Two Autopsy Cases that Cultivated the Foundation of My Interest in Dementia in Clinical Settings

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I have been involved in clinical practice and the research of dementia, focusing on Alzheimer’s disease. Alzheimer’s disease is the most common form of dementia in Japan and Dementia with Lewy Bodies is the second most common form. It was as a psychiatrist at Juntendo Koshigaya Hospital during the early stages of my career that I established the foundation of my interest in dementia. Here, I would like to describe the two autopsy cases of dementia that I experienced there. Although both of the patients were clinically diagnosed as having Alzheimer’s disease, the autopsies revealed a different definitive diagnosis. This discrepancy became the cornerstone of my clinical practice in dementia.

Key words: dementia, Alzheimer’s disease, dementia with Lewy bodies, autopsy

Introduction

In 1981, I graduated from Faculty of Medicine, Juntendo University and decided to pursue a career in psychiatric medicine. The fact that as a little boy I grew up in employee housing adjacent to a psychiatric hospital in Kawagoe-City, Saitama, contributed significantly to this decision. Back then, I used to play freely on the hospital’s property, spend time with in-patients on a daily basis and join their sports festivals and Bon dance festivals. Initially, I was interested in clinical practice and performing research on schizophrenia, however in graduate school, professor Reiji Iizuka (a chief professor of department of psychiatry, Juntendo University at the time) gave me a research topic on Alzheimer’s disease. This sparked my interest in the disease, and since then I have been involved in clinical practice and the research of dementia, focusing on Alzheimer’s disease.

Juntendo Tokyo Koto Geriatric Medical Center, my current workplace, opened in 2002. After its opening, I was in charge of out-patients care on Mondays as a part-time doctor. In 2007, I assumed the position of director of Department of Psychiatry, at ever since I have been engaged in medical practice as a full-time doctor. The Geriatric Medical Center has 404 beds, 129 of which are on the ward for dementia treatment. According to the clinical statistics on demented in-patients of the geriatric medical center in 2018 (Figure 1), 60% of the in-patients had Alzheimer’s disease and 15% had Dementia with Lewy Bodies. These findings indicate that Alzheimer’s disease is the most common form of dementia in Japan and Dementia with Lewy Bodies is the second most common form.

Alzheimer’s disease and Dementia with Lewy bodies

The first patient with Alzheimer’s disease, the most common form of dementia, was a 51-year-old women who was described by the German psychi-
Alzheimer developed dementia at the young age of 51 and died within a little more than 4 years. Neuropathological findings of her brain showed senile plaques and neurofibrillary tangles. Although the concept of senile dementia was established at the time, the case was published because dementia rarely developed at such a young age. Subsequently, in 1908 Kraepelin—an authority in psychiatric medicine at the time—named the disease Alzheimer’s disease. Kraepelin is known for developing the disease concepts of schizophrenia and bipolar disorder.

Alzheimer was born in Würzburg in southern Germany, so to celebrate this fact the first Alzheimer’s Association International Conference was held in Würzburg in 1989. The house where Alzheimer was born is preserved as a museum.

An autopsy case of dementia with Lewy bodies, the second most common type of dementia, was first reported by the Japanese psychiatrist Kenji Kosaka in 1976. In this case, Lewy bodies, previously known to appear in the brain stem, were observed in large numbers in nerve cells in the cerebral cortex. In 1995, the first International Dementia with Lewy bodies Conference was held in England, diagnostic criteria were set and Dementia with Lewy bodies gained international recognition. After studying in Germany, Dr. Kosaka concurrently worked in clinical practice at Tokyo Metropolitan Matsuzawa Hospital. I was also working at Matsuzawa Hospital at that time, and I was able to receive guidance from Dr. Kosaka. He then became a chief professor at the Department of Psychiatry, Yokohama City University.

### Two cases I experienced at Juntendo Koshigaya Hospital

The case reports by Alzheimer and Dr. Kosaka suggested the importance closely examining cases, we encounter in daily clinical practice. Although I have been working predominantly at Juntendo Tokyo Koto Geriatric Medical Center since I become a professor, it was as a psychiatrist at Juntendo Koshigaya Hospital during the early stages of my career that I established the foundation of my interest in dementia. Here, I would like to describe the two autopsy cases of dementia that I experienced there. Although both of the patients were clinically diagnosed as having Alzheimer’s disease, the autopsies revealed a different definitive diagnosis. This discrepancy became the cornerstone of my clinical practice in dementia.

The first patient had prion disease. She was hospitalized at Juntendo Koshigaya Hospital for 21 years with a clinical diagnosis of Alzheimer’s disease. When I was in charge of her, she was confined to her bed and in the terminal phase of the disease. The patient, a 59-year-old woman, made me realize what the terminal phase of Alzheimer’s disease looks like. At age 38, she started to experience memory loss. At age 42, she visited the department of psychiatry at Juntendo University Hospital for the first time, and at age 43 she had difficulty living at home and was admitted to Juntendo Koshigaya Hospital. At age 46, her spontaneous speech started to decrease, and she became bedridden at age 49. At age 50, she developed myoclonus. A cranial computed tomography scan showed severe brain atrophy (Figure 2). At age 59, she died with pneumonia and an autopsy was performed. Her brain weight was 640g. Gerstmann–Sträussler–Scheinker syndrome, a type of prion disease, was diagnosed on the basis neuropathological findings (Figure 3). Gene analysis was performed at the laboratory of professor Tateishi of Kyusyu University and revealed a point mutation at codon 145 of the prion protein. This case is cited in the New Oxford Textbook of Psychiatry.

The second patient had dementia with Lewy bodies. The female patient was hospitalized in...
Juntendo Koshigaya Hospital, and I had been in charge of her since she first visited the out-patient department. Her clinical diagnosis was Alzheimer’s disease with delusion. At age 76, she started complaining her memory loss. At age 77, she sought help from her neighbor saying that a man was in her kitchen, and she visited the department of psychiatry of Juntendo Koshigaya Hospital. She had memory disturbance, disorientation, persecution complex, and muscle rigidity in her upper limbs. A cranial computed tomography scan showed cerebral atrophy that was slightly predominant in the frontal lobe (Figure 4). Considering her medical history, in these day dementia with Lewy bodies would be placed first on the list of possible differential diagnosis, but at that time the clinical diagnosis was Alzheimer’s disease associated with delusion and hallucinations. The patient died with pneumonia at the age of 78, and an autopsy was performed. Her brain weight was 990g. Dementia with Lewy bodies was diagnosed on the basis of the neuropathological findings (Figure 5). I received direct guidance on the pathological findings from Dr. Kosaka, this case was
published at that time (Clinical Atlas of Dementia, 1992)\(^5\). In this book, Alzheimer’s disease is the first item in the table of contents, followed by vascular dementia, Pick’s disease, and Creutzfeldt–Jacob disease (CJD). Dementia with Lewy bodies appears at the end of the list after CJD which occurs in 1 in 1 million people. In these days, dementia with Lewy bodies appear after Alzheimer’s disease at the list. However, in those days it was regarded as a rare disease that was difficult to diagnose.

In both cases presented above, a definitive diagnosis was made through intervention of specialists from the network of Prof. Reiji Iizuka. Looking back on each patient’s medical history after the definitive diagnosis was obtained at autopsy, I could see key point for the diagnosis, which made me realize the importance of carefully analyzing clinical symptoms and obtaining pathological diagnosis.

**Conclusion**

In today’s clinical practice of dementia, various diagnostic image analysis methods are available for clinical diagnosis. However even when some case without dementia is diagnosed clinically, protein deposition is detected by amyloid imaging in the case. Nevertheless, the rate of autopsy is decreasing. We need to recognize again the importance of neuropathological examination at autopsy by following and respect once again to the two autopsy cases described above. They taught me the importance of paying careful attention to signs and symptoms and performing autopsies to final diagnosis, and this knowledge became the cornerstone of my clinical practice.

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