Hashimoto's Disease and Dr. Hakaru Hashimoto

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Introduction

There are many diseases or syndromes designated by a personal name. In the index of Harrison's or Cecil's Textbook of Internal Medicine, there are around 200 names of doctors who discovered diseases that are named for them. Of these, Japanese names are used in Hashimoto's thyroiditis, Kawasaki's disease and Takayasu's arteritis. As a mark of respect for Dr. Hakaru Hashimoto, his picture is used in the logo of the Japan Thyroid Association (Fig. 1). Hashimoto's disease is a very common illness of the thyroid gland; however, surprisingly little is known about its discoverer, Hakaru Hashimoto.

Discovery of Hashimoto's Disease

After joining the first Department of Surgery, Fukuoka Medical College of Kyoto Imperial University, Hakaru Hashimoto examined thyroid tissue samples and discovered new pathological characteristics. He reported this as an independent new disease in Archiv für Klinische Chirurgie, the German journal of clinical surgery in 1912 at the age of 31 (Fig. 2) [1]. This report marked the discovery of Hashimoto's disease. The title of his paper is shown in Fig. 3.

The paper itself was quite long (30 pages and 5 figures). It consisted of five sections, beginning with a brief introduction and followed by clinical descriptions of four middle-aged female patients. Then came the histological changes of thyroid tissues, which were the core of the paper. The fourth section was a review of previous reports and a discussion, and the final section was five precisely drawn illustra-
Zur Kenntniss der lymphomatösen Veränderung der Schilddrüse (Struma lymphomatosa)

Von

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Fig. 3. Title of original paper.

Fig. 4. Cited Fig. 5. in the original paper. Histology of struma lymphomatosa.
   a. Lymphoid follicle.
   b. Degenerated thyroid follicle.
   c. Giant cells.
   d. Hyperplastic interstitium with prominent round cell infiltration.

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However, this epoch-making discovery caught little attention in the world of medicine at that time. It was not until the 1930s when struma lymphomatosa, reported by Hakaru Hashimoto, started to receive recognition in the medical world. In 1931, Drs. Graham and McCullagh reported the same disease as struma lymphomatosa, which had been detailed by Hakaru Hashimoto, and endorsed the conclusion that struma lymphomatosa was an independent illness [2]. Since then this disease has been referred to as Hashimoto's thyroiditis in the United States and European countries.

It was not until the 1950s, after World War II, when the name Hashimoto's disease, was reintroduced back in Japan. This was performed by Dr. Hachine Akita, who had been studying in the United States. He was a younger alumnus of Hakaru’s alma mater.
The life of Dr. Hakaru Hashimoto

Hakaru Hashimoto was born May 5, 1881, the third son in a family that had been practicing medicine for generations in the village of Midai, Nishitsuge about 9 km east of Iga Ueno. Iga Ueno was originally a castle town in the mountainous part of the Kinki district. Historically, it is the home of the Iga school of Ninjia. Iga Ueno is also known as the hometown of Basho Matsuo, the famous Haiku poet. Fig. 5 shows the monument of Dr. Hakaru Hashimoto in front of the house where he was born. Fig. 6 shows his original hospital. The whole area of the hospital grounds must have been around 1,000 tsubo, a little less than one acre. The hospital has been maintained as a home for the aged and was recently rebuilt. After spending his childhood in his birthplace, Hakaru left and entered the First Mie Prefectural Junior High School at Tsu. Today, this is the Mie Prefectural High School at Tsu and is under a new school system. It was about this time when Hakaru started thinking of pursuing medicine. Given the fact that many of his classmates also became active in the medical field, there may have been some underlying factors that inspired the students to pursue studies in medical science. As for Hakaru, he was greatly influenced by his grandfather, Gen’i Hashimoto, a well-known doctor in that region who had studied Dutch medicine at the end of the Edo Era. He was trusted enough to be allowed to wear a sword as a doctor by the feudal lord.

Aspiring to study medicine, Hakaru advanced to the third National High School at Kyoto under the old school system and on to the Department of Medicine at Kyusyu Imperial University. He entered the Department of Medicine at Kyusyu Imperial University in Fukuoka in 1903. Kyusyu Imperial University was founded originally as Fukuoka Medical College of Kyoto Imperial University that same year. In 1910, the college became Kyusyu Imperial University. Hakaru was the first graduate of this school. Upon graduation from the university in 1907, he entered the First Department of Surgery and studied under Prof. Hayari Miyake for four years. During this period, Hakaru Hashimoto examined the thyroid tissues removed from four patients of middle-aged women and discovered new pathological characteristics never reported before.

Soon after the publication of his paper, Hakaru Hashimoto went to Europe for further study. Hakaru must have aspired to test the results of his research in Western countries, where the level of medicine was advanced. For this purpose, he chose Germany. He studied pathology under Prof. Kaufman at Goettingen University. However, within two years, World War I broke out and Hakaru was forced to return Japan without accomplishing his purpose. Upon his return, Hakaru returned to his alma mater for a short time. However, he decided

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Fig. 5. The monument of Dr. Hakaru Hashimoto at his birthplace.

Fig. 6. The hospital of Dr. Hakaru Hashimoto.
to take over the family practice in his hometown because the family was financially strapped.

It was April in 1916 that Hakaru started practicing medicine. He was 35 years old. It quickly became known throughout the countryside that a doctor, a graduate of the Imperial University who had studied abroad, had begun practicing medicine. Surgery was the main field in his hospital. Beside, he treated all patients equally regardless of their status. He was a doctor who put into practice the saying "Medicine is a benevolent art". Riding in the hospital's rickshaw, he traveled great distances across the mountains and fields to visit patients. He did not get married until he was thirty-nine, four years after he opened his practice. He had three sons and one daughter. Hakaru had too many patients to take care of. Fig. 7 shows a photo together with hospital employees at the hospital entrance. There was only one occasion on which he invited his families to a one-day picnic at Mt. Wakakusa in Nara (Fig. 8). Suddenly, at age 52, fate dealt him a crushing blow. He was infected with typhoid fever on one of his house calls. His life ended unexpectedly on January 9, 1934, without recognition for discovering Hashimoto's disease. Hakaru was a man who sincerely loved and cared for his patients. What's more, his pursuit of knowledge was marked by continuous effort and diligence.

**Hashimoto's Disease at Present**

As described above, Hashimoto's disease was initially recognized by characteristic histopathological abnormalities in the thyroid gland, different from the abnormalities of thyroid cancer. In 1956, Drs. Roitt, Doniach et al. [3] found autoantibodies in the sera of patients with Hashimoto's disease [3]. Coincidentally, in the same year, Drs. Rose and Witebsky reported that changes in the thyroid tissue of rabbits that were immunized with thyroid extracts as an antigen were similar to the changes seen in Hashimoto's disease [4]. Following these discoveries, the concept of organ-specific autoimmune disease was established, and Hashimoto's disease was recognized as one such disease. In the nineteen-seventies, an anti-thyroid microsomal hemagglutination antibody test was developed in Japan [5] and these antibodies were found in 10.0% of adult women in the general population. Moreover, one-third of these women were found to have slight enlargement of the thyroid gland [6]. Furthermore, postmortem histological examination has revealed that positive anti-thyroid microsomal antibodies in subjects without overt thyroid disease are associated with the presence of lymphocytic infiltration in the thyroid gland [7]. Thus the concept of Hashimoto's disease has been
expanded on the basis of the concept of autoimmune thyroiditis, and mild cases of Hashimoto's disease are thought to exist in one of 30 adult women in the general population. It has also been clarified that postpartum thyroiditis frequently develops from these subclinical or mild cases of Hashimoto's thyroiditis [8].

Following these discoveries, autoimmune abnormalities have been found in many other diseases. Today, many diseases are known to be autoimmune diseases. The discovery of Hashimoto's disease was a significant step in the history of the discovery of abnormal autoimmunity and endocrine disorders. However, the root cause of the disease has yet to be clarified. Finding answers in this area is among the most important current goals in modern medicine. It just may be the wish of Hakaru Hashimoto, who received little recognition in his life, that this task is to be accomplished by a Japanese. The statue of Dr. Hakaru Hashimoto (Fig. 9) is looking to us, thyroidologists, for break through in discovering the etiology of autoimmune diseases.

Acknowledgements

The authors thank Mr. Kenichi Hashimoto, the eldest son of Dr. Hakaru Hashimoto, for giving us much important information about his father. We also thank Mr. Sunao Tsunetou for his help collecting valuable documents and materials. The skillful assistance of Ms. Yuko Sahara is also acknowledged.

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