Hist. Ophthal. intern. 2, 299 – 321 (1982)

DR. TAKAYASU'S ORIGINAL PAPER AND DR. OHNISHI'S ORIGINAL CASE HISTORY IN CONNECTION WITH MORBUS TAKAYASU - OHNISHI

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Introduction

The concept of the Takayasu-Ohnishi disease was introduced by Dr. TAKAYASU, who reported a case of unusual vascular changes of the retina, and by Dr. OHNISHI, who presented an additional case, before the 12th General Meeting of the *Japanese Ophthalmologic Society* at Fukuoka on 11th April, 1908. According to the excerpted version which appeared in the *Acta Societatis Ophthalmologicae Japonicae* of the same year, TAKAYASU (1908) communicated the case of a young female patient with symptoms characterized by „*wreath-like*" anastomoses and „*globular lumps*" occurring in the retinal blood vessels, and OHNISHI (1908) responded to this by mentioning his own observation of a female patient with similar vascular anomalies and an absence of the radial artery pulses.

Eigtheen years later, the subject was reopened by NAKAJIMA (1926), who admitted that a case of his own which he had formerly reported (1921) as having LEBER's *Aneurysma racemosum arterio-venosum retinae*, resembled much more to the cases reported by TAKAYASU and OHNISHI. Since that time, similar cases, certain and questionable ones intermingled, were occasionally reported in the literature. Nearly 70 cases were published up until 1943, and the disorder became known

as *TAKAYASU disease*. To the best of my knowledge, NIIMI (1941) was the first to use that eponym.

Most reports of the earlier years were chiefly concerned with the ophthalmological findings. Later, some investigators claimed that the disease was due primarily to stenoses of the arteries arising from the aortic arch. After World War II and since the publication of 6 new cases under the designation of „*pulseless disease*" (SHIMIZU and SANO, 1948, 1951), the disease all of a sudden began to draw widespread attention. More recently, UEDA and his associates (1969) coined the name „*aortitis syndrome*" for a group of conditions, including the TAKAYASU-OHNISHI disease.

The term „*TAKAYASU-OHNISHI disease*", adopted in this paper, was proposed by myself in 1957.

In July, 1977, Dr. YAMAGA of Otaru City, Hokkaido, wrote to me concerning a recent report by Dr. SAKAI (1977), who had cited the paper of TAKAYASU (1908a). Dr. YAMAGA asked in his letter specifically, if it had not been I who first pointed out the whereabouts of the original, but actually this was not the case. All the papers published in Japan and dealing with TAKAYASU's case, starting with the paper of NAKAJIMA in 1926 and including my own previous ones, had been based on the brief excerpt of TAKAYASU's (1908b) lecture appearing in the abovementioned journal. Nevertheless, I was particularly gratified at the news of the original's discovery for I had long been wishing to clarify a number of questionable points concerning the excerpt of TAKAYASU's lecture to the Japanese Ophthalmological Society.

The purpose of this paper is to introduce the important parts of TAKAYASU's original paper in contrast to the contents of the excerpt and to discuss some significant discrepancies between the two reports. The result of this comparative study has convinced me of the soundness of my own proposal that the so-called TAKAYASU disease should be renamed „*TAKAYASU–OHNISHI disease*". That is why the original record of Dr. OHNISHI's case will be reproduced in some detail.

Excerpt of Takayasu's Congress Lecture and Ohnishi's Additional Report

TAKAYASU's lecture (1908b) is entitled „*A case of unusual changes of the retinal blood vessels*". The following is a translation of the complete text.

„In May 1905, I met with a strange case in a woman. Before the onset of the present disease, she began to suffer from diminished visual acuity in September of the preceding year. Her vision was blurred in both eyes. At the same time, there occurred hyperemia of the conjunctiva. The symptoms subsided on medical treatment. In March of the following year her eyes became ill again. Up to that time, she had suffered from no other illness. The pupils were slightly dilated and the light reflex was somewhat sluggish. The (retinal) blood vessels were anastomosed in a wreath-like annular configuration encircling the papilla in a distance of 2 – 3 mm.

Another loop of anastomosed blood vessels was found farther peripherically, encircling the wreath-shaped inner anastomosis. In addition, there were arteriovenous communications. A slight elevation of the blood vessels above the plane of the retina was observed in the vascular ring encircling the papilla. The formation of globular lumps was observed here and there in the inner and outer vascular rings and in the blood vessels branching off from them. The location of these lumps changed from day to day, more frequent in the arteries. No inflammations were noted, though slight hemorrhages were seen in some parts. These symptoms were found in both eyes, but more conspicuously in the left. Visual acuity: 50 cm/n.d. No pathological changes were found in the urine and the internal organs. Potassium bromide and iodide was administered orally and saline was injected subconjunctivally. The vision was somewhat improved after that. The patient became able to count fingers at 2 meters. On July 11, injection of pilocarpine was commenced for stimulating perspiration. In August, the pupils became dilated and the eyeballs slightly hard. She developed chronic glaucoma and cataract occurred in the right eye. Cataract was observed in the left on July 14. The patient left hospital for a while on account of her household affairs, and returned on July 21. At that time her vision was worsened. The acuity in the right eye was 50 cm/n.d. and the left 1 meter/n.d. In August, she could hardly count fingers at 20 cm. Very eagerly she asked for cataract excision and was not desuaded by our admonition that any operation might be useless because of the fundal changes. Although the operation was performed without any complications, no improvement of vision was attained. The right eye lost its normal tension and could not distinguish light and dark. The left eye was afflicted with retinal detachment. This is a case in which the disease began at age 21. Otherwise healthy and no signs of tuberculosis. The essentials of the disease are not known to me."

The case of OHNISHI (1908) is reported immediately after the excerpt of TAKAYASU's lecture, and is part of the discussions of TAKAYASU's case:

„In my department, we have a case with similar symptoms. In particular, the annular anastomosis of the (retinal) blood vessels and the aneurysmal lumps bear a striking resemblance to the case reported by Dr. Takayasu. One of the most extraordinary conditions about this patient is that it is not possible to feel the pulsation of the radial arteries, no matter how we try. Her arms are cold. The pupils are dilated and the lenses have gradually become opaque. The extraction of the lenses resulted in hyphema. Now it is almost impossible to observe the eyegrounds. The patient retains a very weak visual acuity."

Takayasu's Original Paper

In 1908, TAKAYASU also published a more detailed account of his case, entitled „*An unusual transformation of retinal blood vessels*" (TAKAYASU, 1908a). Next to the title, he states that the paper was originally presented on April 11, 1908, at the General Meeting of the *Japanese Ophthalmological Society* held at the Fukuoka School of Medicine. This paper is accompanied by an illustration of the fundus of the right eye. (fig. 1). The following is an excerpt from this paper:

„The patient, Mrs. Hayashi, aged 22, was first examined on May 8, 1905. The light-conducting parts of the right eye were normal, but marked anomalies were observed in the retinal blood vessels (fig. 1). They were branching out laterally, 2 – 3 cm away from the papilla, and anastomosed in the form of a ring encircling the papilla. The radial branches from the ring were so thin at their origin as to be barely observable, but lumpy dilatation appeared thereafter followed by gradual narrowing. Some of these branches terminated in cecal pouches. Others anastomosed with each other and formed another ring. Moreover, due to changes in the volume of blood flow, the same blood vessels were sometimes conspicuously dilated and at other times so markedly stenosed as to be hardly visible. Close to the papilla, some blood vessels were slightly elevated into the vitreous space. Strong hyperemia was found on the papilla, and minor extravasations close to or surrounding it. These anomalies occurred mainly in the ar-

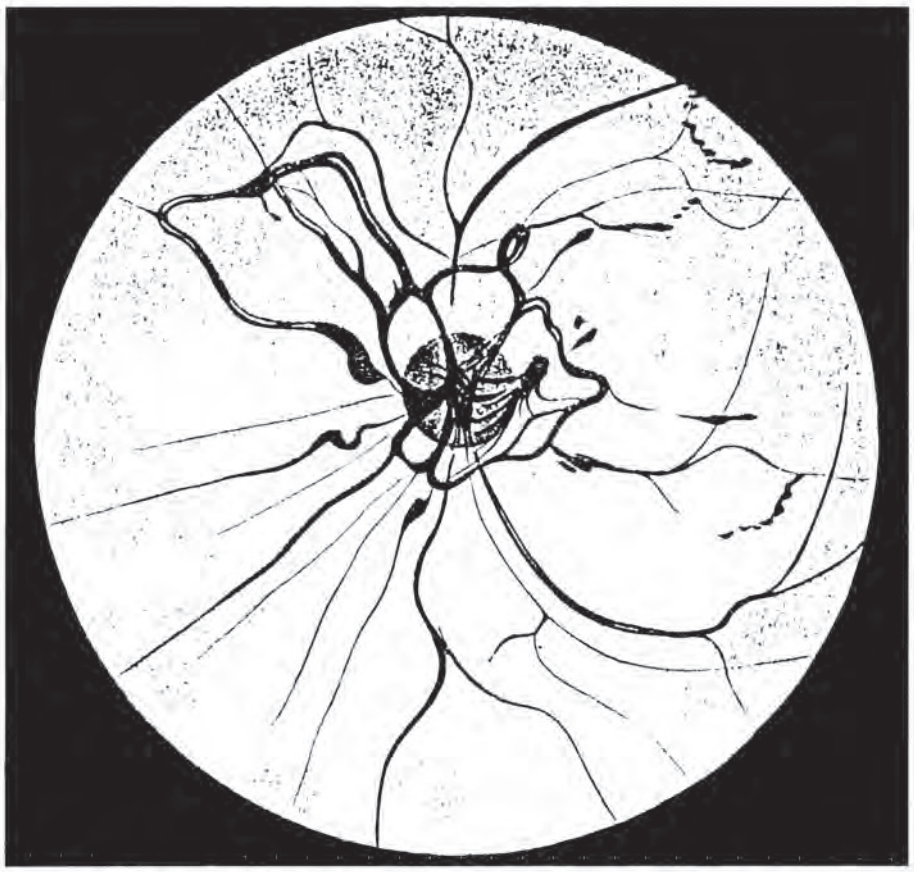

Fig. 1: TAKAYASU's case. Female aged 22. Drawing of the right fundus. Inverted image. 14. May 1905. (TAKAYASU, 1908)

teries, but it appeared that the anastomoses of veins with arteries were causing the blood flow to perfuse from the former to the latter. Examination of the left eye revealed that it was in a state almost identical to that of the right except for the existance of a greater number of blood vessels and hemorrhages around the papilla. The left eye presented therefore an extremely complicated aspect with clots intermingling with blood vessels so that the author had to abandon any attempt to describe the condition in greater detail, to say nothing of drawing any sketches."

The description in the original paper, pertaining to the patient's history and the clinical course of the disease, is almost identical to that in the excerpt. After the first examination, she was admitted on May 11, left hospital on July 16, and was then treated as an outpatient. On September 22, she was admitted again for cataract extraction of the left eye and discharged 3 weeks later. After that, the patient did not visit Dr. TAKAYASU until February 25, 1908, when she received the last examination:

„The left eye was aflicted with retinal detachment and atrophy. The shape of the eyeball was irregular and slightly depressed. A marked mydriasis was observed in the right eye with the iris reduced to a narrow wheel. The lens was turbid like milk and appeared distended. It was assumed that retinal detachment was induced by a pronounced reduction in the intraocular pressure. Vision had been completely lost in both eyes two years before, and the patient was unable to distinguish light and dark."

On general examination, no abnormalities had been found in the urin or internal organs. The patient had no history of gynecologic or internal diseases. Although there are a number of instances where the use of words differs between the original text and the excerpt, there are no contradictions as far as the essential facts are concerned. TAKAYASU sums up his findings as follows:

„The patient became ill at age 21. Although her face had the features of a pulmonary tuberculosis patient, no symptoms of internal disease were found nor did pathological changes ensue. No evidence of past iritis nor syphilitic symptoms were detected. The patient was inflicted by the disease in both eyes. She has been suffering from it since September 1904, and cataracts appeared in early July of 1905. To this, retinal detachment followed at the end of the same year, and within a little over one year after the onset of the illness, she lost her vision completely. The patient's symptoms can be characterized by the anastomosis and lumpy dilatation of the retinal blood vessels. All the symptoms appearing thereafter can be considered induced by these two symptoms."

In the meantime, TAKAYASU searched the literature seaking references for his case and reported as follows.

„The disease bears certain similarities to the first case appearing in VON HIPPEL's (1904) paper. Marked differences exist, however, when compared with the clinical cases reported by FUCHS (1882) and cases reported by MAGNUS (1874) and SEYDEL (1899). Consequently, it is thought that no literature has been published on the disease."

TAKAYASU concludes his paper as follows:

„The author finds exceptional difficulty in trying to determine the essentials of the disease. The case is different from Dr. FUCHS's (1882) so-called traumatic arteriovenous aneurysm and it is not possible to classify it as the very slowly progressive inflammatory disease reported by VON HIPPEL (1904). It can be assumed that the disease is probably a kind of congenital arteriovenous aneurysm suggested by Leplat[1]. The aneurysms had not been found due to the lack of visual disorders at the initial stage. After the patient's physical development was completed, however, anomalies appeared in the walls of the blood vessels due to some changes occurring in the nutritional metabolism and also due to the confluence of the arterial and venous blood flows, leading to softening and dilatation. The patient became aware of her illness only after her visual acuity decreased pronouncedley as a result of chronic glaucoma, induced by congestion and hemorrhage of the retinal blood vessels. The patient is believed to have developed phthisis bulbi following a series of new afflictions such as retinal detachment and cataracts."

The Original Case History of Ohnishi

There had been no published record of OHNISHI's case except for the excerpt mentioned before (OHNISHI, 1908). In 1961, I published a paper on OHNISHI's case on the basis of the copy of his clinical record, borrowed from Dr. IKUI, then Professor of Ophthalmology at Kyushu University (HIROSE, 1961). Since my pa-

[1] TAKAYASU quotes no literature but probably refers to the paper of M. LEPLAT (1902) of Liège.

per was written in Japanese and was not accompanied by a summary in any European language, I should like to reproduce OHNISHI's case in some detail:

The patient, Mrs. Nagata, aged 23, was first examined by Dr. Ohnishi on February 27, 1907. She was a village dweller. Her parents were consanguineous, both healthy, and had no eye illnesses. The grandparents had died but had no noteworthy history of illness. Of her 6 siblings, 3 had died and the other 3 were healthy and had no eye afflications. Five years before their marriage, her husband had suffered from chancre and pains under the clavicle, and had undergone syphilotherapy with non-prescription medicines.

The patient was healthy as a child and married at age 15. After giving birth at age 18, her menstruations became irregular. She had been suffering from wandering pains in the nape of the neck and in the chest two years before she visited Dr. Ohnishi. She complained moreover that she occasionally felt sudden nausea and anxiety before going to sleep. Since April of 1906, she had been afflicted by attacks of syncope preceded by nausea, dizziness and convulsions. She was first diagnosed as having neuroasthenia and then hysteria at the Kumamoto Prefectural Hospital and received treatment for a period of a little over one month. Around September of the same year, her seizures were cured. Two months before she appeared before Dr. Ohnishi, Mrs. Nagata caught a cold and developed a rhinostenosis accompanied by radiating pains around the paranasal parts. Furthermore, she experienced a transitory paralysis of the limbs. Her appetite, physique and nutritional state were normal.

Fig. 2: OHNISHI's case. Cataract of the left lens. Wheel-like opacities in the cortex near the equator and plumous opacities under the posterior capsule. Drawing by Dr. OHNISHI himself on 27. February 1907.

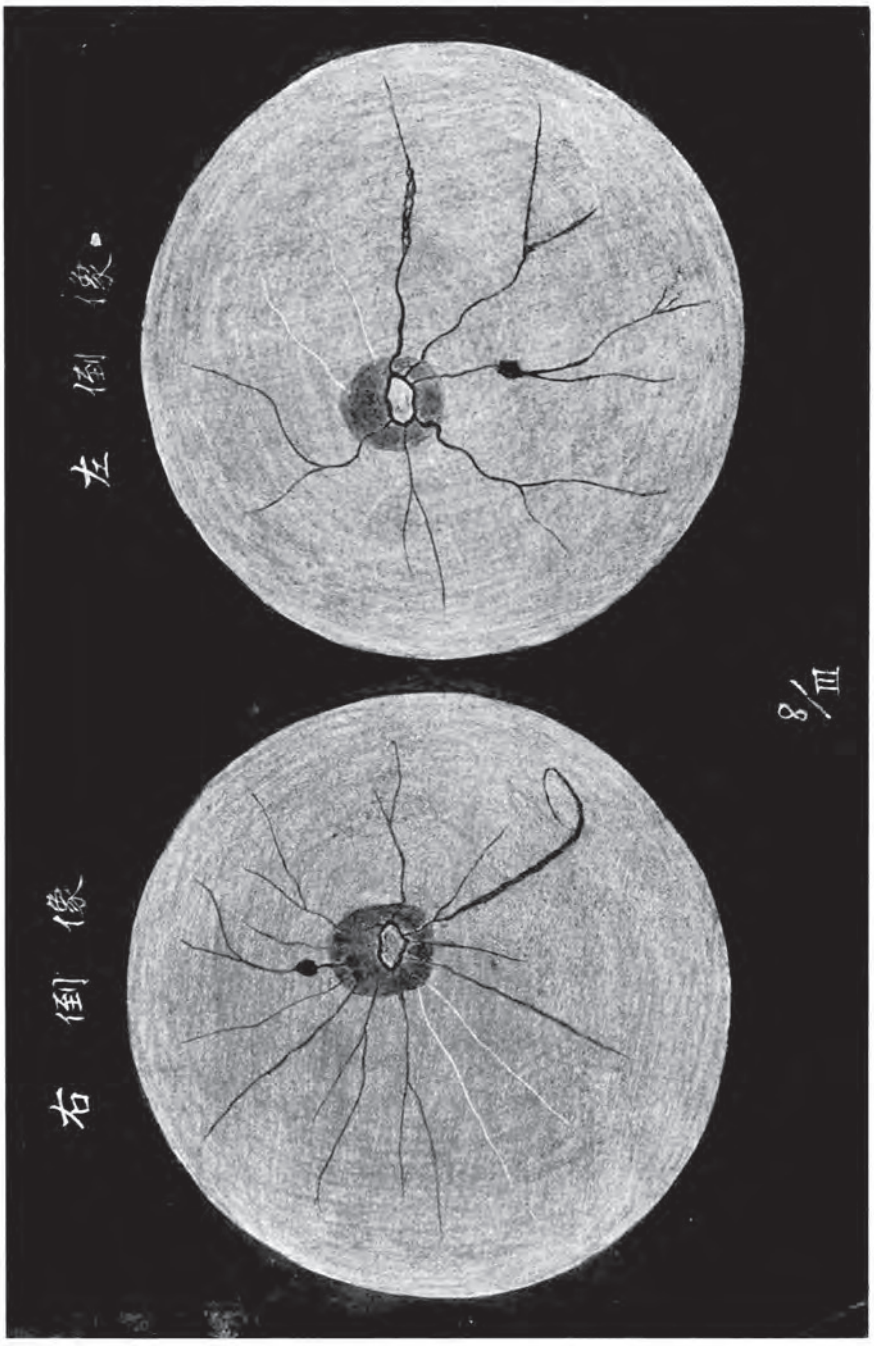

Fig. 3: OHNISHI's case. Fundus of the right (left side) and left (right side) eyes. Inverted images. 8. March. 1907.

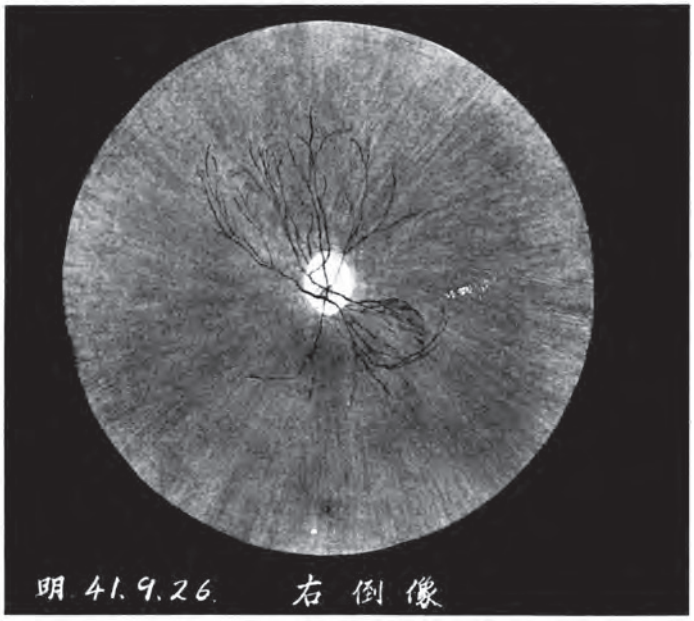

Fig. 4: OHNISHI's case. Right fundus, inverted. 26. September 1908.

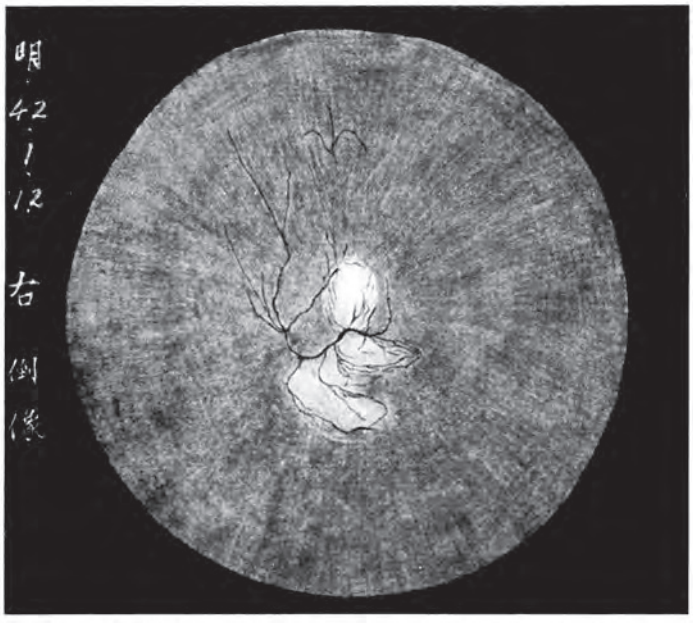

Fig. 5: OHNISHI's case. Right fundus. inverted. 12. January 1909.

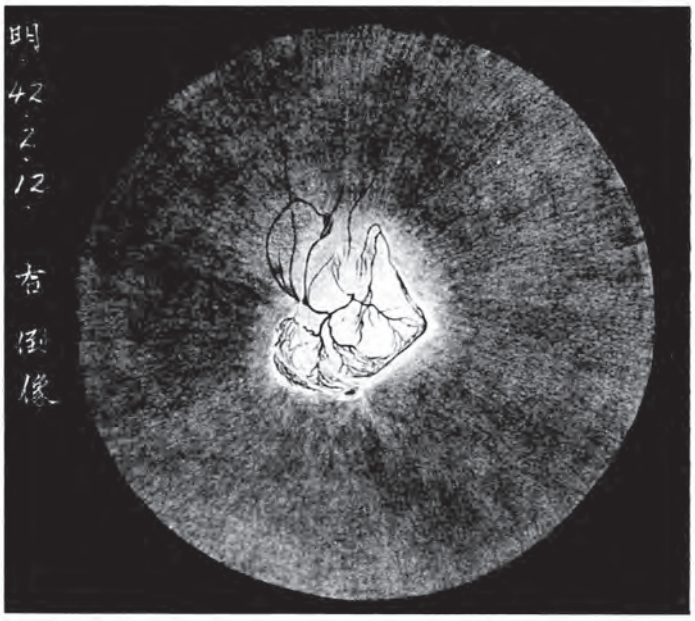

Fig. 6: OHNISHI's case. Right fundus. inverted. 12. February 1909.

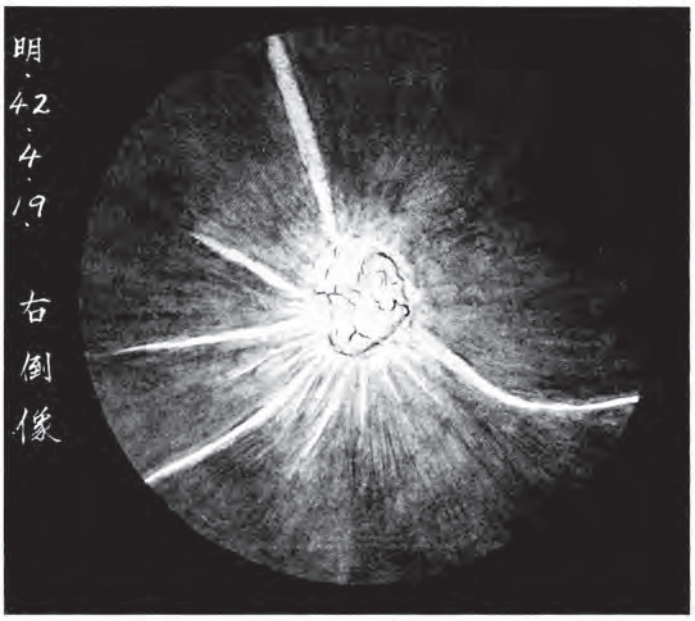

Fig. 7: OHNISH's case. Right fundus. inverted. 19. April 1909.

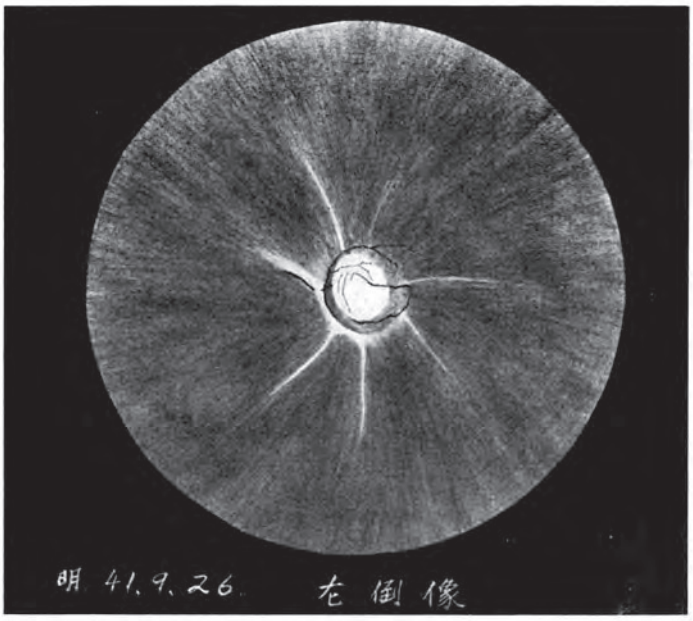

Fig. 8: OHNISHI's case. Left fundus, inverted. 26. September 1908.

Fig. 9: OHNISHI's case. Left fundus, inverted. 3. June 1909.

With the exception of having contracted epidemic conjunctivitis in infancy, she had never experienced any eye problems. However, her vision started to blur from April, 1906, onwards coinciding with the time she began to have the convulsive attacks. Thereafter she noticed paroxysmal darkening of her vision. Visual acuity gradually weakened. At times, she was troubled by headaches and dull pains, deep inside her eyes. When turned upwards, her face became very pale and she was subject to dizziness and syncope.

On the first examination by Dr. Ohnishi, the patient's visual acuity was 0.1 (n.c.) in the right, 30 cm/n.d. in the left and 0.1 in both. A wheel-like shadow was visible in the left lens on examination with retroillumination and a plumose turbidity, on focal illumination (fig. 2). In the right lens, a similar opacity of less extensive degree was found but no dark shadow.

In the fundus of both eyes (fig. 3), a congestion of the papilla was observed. In the right fundus, an annular vascular ring in the form of a side-long ellipse was formed approximately in the center of the papilla. The branches of blood vessels starting from the papilla were very thin at their origin and some of them did not seem to originate from the annular ring. In some distance from the papilla, they widened to some degree. A branch running temporally and inferiorly showed a considerable dilatation and its tip formed an elliptical configuration. An aneurysm was found in the middle of the blood vessel running superiorly. Two vessel branches had transformed into white lines in the superior nasal part.

In the left fundus, a ring of blood vessel of a similar shape as in the right was found around the center of the papilla, and six branches of blood vessels started from the ring. They were somewhat dilated and tortuous. The branch running nasally had a spindle-shaped dilatation in the middle and it appeared that the stream of blood was observable. The branch running superiorly had an aneurysm-like dilatation just before it bifurcated. In both eyes the distinction between arteries and veins was not clear. The number of blood vessels and their ramifications was relatively few, and blood vessels were not seen in the peripheral areas of the fundus. (cf. fig. 1 of TAKAYASU's paper).

The patient was hospitalized on the day of her first examination. Treatment and observation were continued for 3 years and 8 months until she left hospital on November 8, 1910. The patient was examined regularly by Dr. RYUKICHI INADA, then professor of internal medicine at Kyushu University. She ws recorded to have such symptoms as anomalies of the heart on auscultation and percussion, and very weak radial pulses. The common carotid arteries and temporal arteries could not be felt. The pulse waves of the radial arteries, as demonstrated by sphygmography, were very flat, but a result obtained later (June 1909) suggested some improvement of the pulsations. A diagnosis of syphilitic aneurysm of the aortic arch was based mainly on roentgenographic findings. On May 16, 1908, Dr. KENKICHI ASAHI, professor of dermatology, examined her and reported as follows.

„Although it is said that the patient's husband is syphilitic, she has no history of contracting syphilis nor syphilitic symptoms at present. However, aneurysms, among young people in particular, are generally considered syphilitic."

In March 1907, the eyegrounds were extremely difficult to observe due to the rapid maturing of the cataract in both eyes. Cataract extraction was performed on the right eye on June 12, 1907.

Hyphema occurred five days after the operation and lasted, repeating improvement and worsening, for ten months. On September 26, 1908, the visual acuity of the right eye was before face/n.d. (+ 14D). In the fundus (fig. 4) the papilla was hyperemic. Blood vessels, 8 to 9 in number, were seen starting from the papilla but it was not possible to distinguish arteries from veins. The two starting from

the temporal-superior part of the papilla formed a bush-like loop, and those running inferiorly formed three parallelly situated loops through ramification and anastomosis. As time went on, the form and configulation of the blood vessels changed (figs. 5 to 7). The number of blood vessels decreased due to their transformation into white lines. Since June 1909, the light sense of the right eye was completely lost, and retinal detachment followed from August.

The left eye underwent cataract excision on July 7, 1908. Hyphema followed but was absorbed approximately 10 days after.

On September 26, 1908, V.s. = 30 cm/m.m. (+ 14D). In the fundus (fig. 8), the papilla was round in shape, pale in color, and atrophic. A depression of glaucomatous nature was found. There were only three to four retinal blood vessels on the papillary surface and other two skirting half of the papillary circumference were found. An annular turbidity of the retina was seen surrounding the papilla with seven white turbidity lines radiating out from it. These white lines appeared to be the remnants of retinal blood vessels. On June 3, 1909 (V.s. = 30 cm/m.m.), the hub-and-spokes area of turbidity had become less conspicuous (fig. 9). Only two short blood vessels were observed, one starting in the retina just temporally of the papilla, splitting into three branches and spreading to the inferior edge and the surface of the papilla, and the other starting just nasally of the papilla and reaching the nasal edge of the papilla without ramifications.

Until around December, 1909, visual acuity of the left eye remained from 30 cm/m.m. to 1 meter/m.m. On January 8, 1910, V.s. was before face/m.m. The papilla had a pale yellow appearance. Only a short blood vessel was seen starting in the retina just temporally of the papilla, splitting into three branches and spreading in the superior and inferior part of the papillary surface. Ocular tension was found normal at that time but dropped after June 21, 1910. On August 10, the eyeball was extremely soft. Atrophy of the iris was pronounced. Vertical wrinkles were readily formed on the cornea. It seemed that the left eye had also been afflicted with retinal detachment. On November 7, 1910, the left eye retained minimal light perception.

Discussion

I have once tried to reproduce an illustration of the retinal blood vessel configuration of TAKAYASU's case, based on his description in the excerpt (1908b). The result of my effort is shown in fig. 10. It was very difficult to obtain an accurate understanding of what was meant by the term „*wreath-shaped*" anastomosis encircling the papilla. The word wreath-shaped conveyed to me the image of a bunch of flowers arranged in a radial fashion, or of a loop formed by stringing individual flowers. My drawing, however, resembled rather the center of spider's web and does not at all look like a wreath or even a flower. This shows that it is not easy to grasp the actual condition of the eyegrounds of TAKAYASU's case from the description appearing in the excerpt of his lecture.

The problem is that many scholars who took up the study of TAKAYASU's case conceived no doubt about the appropriateness of these terms and took at face value that a „*wreath-shaped*" anastomosis of the blood vessels in the eyeground is an essential symptom of the disease. Nevertheless the drawings presented by these scholars look like anything but a wreath. At best, some might be likened to misshapen flowers and the others only showed the formation of two or three blood vessel communications around the papilla.

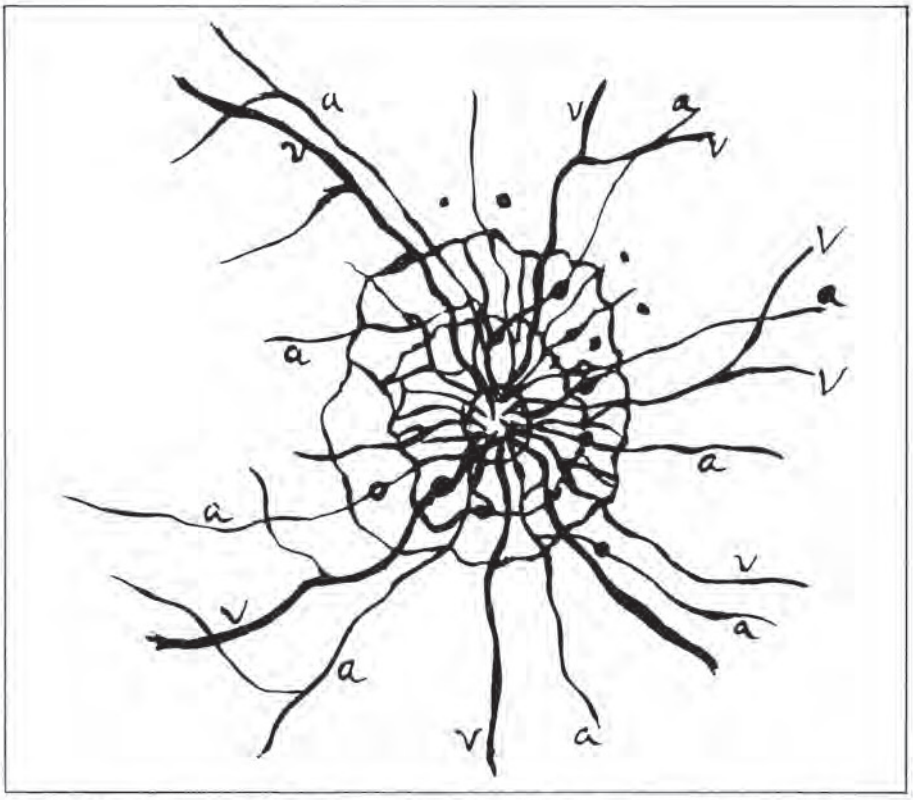

Fig. 10: Vascular changes of the right eyeground in TAKAYASU's case, reproduced on the basis of the description in the excerpt. (HIROSE, 1964)

The original paper of TAKAYASU, however, contains no mention of a wreath-shaped anastomosis. It merely describes that „*the blood vessels were branching out laterally, 2 – 3 mm from the papilla, and anastomosed in the form of a ring encircling the papilla.*" This account corresponds well with Dr. Takayasu's original drawing (fig. 1), and the changes that took place in the eyegrounds are easily understandable, if the form of anastomosis is not called wreath-shaped.

The excerpt reads, moreover, „*another loop of anastomosed blood vessels was found further peripherically, encircling the wreath-shaped inner anastomosis*" and „*in addition, there were arteriovenous communications*". The original paper, however, simply states that some of the radial branches from the ring „*anastomosed with each other and formed another ring*". When checked with the original figure, the „loops" appearing in the excerpt are hardly an appropriate description, as there are only partial communications of a few blood vessels in the superior and inferior nasal quadrants of the retina. In short, it is not possible to liken the retinal anasto-

moses to a wreath on the basis of the description and the drawing in TAKAYASU's original paper and it is quite understandable that he made no use of the term ,,*wreath-shaped*" in this contribution.

I understand that the presently used term ,,*TAKAYASU disease*" has been derived from the belief that the wreath-shaped anastomosis constituted the characteristic symptom of the disease. This can readily be proved by the fact that the above misconception of the *TAKAYASU-OHNISHI disease* is still held by many ophthalmologists today. The fault can be attributed to the fact that the original paper of TAKAYASU had not been available in the past.

In *TAKAYASU-OHNISHI disease* it is well known that the dilatation and tortuosity of the retinal blood vessels occur due to a stagnation or an insufficiency of blood flow. At the terminal stage, when the blood flow can be observed within the vessels, the vessels often become dilated and irregularly shaped, reminding us of a Vienna sausage, and the blood corpuscles flow slowly in *rouleau* form.

In the excerpt of TAKAYASU's lecture, however, no such phenomena are described. It merely mentions the existence of arteriovenous communications and refers to the presence of ,,globular lumps" of the blood vessels, the movement of these lumps from day to day, and relatively greater concentration of these lumps in the arteries.

In the original paper, on the other hand, we find that there were lumpy dilated parts and very thin thread-like parts in the retinal blood vessels branching off from the annular anastomosis, some of these branches becoming thick at the tip and ending in cecal pouches, and others anastomosing with each other forming another ring.

Looking at fig. 1, we notice that there are a number of newly formed blood vessels on the surface of the papilla dotted with aneurysms. Dilatation, stretching, and tortuosity can be observed in many of the blood vessels encircling the papilla, some of them becoming very thin in some places. Such peculiar phenomenona are present also in the blood vessels running radially form the papilla. Small beads of aneurysms appear in the areas slightly above and below the macula.

When we compare the above parts of the original paper to the excerpt, the difference is so significant that it is difficult to believe that these two papers were written by the same author and deal with the same case. With regard to blood flow, Dr. TAKAYASU reports his observation in the original paper that, due to a ,,change" of blood flow, the same blood vessels were sometimes markedly dilated and at other times became so contracted that they were scarcely visible. He relates moreover that the retinal arteriovenous anastomoses were seemingly causing the blood to perfuse into the arteries, suggesting the existence of abnormal blood flow where venous blood is flowing into the arteries. Such anomalies in blood flow, however, are completely different from the symptoms observed in what we call today *morbus TAKAYASU-OHNISHI*.

As has been mentioned, the excerpt relates the formation of ,,*globular lumps*'' and the change in location of these lumps from day to day, more frequently in the arteries, but does not explain the nature of these lumpy formations.

In the meantime, the author and his colleagues have conducted an experiment on rabbits (HIROSE and KIYA, 1963). When the ascending aorta and/or the arteries originating from the aortic arch were constricted in these animals, the formation of small aneurysms in branches of the central retinal vessels could be observed. These small aneurysms were not necessarily migratory nor concentrated in the arteries, but it was assumed that these must have been the ,,*globular lumps*'' described in TAKAYASU's report. We considered at the time that TAKAYASU himself had been the first to observe the small aneurysms that are so commonly found in patients with TAKAYASU-OHNISHI disease and that he had used the term ,,globular lumps'' to describe them.

In the original paper, however, no mention is made of ,,globular lumps''. We merely find a passage mentioning ,,lumpy dilatation'' but it is difficult to determine from the context whether the globular lumps refer to ,,lumpy dilatation'' or to small aneurysms. To put it simply, the symptom of globular lumps, as recorded in the excerpt, is quite incomprehensible. Had I had the original text available instead of the excerpt, I would never have erred in citing TAKAYASU as the discoverer of the small aneurysms.

As for the etiology of the disease, TAKAYASU states in the excerpt that ,,*the essentials of the disease are unknown*'' to him. On the other hand, the original paper reads ,,*It can be assumed that the disease is probably a kind of congenital arteriovenous aneurysm suggested by Leplat.*'' After this, TAKAYASU presents his inference on the genesis and progress of the disease. In the concluding part, he avoids a clear-cut difinition and his words are less assertive. Nevertheless, it can safely be said that TAKAYASU assumed the patient to suffer from a congenital arteriovenous aneurysm. I am therefore convinced that if all the scholars after him had referred not to the excerpt but to the original paper, no one would have concluded the case as a disease of unknown etiology.

With regard to the patient's general condition, we find that the descriptions are virtually the same in the excerpt and original paper, though in more detail in the latter. In short, TAKAYASU reports that otherwise no disease was found in the patient. I deeply regret that the original paper does not contain an account of the results of circulatory tests and main artery pulse count. If we assume that TAKAYASU's account on the general state was correct, then the disease which he described is not the disease which we think of as *TAKAYASU-OHNISHI disease* today. Needless to say, the disease is caused by the stricture of the arterial trunks originating from the aortic arch, its main symptoms being the loss or weakening of the pulsations of the affected arterial trunks and branches.

In 1926, 18 years after TAKAYASU and OHNISHI reported their cases, NAKAJIMA reopened the study of this disease. Already in 1921, he had published a paper entitled „*Über einen Fall von Anastomose der Netzhautgefäße mit verschiedenartigen congenitalen Anomalien*". In this earlier paper, NAKAJIMA had concluded that his case should be classified as LEBER's so-called retinal arteriovenous cirsoid aneurysm (*aneurysma racemosum arterio-venosum retinae*). Five years later, however, he came to change his opinion after reading the excerpt of TAKAYASU and OHNISHI's report. In this second paper NAKAJIMA concludes as follows:

„My case first appeared to resemble very closely LEBER's cirsoid aneurysm and was thought to be resonably diagnosed as such. But when the two cases reported by Takayasu and Ohnishi were taken in account, it has obviously become necessary to admit that my case differs in not a few respects with Leber's. Therefore it can be thought that the case comes under a completely different type of disease."

In NAKAJIMA's case, the patient was a 19-year-old female. At age 18, she developed a number of symptoms including an extensive retinal arteriovenous anastomosis with sporadic occurence of spindle-shaped blood vessel dilatations. No globular aneurysms were found. No blood vessels were found in the peripheral areas of the retina. Such symptoms were observed in the fundus of both eyes. (fig. 11). Vision was extremely week and the patient later developed cataracts. Hams were heard in different pitches on both side of the neck and in the subclavian fossae indicating the existence of anomalities of the cardiovascular system. The pulse of the right subclavian artery was palpable at the back of the right clavicle. The heart was enlarged and the sounds were dull. Noises were heard over the abdominal aorta and femoral arteries. Palpation of the antebrachial arteries and dorsal arteries of the feet was not possible.

Had NAKAJIMA not quoted from the excerpt but directly from the original paper when comparing his own case with that of TAKAYASU, the result would probably have been different. NAKAJIMA had originally diagnosed his case as LEBER's retinal arteriovenous cirsoid aneurysm, while TAKAYASU had assumed his to be LEPLAT's congenital retinal arteriovenous aneurysm. Had NAKAJIMA known about this, he would most probably never have declared, as he did, that these three cases belong to a new type of disease different from other reported cases. Nor would he later have published a paper entitled „*Some corrections with regard to a case of retinal arteriovernous anastomosis accompanied by various congenital anomalies previously reported by the author*".

But, in fact, NAKAJIMA had also come across OHNISHI's additional report and he found that it described the loss of both radial pulses in addition to the retinal changes and the developement of cataracts. Because in his own case, the loss of radial pulses had been one of the major symptoms, this coincidence of circulatory and ocular disorders must have prompted him to conclude that all three cases fell under a new type of disease, completely different from any others.

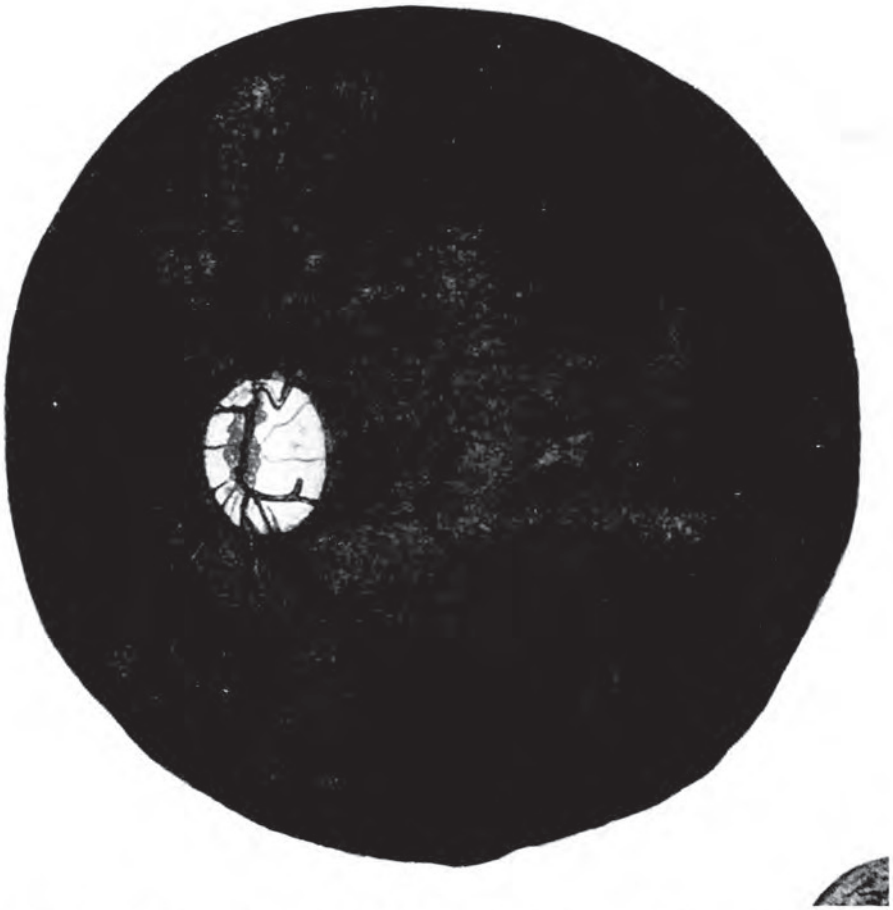

Fig. 11: Nakajima's case. Drawing of the left fundus. Inverted image. (NAKAJIMA, 1921)

The report of OHNISHI's additional case is particularly significant in that it pointed out for the first time the loss of both radial pulses. Although this attracted the attention of NAKAJIMA, the other researchers taking up the study of TAKAYASU's case failed to take due note of OHNISHI's report. Because this case was first reported by an ophthalmologist as ,,*unusual changes of the retinal blood vessels*'', the focus of the researchers' attention was directed to the fundal changes of the eye. Most of the studies on this subject were made by ophthalmologists and the ,,*wreath-shaped*'' anastomosis encircling the papilla was considered the characteristic symptom of the disease. As the result, it has come to be known as TAKAYASU disease.

Thereafter, not only ophthalmologists but also internists, surgeons and psychiatrists started to make this disease the subject of their studies and researches were conducted from an interdisciplinary viewpoint. It has thus become known that the disease is not simply a local eye affliction but has a certain relationship with disorders of the blood flow in the arterial trunks originating from the aortic arch. Still at this stage many scholars, including even those who raise the loss of radial artery pulses as one of the trias of the disease, seem to be ignorant of the name of Dr. OHNISHI who was the first to ever mention this symptom.

In 1959, I asked the late Dr. TAMURA, a student of Dr. OHNISHI and then professor of ophthalmology at Kyushu University, to produce a summary of the record of OHNISHI's case. Based on it, I published a paper and proposed that the so-called TAKAYASU disease should be renamed *TAKAYASU-OHNISHI disease* (HIROSE, 1967). The ethiology and developement of the disease can better be understood by adding OHNISHI's case to that of TAKAYASU. The proposal was accepted by not a few, while some ignored it. Now that the essentials of the disease are almost accurately comprehended and it is generally accepted that the ,,*wreath-like*'' anastomosis is not necessarily an essential symptom of the disease, the name of Dr. OHNISHI should not be forgotten as the reporter of the first case manifesting the cardinal symptom of the disease, the loss or weakening of the radial artery pulses.

Tables I and II give a comparison of the ophthalmological and general symptoms of the cases of TAKAYASU (1908), OHNISHI (1908) and NAKAJIMA (1921).

Regarding the ophthalmological changes, the cases of TAKAYASU and NAKAJIMA have many symptoms in common, whereas only aneurysms and spindle-shaped vessel dilatations are found in OHNISHI's case. Nevertheless, it is quite reasonable to consider OHNISHI's case to be the first reported case of *morbus TAKAYASU-OHNISHI*, because we now know that the disease can occur without an annular anastomosis around the papilla and that there are several other diseases which are accompanied by annular anastomoses. On the other hand a weakening or loss of the arterial pulses (induced by a stricture of the arterial trunks originating from the aortic arch) is recognized today as the major symptom of *morbus TAKAYASU-OHNISHI*, and this was first found in OHNISHI's case. NAKAJIMA only mentions the loss of the radial and dorsal feet pulses.

Table I Comparison of ophthalmological symptoms observed in cases reported by Takayasu (1908), Ohnishi (1908) and Nakajima (1921).

Takayasu's case (Fig. 1)	Ohnishi's case (Fig. 3)	Nakajima's case (Fig. 11)
Patient: Age 22, female, married	Patient: Age 23 years 10 months, female, married	Patient: Age 19, female
Irregular blood vessel anastomosis encircling the papilla of both eyes. Blood vessel communications were found further out, partially encircling the former.	Small annular blood vessels in the center of the papilla of both eyes. 11 branches of blood vessels radiating from the papilla, almost independent from the vascular ring (right eye) and 6 branches from the central ring (left eye). No blood vessel anastomosis.	Annular anastomosis encircling the papilla. Many similar symptoms to Takayasu's case observed. Extensive blood vessel communications.
No transformation of blood vessels in white lines. Thread-thin parts and lumpy dilatation of blood vessels.	Transformation of blood vessels into white lines observed. No clear arteriovenous distinction. Blood vessels slightly tortuous with some spindle-shaped dilatation. One aneurysm formed in each eye.	No transformation of blood vessels into white lines. Most of the anastomosed branches dilated and totuous except for some thin ones. Though spindle-shaped dilatation recorded, no description about lumpy aneurysms.
Abnormal blood flow causing the change in location of dilated and narrowed parts of blood vessels. Paradoxical blood flow where venous blood is flowing into arteries.	No description concerning blood flow except that blood flow seemed to be observable in one branche of blood vessel.	No description on blood flow abnormalities.
Many newly formed blood vessels on the papillary surface. Extensive hyperemia of the papillae. No inflammatory symptoms.	Very small number of blood vessels on the papillary surface. No newly formed blood vessels. Hyperemia observed. No inflammatory symptoms.	Newly formed blood vessels (?) on the papillary surface. Papilla hyperemic. No inflammation.
Blood spots on the retina. No blood vessels observed in the peripheral eyeground.	No retinal bleeding. No blood vessels in the perphery of retina. The fundus remained dark, in particular at the terminal stage.	Dotty blood spots or small aneurysms (?) noted. No blood vessels found in the perpheral retina. Dark fundus.
Cataract extraction afterwards. Prognosis not good. Retinal detachment (both eyes).	Cataract extraction afterwards. Prognosis not good. Retinal detachment (both eyes).	Cataract extraction. Prognosis not good.
Ophthalmologic diagnosis: Congenital retinal arteriovenous aneurysm.	Retinal atrophy induced by syphilitic aneurysm of the aortic arch.	Retinal arteriovenous cirsoid aneurysm (1921) and later unknown eyeground disorder.

Table II Comparison of general symptoms observed in cases reported by Takayasu (1908), Ohnishi (1908) and Nakajima (1921).

Takayasu's case	Ohnishi's case	Nakajima's case
No abnormalities noticed.	Thoracic dermal venous network conspicous.	
	Pulse can be felt in the juglar fossa.	Humming over the upper and lower clavicular fossae.
	Heart enlarged and heart sounds dull.	Heart enlarged. Heart sounds dull.
	Second sound of the aorta slightly accelerated. Very weak radial pulse (both). Vessel walls not hardened. Very weak pulse in upper arm arteries; vessel walls hardened and tortouos. Palpation of common carotid arteries very difficult (both sides). Pulse almost absent in the right carotid artery and very weak on the left. Temporal artery pulse very weak.	No radial pulse felt since childhood. At times forearm pulse extremely weak.
	Abdominal artery pulse clear and normal. Femoral artery pulse clear and normal. Palpation of the dorsal arteries of the foot very clear. Diagnosis: Aortic arch artery aneurysm of syphilitic nature. Face very pale when turned upwards. Attacks of vertigo and syncope.	Murmurs over the abdominal aorta and femoral arteries. Palpation of the dorsal arteries of foot not possible

Summary

Since Nakajima (1926) first paid attention to the case reports by Takayasu and Ohnishi, all papers dealing with the Takayasu-Ohnishi disease have cited the excerpts of their congress communications, which appeared in the Acta of the Japanese Ophthalmological Society in 1908. Only recently has it become known that Takayasu had published, in the same year, another more detailed paper about his case elsewhere.

On reading this original paper we find a number of significant discrepancies in the description beween the original version and the excerpt. The terms ,,wreath-shaped'' anastomosis and ,,globular lumps'' of the except read ,,annular'' anastomosis and ,,lumpy dilatation'' in the original. And while Takayasu speaks of an ,,unknown'' etiology in the excerpt, his conclusion in the original paper is that the case should be classified as a congenital arterio-venous aneurysm of the type described previously by Leplat. The presence of general symptoms is denied in both the excerpt and the original. The anomalies of blood flow described in the original are not those commonly observed in what we call ,,morbus Takayasu-Ohnishi'', today.

When compared with Takayasu's patient, another case described by Nakajima (1921, 1926) has many of the ophthalmological findings in common, with the additional absence of the radial pulses, a change that had up to then only been reported by Ohnishi. On the other hand, Ohnishi's case differs with respect to the ophthalmological findings in that only retinal aneurysms and spindle-shaped blood vessel dilatations were observed. Nevertheless, it appears that Ohnishi's case is actually the first reported case of ,,morbus Takayasu-Ohnishi''. We can therefore conclude that the term ,,morbus Takayasu'' is an erroneous nomination, based on an insufficient description in the excerpted lecture and due to the ignorance of the more detailed original paper.

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Zusammenfassung

Seit Nakajima (1926) erstmals auf die Fallbeschreibungen von Takayasu und Ohnishi aufmerksam wurde, haben sich alle Veröffentlichungen zum Thema Morbus Takayasu-Ohnishi auf die auszugsweisen Darstellungen der beiden Autoren bezogen, die im Sitzungsbericht der Japanischen Ophthalmologischen Gesellschaft vom Jahre 1908 erschienen waren. Erst seit kurzer Zeit ist bekannt, daß Takayasu eine ausführlichere Darstellung seines Falles schon einmal im selben Jahr an anderer Stelle veröffentlicht hatte,.

Bei Studium dieser Originalarbeit finden wir eine Reihe wesentlicher Unterschiede in der Beschreibung des Krankheitsbildes gegenüber der späteren Darstellung im Kongreßbericht. Statt der Begriffe ,,girlandenförmige'' Anastomosen und ,,globuläre Klümpchen'' des Kongreßberichtes heißt es in der Originalarbeit ,,ringförmige'' Anastomosen und ,,plumpe Erweiterung'' der Gefäße. Und während der Kongreßbericht von ,,unbekannter'' Ätiologie spricht, wird das Krankheitsbild in der Originalarbeit als ,,kongenitales arterio-venöses Aneurysma'' der von Leplat beschriebenen Form klassifiziert. Das Vorkommen von Allgemeinsymptomen wird sowohl in der Originalarbeit als auch im Kongreßbericht geleugnet. Die Durchblutungsanomalien, die in der Originalarbeit beschrieben werden, entsprechen demnach nicht der Vorstellung, die wir uns heute vom Morbus Takayasu-Ohnishi machen.

Beim Vergleich des von Takayasu beschriebenen Patienten mit dem später von Nakajima mitgeteilten Fall finden wir deutliche Übereinstimmungen im ophthalmologischen Befund. Zusätzlich imponierte bei diesem jedoch ein Fehlen der Radialispulse, ein Symptom, das als erstem Ohnishi bei seinem Patienten aufgefallen war. Andererseits bietet der Fall von Ohnishi gewisse Unterschiede hinsichtlich des Augenbefundes, wobei lediglich Netzhautaneurysmen und spindelförmige Gefäßerweiterungen auffielen. Trotzdem scheint die Annahme berechtigt, daß der Fall von Ohnishi tatsächlich die Erstbeschreibung eines Falls mit „Morbus Takayasu-Ohnishi" darstellt. Wir können daher feststellen, daß der Begriff „Morbus Takayasu" irreführend ist. Er wurde geprägt aufgrund einer unzureichenden Fallbeschreibung bei verschollener Originalarbeit.,

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