An Atypical Case of Progressive Supranuclear Palsy

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SUMMARY: We report a 59 year old woman who presented with double vision, nuchal pain and mild dementia. On neurological examination she demonstrated third, sixth and seventh nerve palsies and ataxia. Following intravenous ACTH and oral prednisone therapy she showed a remarkable recovery which left her with only a left facial weakness. She remained well for two years. She then developed bulbar palsy and profound dementia. Pathological examination revealed progressive supranuclear palsy (PSP). This patient demonstrated a greater variability in the course of PSP than has previously been recognized.

RESUME: Nous rapportons le cas d’une femme de 59 ans se presentant avec diplopie, douleur à la nuque et une demence legere. L’examen neurologique montrait des paresies du 3e, 6e et 7e nerfs cranien. Après l’administration intraveineuse d’ACTH et une traitement orale avec Prednisone elle montra une rémission remarquable qui ne laissa qu’une faiblesse faciale. Elle fut bien pour 2 ans et dévelooppa ensuite une paresie bulbaire et une demence profonde. L’examen pathologique révéla une paralysie supranucléaire progressive (PSP). Son évolution fut plus oscillatoire que ce qu’on avait décidé auparavant.

CAN. J. NEUROL. SCI. 1984; 11:48-52

The clinical and pathologic features of progressive supranuclear palsy (PSP) were first described by Richardson, Steele, and Olzewski (Richardson et al., 1963; Steele et al., 1964). Several subsequent reports have provided additional details concerning this disorder (David et al., 1968; Behrman et al., 1969; Pfaffenbach et al., 1972; Steele, 1972; Perkin et al., 1978). The disease is characterized by supranuclear ophthalmoplegia, pseudobulbar palsy, nuchal dystonia, cerebellar and pyramidal signs and progressive dementia. It follows a progressive and relentless course ranging from two to ten years in duration. The characteristic pathological changes are cell loss, neurofibrillary degeneration and gliosis in brainstem, diencephalic and cerebellar nuclei.

The pathognomonic ultrastructural finding is neurofibrillary tangles consisting of 15 nm straight tubules. (Tellez-Nagel and Wisniewski, 1973; Roy et al., 1974; Powell et al., 1974). We report a patient with an unusual presentation of the disease and an atypical course. She had a two year remission followed by a rapid terminal course. Pathological examination revealed the classical abnormalities.

CASE REPORT

A 59 year old woman was admitted to the Health Sciences Centre, Winnipeg, in May of 1980. She had been well until two weeks prior to admission when she complained of double vision, nuchal pain and mild dementia. On neurological examination she demonstrated third, sixth and seventh nerve palsies and ataxia. Following intravenous ACTH and oral prednisone therapy she showed a remarkable recovery which left her with only a left facial weakness. She remained well for two years. She then developed bulbar palsy and profound dementia. Pathological examination revealed progressive supranuclear palsy (PSP). This patient demonstrated a greater variability in the course of PSP than has previously been recognized.


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An electroencephalogram showed intermittent bilateral polymorphic and arrhythmic delta activity most pronounced in the left temporal region. Brainstem auditory evoked potentials and pattern reversal visual evoked potentials showed normal latencies and amplitudes. CT-scan of the brain was unchanged.

The patient was not examined by us again, but we were informed that she developed a gradually progressive course with dementia and inability to move her eyes in any direction. In June 1982, she was admitted to a local hospital because of difficulty swallowing and aspiration. Terminally she was in a helpless bedridden state and died of bronchopneumonia a month later. Her brain was sent to us for examination.

**PATHOLOGY**

**Gross Examination of the Brain.** The brain weighed 1250 grams in the formalin fixed state. The meninges were thin and translucent. Coronal sections revealed mild dilatation of the ventricles. The cerebral cortex, white matter, thalamic and lenticular nuclei appeared normal. Sections of the brainstem showed pallor of the substantia nigra. The cerebellum was unremarkable on sectioning. The spinal cord revealed no gross abnormalities.

**Light Microscopic Examination.** No demyelinated plaques suggestive of multiple sclerosis were found in the cerebrum, cerebellum, brainstem or spinal cord, and no changes indicative of encephalitis or vasculitis could be demonstrated. Widespread neurofibrillary tangles were found in nuclei of the diencephalon, brainstem and cerebellum. They consisted of argyrophilic cytoplasmic inclusions of either flame-shaped or globoid types. They were most numerous in the inferior olivary, the dentate (Figure 1), the accessory cuneate, the subthalamic nuclei, and in the substantia nigra (Figure 2). They were also found in the zona incerta, the red nucleus, the periaqueductal grey matter and in the dorsal raphe nucleus and locus ceruleus of the pons, and in the vestibular and ambigu nuclei of the medulla.

In addition, a few tangles were identified in the medial globus pallidus, and in the anterior and reticular nuclear complexes of the brainstem.

![Figure 1 — Dentate nucleus showing two neurons containing neurofibrillary tangles and a moderate neuronal loss. (Bielschowsky's silver stain). Mag. 730x](https://www.cambridge.org/core/terms). https://doi.org/10.1017/S0317167100045315

![Figure 2 — Detail of a substantia nigra neuron showing most of the cytoplasm occupied by globoid neurofibrillary tangle. (Bielschowsky's silver stain). Mag 1340x](https://www.cambridge.org/core/terms).
the thalamus. Furthermore, tangles were demonstrated in the fourth and sixth cranial nerve nuclei. The third cranial nerve nuclei appeared unremarkable, apart from the occasional tangle. The seventh cranial nerve nuclei showed no tangles but marked neuronal loss, and preserved neurons revealed central chromatolysis (Figure 3). The exit tracts of the third and the seventh nerves showed moderate myelin pallor. The substantia nigra and the subthalamic nuclei showed moderate to marked neuronal loss and astrogliosis. The substantia nigra also revealed neurons containing Lewy bodies (Figure 4).

The hippocampi and cerebral cortex appeared unremarkable and failed to show any neurofibrillary tangles. The intensity of neurofibrillary tangle involvement and severity of neuronal loss and gliosis in various nuclei are listed in Table 1. Peripheral nerves were not available for examination.

Electronmicroscopy

Tissue from the subthalamic nucleus, locus ceruleus and substantia nigra were processed for electronmicroscopy. Examination of these revealed the presence of focal cytoplasmic accumulation of straight tubules which were beaded with granules (Figure 5). No parahelical filaments were demonstrated. The straight tubules revealed a mean diameter of $16.2 \pm 1.4 \text{ nm}$.

DISCUSSION

The pathological findings in this patient were typical of PSP (Steele et al., 1964; Jellinger, 1971; Steele, 1972). This diagnosis was confirmed ultrastructurally by the presence of straight intracytoplasmatic tubules measuring approximately 15 nm (Tellez-Nagel and Wisniewski, 1973; Roy et al., 1974; Tomonaga, 1977).

**Figure 3** — Central chromatolysis in a preserved neuron of the seventh nucleus. (Hematoxylin-Eosin (H-E) and Luxol-fast-blue (LFB). Mag. 920 x

**Figure 5** — Electronmicrograph of a neurofibrillary tangle in the substantia nigra. The tangle consists of straight tubules which measured a mean diameter of 16.2 nm. Note granular beading of the individual tubules. Mag. 83,700 x

**Figure 4** — Mature Lewy body in the substantia nigra. (H-E and LFB). Mag. 1840 x
PSP is of unknown etiology and progresses in two to ten years to severe physical disability, dementia, and death. Temporary improvement has been noted, often coinciding with various treatments and lasting from weeks to months (Derenzi and Vignolo, 1969; Haldeman et al., 1981; Rafal and Grimm, 1981; Jackson et al., 1983). The clinical picture has been well documented (Steele et al., 1964; Albert et al., 1974; Perkin et al., 1978). The main features are impairment of voluntary vertical eye movements, difficulties with locomotion, balance, speech, swallowing and the development of dementia. Occasionally, absence of the typical eye signs may cause delay in the diagnosis (Perkin et al., 1978; Nuwer, 1981). Other features are slow, labored speech, and cerebellar dysfunction. Several authors have documented involvement of cranial motor nuclei with neuronal loss of the third, fourth and sixth nuclei as well as demyelination of their emerging nerves (Blumenthal and Miller, 1969; Ishino et al., 1974). These findings are similar to those found in our patient who showed lower motor neuron involvement of the third, sixth and seventh cranial nerves, all verified on pathological examination. The initial clinical features of double vision and unilateral cranial nerve symptoms in our patient were atypical. At this stage she showed mild dementia and complained of nuchal pain. Only at the terminal state did she show gaze palsy as well as profound dementia.

Since peripheral nerves were not examined pathologically, the coexistence of a peripheral nerve disorder, such as acute intermittent porphyria or the Fisher variant of Guillain-Barré syndrome, cannot be excluded. However, the normal nerve conduction velocity and normal CSF protein as well as the lack of further clinical evidence do not support these possibilities.

In PSP defective voluntary conjugate gaze with preservation of reflex eye movements is due to supranuclear lesions involving diencephalic and midbrain structures as in our patient. The lesions are usually bilateral, thus vertical eye movements can similarly be affected (Bender, 1980).

The dementia in our patient may have been due in part to lesions of the thalamomesencephalic junction, resulting in a disconnection of the ascending impulses from the mesencephalic reticular formation (Albert, 1978; Albert et al., 1974; Segarra, 1970). In addition, there may have been biochemical disorders involving cortical neurons not evident on pathologic examination (Drachman, 1981).

While receiving intravenous ACTH therapy and tapering doses of prednisone the patient showed a remarkable recovery. When she was discharged from hospital she had only a mild residual facial weakness. This remission lasted for two years before she developed a rapidly fatal progressive course.

Whether her improvement and long remission were an effect of the therapy is not known. The atypical presentation and prolonged remission in this patient indicate a greater variability in the natural course of the Steele-Richardson-Olszewski syndrome than has been previously recognized.

ACKNOWLEDGEMENTS

We are indebted to Dr. R.T. Ross, who provided helpful comments, and to Mrs. J. McKane for preparing this manuscript.

REFERENCES


Table 1: Intensity of neurofibrillary tangles and severity of neuronal loss and gliosis in various nuclei.

<table>
<thead>
<tr>
<th>SITE*</th>
<th>Intensity of neurofibrillary tangles</th>
<th>Neuronal loss</th>
<th>Gliosis</th>
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<tbody>
<tr>
<td>Anterior thalamic nucleus</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Reticular nucleus of thalamus</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Medial globus pallidus</td>
<td>++</td>
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<td>+</td>
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<tr>
<td>Substantia innominata</td>
<td>+</td>
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<td>-</td>
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<tr>
<td>Subthalamic nucleus</td>
<td>+++</td>
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<tr>
<td>Zona incerta</td>
<td>+</td>
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<tr>
<td>Periaqueudal grey matter</td>
<td>++</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Third nucleus</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Fourth nucleus</td>
<td>++</td>
<td>-</td>
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<tr>
<td>Red nucleus</td>
<td>+</td>
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<td>-</td>
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<tr>
<td>Substantia nigra; pars reticulata</td>
<td>+++</td>
<td>+++</td>
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<tr>
<td>pars compacta</td>
<td>-</td>
<td>+</td>
<td>++</td>
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<tr>
<td>Sixth nucleus</td>
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<tr>
<td>Seventh nucleus</td>
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<td>+++</td>
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<tr>
<td>Dorsal raphae nucleus</td>
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<tr>
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<tr>
<td>Accessory cuneate nucleus</td>
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+ = mild; ++ = moderate; +++ = severe.*The degree of involvement of various paired nuclei showed no significant differences.


