Current Survey

PRE-PULSELESS AND PULSELESS TAKAYASUS' ARTERITIS

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The Confused Terminology and Changing Concept of Takayasu's Arteritis

In 1908 the Japanese ophthalmologist, Takayasu, reported an unusual wreath-like vascular anastomosis surrounding the optic discs of a young female patient who was nearly blind, but who showed 'no general physical changes'. He was unable to explain this abnormality. Later a colleague, Onishi, referred to a similar case who had the further 'peculiarity' of pulselessness of the arms. Eventually it was established that these widely separated abnormalities were but two of many remarkable features which could occur when disease caused severe stenosis or obstruction of the arterial trunks arising from the aortic arch. The full spectrum, which is best termed the aortic-arch syndrome (Froviq, 1946), included bizarre features such as premature aging of the face, masseter claudication and ulceration of the palate, nasal septum, ears or nose in addition to the commoner consequences of ocular, cerebral and arm ischaemia such as blindness, strokes and arm claudication.

Because of the rarity of atheroma in the Orient it became apparent early that the aortic-arch syndrome could be due to an arteritis of obscure aetiology. In the absence, however, of aortography or specific serological tests neither early diagnosis nor accurate distinction of this arterial disease from the other causes of the syndrome such as syphilis, polyarteritis, chronic dissecting aneurysm or atheroma was possible. During the first half of this century these circumstances and the variable presentations of the aortic-arch syndrome obscured the early natural history of this new arteritis and led to nosological confusion (Table 1). Unfortunately, the misleading term 'pulseless disease' gradually became dominant, being used by some as a synonym for the syndrome and by others specifically for the arteries first referred to, albeit unknowingly, by either Takayasu or Savory (1856). The last decade has added to the confusion since descriptions of Takayasu's arteritis distal to the aortic arch have resulted in a further selection of terms. These include central aortitis, middle aortic syndrome, stenosing aortitis, elongated coarctation and sub-isthmic coarctation.

Largely because of the term 'pulseless disease' Takayasu's arteritis came to be regarded essentially as a cause of arm pulselessness, blindness or cerebro-vascular insufficiency. Recently, however, several papers (Sandring and Welin, 1961; Judge, Currier, Gracie and Figley, 1962; Strachan, 1964;

TABLE 1

TERMINOLOGY OF TAKAYASU'S ARTERITIS

Takayasu's disease
Pulseless disease
Takayasu-Onishi disease
Branchial arteritis
Reader-Harbitz syndrome
Arteritis of aorta in young women
Aortic arch arteritis
Syndrome of occlusion of supra-aortic trunks
Young female arteritis
Rheumatic brachio-cephalic arteritis
Reversed coarctation
Martorell's syndrome
Takayasu-Martorell-Fabre syndrome
Aortic arch syndrome
Thrombo-arteritis obliterans subclavico-carotica
Chronic subclavian-carotid obstructive syndrome

The above is a selection of the terms which have been used in the literature as synonyms for Takayasu's arteritis.

Hirsch, Aikat and Basu, 1964; Schrire and Asherson, 1964; Falicov and Cooney, 1964) have focused attention on various systemic and other manifestations which may occur before arterial obstruction can cause these classical features. Moreover, pulselessness may not occur for several reasons, e.g. the development of arterial dilatation rather than stenosis, mildness of the disease and involvement of the abdominal aorta rather than the aortic arch. In recognition of these points, Strachan (1964) suggested the division of the disease into early and late phases to be designated 'Pre-pulseless Takayasu's Arteritis' and 'Pulseless Takayasu's Arteritis'. It was appreciated that the manifestations of these stages could overlap and that the pulseless artery might be inaccessible in the abdomen making the term 'occlusive' preferable to 'pulseless'. Such a concept was also in alignment with the pathological progression of the disease from a periarteritis to a panarteritis and finally to intra-arterial thrombosis (Judge and others, 1962). The above terminology should encourage early diagnosis and end the inadequate concept of Takayasu's disease as a cause solely of the aortic arch syndrome.

Pre-Pulseless (Pre-occlusive) Takayasu's Arteritis

Takayasu's arteritis is a chronic relapsing disease which may extend from childhood to late adult life. It is commoner in the Orient (McKusick, 1962) and shows a predilection for young females, but it occurs in male patients and has been reported throughout the world. The pre-

DIAGNOSTIC FEATURES:

Bruits: Raised E.S.R.: Hyperglobulinaemia:
Segmental aortic dilatation.
Aortography—early stenosis or dilatation

FIG. 1.— Pre-pulseless Takayasu's arteritis.

pulseless phase is of variable severity and duration and its manifestations may occur episodically over many years. Analysis of the literature has shown that a few months to 39 years, with a mean of about 8 years, have lapsed between the onset of the disease and the observation of any abnormality of the pulses (Strachan, Wigzell and Anderson, (1966).

The early systemic features of the disease first became apparent in the writings of Ask-Upmark (1954) and Sandring and Welin (1961). Strachan (1964) has recently emphasised that the full spectrum (Fig. 1) of pre-pulseless manifestations included anaemia, prolonged fever, pleurisy with or without effusion, haemoptysis, pericarditic pain, myalgia, arthralgia, migratory polyarthritides, erythema-nodosum-like lesions, ulceration of the legs, transient skin rashes, Raynaud's phenomenon, iritis, episcleritis, cranio-cervical pain and perhaps splenomegaly. Isolated examples of superficial

thrombophlebitis (Hirsch and others, 1964) and occlusion of the venae cavae (Schrirre and others, 1964) have been reported but whether these were coincidental or a very rare feature of Takayasu's disease is uncertain. As in chronic rheumatic heart disease the earlier phase of acute rheumatic fever is inconsistent, so it appears that some patients pass through the pre-pulseless phase of Takayasu's arteritis without symptoms (Sandring and Welin, 1961) or with nothing more definite than intermittent malaise and fatigue.

The diagnosis may be easily overlooked at this stage for many of the early symptoms do not direct attention to the vascular system and result in referral to various specialties, to which, by long tradition, this arteritis is not considered a relevant disease. Pre-pulseless Takayasu's arteritis, however, now requires inclusion in the differential diagnosis of rheumatoid disease, Still's disease, rheumatic fever, systemic lupus erythematosus,

CEREBRAL ISCHAEMIA

Syndromes of carotid and vertebro-basilar insufficiency

OCULAR ISCHAEMIA

Corneal opacities: cataract
Haemorrhage—vitreous: retinal
Optic atrophy: retinal atrophy
Amaurosis—transient: persistent
Arterio-venous anastomosis, etc.

Hypertension—renal artery
stenosis; coarctation
Intestinal angina } stenosis-
Haematemesis } mesenteric,
Melaena } coeliac

Limbs (symptoms)

Fatigue
Pallor
Paraesthesiae
Gangrene
Claudication pain

FACIAL ISCHAEMIA

Face—premature aging atrophy
Ulceration—palate, nose, ears
Saddle nose: gum atrophy
Jaw claudication

Heart failure (hypertensive)
Aortic incompetence
Angina: myocardial infarction
Aneurysm: coarctation (supra
or infra-diaphragmatic)

Leriche syndrome

Limbs (signs)

Pulses—weak, absent,
asynchronous

B.P.—unrecordable
low
normal
high

DIAGNOSTIC FEATURES: As for pre-pulseless phase + pulse abnormalities.
E.S.R. however may be normal. Aortography—positive.

FIG. 2.— Pulseless (occlusive) Takayasu's arteritis.

bacterial endocarditis, erythema nodosum syndrome, brucellosis, pericarditis, 'P.U.O.' and unexplained anaemia (Strachan and others, 1966). Aortic incompetence occasionally occurs due to dilatation of the aortic valve ring or rupture of an aneurysm (Schnire and others, 1964) and consequently the disease must also be considered in instances of isolated aortic incompetence.

Features which support the diagnosis in this early phase are persistent vascular bruits over the neck, abdomen and inter-scapular area, tenderness of the carotid arteries, slight inequality or asynchronism of the neck or limb pulses, elevation of the ESR and hyperglobulinaemia. Until examination for murmurs and pulse abnormalities becomes part of the initial assessment and re-assessment of patients presenting at the many specialist departments implicated, examples of this disease will undoubtedly be overlooked. Although bruits are the most specific

feature they may not be a *sine qua non* for the diagnosis for during the initial stage of peri-arterial inflammation this valuable sign is presumably absent. LE cells, rheumatoid factor and anti-nuclear antibodies (Hirsch and others, 1964) have occasionally been reported in the arteritis and these do not automatically exclude the diagnosis.

Radiology: Radiological investigation is essential. Routine plain radiography of the chest may show dilatation of the ascending aorta or the aortic arch and a film with increased penetration to demonstrate the descending thoracic aorta within the heart shadow may reveal unsuspected segmental dilatation. Calcification may occur anywhere in the aorta although it is very rare in the ascending part (Cheitlin and Carter, 1965). Rib notching has been reported but is a late feature. In suspected cases thoracic and abdominal aortography and lower limb arteriography should be

employed early rather than late in the hope of confirming the diagnosis before there is more than slight arterial narrowing or dilatation. At any stage these procedures delineate the extent, severity and character of the arteritis and allow the place of corticosteroid drugs, anti-coagulant therapy and surgery in treatment to be assessed. These aspects of the radiology of this disease have been reviewed by Grollman and Hanafé (1964) and Gillanders and Strachan (1965).

Pulseless (Occlusive) Takayasu's Arteritis

The features (Fig. 2) and differential diagnosis of this stage are quite different and have been dealt with in several excellent publications (Caccamise and Whitman, 1962; Ross and McKusick, 1963; Ash-Upmark, 1954; Currier, De Jong, and Bole, 1954). The symptom complexes which occur depend on whether the thoracic or abdominal aorta or the lower limb arteries are maximally involved.

Arteritis of the thoracic aorta: The protean ocular, cerebral, trophic and upper limb manifestations of classical Takayasu's disease are well known. Occasionally angina or myocardial infarction may result from coronary ostial stenosis.

Arteritis of the abdominal aorta and its branches: Hypertension due to renal artery stenosis is the commonest consequence of the arteritis in this site. Stenosis of other major branches has occasionally resulted in gastric ulceration, intestinal angina, melaena or the Leriche syndrome (Danaraj, Wong and Thomas, 1963; Sen, Kinare, Engineer and Parulkar, 1963; Hirsch and others, 1964). In both the abdomen and the chest aneurysm formation rather than stenosis may occur.

Arteritis of the lower limb vessels: Only if this arteritis is considered routinely will the occasional case be distinguished from the innumerable patients with atheroma and the rare instances where systemic lupus erythematosus, rheumatoid disease, pseudo-xanthoma elasticum or thromboangiitis obliterans are responsible for intermittent claudication and pulse deficiencies. An early history compatible with the pre-pulseless phase, unexplained elevation of the ESR segmental aortic dilatation and smoothness of arterial constrictions on arteriography (Wickbom, 1957) all warn of the possibility of Takayasu's disease, particularly in the female patient. Limited studies (Strachan and others, 1966) have also suggested that ultracentrifugal analysis of serum may be helpful by demonstrating a marked increase in the high density or alpha-lipoprotein fraction.

Aetiology and Pathology

The aetiology remains obscure. No spirochaetal, bacterial, fungal or viral agents have been directly incriminated. There is no good evidence that it represents a peculiar tissue reaction to tuberculous, syphilitic or streptococcal infection. It may be a form of hyper-sensitivity angiitis which can

be triggered by various aetiological agents. Judge and others (1962) offered the suggestion that it was an auto-immunopathy affecting vascular elastin with non-specific aggravation of the pathology at the aortic arch due to severe haemodynamic stress. Initial studies, however, have so far not demonstrated circulating auto-antibodies to constituents of the aorta or its branches (Hirsch and others, 1964; Wakisaka, Nagata and Swada, 1964; Strachan and others, 1966).

Pathology: The arteritis classically occurs in the aorta and its branches, particularly in their proximal segments but involvement of the pulmonary (Gillanders and others, 1965) and possibly the cerebral (Riehl and Brown, 1965) arteries has been reported. Macroscopically the arterial wall is thickened, the intima wrinkled, ostial stenosis obvious, and superimposed atheroma common. Histologically there is a panarteritis with necrosis and fragmentation of the elastic tissue and proliferation of the fibrous connective tissue. Round cell infiltration is characteristic but neither fibrinoid change nor eosinophils are seen. Giant cells have been described but cannot be taken to suggest any close relationship to giant-cell arteritis.

Treatment

Lifelong supervision is necessary. Activity of this chronic relapsing disease is reflected by the symptoms, elevation of the ESR and the development of bruits. The disappearance of a murmur may indicate improvement or progression to complete obstruction in a stenosed vessel. Aortography, repeated at intervals of months or years, to judge improvement or deterioration accurately is required for sound treatment.

Steroid drugs may be necessary for the suppression of the early systemic symptoms and to prevent progression of visualised stenotic lesions at this time or in the pulseless stage (Hirsch and others, 1964). Prolonged treatment may be necessary to carry a patient into a quiescent phase. It requires to be more vigorous and prolonged if stenosis is developing in vital arteries such as those feeding the cerebral circulation. In such circumstances long-term anti-coagulant therapy also appears advisable whether the disease is active or inactive. In general arterial dilatation requires less energetic treatment unless aortic incompetence or aneurysm formation appears likely.

Salicylates and vasodilator drugs have been used but their value is uncertain and requires further critical appraisal. Immuno-suppressive drugs such as azathioprine (Imuran) may have a role to play, particularly if steroids fail, but so far no reports of the use of such agents have been published.

Surgical procedures such as endarterectomy or by-pass grafting may be necessary to preserve an adequate cerebral circulation or to avoid an abdominal catastrophe. Hypertension due to renal artery stenosis may respond to nephrectomy but as the disease may be progressive by-pass grafting is preferable, if practicable.

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