The First Neuropathological Studies on HDLS

I read with considerable interest the article in the Journal by Riku et al on hereditary diffuse leukoencephalopathy with spheroids (HDLS) describing the early changes in this relatively rare disease (1). Riku et al referred to the original article as a source of the primary clinical findings. In our original article, however, we presented the first detailed neuropathology studies of HDLS (2). At that time, we used routine histological and histochemical techniques as well as electron microscopy. The findings of Riku et al look quite similar to ours, but the pictures are now in color. Nevertheless, the first neuropathological analyses of this disease were published more than 30 years ago.

The brief history behind this disease is as follows: I went to Professor Patrick Sourander’s laboratory, Sahlgren Hospital in Gothenburg, Sweden, for neuropathology training in 1980. Patrick had 2 cases in which both clinical and neuropathological findings resembled those of multiple sclerosis (MS), as has also recently been reported (3). Because I had done my thesis on MS, Patrick gave me these cases to determine whether they represented some form of MS or something else. Initially, the findings seemed to resemble MS; however, after careful studies, we found eosinophilic swollen axons, which also stained positively with silver staining. The 2 patients studied belonged to the same family. We were additionally able to investigate the third patient who also belonged to this family. I continued the electron microscopy studies while working in Albert Einstein College of Medicine with help from Professor Cedric S. Raine. On the basis of the neuropathology findings, Patrick and I named this disease, “hereditary diffuse leukoencephalopathy with spheroids” (2). The first neuropathological report of this disease was presented in 1982 in the 24th Scandinavian Congress of Neurology by Röyttä et al (2). The clinical and neuropathological data were subsequently published as a Supplement in Acta Psychiatr Scandinavica in 1984 (4). In the preface of this Supplement, the exact role of each author was described.

At that time, we did a wide literature search on diseases that had changes similar to those observed in this proposed new disease. One disease that had some resemblance to HDLS was Nasu disease (now called as Nasu-Hakola disease) or “polycystic lipomembranous osteodysplasia with sclerosing leucoencephalopathy” (5–7); in this disorder, the mode of inheritance is different, however. These diseases appeared at that time to be more common in Japan and Nordic countries. When the genetic cause of HDLS was determined and the mutation in the colony stimulating factor 1 receptor (CSF1R) gene was found (8), it was then determined that both diseases were related to CSF1R signaling. This shows that when examining new unknown diseases, the histopathology studies gave important clues to their pathogenesis.

I would like to take the opportunity to acknowledge and express my warmest thanks to the late Professor Patrick Sourander. He was my friend as well to many others, a spiritual father and one of the Grand Old Men whom I have met during my journey in clinical neuropathology and neuroscience.

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REFERENCES