A CASE OF TAKAYASHU'S SYNDROME: THE PULSELESS DISEASE

BY

L. TRIAS DE BES, J. G. SANCHEZ LUCAS, AND F. BALLESTA BARCONS

From Barcelona, Spain

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The Takayashu disease (or pulseless disease according to Anglo-Saxon authors) is universally considered as an exceptional clinical rarity, worthy of detailed study and of being placed on record. Thus an addition to the small group of cases so far reported throughout the world may represent an important step towards the better knowledge of this most unusual ischæmic syndrome. The instance of Takayashu disease that we now recount possesses all the characteristics of that malady and presents, at the same time, some new features worthy of comment.

The most striking feature of the disease is the complete absence of arterial pulsation in the main arterial trunks arising from the aortic arch. It was first described by the Japanese ophthalmologist Takayashu (1908) whose attention was drawn to the serious ocular accompaniments that inevitably develop. From 1908 till the present time Japanese authors have described a total of 58 cases, which have been previously brought together by Caccamise and Whitman (1952) in a comprehensive survey of the pulseless disease.

Very few cases have been reported from other sources. However, two important reviews of those observed in Europe have lately been published by Skipper and Flint (1952) and by Ask-Upmark (1954). These authors concur in noting the actual and relative infrequency of the disease in the white race, although they do not entirely agree as to the total number of cases recorded. A critical study comprising some other cases not hitherto reported has been published by Anton Garrido and Ramirez Guedes (1953). Finally our very typical case is now added, making a total of 37 non-Japanese cases. It should, however, be noted that some few of the recorded cases do not fulfil the strict criteria necessary for the diagnosis to be established beyond doubt.

Case Report

An unmarried woman, aged 19, was admitted to hospital on June 30, 1953. She had been able to work in the household and on the farm. There was no significant family or past personal history. She was of asthenic constitution. Weight 48 kg., height 1·46 m.; menses irregular.

At the age of 18 she had aural vertigo and some short syncopal attacks with slight convulsions. She was complaining of progressive weakness and had noticed undue muscular tiredness in both arms, so that she was apt to drop things; this symptom was of the nature of intermittent claudication of the arms. In 12 months there had been three bouts of transitory hemiparesis, lasting for about half an hour, accompanied by dysarthria. Abrupt movements of the head accentuated the giddiness and even provoked syncope. The patient presented an obvious hypersensitivity of the carotid sinus. She suffered from frequent pains in the head. A few weeks after the onset of the illness, ocular troubles set in with progressive blurring of vision. There was total loss of sight in the right eye two months before admission to hospital.

The clinical examination of the heart showed only an accentuation of the aortic second sound. The aorta showed increased pulsation but none could be felt in the carotid, axillary, brachial, or radial arteries. Oscillometry in the superior extremities showed a greatly reduced amplitude on both sides, while in the legs the blood pressure was 180/80 mm. Hg. The oscillometric index in both thighs was 3·5. Pulsation was normal in the femoral, posterior tibial, and dorsalis pedis arteries in both legs. The electrocardiogram at rest and after effort was normal. No abnormality was found in the veins. There was a slight decrease of skin temperature in both arms. No abnormal signs were found in the respiratory system and no septic foci were discovered. Examination of the alimentary and nervous systems gave negative results. There was slight bilateral hypoacusis.

The results of laboratory examinations were as follows. E.S.R.: 32 mm. in one hour. Erythrocytes: 3,870,000/cu. mm. Leucocyte count: 10,300, with normal differential count. Urine examination, no albumin or sugar. Wassermann reaction, negative. Blood sugar, 89 mg.; cholesterol, 134 mg.; plasma protein: 8·24 g.; albumin, 3·24 g.; globulin, 5·0 g.; in each case per 100 ml. The leucocytosis and increased E.S.R. persisted at subsequent examinations. Coagulation time, 3·5 minutes. Bleeding time, 1 minute. Ocular examination on 13/7/53 showed cataract in the right eye. In the left fundus the veins were overfilled and showed irregular dilatation. The discs were normal.

Ophthalmological examination (21/2/54). Anterior chamber: adhesions between the cornea and the iris causing obstruction to the flow of aqueous humour. There were extensive atrophic zones of the pigmentary layers and parenchyma in the peripheral part of the iris. The pupil was dilated and fixed. In the right eye there was a total cataract of a mother-of-pearl colour. In the left eye, the lens showed slight peripheral opacities in the equatorial zones and small peripheral and central punctiform opacities.

Fundus of the eye. In the right eye it was not possible to see the fundus on account of the cataract. In the left eye, irregular sinuous filaments and floating bodies were observed. These findings were most marked in the posterior region of the vitreous.

Retina and optic nerve: the retina showed a yellowish colour. The veins were tortuous and of a calibre larger than normal. Within, the blood flow could be observed, having the appearance of coffee grounds, and circulating slowly and irregularly. In the temporal zones there was seen an arteriovenous anastomosis in the form of a wide arch. In the superior peri-papillary portion of the retina there were small patches of whitish exudate, possibly remains of previous hæmorrhage.

The optic nerve was in process of atrophy, as was shown by its colour and the well defined cribriform lamella. The disc margins were irregular and indistinct. In the temporal portion there was a conspicuous accumulation of choroidal pigment. The visual acuity of the right eye was nil on account of the total cataract. In the left eye it was scarcely 1/10. The visual field was much reduced as a consequence of the optic nerve atrophy. Tension in the right eye was 50, in the left eye 20.

The assessment of the exceptional circulatory symptoms and signs and the peculiar features of the ocular disturbance combined to clinch the diagnosis of Takayashu disease. Throughout the year in which the patient has been under our clinical observation, there has been no change in the cardiovascular state. In a quiet environment and with avoidance of effort, there has been no repetition of the cerebral ischaemic episodes or the claudication of the superior extremities. The ocular disturbances have, on the other hand, become progressively worse. In the right eye, in which intraocular pressure was abnormally high, a malignant glaucoma developed necessitating the enucleation of the eye on 8/1/54. Subsequently the cataract in the left eye was removed in order to ameliorate, as far as possible, the serious defect of vision in that eye.

Morphological Examination of the Enucleated Eye. Sclera thin. No pathological products in the vitreous or in the chambers.

The microscopical examination revealed the presence of a connective vascular lamina, histologically of embryonic aspect, extending in front of the retina, with its greatest thickness at the level of the periphery of the papilla, becoming progressively thin peripherally, till it ends by a sharpened edge in the equatorial zone. In front of the papilla there exists a sort of truncated cone which at its vertex gets lost in the vitreous (Fig. 1). The conoid formation is not centred on the papilla but corresponds to an edge of it. It is formed by a very delicate fibrous connective tissue with blood vessels, very few cells and fine collagenous fibrils, with

abundant œdematous matrix. Towards the vertex of the " cone " the cellular density increases progressively, the cells being of two types, starred mesenchymal or fusiform and lymphoid cells, the former predominating. There were also some occasional isolated neutrophile granulocytes but without inflammatory foci or recent or old hæmorrhage. The vascular structure is very remarkable with dilated capillaries or venules with very fine walls (Fig. 1). Through the contour of the papilla the tissue proper of the " cone " extends in all directions before the retina, getting progressively thin in its advance till there finally appears a fine chink between it and the latter. The pellicle in question has the same structure as the suprapapillar cone, with predominance of the zones where the fundamental substance abounds; cells and fibrils are very scanty (Fig. 2 and 3).

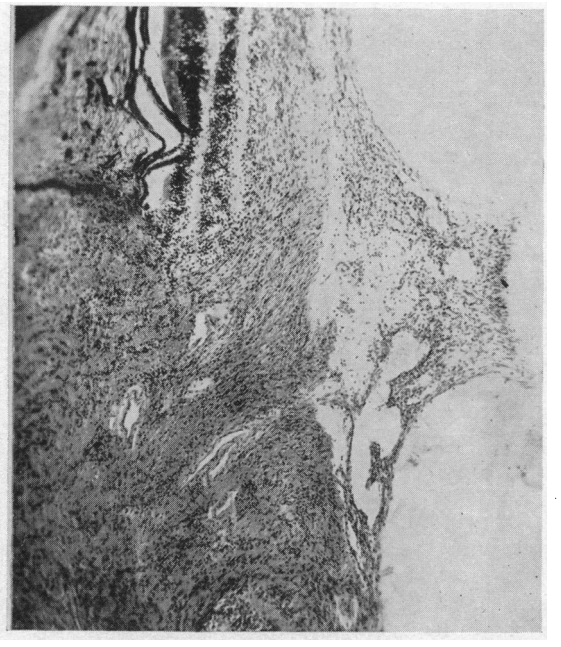

FIG. 1.—Hyaloid " cone " on the papilla (somewhat peripheral side of it). Note large vessel with aneurysmal dilatations.

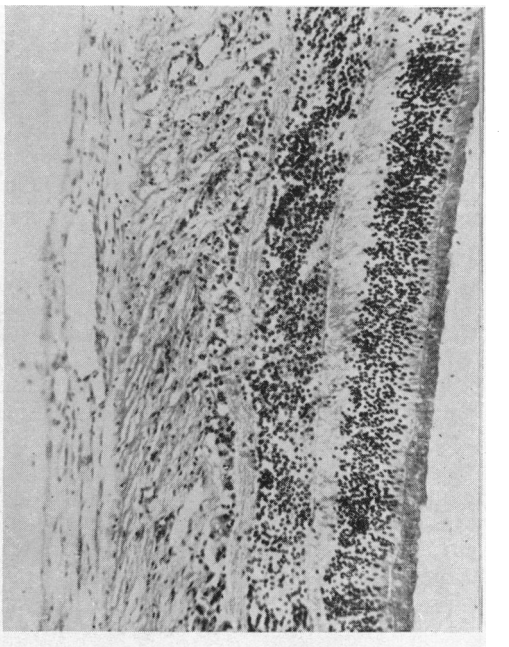

FIG. 2.—Disorganization of retina, with enlargement. Gliosis and rich vascularization of the layers of optic nerve fibres. Pre-retinal membrane with a large vein.

There is a cataract in the lens. The iris is atrophic. In the retina, apart from the lesions due to glaucoma, there are large calibre vessels sometimes with thick walls (especially of the arteries) in the nerve fibre layer, this condition being specific for this malady (Fig. 4). Neither lesions of the vascular walls nor thrombosis have been observed.

It is thought that the glaucoma has been provoked in this case by the synechiæ of the iris, being therefore a secondary glaucoma. However, it is noted that at the level of the irido-corneal angle there are not even vestiges of an earlier pathological process, which is important if we take into account the rapidity of the process. All the other lesions except the " pre-retinal membrane " of the " cone " may be attributable to the glaucoma. The " cone " and the membrane are therefore lesions peculiar to this disease, not hitherto described as far as we know.

No trace whatever of the hyaloid artery has been found nor cords resulting from its obliteration; nor are there indications of inflammation or hæmorrhage, old or recent, or other morbid process in the vitreous or the retina.

Have these ocular lesions any pathogenetic connection with the pulseless disease or are they in this case a pure coincidence with the fundamental process? The former hypothesis is supported by the evidence of mesenchymal derangements in the eye (the cone and its peripheral extension) and by the unusually large calibre of the retinal arteries.

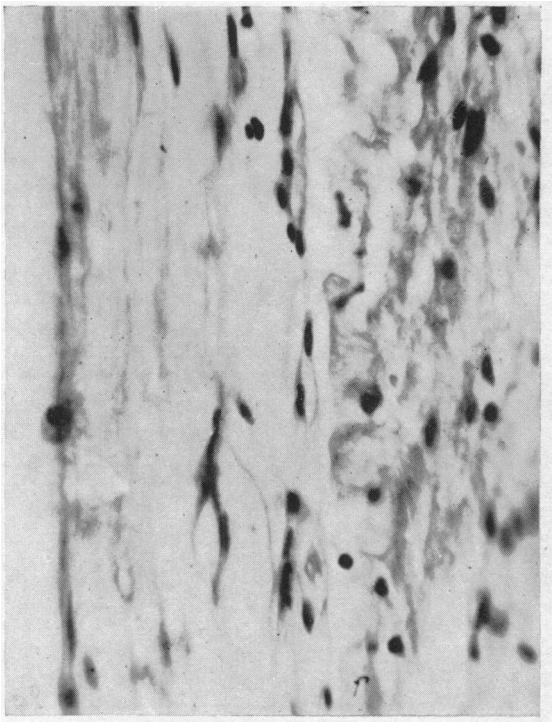

FIG. 3.—Pre-retinal membrane highly enlarged. Notice a fine crevice between it and the retina.

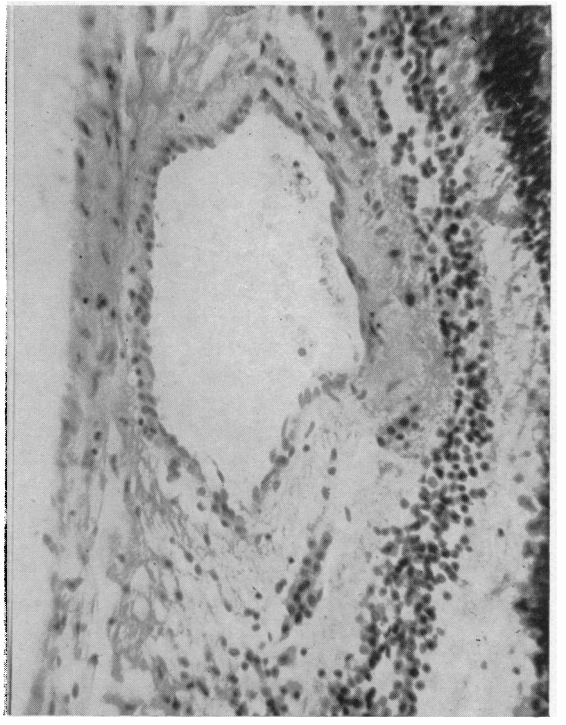

FIG. 4.—Inner part of retina with a large calibre artery in the layer of optic nerve fibres, making a bow on the inner molecular layer. Groups of disintegrated ganglion cells, above and on either side of artery.

DISCUSSION

Among previously reported cases there are few that present the classical features of pulseless disease manifested in the present example. These may be grouped as follows.

Suppression of the Arterial Pulsation in the Upper Half of the Body. Complete bilateral abolition of arterial pulsation of the carotid, axillary and radial arteries.

Symptoms due to this Circulatory Insufficiency. Claudication provoked by minimal muscular effort of either arm, headache, syncopal crises in connection with a hypersensitivity of the carotid sinus, and occasionally convulsions that occur either spontaneously or on sudden change of posture of the head. There may also be transitory hemiparesis.

Ocular Anomalies. Structural defects in the retinal vessels, particularly in the veins, leading to papillary degeneration and to progressive blindness; aneurysmal dilatations and arterio-venous communications of retinal vessels and formation of bilateral cataracts. In our case, glaucoma necessitating the enucleation of the right eye developed as well.

Precocious Appearance of the Ischæmic Syndrome. This patient was aged nineteen years.

The diagnosis of the Takayashu's syndrome is based not only on the existence of ischæmic disturbances of unusual distribution, but also on the circumstance of its appearing in youth. If we consider that the pathological basis of the disease is an obliterating thrombo-arteritis of the large vessels that arise from the aortic arch, the discovery in some necropsies of an obliterating panarteritis affecting the initial portion of the big arterial trunks of the aortic arch has suggested an inflammatory process caused by infection. The peculiar morbid process has to be distinguished from arterial obliteration that may occur in adult life by reason of syphilitic infection or arteriosclerosis, and in young adults of both sexes through malignant hypertension and arteriosclerosis. The evidence in this case of congenital mesenchymal abnormalities in the enucleated eye (pellicle, cone) support the pathogenetic hypothesis of the disease as developing on a

dysontogeneto basis. Among the 58 cases published by Japanese workers, the age is known in 44; in 36 of these the illness began before the age of twenty-five. Among these 36 there were 33 females. Of the 39 cases reported from other countries than Japan, only 10 (including the present instance) began to suffer from the disease before the age of 25 and all of these were females. Griffin (1939) has described a case in which a woman of 19 years showed this ischæmic syndrome in conjunction with persistent ductus arteriosus. The example recorded by Elliot *et al.* (1939) presented a combination of ischæmic disorders causing syncopal attacks and congenital abnormality of those arteries usually affected in Takayashu's syndrome.

SUMMARY

A case of Takayashu's syndrome (pulseless disease) has been described. The patient presented the classical features of this disorder comprising arterial disease of obliterative type involving the main trunks arising from the aorta in a woman aged 19. Absence of pulses and intermittent claudication in the arms, and syncopal attacks associated with carotid sinus sensitivity were the main cardiovascular symptoms.

Progressive and severe ocular disease leading to glaucoma and the ultimate enucleation of one eye was associated with the cardiovascular disease. These lesions occurring precociously in a young woman clinched the diagnosis. Mesenchymal abnormalities observed in the enucleated eye suggested a possible congenital basis for the disease.

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