Thalamo-olivary degeneration in a patient with laryngopharyngeal dystonia

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Abstract
A 67 year old woman with a two year history of laryngopharyngeal dystonia, spasmodic dysphonia, and parkinsonism succumbed to Wernicke’s encephalopathy and died six months later. Necropsy showed, besides Wernicke’s encephalopathy, degenerative changes in selected thalamic nuclei (dorsomedial, pulvinar, and the medial geniculate bodies) and the inferior olives and numerous cerebellar torpedoes. The substantia nigra and basal ganglia were spared. Immunostaining for prion protein was negative. This patient indicated a new type of presentation of so-called pure thalamic degeneration, or more precisely thalamo-olivary degeneration.

Keywords: thalamo-olivary degeneration; thalamic degeneration; spasmodic dysphonia; laryngopharyngeal dystonia

Thalamic degeneration is a rare condition, the clinical manifestations of which have been variable cognitive memory and behavioural disorders.1 Three types of selective thalamic degeneration have been distinguished2: firstly, combination with a variety of neurodegenerative3–5 and metabolic disorders such as Menke’s kinky hair disease; secondly, the thalamic form of Creutzfeldt-Jakob disease6; thirdly, isolated or pure thalamic degeneration.5,6,10 Now that a mutation at codon 178 of the prion protein gene has been detected in fatal familial insomnia7,8 that used to belong to the third category,2,13 these patients may well be recategorised to the second or prion disease group despite different clinical manifestations. Therefore the patients with pure thalamic degeneration who were negative or not tested for prion protein were only seven2,6,11; among these were four Japanese and one Chinese; and two of the seven patients were familial. The thalamic involvement has been roughly selective among its divisions and there has been no patient in whom the thalamus was the only site of degeneration. Interestingly, degeneration of the inferior olives accompanied the thalamic changes not only in all the patients with pure thalamic degeneration except one1 but also in patients with prion disease. The oligary degeneration is associated with no6,7 or mild8,11 cerebellar cortical changes; thus a trans-synaptic degeneration was unlikely. Therefore we think that the term thalamo-olivary degeneration is more appropriate to designate this condition.

We experienced such a patient with thalamo-olivary degeneration, who presented mainly with parkinsonism, dystonia, and spasmodic dysphonia over 18 months. Her family history was not relevant. She had been living alone and her relatives had noticed subtle abnormalities in her behaviour after the surgery. For example, she refused gifts of food based on her assumption that it was old and she removed the petals from arranged flowers to detect presumed insects. Because of increasing anorexia and discomfort when breathing the patient was again admitted to our hospital in December 1992. There was no evidence of recurrence of cancer or presence of other disorders to account for her loss of appetite and a neurological consultation was made. Her mental state was unremarkable except for depression; and she scored 28/30 on the mini mental state examination. Cranial nerves were intact and swallowing was not disturbed. There was moderate parkinsonism with hypokinesia, cogwheel rigidity of the limbs, neck, and trunk, a mask-like face, and a shuffling gait. Tremor was absent and postural response was intact. Tendon reflexes were normal and the plantar response was flexor. There were involuntary movements in the throat muscles that were characterised by irregular abrupt stops in the inhalation phase,
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producing faint unintentional phonation. These abnormalities were confirmed by pneumotachogram (fig 1). Fibre laryngoscopy also showed irregular, repetitive, vocal fold closing during the resting state of respiration. Synchronous with the unintentional phonation was raising of her throat as if to swallow, nodding-like neck flexion, and slight forward bending of the trunk. Ataxia was not evident. Brain CT was normal. Levodopa up to 400 mg/day with a decarboxylase inhibitor and antidepressants were tried without an appreciable effect.

Fluid infusion without supplementation of vitamins induced Wernicke's encephalopathy in April 1993. Thereafter, no more spasmodic dysphonia, dystonia, or dyskinesia was observed. Although the patient partially recovered, she was kept confined to bed and her mental state deteriorated again five months after the attack of Wernicke's encephalopathy. Eventually she entered a state of akinetic mutism. Her ECGs showed background disorganisation with diffuse theta and delta slowing no periodic sharp discharges15 were recorded on any occasion. She died two months later of uncontrollable respiratory infection in October 1993.

Postmortem examination showed bronchopneumonia and widespread microabsces formation. There had been no recurrence of cancer. The brain weighed 1140 g. Macroscopic abnormalities were limited to the necrotising lesions around the third ventricle and the aqueduct and a mild atrophy of the mammillary bodies. Histological examination confirmed tissue destruction with macrophages and hypertrophic astrocytosis, which was consistent with Wernicke's encephalopathy. There was severe thalamic degeneration distinct from the changes of Wernicke's encephalopathy, consisting of isomorphic fibrillary gliosis and loss of neurons (fig 2). The dorsomedial, pulvinar, and the medial geniculate bodies were mainly affected bilaterally (fig 3). The anterior nuclei were mostly preserved. The superior and inferior colliculi were moderately gliotic. The inferior olives and the accessory olivary nuclei showed severe degeneration (fig 4). Although the cerebellar cortex escaped neuron loss, there were profuse torpedoes (fig 5). A few Lewy bodies were seen in the pigmented brainstem neurons. Otherwise, the basal ganglia, substantia nigra, subthalamus, the rest of the brainstem, and the spinal cord were intact except for scattered microabscesses and mild gliosis. A few Alzheimer's neurofibrillary tangles were seen in the hippocampus and senile plaques or ballooned neurons were not detected. Spongy changes characteristic of Creutzfeldt-Jakob disease were not found and immunostaining for prion protein was negative.

Discussion

"Pure" thalamic degeneration, even in its broad sense, has been reported in only a few cases.2 6-11 14 The precise mapping of subdivisions of thalamic involvement in these patients is hampered by variable nomenclature. According to the standard text of Carpenter and Sutin and the schematic illustrations in the medical literature, the most consistent affected regions were dorsomedial, anterior, ventral anterior, and pulvinar. Our patient was unique both in the affected medial geniculate body, that was intact in all except one patient reported by Hori et al,16 and the spared anterior nuclei, that were always affected in other patients described. The constant involvement of the inferior olives in pure thalamic degeneration is a peculiar finding as there is no direct functional connection between these two structures. Of related interest both in pure thalamic degeneration and in prion disease were minor cerebellar changes that included torpedoes of the Purkinje cell axons,3 11-13 20 which are not specific,21 but are intriguing accompaniments.

There were patients with multiple system degeneration in which thalamic changes were
disproportionally severe. These patients were not different in the distribution pattern of thalamic lesion from patients with pure degeneration. Similarly, cases of the thalamic form of prion protein disease showed changes indistinguishable from pure cases. A normal prion protein gene but positive prion protein immunoblot were seen in one patient with mild spongiform encephalopathy. Wernicke's encephalopathy is another disorder in which the thalami, particularly the dorsomedial and pulvinar areas, are always involved. Involvement of the anterior nucleus is frequent, whereas that of the medial geniculate body is uncommon in Wernicke's encephalopathy: both of these are contrary to the findings in our patient. Furthermore, olivary degeneration is not a part of Wernicke's encephalopathy.

Clinical presentation of this patient was distinct from the other reported cases and indicates a wide clinical range of thalamic degeneration despite rather uniform pathological findings. Spasmodic dysphonia is a term that describes a family of strained, strangled voices, voice tremor, or stridor, resulting from vocal fold spasm. Three types—adductor, abductor, and mixed—of spasmodic dysphonia are known, among which the adductor type is by far the most common. For dystonia in general, there has been uncertainty as to the underlying pathology. Not infrequently psychogenic dysfunction (psychoneurosis) is the only explanation for spasmodic dysphonia. Pool et al. however, found neurological abnormalities in about 70% of their patients. Disturbed rapid alternating movements, weakness, and tremor were some of the abnormalities. The authors suggested, from anatomical and functional brain imaging studies, that the pallidothalamic area (pars oralis of the ventro-
lateral nucleus of the thalamus)—the supplementary motor area—could account for the neurological findings. Rosenfield et al. evaluated 100 patients with spasmodic dystonia and showed that 71 had essential tremor, 25 had Meige’s syndrome, and 12 were hypothyroid. Among the reported patients with thalamic degeneration only one had abnormal phonation: she showed strong inspiratory effort due to whoop-like laryngeal spasms. Even this patient’s sign was unlike the rhythmic spasmodic dystonia of our patient, who showed nodding-like neck movement and pharyngeal components.

Regarding other clinical signs in thalamic degeneration, particularly different in our patient was an apparent absence of both dementia at the early stages and sleep disturbance. Superimposition of Wernicke’s encephalopathy could have terminated the natural course of the disease, muting these important signs and making the laryngopharyngeal dystonia disappear. The necrotising changes in Wernicke’s encephalopathy could possibly interrupt neural circuits underlying the movement disorder as in surgical procedures for tremor.

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