore become widely accepted that the aetiology of this disease is similarly non-specific and hence it is regarded as the general reaction of the arterial wall to non-specific antigenic agents. Thus it may be grouped aetiologically with the arterial lesions of rheumatoid arthritis, giant cell arteritis, temporal arteritis and polyarteritis nodosa. In none of these conditions has a specific pathogen been demonstrated and it is unlikely that a single pathogen exists. In several reports on this group of diseases, the association with tuberculosis has been noted;[10] it is not yet clear whether this association is more than fortuitous but it is possible that the tubercle bacillus may be one of the non-specific agents concerned in the pathogenesis.

In browsing through some of the relevant literature, we have gained the impression that the frequency of this disease is apparently greatest in the less developed countries and among the poorer classes of mankind. If this is true, the conditioning effects of malnutrition and recurrent low-grade infections will also have to be considered when studying the pathogenesis of this disease.

While reading the literature, we have also been impressed by the great many names — eponymous, descriptive and speculative — which have been attached to this condition. At the risk of increasing the confusion, but with the sincere intention of simplification, we suggest *Central arteritis* as a convenient label. This is by analogy with 'peripheral arteritis', a term which has proved useful in describing various afflictions of the smaller arteries. In the present state of our knowledge of the aetiology of this group of diseases, it is recommended that the term 'central arteritis' be further qualified by one of the conventional expressions of ignorance such as 'agnogenic, 'cryptogenic', or 'idiopathic'.

Addendum

In May 1964 the patient was again admitted to hospital after a subarachnoid haemorrhage with hemiplegia. Her BP in the right arm was 280/160 mm. Hg. The BP was gradually reduced to about 160/100 mm. Hg by means of intramuscular reserpine and has been maintained at about that level on 50 mg. of hydrochlorthiazide and 0·25 mg. of reserpine, each given twice daily by mouth. She has been kept quietly in bed except for intensive physiotherapy aimed at strengthening the motor power of the right arm and leg. On this regime, she has made a good recovery. There are no signs of subarachnoid haemorrhage and the power in the arm and leg have almost returned to normal.

SUMMARY

The case is reported of a young Cape Coloured girl with severe hypertensive disease. Arteriography revealed a diseased descending aorta, narrowing of the right renal artery and an aneurysm of the first part of the superior mesenteric artery. The condition from which this patient is suffering is one of an ill-defined group for which we have suggested the general designation of 'Idiopathic central arteritis'.

We are obliged to Dr. J. G. Burger, Medical Superintendent of Groote Schuur Hospital, for permission to publish this report. We are also indebted to Dr. R. Kottler for the arteriography. The facilities of the Ecology of Hypertension Research Project have been used to ensure the continuing care of the patient; this project is sponsored by the National Institutes of Health of the US Public Health Service (Grant HE 06267).

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