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## Palatal Tremor and Orofacial Stereotypies Within the Locked-In Syndrome

Video



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The term locked-in syndrome (LIS) was coined by Plum and Posner in 1966 to describe a state of tetraplegia and mutism with retained consciousness.<sup>1</sup> Typically, LIS arises when descending corticospinal, corticobulbar, and corticofacial tracts are interrupted within the ventral pons.<sup>2</sup> A lesion at this site spares descending motor projections to the oculomotor apparatus in the mid-brain and allows voluntary eye opening and vertical eye movement. We describe an individual who developed a variety of involuntary movements within LIS complicating pontine infarction.

A 64-year-old man was brought to hospital after being found one morning in a state of apparent unconsciousness. Enquiry revealed that, 5 years earlier, the patient experienced transient left-sided weakness and sensory disturbance thought to represent transient cerebral ischemia. He was prescribed aspirin at that time but was not investigated. Recovery was complete. The remainder of the medical history was unremarkable.

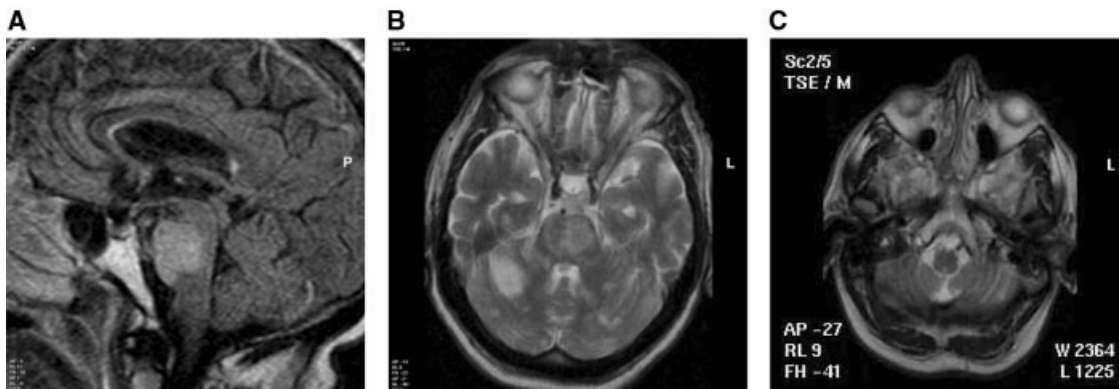
Examination revealed normal vital signs and no abnormality within the cardiovascular, respiratory, and abdominal systems. The eyes were open and the pupils were reactive. The diameter of the right pupil was 3 mm and the left 2 mm. Voluntary elevation of the eyes was present. Voluntary lateral gaze was impaired, particularly to the right. Voluntary facial and bulbar movements were absent. Tone of the limbs was mildly increased, and there was no voluntary limb movement. Limb tendon reflexes were brisk, and the plantar response was bilaterally extensor. Sensation was preserved (see Video). A diagnosis of locked-in syndrome complicating basilar artery thrombosis was suspected.

Routine biochemical and hematological indices were normal. Magnetic resonance imaging (MRI) of the brain demonstrated abnormality of the ventral pons and both cerebellar hemispheres in keeping with infarction (Fig. 1). Magnetic resonance angiography demonstrated occlusion of the proximal basilar artery.

During subsequent months, the patient's condition changed very little, although he regained minimal head turn. One year after first presenting, synchronous, involuntary movement of the soft palate and tongue was noted (see Video). The movement was incessant but the degree was variable. Occasionally, there was also synchronous movement of orbicularis oris, dilator naris, and auricularis anterior. There was no accompanying ocular or limb movement. The movements were not ameliorated by baclofen or clonazepam. Further therapeutic trials were declined by the patient's family.

This article includes Supplementary Video, available online at <http://www.interscience.wiley.com/jpages/0885-3185/suppmat>

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**FIG. 1.** A: Midline sagittal FLAIR magnetic resonance imaging (MRI) scan at presentation. B: Axial T2-weighted FSE MRI at presentation. C: Axial T2-weighted FSE MRI at presentation at the level of the olives.

Several months later, the patient began to exhibit chewing and pouting movements and bruxism in addition to his established palatal tremor. These movements are involuntary and intermittent. Their periodicity has been variable and more visibly influenced by external factors, such as intercurrent illness, than the coexistent palatal tremor. The tendency to generate chewing movements has at times been severe and sufficient to cause alarming degrees of buccal bleeding. Imaging of the brain 44 months after the initial presentation demonstrated infarction within the ventral pons and, to a lesser degree, the cerebellum but no olivary hypertrophy (Fig. 2).

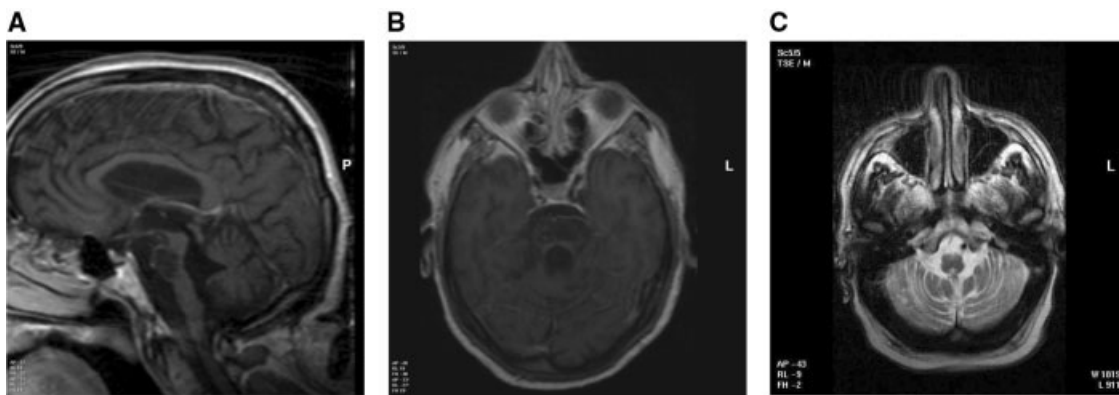
Ironically, LIS complicating pontine is commonly complicated by involuntary movement. In the series of 139 cases of LIS reviewed by Patterson and Grabois, some form of involuntary movement was seen in 50 patients.<sup>3</sup> The movements encountered may be divided into three categories: first, LIS complicated by symptomatic palatal tremor (SPT); second, complex patterned movements, which may be stimulus induced, such as yawning and chewing; and third, miscellaneous movements such as mirror movements and abnormal posturing. In addition, there may be ocular bobbing.<sup>3,4</sup> SPT is frequently associated with hypertrophy of the medullary olivary nuclei. When SPT is unilateral, olivary hypertrophy, if present, is contralateral to the side in motion. The responsible lesion is supraolivary, either in the central tegmental

tract ipsilateral to the hypertrophied olive or in the contralateral dentate nucleus.<sup>5,6</sup>

Typically, olivary hypertrophy occurs several months after the initial insult to the dentato-olivary pathway.<sup>7</sup> SPT follows shortly afterward but persists despite subsequent olivary neuronal loss and atrophy. The dentato-olivary pathway is thought to be  $\gamma$ -aminobutyric acid-ergic and inhibitory and it may be that cells within the olive, deprived of this inhibitory input, experience unchecked excitotoxicity, leading initially to cellular hypertrophy but ultimately to cellular death. The persistence of SPT, despite marked loss of olivary neurons and degeneration of efferent tracts from the olive may indicate that the movements of SPT are actually generated elsewhere in neurons liberated from control of the olive.<sup>7</sup>

The process of olivary degeneration leading to SPT is frequently, but not invariably, accompanied by olivary hyperintensity on T2-weighted MRI. This change may occur within weeks of the responsible brainstem insult, precedes the onset of olivary hypertrophy, and persists.<sup>8</sup>

In this case, emergence of SPT was followed by emergence of a second movement disorder characterized by involuntary, exaggerated chewing movements and pouting. Involuntary chewing movements were reported in 6 of the 139 patients with LIS reviewed by Patterson and Grabois.<sup>3</sup>



**FIG. 2.** A: Midline T1-weighted SE magnetic resonance imaging (MRI) follow-up scan taken 44 months after presentation. B: Axial T1-weighted SE follow-up scan taken 44 months after presentation. C: Axial T2-weighted FSE MRI follow-up scan taken 44 months after presentation.

Sucking and swallowing movements sometimes accompanied by pouting have also been observed, and together, these movements have been termed oral automatisms.<sup>3,9</sup> The spectrum of involuntary, patterned movement encountered in LIS also includes movements that appear emotionally charged, including movements accompanied by vocalization. Grunting, groaning, sighing, yawning, moaning, crying, and the pain reaction are all described.<sup>3,9</sup> The presence of these movements would suggest spontaneous activity within the motor component of the emotional motor system thought to reside between the midbrain periaqueductal gray matter and interneurons in the caudal medulla.<sup>10</sup> We believe that the locked-in state and development of symptomatic palatal tremor is particularly well illustrated by this case.

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### Legend to the Video

The films demonstrate abnormal signal within the ventral pons and cerebellum indicative of infarction and subsequent gliosis but no olivary hypertrophy.

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## Over 10 Years of Isolated Autonomic Failure Preceding Dementia and Parkinsonism in 2 Patients with Lewy Body Disease

Parkinson's disease (PD), Parkinson's disease with dementia (PDD), dementia with Lewy bodies (DLB), and pure autonomic failure (PAF) are characterized neuropathophysiologically by Lewy bodies.<sup>1</sup> PDD and DLB are two common syndromes with overlapping clinical symptoms, and they share a common pathological substrate.<sup>2</sup> Consensus criteria for DLB lists repeated falls and syncope, transient loss of consciousness, and severe autonomic dysfunction as supportive features.<sup>3</sup> Recently, autonomic failure, as well as multiple system atrophy, has been reported to be frequent in DLB,<sup>4,5</sup> but autonomic dysfunction has not been well investigated in DLB/PDD. We report 2 patients whose initial clinical manifestation was isolated autonomic failure, which lasted for over 10 years before the appearance of Parkinsonism and dementia.

### Case 1

A 65-year-old man, who had no familial history and environmental exposures, suffered light-headedness on standing at age 51, and he was found to have orthostatic hypotension on admission for early esophageal cancer at age 52. He experienced urinary frequency and constipation at age 53 and erectile dysfunction at age 55. His postural symptoms worsened, and occasionally he fainted. A neurological examination at age 61 found generalized anhidrosis and severe orthostatic hypotension, but no other neurological abnormalities. Head-up tilt (30 degrees) reduces blood pressure from 140/94 mm Hg (heart rate, 82/min) to 78/44 mm Hg (96/min). Plasma noradrenalin levels were 65 pg/ml when supine and 84 pg/ml 10 minutes after head-up tilt. The coefficient of variation of R-R intervals (CV<sub>R-R</sub>) was a low (0.27%; normal > 1.41%). Brain magnetic resonance imaging (MRI) showed no abnormalities. Administration of L-threo-3,4-dihydroxyphenylserine (L-DOPS) lessened his orthostatic symptoms. At age 63, limb rigidity and bradykinesia appeared. In addition, he experienced visual hallucination and fluctuating cognition with pronounced variations in attention and alertness. Neurological examination at age 65 detected mild dementia (Mini-Mental State Examination [MMSE] score 17/30). There was impaired sense of smell. There was rigidity of the limbs, resting tremor of the hands, bradykinesia, and gait disturbance. Muscle strength, muscle stretch reflexes, and coordination were normal. Head-up tilt (70 degrees) reduced blood pressure from 157/91 mm Hg (86/min) to 58/18 mm Hg (86/min) under L-DOPS medication. Brain MRI detected mild cerebral atrophy, but there was no brainstem or cerebellar atrophy (Fig. 1A). Single photon emission computed tomography study showed reduced accumulation of <sup>123</sup>I-N-isopropyl-P-iodoamphetamine in the cerebral cortex. An administration of levodopa with decarboxylase slightly improved Parkinsonism.

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