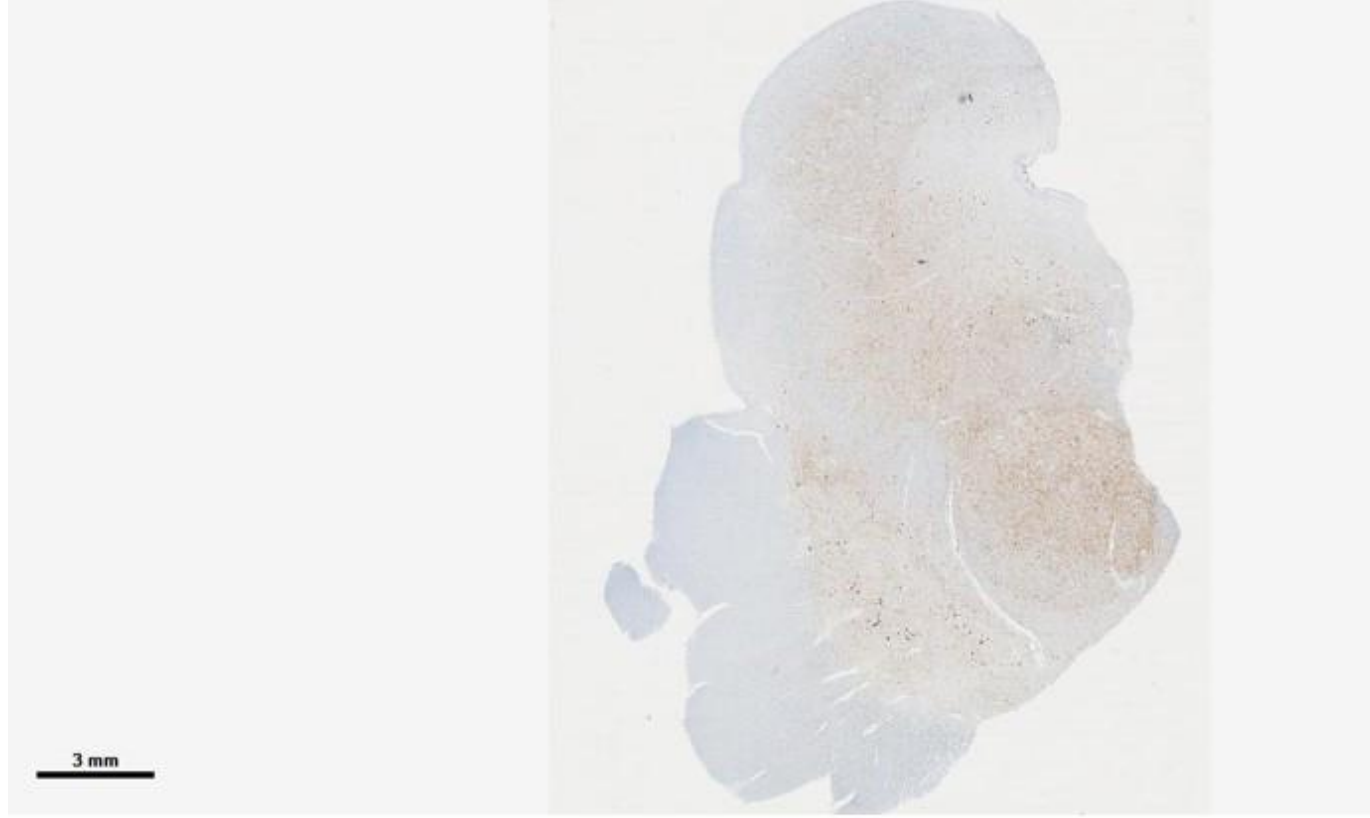
Case #60

NAME Educational Activities Committee

Case provided by:

Daniel Kirsch (MD, PhD student and EAC member) and
Dr. Bertrand R. Huber (Boston University).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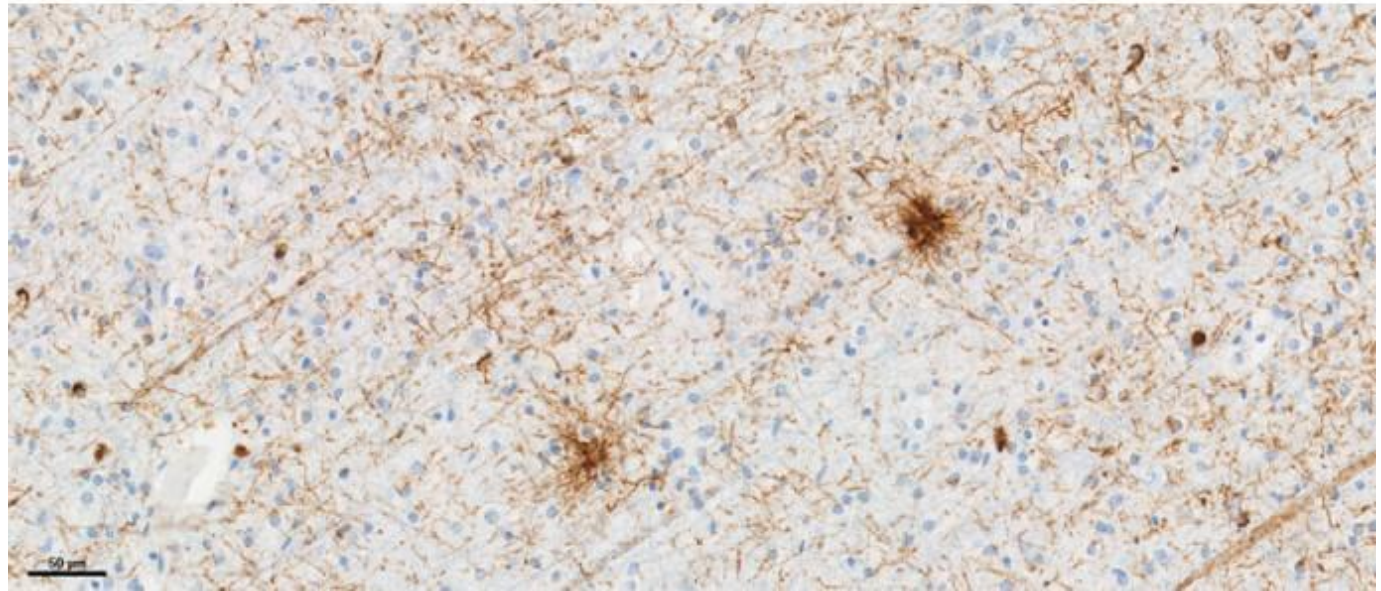
50 µm

1. A 70-year-old man with pronounced cognitive impairment died in a long-term care facility. Gross examination of the brain showed pallor of substantia nigra (SN). Sections of the SN were stained for hyperphosphorylated tau protein. The finding in the higher magnification image is most specifically associated with which antemortem clinical symptom or observation?

- ◯ Alien hand sign
- ◯ Parkinsonian movement abnormalities
- ◯ Vertical gaze palsy
- ◯ Excellent response to treatment with levodopa
- ◯ Mood and behavioral changes

Answer...

2 answers accepted: B and C

C. Vertical gaze palsy (7.11% responses)

This a is a case of progressive supranuclear palsy (PSP), a sporadic, neurodegenerative tauopathy, characterized by accumulation of hyperphosphorylated tau protein (p-tau). It the most common cause of atypical parkinsonism, and presents with gait disturbances and motor impairment, similar to Parkinson's Disease. Gross findings supportive of PSP include pallor of the substantia nigra and midbrain atrophy with tectal plate flattening. p-Tau pathology is most commonly seen in the midbrain and brainstem regions, while also affecting the peri-Rolandic regions of the cortex. Histological hallmarks of PSP are globose neurofibrillary tangles (NFTs) and tufted astrocytes (TAs). TAs are composed of proximal p-tau accumulation in astrocytes (as opposed to astrocytic plaques in corticobasal degeneration).

The histology highlighted tufted astrocytes, commonly seen in PSP. One of the most specific and earliest clinical presentations is a vertical gaze palsy, making C the best and most specific answer.

The majority of our 422 respondents chose:

B. Parkinsonian movement abnormalities (54.5% responses)
True, but not the most specific choice given. While this patient had parkinsonian movement disorder symptoms, these are not specific to PSP. Parkinsonian symptoms are observed in multiple neurodegenerative processes that affect the basal ganglia, including Parkinson's disease, CBD, progressive supranuclear palsy, and chronic traumatic encephalopathy, as well as vascular insults leading to damage to component structures.

Other responses:

A. Alien hand sign (1.18%)
Alien limb sign is classically associated with corticobasal degeneration (CBD). The hallmark lesion of CBD is a p-tau positive astrocytic plaque, which is a collection of p-tau in the distal processes of the astrocyte. The lesion in the above high-power section is a tufted astrocyte, which forms due to proximal accumulation of p-tau in an astrocyte.

D. Excellent response to treatment with levodopa (4.98% responses)
PSP causes a parkinsonian movement disorder that is minimally or non-responsive to treatment with medications for Parkinson's disease, including levodopa.

E. Mood and behavioral changes (32.23% responses)
While patients with PSP can exhibit mood and behavior changes across the course of their disease, this observation is not specific to PSP and can be seen in many neurodegenerative processes, such as CTE, behavioral variant frontotemporal dementia, and Alzheimer disease, among others.

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