

Dystonia in progressive supranuclear palsy

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Abstract

Objectives—To document the nature, distribution, and frequency of dystonic symptoms in progressive supranuclear palsy (PSP).

Methods—Charts and videotapes of all clinically diagnosed patients with PSP seen between 1983 and 1993 were reviewed and the occurrence, nature, and distribution of all dystonic symptoms were recorded.

Results—Of 83 identified cases 38 had some dystonic features. Twenty (24%) had blepharospasm (one was induced by levodopa), 22 (27%) had limb dystonia (one was induced by electroconvulsive therapy and another by levodopa), 14 (17%) had axial dystonia in extension, one had oromandibular dystonia induced by levodopa, and two had other cranial dystonias. Six patients had limb dystonia as an early or presenting feature, sometimes leading to misdiagnosis of cortical-basal ganglionic degeneration. All three patients who had postmortem confirmation of the diagnosis had other concurrent disease. One patient with bilateral limb dystonia and blepharospasm had evidence of previous hydrocephalus and severe arteriosclerotic changes. One with arm dystonia also had cerebrovascular disease and one with hemidystonia also had rare swollen chromatolytic neurons in the frontotemporal cortex.

Conclusions—Dystonia is a common manifestation of PSP. Limb dystonia is particularly common and may indicate the presence of concurrent disease. When dystonia occurs in PSP, dopaminergic medication should be cautiously reduced or discontinued to rule out the possibility of treatment induced symptoms.

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Since progressive supranuclear palsy (PSP) was first characterised in 1964,¹ dystonic manifestations have been reported only sporadically.²⁻⁷ "Axial dystonia in extension" is the only such manifestation which has been emphasised; however, the pathogenesis of this tonic, rigid extended posture is probably distinct from other forms of dystonia.⁸ Blepharospasm has also been reasonably well

recognised in this setting, whereas limb dystonia, oromandibular dystonia, and treatment induced dystonia have all but been ignored. In reviewing a large series of patients with PSP, we were impressed with the frequency of dystonia and report our findings below.

Methods

The charts of all patients with a diagnosis of PSP who were seen in the Toronto Hospital movement disorders clinic between January 1983 and February 1993 were reviewed. All videotaped examinations available on these patients were reviewed. The clinical diagnosis was considered correct if the patient had a progressive, non-familial neurodegenerative disorder with onset after the age of 40 which included supranuclear ophthalmoplegia with downgaze abnormalities and at least two of the following features: postural instability with backward falls, pseudobulbar palsy, bradykinesia and rigidity, frontal lobe signs, or axial dystonia and rigidity (Lees' criteria).⁹ Any patient with limb apraxia, cortical sensory loss, or dysphasia was excluded. All patients satisfying the criteria were reviewed for the presence of dystonia. This was defined as a syndrome of involuntary movement dominated by sustained muscle contractions causing twisting and repetitive movements or abnormal postures.¹⁰ Clinical aspects of the dystonic manifestations were reviewed including the location, nature, accompanying clinical features, and the time of onset. Accurate information on the time of onset in relation to onset of disease was not always available.

Results

Eighty three patients met the diagnostic criteria for PSP; 45 were men and 37 were women (1.2:1). Twenty seven had at least one videotaped examination. The age at onset of PSP symptomatology ranged from 47 to 81 years of age with a mean of 62.9 years. Duration of PSP symptoms to last follow up visit or death was 4.7 (range 1-20) years. Thirty eight (46%) had at least one dystonic feature at some point in their illness. Twenty had blepharospasm (24%), 22 had limb dystonia (27%), 14 were noted to have so called axial "dystonia" in extension (17%), and three had other cranial dystonias. In three patients, the dystonia was clearly induced by treatment (one with oromandibular dystonia and blepharospasm and two with limb dystonia).

Blepharospasm occurred either sponta-

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neously or reflexively in response to facial stimuli or voluntary facial movements (reflex blepharospasm). Because of incomplete reporting, it was not possible to discern how many patients had isolated spontaneous blepharospasm, reflex blepharospasm only, or a combination of the two. Ten of the 20 patients with blepharospasm also had "apraxia of eyelid opening" (referred to elsewhere as levator inhibition or eyelid freezing). Reflex blepharospasm was a common accompaniment of this disorder. Two patients had blepharospasm with apraxia of eyelid closure. In nearly all those affected, blepharospasm occurred as a late manifestation of their disease, with only one patient reporting difficulty with eyelid opening within one year of onset of symptoms. One patient with blepharospasm and other dystonic features had a postmortem performed and the results are reported below.

One patient developed blepharospasm and oromandibular dystonia while receiving levodopa/carbidopa 100/25 thrice daily. On withdrawal of the drugs, the blepharospasm resolved but apraxia of eyelid opening remained. The oromandibular dystonia also resolved on stopping levodopa. No other patient had oromandibular dystonia although one had a dystonic grin with repetitive lower facial grimacing and one had sustained involuntary smiling.

Limb involvement was the most common dystonic manifestation in our PSP population (22 patients, 27%) and hemidystonia the most frequent distribution (nine patients (11%)). Although in many instances the precise limb posture was not recorded, a "pointing gun" posture, with extension of the index finger and thumb, was often noted. In four patients, hemidystonia was a very early or presenting feature of their disease. Two were initially diagnosed elsewhere as having cortical-basal ganglionic degeneration because of the pronounced unilateral (left sided) dystonia. However, these patients had a vertical supranuclear gaze palsy at presentation and no cortical sensory loss or stimulus sensitive myoclonus. Significant limb apraxia was also absent but was difficult to assess due to the pronounced disability caused by their dystonia, bradykinesia, and rigidity. One patient, last seen six years after symptom onset, remains free of manifestations of cortical-basal ganglionic degeneration. The other died five years after onset of symptoms. Postmortem examination disclosed the typical pathological abnormalities of PSP. In addition, rare swollen chromatolytic neurons were noted in the frontotemporal cortex and there was neuronal loss and gliosis in the left motor cortex and right posterior middle frontal gyrus. These findings, although suggestive of cortical-basal ganglionic degeneration, have been described in PSP¹¹⁻¹³ and due to the overwhelming predominance of the findings of this disorder, the final neuropathological diagnosis was that of "atypical PSP".¹⁴

Single limb involvement occurred in eight patients (10%). In seven, an arm was involved. In one the patient developed dystonia in his

left leg during a course of electroconvulsive therapy.¹⁵ Within one month of cessation of that treatment, this symptom resolved. It spontaneously recurred and gradually worsened over the subsequent 18 months of follow up. One patient developed right arm dystonia with associated choreic movements while receiving levodopa/carbidopa. All involuntary movements ceased on discontinuation of the drug.

In two other cases, arm dystonia was the initial manifestation of disease. One of these, with right arm involvement, died after an eight year history of gradually progressive neurological dysfunction compatible with a clinical diagnosis of PSP. Postmortem examination, in addition to the typical pathological changes of PSP, showed severe arteriosclerosis with microinfarcts in the left caudate, left lateral thalamus, right dorsomedial thalamus, and multiple neocortical regions.

The one patient with dystonic posturing in all four limbs late in the course of his illness also had PSP confirmed at necropsy. This patient is reported elsewhere.¹⁶ He presented at age 69 with incontinence, gait impairment, falls, and cognitive dysfunction. Brain CT suggested normal pressure hydrocephalus and ventricular shunting was performed. His symptoms improved greatly for a few months; however, his gait then worsened, dysphagia and dysarthria occurred, and he developed a vertical supranuclear gaze palsy, blepharospasm, and mild bilateral limb dystonia. He died aged 75 and in addition to the typical findings of PSP, his postmortem examination showed evidence of previous hydrocephalus and severe arteriosclerotic changes in the white matter and deep grey structures with numerous small infarcts (1-8 mm in diameter) bilaterally in the centrum semiovale and basal ganglia.

Whereas we do not consider the neck posture typically seen in PSP to be dystonic in nature, as some authors consider it such, we recorded the frequency of this feature. Fourteen patients (17%) were documented as having "axial dystonia in extension". This was characterised by constant extensor posturing of the neck with severe nuchal rigidity. No patient had phasic or intermittent dystonic neck movements, improvement with antagonistic gestures, "morning benefit", or other clinical features characteristic of classic cervical dystonia.

With the retrospective nature of this review, the lack of a consistent approach to treatment, and the complex symptomatology that our patients experienced, an accurate assessment of the response of the patients' dystonia to medical management could not be obtained. None of the patients receiving levodopa or dopamine agonists were reported to experience a lessening of their dystonic symptoms. Rarely, patients with limb dystonia or blepharospasm were noted to have some beneficial response to tricyclic agents whereas only those who received botulinum toxin injections for blepharospasm clearly experienced a good response to therapy. No patient in this series

with any other form of dystonia received botulinum toxin injections.

Discussion

Dystonia was first reported in association with PSP with the initial description of the disorder by Steele, Richardson, and Olszewski in 1964.¹ Whereas they emphasised "axial dystonia in extension", one of their patients also showed unilateral arm dystonia.

Axial dystonia in extension is by far the most commonly recognised and reported "dystonic" manifestation of PSP. De Bruin and Lees noted that 48.3% of all necropsied patients with PSP reported in the literature had axial dystonia of some sort.¹⁷ The posturing seen in this condition, however, lacks the typical features of dystonia and many authors think that this term should be avoided.^{8,18} The neck positioning in PSP tends to be fixed and does not alter with posture or activity as idiopathic dystonia does. Patients fail to show sensory tricks for improving the posturing, diurnal variation ("morning benefit") is absent, and painful neck spasms and hypertrophic muscles are not seen. For these reasons, nuchal rigidity in extension would be a more appropriate term. We would reserve the term "axial dystonia" for those rare cases reported in which torticollis was described.^{19,20} In our series, no patient had such neck movements. Fourteen (17%), however, were noted to have overt nuchal rigidity in extension. This is likely an underrepresentation of the true prevalence of this sign as the position of the neck was not always specified and so milder examples may have been overlooked or not documented.

The most widely accepted dystonic manifestation of PSP is blepharospasm.²¹ In two clinic based series, blepharospasm was noted in between 8% and 23% of cases.^{22,23} Golbe *et al* reported a community based series of 38 patients with PSP in whom 10 (26%) had blepharospasm, or "levator inhibition" ("apraxia of eyelid opening"), or both.²⁴ It should be noted that "levator inhibition" is probably an uncommon cause of "apraxia of eyelid opening". Recent studies have emphasised the presence of isolated contraction of the pretarsal component of the orbicularis oculi muscle in a high proportion of cases, making this a subtype of dystonic blepharospasm.^{25,26} Golbe *et al* noted that the duration and severity of disease in patients with disturbances of eyelid function was not significantly different from those lacking this feature although they did note the presence of more severe upgaze abnormalities.²⁴ In our series, 31 patients (40%) had disturbances of eyelid function including eight with blepharospasm alone, and 12 with a combination of blepharospasm and apraxia of eyelid opening or closure. The retrospective nature of our series, with insufficient recording of some clinical features, does not allow us to confirm the findings of Golbe *et al* of more severe upgaze impairment in these patients. However, in our patients, blepharospasm tended to be a late manifestation of disease, occurring within one year of onset

of symptoms in only one patient.

One patient with blepharospasm in our series had postmortem confirmation of diagnosis but he also had severe arteriosclerotic changes and normal pressure hydrocephalus which may have contributed to the development of this symptom. The pathological distribution of degenerative changes in classic PSP includes extensive involvement of the midbrain and as midbrain lesions have been known to result in blepharospasm,²⁷ it is not surprising that this sign occurs so often in PSP. The more severe abnormalities of eye movement noted by Golbe *et al* would also be consistent with this.²⁴

De Bruin and Lees recently reviewed reports of patients with pathological changes of PSP and found 90 cases.¹⁷ Only five (5.6%) had blepharospasm; however, only 68.5% of their cases actually met clinical criteria for a diagnosis of PSP. The patients who did not fulfill the criteria lacked the appropriate eye findings, suggesting that they had less severe pathological involvement of the midbrain, perhaps explaining the low frequency of this sign. In addition, after the initial characterisation of the disease, necropsied cases reported in the literature are more likely to be atypical and so this series may have underestimated the true prevalence of this sign in PSP.

Oromandibular dystonia or other cranial dystonias are rare features of PSP. In 1968, David *et al* described a patient with "dystonic stiffness" of the face²⁸ and Anzil reported another with "trismus".²⁹ Although in both cases, the diagnosis was confirmed at necropsy it is not clear from the case summaries that these signs were truly dystonic. A recent necropsy series of 12 patients with PSP reported one with dystonia of the face³⁰ but the necropsy series of 90 cases reported by De Bruin and Lees does not comment on this sign at all.¹⁷ Details in clinical series are similarly lacking. Jankovic *et al* reported that 28 of 104 patients had blepharospasm "or other facial spasms".²² Elsewhere they noted that 24 of these had blepharospasm but there is no mention of the nature of the "facial spasms" in the other four or whether any of the patients with blepharospasm had other associated facial movements. Hayashi *et al* described a case of otherwise typical PSP in which the patient developed tonic contraction of the orbicularis oris and palatal muscles when attempting to make certain sounds.³¹ Although they considered that this was analogous to apraxia of eyelid opening, it may represent a form of facial dystonia.

Whereas one of our patients had a dystonic grin with intermittent repetitive semirhythmic movements of the muscles of her lower face and one had sustained involuntary smiling which appeared dystonic, many patients had facial "stiffness" which was not clearly dystonic in nature. In these patients, the facial stiffness was accompanied by a concomitant increase in facial reflexes and we therefore considered this appearance to be due to spasticity rather than dystonia. Although the characteristic sustained eyebrow elevation

commonly seen in PSP may represent dystonic involvement of the frontalis muscle, it could also represent a variable combination of spasticity, rigidity, and a response to difficulty with eyelid opening. In view of the uncertainty of classification, we chose, for the purpose of this report, not to record the furrowing of the brow or the deepening of the nasolabial folds as features of dystonia.

No patient in this series had spontaneous oromandibular dystonia. One patient with long standing PSP, however, had jaw closure dystonia and blepharospasm while taking levodopa. On discontinuation of this medication, both dystonic symptoms resolved completely. It is important to emphasise that the cause and effect relation between the dystonic symptoms and levodopa therapy was not readily apparent in this patient until long term levodopa treatment was withdrawn. The same is true of the one patient with limb dystonia induced by levodopa. Given our experience, the potential role of medication, especially levodopa, must be considered when dealing with dystonia in patients with PSP.

Despite a lack of emphasis on this feature in the literature, we found limb involvement to be the most frequent type of dystonia in our series. When Steele, Richardson, and Olszewski first described this condition in 1964, they reported seven necropsied cases and two clinical cases. One of the necropsied cases had "athetoid posturing of the limbs"¹ and one of the clinical cases, which subsequently came to necropsy, developed a "hemiplegic dystonic posture".³²

Very little emphasis has been placed on this feature since then. Jankovic *et al* reported the only large clinical series in which limb dystonia was not a rare or absent sign.²² They described "hand or foot deformity" that was elsewhere called dystonia, in 14% of a series of 104 patients. Unfortunately no further details were given regarding these patients. Similarly, De Bruin and Lees reported that 18 of 90 patients with PSP had "segmental dystonia" on necropsy but no further details were provided here either.¹⁷ It is not clear if all of these patients had limb dystonia or if some had craniocervical dystonia. The same difficulty exists with the series of 21 necropsied cases reported by Verny *et al*.³³ Two of these patients with typical pathologically established PSP were reported to have "focal or segmental dystonia". A review of the text suggests that they were referring to limb dystonia, but this was never clarified. Leger *et al* described two otherwise typical clinical cases of PSP with isolated upper limb dystonia as a presenting feature³⁴ and Rafal and Friedman described the presence of limb dystonia in eight of 30 patients (27%) with clinically diagnosed PSP.³⁵ In the last series, the dystonia occurred before the onset of the typical abnormalities of eye movement in half of the patients. In our larger series, we noted limb dystonia in a similar proportion with 22 of 83 patients being affected. This was a presenting feature in a small proportion (6/22 or 27%).

All of our patients with limb dystonia who

went on to postmortem examination showed other concurrent diseases (two had cerebrovascular disease and one had additional cortical findings). It is possible that limb dystonia in PSP is an indicator of concomitant neuropathological changes, but it must be emphasised that a necropsy was more actively sought in those patients who had atypical clinical features. The pathological findings described in our three patients undergoing postmortem examination, therefore, may not be representative of the entire subgroup of patients with limb dystonia. However, it is becoming increasingly recognised that cortical pathology such as described in one of these patients does occur in PSP.^{11-13 36} These changes may not necessarily imply the presence of a concurrent second disease but might simply represent part of the range of the disease. A recent clinicopathological conference in the *New England Journal of Medicine*,³⁷ a necropsied case of PSP with arm dystonia described in the French literature,³⁸ and Steele's experience³² clearly show that limb dystonia can be prominent in pathologically established typical PSP without any other associated disease. Our experience and that described in the *New England Journal of Medicine*³⁷ emphasise the potential for the presence of focal limb dystonia to encourage a misdiagnosis of cortical-basal ganglionic degeneration. Caution then must be exercised in diagnosing ideomotor apraxia in the presence of severe dystonic posturing, rigidity, and bradykinesia.

Although referral bias in this series may have resulted in the accrual of a higher proportion of atypical cases and, consequently, an overestimate of the frequency of dystonia in PSP, our findings clearly indicate that dystonia is a common manifestation of PSP. Limb dystonia, although sometimes indicative of other concurrent pathology, may be the presenting symptom of this disorder. Recognition of this may avoid misdiagnosis of cortical-basal ganglionic degeneration or some other condition.

Our series also shows the potential for dopaminergic medication to induce dystonia in PSP. Although this may be an infrequent cause, when dystonia is noted in patients on such medications, the dosage should be cautiously reduced or eliminated in an attempt to establish the role of drug therapy in the causation of this disabling complication.

Further study of community based populations with associated clinical-pathological correlation is necessary if the true frequency and anatomical substrates of the dystonic manifestations of this disorder are to be clarified.

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- 1 Steele JC, Richardson JC, Olszewski J. Progressive supranuclear palsy. *Arch Neurol* 1964;10:333-59.
- 2 Singh S, Smith BH, Lal A. Progressive supranuclear palsy: report of 4 cases with particular reference to blepharospasm and levodopa therapy. *Neurology India* 1974; 22:65-71.
- 3 Jackson JA, Jankovic J, Ford J. Progressive supranuclear palsy: clinical features and response to treatment in 16 patients. *Ann Neurol* 1983;13:273-8.
- 4 Kristensen MO. Progressive supranuclear palsy—20 years later. *Acta Neurol Scand* 1985;71:177-89.

- 5 Duvoisin RC, Golbe LI, Lepore FE. Progressive supranuclear palsy. *Can J Neurol Sci* 1987;14:547-54.
- 6 Khunadorn N, Kalumpaheti R, Saipetara K. Blepharospasm in progressive supranuclear palsy. The first case in Thailand. *Journal of the Medical Association of Thailand* 1979;62:89-92.
- 7 Mastaglia FL, Grainger E, Kee F, Sadka M, Lefroy R. Progressive supranuclear palsy (The Steele-Richardson-Olszewski syndrome). Clinical and electrophysiological observations in eleven cases. *Proceedings of the Australian Association of Neurology* 1973;10:35-44.
- 8 Fukushima-Kudo J, Fukushima K, Tashiro K. Rigidity and dorsiflexion of the neck in progressive supranuclear palsy and the interstitial nucleus of Cajal. *J Neurol Neurosurg Psychiatry* 1987;50:1197-203.
- 9 Lees AJ. The Steele-Richardson-Olszewski syndrome (progressive supranuclear palsy). In: Marsden CD, Fahn S, eds. *Movement disorders 2*. London: Butterworths, 1987: 272-87.
- 10 Weiner W, Lang AE. Idiopathic dystonia. In: Weiner W, Lang AE, eds. *Movement disorders: a comprehensive survey*. Mount Kisco: Futura Publishing, 1989:348.
- 11 Vermersch P, Robitaille Y, Bernier L, Watzet A, Gauvreau D, Delacourte A. Biochemical mapping of neurofibrillary degeneration in a case of progressive supranuclear palsy: evidence for general cortical involvement. *Acta Neuropathol* 1994;87:572-7.
- 12 Giaccone G, Tagliavini F, Street JS, Ghetti B, Bugiani O. Progressive supranuclear palsy with hypertrophy of the olives. An immunocytochemical study of the cytoskeleton of argyrophilic neurons. *Acta Neuropathol* 1988;77:14-20.
- 13 Paulus W, Selim M. Corticospinal degeneration with neuronal achromasia and basal neurofibrillary tangles. *Acta Neuropathol* 1990;81:89-94.
- 14 Lantos PL. The neuropathology of progressive supranuclear palsy. *Journal of Neural Transmission* 1994;42: 137-52.
- 15 Barclay CL, Lang AE. Electroconvulsive therapy in progressive supranuclear palsy. *Neurology* 1994;44(suppl 2): A152-3.
- 16 Curran T, Lang AE. Parkinsonian syndromes associated with hydrocephalus: case reports, a review of the literature and pathophysiological hypotheses. *Mov Disord* 1994;9:508-20.
- 17 De Bruin VMS, Lees AJ. Subcortical neurofibrillary degeneration presenting as Steele-Richardson-Olszewski and other related syndromes: a review of 90 pathologically verified cases. *Mov Disord* 1994;9:381-9.
- 18 Rivest J, Quinn N, Marsden CD. Dystonia in Parkinson's disease, multiple system atrophy and progressive supranuclear palsy. *Neurology* 1990;40:1571-8.
- 19 Weinmann RL. Heterogenous degeneration of the central nervous system associated with peripheral neuropathy. *Neurology* 1967;17:597-603.
- 20 Constatinidis J, Tissot R, De Ajuriaguerra J. Dystonie oculo-facio-cervicale ou paralysie supranucleaire progressive de Steele-Richardson-Olszewski. Pseudo-paralysie du regard, troubles visuo-spatiaux, pseudo-démence, alterations neuronales. *Rev Neurol* 1970;122:249-62.
- 21 Pfaffenbach DD, Layton DD, Kearns TP. Ocular manifestations in progressive supranuclear palsy. *Am J Ophthalmol* 1972;74:1179-84.
- 22 Jankovic J, Friedman DI, Pirozzolo FJ, McCrary JA. Progressive supranuclear palsy: motor, neurobehavioural and neuro-ophthalmological findings. In: Streifer MB, Korczyn AD, Melamed E, Youdim MBH (eds). Raven Press, New York, *Advances in Neurology* 1990;53: 293-304.
- 23 Maher ER, Lees AJ. The clinical features and natural history of the Steele-Richardson-Olszewski syndrome (progressive supranuclear palsy). *Neurology* 1986;36:1005-8.
- 24 Golbe LI, Davis PH, Lepore FE. Eyelid movement abnormalities in progressive supranuclear palsy. *Mov Disord* 1989;4:297-302.
- 25 Krack P, Marion MH. "Apraxia of lid opening", a focal eyelid dystonia: clinical study of 32 patients. *Mov Disord* 1994;9:610-15.
- 26 Aramideh M, Ongerboer de Visser BW, Koelman JHTM, Bour LJ, Devriese PP, Speelman JD. Clinical and electromyographic features of levator palpebrae superioris muscle dysfunction in involuntary eyelid closure. *Mov Disord* 1994;9:395-402.
- 27 Jankovic J, Patel SC. Blepharospasm associated with brainstem lesions. *Neurology* 1983;33:1237-40.
- 28 David NJ, Mackey EA, Smith JL. Further observations in progressive supranuclear palsy. *Neurology* 1968;18: 349-56.
- 29 Anzil AP. Progressive supranuclear palsy: case report with pathological findings. *Acta Neuropathol* 1969;14:72-6.
- 30 Collins SJ, Ahlskog JE, Parisi JE, Maraganore DM. Progressive supranuclear palsy: neuropathologically based diagnostic clinical criteria. *J Neurol Neurosurg Psychiatry* 1995;58:167-73.
- 31 Hayashi M, Isozaki E, Suga M, Horiguchi S, Hayashida T. A case of progressive supranuclear palsy presenting mouth opening difficulty with tonic contraction of the orbicularis oris muscle. *Rinsho Shinkeigaku—Clinical Neurology* 1992;32:1250-5.
- 32 Steele JC. Progressive supranuclear palsy. *Brain* 1972; 95:693-704.
- 33 Verny M, Jellinger KA, Hauw JJ, Bancher C, Litvan E, Agid Y. Progressive supranuclear palsy: a clinicopathological study of 21 cases. *Acta Neuropathol* 1996;91: 427-31.
- 34 Leger JM, Girault JA, Bolgert F. Deux cas de dystonie isolée d'un membre supérieur inaugurant une maladie de Steele-Richardson-Olszewski. *Rev Neurol* 1987;143: 140-2.
- 35 Rafal RD, Friedman JH. Limb dystonia in progressive supranuclear palsy. *Neurology* 1987;37:1545-9.
- 36 Nishimura T, Ikeda K, Akiyama H, et al. Immunohistochemical investigation of tau-positive structures in the cerebral cortex of patients with progressive supranuclear palsy. *Neurosci Lett* 1995;201:123-6.
- 37 Scully RE, Mark EJ, McNeely WF, McNeely BU. Case records of the Massachusetts General Hospital, Case 46-1993. *N Engl J Med* 1993;329:1560-7.
- 38 Feneelon G, Guillard A, Romatet S, Feve A, Mahieux F. Les signes parkinsoniens du syndrome de Steele-Richardson-Olszewski. *Rev Neurol* 1993;149:30-6.