
To the Editor:

We read with interest the recent publication, “Selective Deposition of 4-Repeat Tau in Cerebral Infarcts,” by Ichihara et al (1). The authors reported that Gallyas-positive structures that usually indicate neurodegenerative processes may also appear around ischemic foci. Since Gallyas-positive structures can appear in these apparently distinct processes, it is necessary to distinguish the nature of the process with which they are associated (2).

We recently studied the brain of a 71-year-old female patient with Parkinson disease and additional clinical manifestations that suggested the diagnosis of progressive supranuclear palsy (PSP); these included supranuclear gaze palsy, rigidity and dorsiflexion of the neck, subcortical dementia and parkinsonism not responsive to L-dopa. In addition to Lewy bodies in the substantia nigra, oculomotor nucleus, locus ceruleus, and dorsal motor nucleus of vagus, ischemic foci were widely scattered in the brain, including in the putamen, neocortex, hippocampus, substantia nigra, and pons. Gallyas-positive structures were found in the substantia nigra, subthalamic nucleus, putamen, and hippocampal dentate gyrus and CA4, partly overlapping with neurofibrillary tangles observed in PSP. This led us to the initial diagnosis of PSP, but after reading the study of Ichihara et al (1), we determined that the Gallyas-positive structures were found preferentially around ischemic foci in our patient. Moreover, they were AT8-negative and exhibited granular appearances, both suggestive of ischemia and distinct from neurodegenerative processes (2); tuft-shaped astrocytes were also absent. In light of the recent study, we felt, therefore, that it would be reasonable to negate our initial pathological diagnosis of PSP in favor of Parkinson disease with hypoxic-ischemic encephalopathy.

We conclude that careful cytopathologic differentiation of Gallyas-positive structures is necessary and useful to avoid this diagnostic pitfall, especially when clinical manifestations are compatible with PSP, as in our patient.

Naoki Kasahata, MD
Department of Neurology
Chigasaki Tokushukai General Hospital
Chigasaki City
Kanagawa Prefecture, Japan

Yoshio Miyazawa, MD
Department of Pathology
Chigasaki Tokushukai General Hospital
Chigasaki City
Kanagawa Prefecture, Japan

Tetsumasa Kamei, MD
Department of Neurology
Chigasaki Tokushukai General Hospital
Chigasaki City
Kanagawa Prefecture, Japan

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Authors’ Reply:

We thank Dr Kasahata and his colleagues for confirming the induction of Gallyas-positive neurons in ischemic foci. The cytopathological changes described in their patient seem to be in agreement with our series on cerebral infarcts (1). They demonstrate the use of this distinction in ruling out progressive supranuclear palsy in their patient with progressive supranuclear palsy—like clinical features. Since ischemic complications are very frequent in human autopsy brains, awareness of this potential pitfall may improve the accuracy of histological diagnoses. It remains to be clarified, however, whether these cytopathological features are unique to ischemia or are shared with other nondegenerative processes that may harbor tau-positive structures, such as inflammation, trauma, and demyelination (2, 3). Careful comparison of these categories by looking for possible argyrophilia and tau-like immunoreactivity in a broader disease spectrum will specify the diagnostic use and pitfalls of these findings. Furthermore, this may provide insight into the mechanisms of tau deposition induced by ischemia, possibly distinct from but partly shared with neurodegeneration.

Kazuaki Ichihara, MD, PhD
Department of Neurology
Tokyo Metropolitan Institute for Neuroscience
Tokyo, Japan

Toshiki Uchihara, MD, PhD
Ayako Nakamura
Department of Pathology
Tokyo Metropolitan Institute for Neuroscience
Tokyo, Japan

Yoshio Suzuki, MD, PhD
Department of Pathology
Asahi General Hospital
Chiba, Japan

Tomohiko Mizutani, MD, PhD
Division of Neurology
Department of Medicine
Nihon University School of Medicine
Tokyo, Japan

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