ARTERITIS OF THE AORTA AND ITS MAJOR BRANCHES

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SYNOPSIS

Six patients presenting with arteritis of the aorta and its major branches of unknown aetiology are described. The varied mode of clinical presentation as shown by these 6 cases and others documented in the literature is stressed.

Four of the 6 patients had a raised IgG level in the sera and 5 patients had persistently raised ESR. The significance of these findings with reference to the aetiology of the syndrome is described.

The aorta and its branches is sometimes affected by an arteritis of unknown cause. This syndrome has in the past been known by a host of different names such as Takayasu's arteritis, aortic arch arteritis, reversed coarctation, pulseless disease and young female arteritis (Strachan, 1966). Each of these terms emphasises a different mode of clinical presentation of the disease. Since any segment of the aorta and any of its main branches may be involved, the term "Arteritis of the aorta and its major branches" as coined by Schrire and Asherson (1964) would probably be the most appropriate.

This disease occurs in most of the countries in this world, but is specially prevalent in Japan, Singapore, India and in Africa. In 1963, Danaraj, Wong and Thomas described 8 cases seen in Singapore presenting with hypertension due to renal artery stenosis. In this paper, we document 6 cases of arteritis of the aorta, with special emphasis on the immunoglobulin levels found in these patients.

CASE RECORDS

Case 1

A 20 year old Malay girl was first seen on 12.8.66 for exertional dyspnoea. Clinical examination revealed delayed femoral pulses. The blood pressure reading in both the upper limbs was 180/95 whilst that in the lower limbs was 130/90. A systolic bruit was heard over the spine extending from the second thoracic to the first lumbar vertebra region, over both carotid arteries and on both sides of the umbilicus. The fundi showed Grade 2 changes (Keith, Wagener and Barker, 1939). A clinical diagnosis of coarctation of the aorta was made and this was thought to be due to arteritis of the aorta.

The Mantoux test 1/1,000 was positive. A skiagram of the chest showed cardiomegaly, but normal lung fields. The intra-venous pyelogram was normal. The ECG showed changes of left ventricular hypertrophy. The serum protein electrophoresis showed—Albumin 3·7 gms.%, α_1 globulin 0·3 gms.%, α_2 globulin 0·9 gms.%, β globulin 1·2 gms.%, γ globulin 2·4 gms.%. The results of the other investigations are listed in Table I. Retrograde aortography via the femoral route showed a large dilated ascending aorta with marked narrowing and irregularity of the descending and the abdominal aorta. There was also irregular narrowing and dilatation of the left common carotid and left subclavian arteries (Fig. 1). Both renal arteries appeared normal. Right and left sided cardiac catheterization showed normal findings.

She has been treated with anti-hypertensive drugs and the blood pressure in the upper limbs has been maintained at around 140/80.

Case 2

A 10 year old Chinese boy was admitted on 10.7.68 for severe headache of 2 years duration. On clinical examination the blood pressure was 230/140 in both the upper limbs and 250/160 in both the lower limbs.

Urine chemical and microscopical analysis, blood urea and serum electrolytes estimation were all normal. A skiagram of the chest showed cardiomegaly and this was confirmed in the ECG. The intra-venous pyelogram showed prompt excretion of the dye in the left kidney with normal appearance of the collecting system. The right kidney showed delayed excretion with poor filling of the calyces. It was therefore thought that there was a stenosis of the right renal artery. The serum protein electrophoresis estimation showed—Albumin 4·5 gms.%, α_1 globulin 0·2 gms.%, α_2

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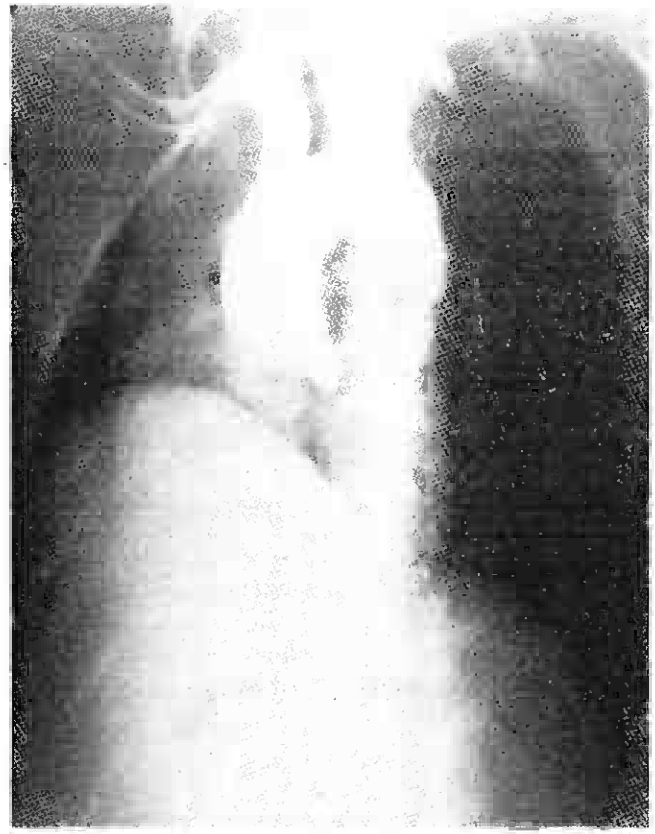

Fig. 1. Retrograde aortogram — Case 1 (see text).

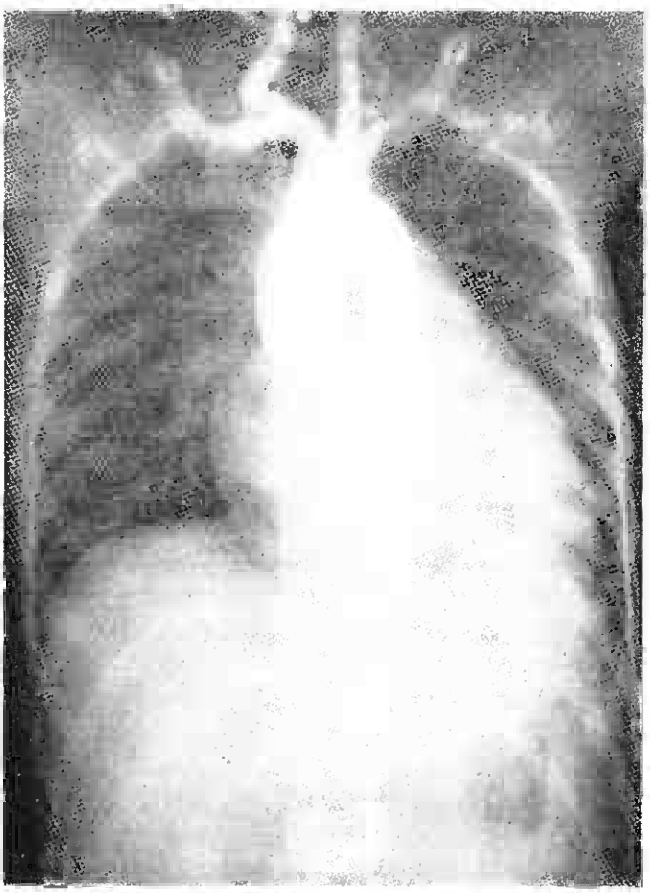

Fig. 3. Retrograde aortogram — Case 3 (see text).

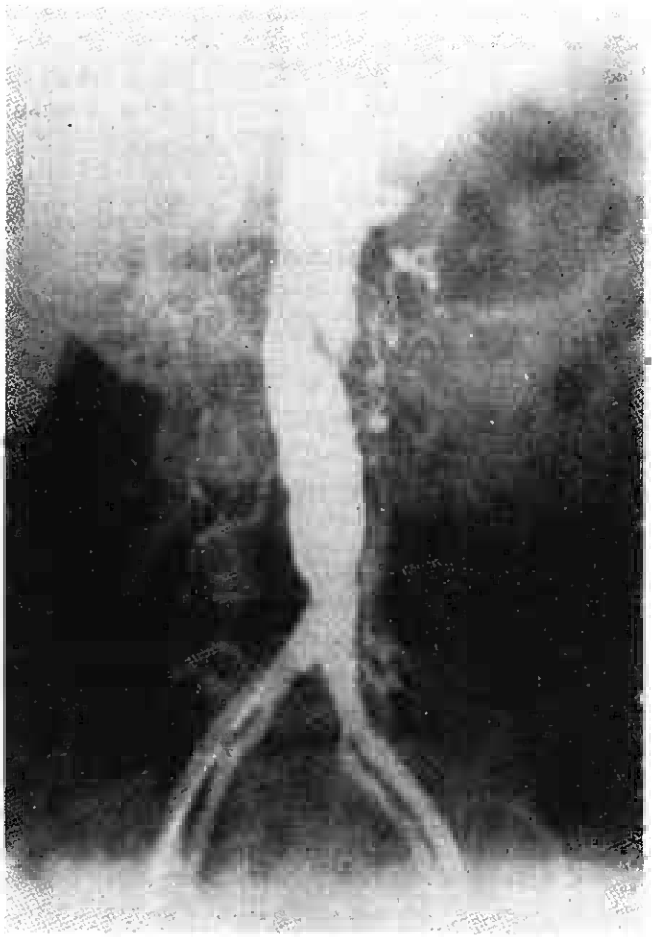

Fig. 2. Retrograde abdominal aortogram—Case 2 (see text).

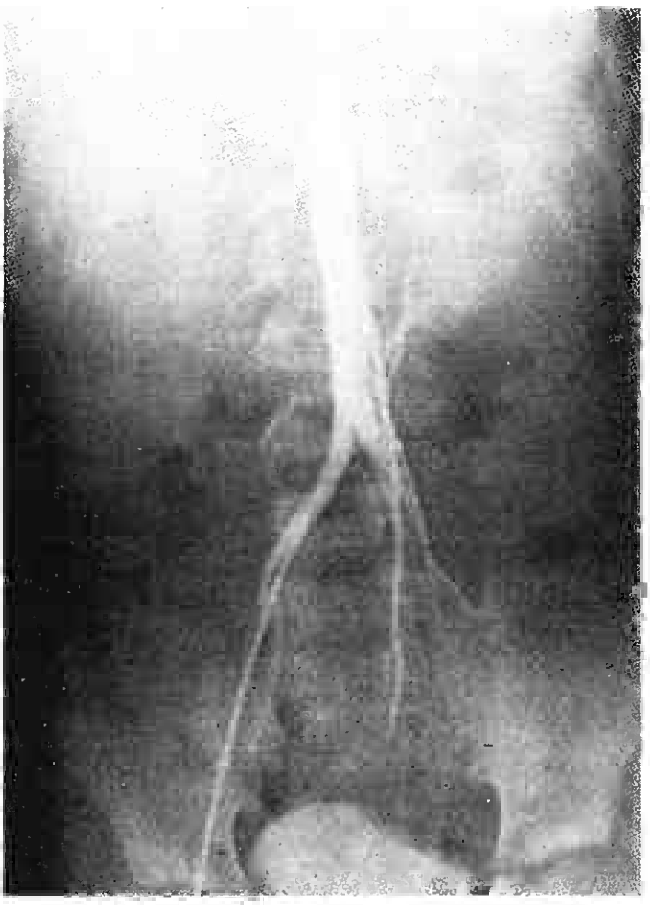

Fig. 4. Retrograde aortogram — Case 3 (see text).

TABLE I

LABORATORY FINDINGS IN 6 PATIENTS WITH ARTERITIS OF THE AORTA AND ITS MAJOR BRANCHES

Case No.	Serum IMGS -- MGMS %			Antinuclear Factor	L.E. Cell	R.A. Factor	B.S.R. mms./hr.	Serum Cholesterol MGM %	Blood K.T.
	IgG	IgA	IgM						
1	1690	322	70·0	Negative	Negative	Negative	62	215	Negative
2	1460	225	62·5	Negative	Negative	Negative	27	175	Negative
3	1060	288	60·0	Negative	Negative	Negative	70	198	Negative
4	1340	384	68·5	Negative	Negative	Negative	50	225	Negative
5	1060	276	85·5	Negative	Negative	Negative	102	Not done	Negative
6	1860	216	74·8	Negative	Negative	Weak Positive	63	184	Negative

globulin 0·7 gms.%, β globulin 0·9 gms.%, γ globulin 1·2 gms.%. The results of the rest of the investigations done are shown in Table I.

A retrograde aortogram via the femoral route showed that there was marked variation in calibre and irregularity of outline of the abdominal aorta from the first lumbar vertebra region downwards. The right renal artery was totally occluded, whilst the left was severely narrowed (Fig. 2).

Anti-hypertensive therapy was instituted. Since he was first seen, he has been admitted to the hospital on 9 other occasions, for either headache, giddiness or difficulty in control of the hypertension. When recently reviewed, his blood pressure was 190/120.

Case 3

A 13 year old Malay boy was admitted on 28.12.66 for investigation of hypertension. All his peripheral pulses were palpable except for those in the left upper limb. The blood pressure was 180/120 in the right brachial artery, 170/130 in both the popliteal arteries but unrecordable in the left brachial artery.

The ECG showed left ventricular hypertrophy. A skiagram of the chest showed cardiomegaly. The intra-venous pyelogram was normal. The serum electrolytes estimation were Sodium 141 meq./L., Potassium 4·1 meq./L., Chloride 100 meq./L. Serum protein electrophoresis estimation showed —Albumin 3·5 gms.%, α_1 globulin 0·5 gms.%, α_2 globulin 1·5 gms.%, β globulin 1·3 gms.%, γ globulin 1·9 gms.%. The results of the rest of the investigations are listed in Table I.

A retrograde aortogram was done via the femoral route. The left subclavian artery was found to be narrowed at 2·5 cms. distal to the origin of the left vertebral artery. The descending aorta was found to be extremely tortuous and irregular from the junction of the arch and descending aorta downwards (Fig. 3) with severe narrowing at the junction of the twelfth thoracic and the first lumbar vertebra region where the right renal artery originated. The left renal artery was absent and the left kidney appeared to be supplied by collaterals from the lumbar and the superior and inferior mesenteric arteries. The aorta bifurcated at the third lumbar vertebra region and there was narrowing of the left iliac artery (Fig. 4).

He was started on hypotensive therapy together with prednisolone. He has been followed up closely as an outpatient and has been maintained on this therapy with the blood pressure in the right brachial artery maintained around 170/110.

Case 4

This patient was reported in full by Danaraj, Wong and Thomas (1963) (Case 6 in their series). However no immunoglobulin studies were done previously. In brief, she was an 18 year old Chinese girl and was found in October 1968 to have hypertension in the lower limbs with a blood pressure of 230/130 and absent upper limb pulses and unrecordable blood pressure and subsequently she was readmitted for congestive heart failure. Aortography revealed a normal aortic arch with the innominate and left common carotid arteries arising from a common root. The right subclavian artery was not visible and the left subclavian artery was seen only at its origin. The descending aorta was irregular in outline and the right renal artery was constricted. A right nephrectomy was done in December 1959. On microscopical examination, a chronic inflammatory reaction consisting of lymphocytes and plasma cells were present, especially in the cortex. The intra-renal arteries and arterioles were normal. The renal artery was normal except for some focal intimal thickening.

Since the operation, she has been on hypotensive therapy and the blood pressure in the lower limbs has been maintained around 130/80.

The results of some of the other investigations done are seen in Table I.

Case 5

The patient, a 29 year old Indian woman, was first seen on 18.12.67 for a 4 month history of pain over the left carotid artery. On clinical examination, the left carotid artery was found to be slightly swollen and tender but pulsatile. There was a systolic thrill felt over both the right and left carotid arteries. Both the brachial and radial pulses were not felt, but the femoral, dorsalis pedis and posterior tibial arteries were easily palpable. The blood pressure in both the upper limbs was not recordable, but that in the lower limbs was 100/80. A systolic bruit was heard on both sides of the umbilicus and over the spine from the second thoracic vertebra region to the lumbar region.

The Mantoux test 1/1000 was positive. The blood urea, haemoglobin and the total white count were all within the normal limits. The skiagram of the chest and the intra-venous pyelogram were all normal. The serum protein electrophoresis pattern showed an Albumin of 4·6 gms.%, α_1 globulin 0·3 gms.%, α_2 globulin 0·4 gms.%, β globulin 0·3 gms.%, γ globulin 1·7 gms.%. The results of the rest of the investigations are listed in Table I.

She has been maintained on Prednisolone and has been well except for occasional pain over the left carotid artery region, over the chest and over the knee and ankle joints.

Case 6

A 26 year old Chinese woman was treated in July 1960 for tuberculosis of the left hip. On clinical examination, the upper limb and the right femoral pulses were easily felt but the left femoral pulse was rather weak. The blood pressure in both the upper limbs was 170/80, but that in the lower limbs could not be recorded. A systolic bruit was heard widely over the abdomen.

A radiogram of the abdomen revealed calcification of the aorta at the eleventh and twelfth thoracic vertebra level (Fig. 5). The ECG and skiagram of the chest were normal. The urine microscopical and chemical analysis, the blood urea and the serum electrolytes were all normal. The serum protein electrophoresis pattern showed albumin 4·2 gms.%, α_1 globulin 0·3 gms.%, α_2 globulin 0·4 gms.%, β globulin 1·2 gms.%, γ globulin 1·8 gms.%. The results of the rest of the investigations are shown in Table I. A retrograde aortogram was done but unfortunately the films are missing from the files.

Fig. 5. Lateral radiogram of the abdomen showing calcification of aorta (arrowed) — Case 6.

She was followed up closely and was well until 4.7.70 when she was admitted for polyarthritis of unknown cause. During this admission, the LE cell and antinuclear factor were repeatedly negative. The R.A. factor was weakly positive, the anti-streptolysin 0 titre was 400 Todd units and the erythrocyte sedimentation rate was 110 mms./hr. She improved with the symptomatic treatment given and was discharged from hospital.

DISCUSSION

Arteritis of unknown aetiology affecting the aorta and its main branches has been documented as far back as 1827 (Adams, 1827). In 1908, Takayasu described an unusual wreath-like vascular anastomosis surrounding the optic disc of a young Japanese female patient who was almost blind, but otherwise physically well (Takayasu, 1908). His colleague, Onishi, found another patient with similar eye changes but with the additional feature of pulselessness of the arms. Subsequently, it was established that both the absence of upper limb pulses and the unusual eye changes were the manifestations of an arteritis involving the aortic arch and its main branches.

Since any segment of the aorta and any of its major branches can be involved, the symptoms and signs encountered in this syndrome are typically protean. Thus Schrire (1967) in a review of 34 patients, found that the mode of presentation

was cardiac in 20 (symptoms 17, hypertension only 3), peripheral vascular 7, cerebral 3, thoracic aneurysm 2, constitutional symptoms 1 and incidental 1.

An absent or diminished pulse in the upper or lower limb artery constitutes one of the most dramatic findings in this syndrome, giving rise to the term "pulseless disease". In this series of 6 cases, there was an absence or diminution of pulses in 5 patients—the left brachial in Case 3, both brachials in Cases 4 and 5, left femoral in Case 6 and both femorals in Case 1. Aortography revealed that there was a marked narrowing and irregularity of the descending and the abdominal aorta in Case 1 producing a coarctation of the aorta with hypertension in the upper limbs. Similarly, the absent left brachial artery pulse in Case 3 was demonstrated by aortography to be due to narrowing of the left subclavian artery and in Case 4, the absence of both upper limb pulses was shown to be due to the occlusion of both the subclavian arteries. In Schrire's series of 34 patients (1967), pulse abnormality was found in 26.

Other symptoms which may occur are best classified according to the segment of aorta involved by the disease. Involvement of the aortic arch and its major branches gives rise to the "aortic arch syndrome". The symptoms of aortic arch insufficiency due to aortic arch syndrome are usually very varied. Syncope, headaches, fits, hemiplegia, blurring of vision and other neurological deficits were the presenting complaints in the series published by Hirsch, Aikat and Basu (1964). Changes in the fundi as first described by Takayasu (1968) may also be seen. In this series, only 1 patient exhibited symptoms which were referable to the disease of the aortic arch; this patient presented with pain over the left carotid artery which was found to be swollen but pulsatile.

In Schrire's series (1967), 21 of the 26 patients examined by aortography showed occlusion of the abdominal aorta. Occasionally this is seen on a plain abdominal radiogram as calcification of a segment of the abdominal aorta as is shown in Case 6. Furthermore, 8 patients had occlusion of one or both renal arteries producing hypertension. Occlusion of one renal artery occurred in 2 patients and both renal arteries were occluded in 1 patient in this series and all these 3 patients presented with hypertension. In Case 4, this was detected only in the lower limbs as both the subclavian arteries were occluded by the disease process.

Other arteries may be stenosed or occluded are the mesenteric, the coronary and the pulmonary arteries. The heart in this syndrome may be affected by involvement of the cardiac valves, the coronary arteries, systemic hypertension or primary muscle disease (Schrire, 1967).

Strachan (1966) has divided arteritis of the aorta into 2 stages—an early prepulseless (pre-occlusive) stage and a later pulseless (occlusive) stage. In the former, there is no occlusion of any of the major branches of the aorta and the presenting signs and symptoms may be anaemia, prolonged fever, polyarthritis, myalgia, thrombophlebitis, a raised erythrocyte sedimentation rate (ESR) and hyperglobulinaemia. The clinical presentation of the pulseless stage has been described above (vide supra) but Strachan commented that at this later stage, the ESR may sometimes be normal.

In this series of 6 cases, other possible causes of occlusive disease of the aorta and its branches have been excluded as far as possible. Thus the blood Kahn test was negative in all 6 patients excluding syphilis as a cause. Antinuclear factor and L.E. cells were negative in all. The ages of the patients in this series ranged from 10 to 29. It is unlikely that atheroma is the aetiological factor here, the serum cholesterol being normal in 5 of the 6 patients. Furthermore, 5 of the 6 patients in this series had persistently high ESR reading and this would certainly favour arteritis of the aorta where the ESR is often raised rather than atheroma, where the ESR is normal.

The exact aetiology of arteritis of the aorta has remained a mystery. A tuberculosis aetiology was proposed by Sen *et al* (1963). However, since the incidence of tuberculosis is high in both India and Singapore, this disease detected in patients with arteritis of the aorta in both Sen's series and in Case 6 in the present series was more likely to be coincidental rather than of any aetiological significance. Most recently, Munoz and Correa (1970), on the basis of autopsy studies on 7 cases, suggested that arteritis of the aorta may be related to the rheumatoid syndrome or may be due to an infection by an unidentified nematode with arterial tropism in children and young adults.

However, the most consistent hypothesis probably would be that this syndrome represents yet another member of the big family of auto-immune diseases. The protean nature of the disease, the raised gamma globulin and the occurrence of "rheumatic" symptoms preceding or accompanying the arteritic phase, as seen in Case 6 in this series, all point to an auto-immune aetiology. The L.E. cell has also been reported to be positive in a few instances (Hirsch and Basu, 1964), although both the L.E. cells and the antinuclear factor were repeatedly negative in this series.

In a study of the serum immunoglobulin levels, Asherson *et al* (1968) found that patients with arteritis of the aorta have a raised level of IgG, IgM and IgA as compared to a control group of patients with functional disorders. However, unlike Ito (1966) they could find no antibodies against aorta by complement fixation, gel precipitation or immunofluorescence techniques.

In this study, immunoglobulin levels in the sera of all 6 patients were estimated and the results are shown in Table I. Serum levels of immunoglobulin (IgG, IgA and IgM) in normal people comprising the 4 races—Chinese, Malays, Indians and Europeans—living in Singapore have been studied by Chew *et al* (1969). The immunoglobulin levels in a normal population vary with both sex and race. Using their results as a baseline of normality, IgG was found to be raised in 4 patients in this series—Cases 1, 2, 4 and 6. IgA and IgM levels in all 6 patients were within the normal limits.

According to Asherson *et al*, high immunoglobulin levels in arteritis of the aorta may be due to one of these 4 main possibilities:

"1. The disease may be due to an infection by a parasite or micro-organism.

2. The disease may be due to an immune process.

3. The disease may be due to antibody antigen complexes which selectively damage the aorta because of some other (unknown) agent which also acts on the aorta.

4. The raised immunoglobulin may be due to an immune response to damage to the aorta and may throw no light on the cause of the damage".

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