PostScript

LETTERS

''Who came with you?'' A diagnostic observation in patients with memory problems?

The importance of obtaining collateral history when assessing patients attending the neurology clinic complaining of memory difficulties is well known.[1 2] Patients developing amnesia in the context of Alzheimer's disease may underplay their difficulties because of cognitive anosognosia, whereas those with purely subjective memory complaints (the ''worried well'') may overemphasise difficulties. Memory complaint, preferably corroborated by an informant, is one of the suggested diagnostic criteria of mild cognitive impairment (MCI).[3] Misdiagnosis of memory complaints may occur when no collateral history is available.[4]

For these reasons, all patients referred to my cognitive function clinic are sent, as part of their clinic appointment letter, a request asking them to bring a relative, friend, or carer from whom additional clinical information may be obtained; this is printed in bold type and in a separate paragraph. Despite this, some patients attend the clinic alone. A study was undertaken to measure the diagnostic value of this observation.

As part of an audit of referrals over a 2 year period (September 2002 to August 2004 inclusive), attendance or non-attendance of a relative or friend at each consultation was noted. Diagnosis of dementia was based on DSM-IV criteria, established by clinical interview, neuropsychological assessment and structural neuroimaging. Diagnosis of dementia subtype (Alzheimer's disease, vascular dementia, dementia with Lewy bodies, frontotemporal dementia) and of MCI followed widely accepted diagnostic criteria. All patients had minimum follow up of 6 months.

Of 183 new referrals seen, 150 (82%; 95% confidence interval (CI) 76 to 88%) followed the written instruction in the clinic appointment letter and attended with a relative, friend or carer; the remaining 33 (18%; 95% CI 4 to 31%) attended alone. In this cohort, 90 patients were diagnosed with dementia and 93 were not demented; three had MCI. Of the 150 patients accompanied to the clinic, 90 (60%; 95% CI 52 to 68%) had dementia; of the 60 not demented, one had MCI. None of the 33 patients attending alone had dementia, although two had MCI.

Hence, if attending the clinic with a relative, friend, or carer (that is, following the instructions given in the appointment letter) were considered a diagnostic test for dementia, it would have a sensitivity of 100% (95% CI 96 to 100%, Wilson method), specificity of 35% (95% CI 26 to 46%), and positive and negative predictive values of 60% (95% CI 52 to 67%) and 100% (95% CI 90 to 100%) respectively. Positive likelihood ratio was 1.55 (95% CI 1.33 to 1.80, log method), judged unimportant, but negative likelihood ratio (0) was large.

Although not absolute, as those unaccompanied patients with MCI might yet evolve to dementia, the period of follow up for some patients is brief, and clinically established diagnoses may require revision (for example, when neuropathological data become available), these findings nevertheless support the belief that attending the neurology clinic alone despite written instructions to the contrary is a robust sign of the absence of dementia.[5]

A J Larner
Cognitive Function Clinic, Walton Centre for Neurology and Neurosurgery, Liverpool, UK

Correspondence to: Dr A J Larner, Cognitive Function Clinic, Walton Centre for Neurology and Neurosurgery, Lower Lane, Fazakerley, Liverpool, L9 7LJ, UK; a.larner@thewaltoncentre.nhs.uk

doi: 10.1136/jnnp.2005.068023

Competing interests: none

References

1 **Tierney MC**, Szalai JP, Snow WG, *et al*. The prediction of Alzheimer disease: the role of patient and informant perceptions of cognitive deficits. *Arch Neurol* 1996;**53**:423–7.
2 **Carr DB**, Gray S, Baty J, *et al*. The value of informant versus individual's complaints of memory impairment in early dementia. *Neurology* 2000;**55**:1724–6.
3 **Petersen RC**. Mild cognitive impairment as a diagnostic entity. *J Intern Med* 2004;**256**:183–94.
4 **Larner AJ**. Getting it wrong: the clinical misdiagnosis of Alzheimer's disease. *Int J Clin Pract* 2004;**58**:1092–4.
5 **Matthews WB**. *Practical neurology*, 3rd ed. Oxford: Blackwell Science, 1975:111.

Laryngeal abductor paralysis can be a solitary manifestation of multiple system atrophy

Laryngeal abductor paralysis (LAP) and stridor are well known features that occur in over one third of patients with multiple system atrophy (MSA).[1] The pathogenesis of LAP is thought to be crico-arytenoid abductor muscle denervation,[2] although there is a lack of consistent evidence of motor cell loss in the nucleus ambiguus.[2 3] More recently, dystonia of the laryngeal adductor muscle has also been proposed.[4] LAP/stridor usually occurs in the advanced stages of the disease,[6] and is considered to be a poor prognostic feature.[1 2] In contrast, some MSA cases have shown LAP initially, with most of these reported by otolaryngology departments.[5–7] However, there are no systematic surveys as to the extent to which MSA patients initially present with LAP. We describe the result of a survey of 200 MSA inpatients conducted in a neurology department.

We reviewed the case records of 200 consecutive ''probable'' MSA patients who met the inclusion and exclusion criteria.[8] They were 119 men and 81 women, mean age 60 years; 29 had the Parkinsonian form (MSA-P) and 171 the cerebellar form (MSA-C). Among these, eight patients (4%) (four MSA-P, four MSA-C) were shown to have stridor as the initial manifestation (table 1). Stridor was the solitary manifestation in six of the patients, though it was combined with minimal laryngeal signs in two of these six patients (inspiratory gasp in one; hoarseness in one) and REM (rapid eye movement)-sleep related behavioural disorder (''night terror'') in one. In the remaining two patients stridor occurred together with bladder dysfunction or gait ataxia. In the former six patients, stridor was followed by bladder dysfunction in four, constipation in three, tremor/akinesia in one, ataxia in one, and postural hypotension in one. The average interval between the development of stridor and these later symptoms and signs was 3.3 years (range 1 to 6). The average interval between stridor and hospital admission was 5.4 years (1–10). In all eight patients, laryngoscopy confirmed that the stridor was caused by LAP. The grade of LAP at the first admission to our hospital (table 1), according to Isozaki's laryngoscopy classification,[9] was moderate (abductor paresis during waking; paradoxical adduction during sleep) in three and severe (complete paralysis) in five. Among those patients, continuous positive airway pressure was introduced in three, laser incision of the vocal fold was carried out in one, and subsequent tracheostomy was necessary in five.

In the cases presented, it proved true that LAP/stridor can be a solitary manifestation of MSA. The interval between LAP/stridor and hospital admission was rather long (on average 5.4 years), suggesting that the progression of LAP was not very rapid in those patients. Although the initial presentation of LAP/stridor was not common (it occurred in only 4% of all MSA patients), it is clinically relevant because patients with LAP/stridor but without obvious neurological symptoms may see general physicians or otolaryngologists first. Laryngeal stridor also occurs because of local inflammation or tumours, or from distant causes that affect the vagal nerves, such as upper thoracic or nasopharyngeal carcinoma. If such conditions have been excluded, central neurological causes should be considered. Co-morbid bladder dysfunction (particularly urinary incontinence and post-voiding residual volume of more than 100 ml), postural and postprandial syncope, parkinsonism, and ataxia are all red flags suggestive of MSA.[10] In our eight patients, bladder dysfunction was an early sign and was chronologically correlated with LAP/stridor; this finding is in line with a previous report.[9] These atypical features for a local laryngeal pathology suggest that further studies of the brain are necessary to confirm the diagnosis of MSA.

A Uzawa, R Sakakibara, N Tamura, M Asahina, Y Yamanaka, T Uchiyama, T Ito, T Yamamoto, Z Liu, T Hattori
Department of Neurology, Chiba University, 1-8-1 Inohana Chuo-ku, Chiba 260-8670, Japan

Correspondence to: Dr Ryuji Sakakibara; sakakibara@faculty.chiba-u.jp

Table 1 Patients with multiple system atrophy who initially presented with laryngeal abductor paralysis/stridor

	Years from the onset of illness														Laryngoscopy findings†
Patient*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	
1. 62/M MSA-P	Laryngeal stridor						BD	Decreased sweating	Akinesia, cerebellar ataxia, PH		**Admission:** *tracheotomy*				++
2. 74/F MSA-P	Laryngeal stridor					Constipation, BD, PH, akinesia	**Admission:** inspiratory gasp, hoarseness								+++
3. 83/F MSA-C	Laryngeal stridor, inspiratory gasp					Ataxic gait, BD, constipation			PH	**Admission:** *tracheotomy*	Akinesia			Pneumonia, **Admission:** *gastrostomy*	+++
4. 59/F MSA-C	Laryngeal stridor, RBD		Ataxic gait			BD	**Admission:** *CPAP >tracheotomy*								++
5. 62/M MSA-C	Laryngeal stridor	Constipation, BD		**Admission:** ataxic gait, akinesia, inspiratory gasp; CPAP		**Admission:** *tracheotomy*									+++
6. 57/F MSA-P	Laryngeal stridor, hoarseness	Hand tremor	Dysphasia	akinesia, ataxic gait, BD	**Admission:** *laser incision >tracheotomy*										+++
7. 53/M MSA-P	Laryngeal stridor, hoarseness, BD, erectile dysfunction, constipation	PH, decreased sweating, ataxic gait			**Admission:** dysphagia										++
8. 63/F MSA-C	Laryngeal stridor, ataxic gait	Admission hoarseness, akinesia; *CPAP*													+++

*Age, sex, diagnosis.
†Laryngeal abductor paralysis: +(mild), ++(moderate), +++(severe), Isozaki's classification.
AHI, apnoea hypopnoea index; BD, bladder dysfunction; CPAP, continuous positive airway pressure; F, female; HUT, head up tilt (60° for 10 min); M, male; MSA-C, cerebellar form of multiple system atrophy; MSA-P, parkinsonian form of multiple system atrophy; ODI, oxygen desaturation index (dips per hour); PH, postural hypotension; RBD, REM sleep behavioural disorder; SAS, sleep apnoea syndrome.

doi: 10.1136/jnnp.2005.069344

Published Online First 9 June 2005

Competing interests: none declared

References

1 **Wenning GK**, Tison F, Ben Shlomo Y, *et al*. Quinn NP. Multiple system atrophy: a review of 203 pathologically proven cases, *Mov Disord* 1997;**12**:133–47.
2 **Bannister R**, Gibson W, Michaels L, *et al*. Laryngeal abductor paralysis in multiple system atrophy. A report on three necropsied cases, with observations on the laryngeal muscles and the nuclei ambigui. *Brain* 1981;**104**:351–68.
3 **Isozaki E**, Matsubara S, Hayashida T, *et al*. Morphometric study of nucleus ambiguus in multiple system atrophy presenting with vocal cord abductor paralysis. *Clin Neuropathol* 2000;**19**:213–20.
4 **Isono S**, Shiba K, Yamaguchi M, *et al*. Pathogenesis of laryngeal narrowing in patients with multiple system atrophy. *J Physiol (Lond)* 2001;**536**:237–49.
5 **Martinovits G**, Leventon G, Goldhammer Y, *et al*. Vocal cord paralysis as a presenting sign in the Shy-Drager syndrome. *J Laryngol Otol* 1988;**102**:280–1.
6 **Kew J**, Gross M, Chapman P. Shy-Drager syndrome presenting as isolated paralysis of vocal cord abductors. *BMJ* 1990;**300**:1441.
7 **Hughes RG**, Gibbin KP, Lowe J. Vocal fold abductor paralysis as a solitary and fatal manifestation of multiple system atrophy. *J Laryngol Otol* 1998;**112**:177–8.
8 **Gilman S**, Low PA, Quinn N, *et al*. Consensus statement on the diagnosis of multiple system atrophy. *J Auton Nerv Syst* 1998;**74**:189–92.
9 **Isozaki E**, Miyamoto K, Osanai R, *et al*. Clinical studies of 23 patients with multiple system atrophy presenting with vocal cord paralysis. *Rinsho Shinkeigaku (Clinical Neurology)*. 1991;31: 249–54, (in Japanese with English abstract.).
10 **Kirby R**, Fowler C, Gosling J, *et al*. Urethrovesical dysfunction in progressive autonomic failure with multiple system atrophy. *J Neurol Neurosurg Psychiatry* 1986;**49**:554–62.

Disseminated *Pseudallescheria boydii* infection successfully treated with voriconazole

A 56 year old, right handed African-American man with past history of left knee osteoarthritis, remote intravenous drug use, remote alcoholism, and seropositivity for hepatitis C was admitted to a local hospital for fatigue, chest pain, 13.6 kg weight loss, night sweats, and vision loss. On examination, a loud systolic murmur was present. An electrocardiogram (ECG) displayed T wave alternans and a transoesophageal echocardiogram revealed severe mitral regurgitation with mitral valve vegetations, ruptured chordae tendineae, and left ventricular ejection fraction of 75%. He was diagnosed as having endocarditis and cytomegalovirus endophthalmitis, and was treated with ceftriaxone, vancomycin, ganciclovir, foscarnet, aspirin, metoprolol, lisinopril, nifedipine, and intravenous esmolol. He developed fever (39.3℃) and his mental status declined. A head computed tomography (CT) scan showed left occipital haemorrhage. His left leg became cold and pale with an ankle:brachial index of 0.4. Blood cultures grew yeast. Amphotericin B was started and he was transferred to our hospital for further care.

Upon arrival his temperature was 36.4℃, pulse was 80 beats per minute and regular, respiratory rate was 25 per minute, and blood pressure was 106/76 mm Hg on the right and 160/83 mm Hg on the left. On auscultation a II/VI holosystolic murmur over the apex and bibasilar rales were heard. His left leg was cold with pulses detectable only by Doppler. He was alert and oriented to person and place only, and recalled 1/3 items after short delay. His speech was fluent and well articulated. He had light perception on the right and was only able to count fingers centrally on the left. He displayed mild left leg weakness, normal reflexes and flexor plantar responses, mild right pronator drift, and diminished left sided proprioception. Ophthalmological examination disclosed dense bilateral vitreous infiltrates, retinal lesions, segmental retinal detachments, and scattered choroidal inflammation worse on the right. Flucytosine was added.

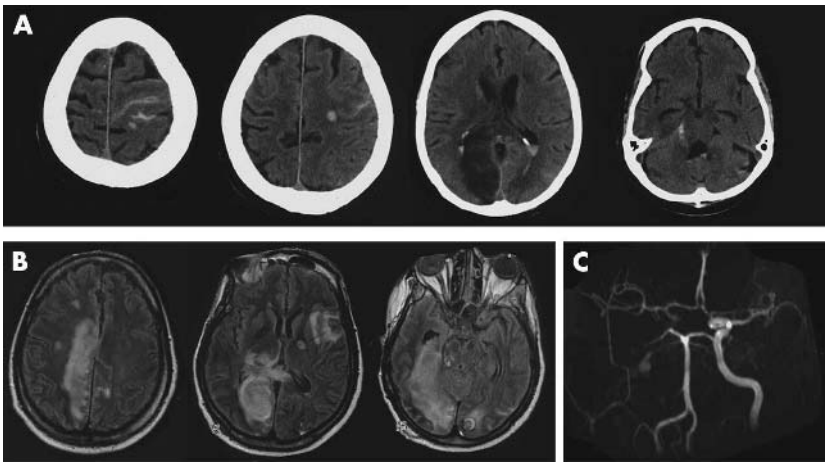

Figure 1 (A) Head computed tomography scan showing left parietal intraparenchymal, subarachnoid, and intraventricular haemorrhages, right middle cerebral and anterior cerebral arteries, bilateral posterior cerebral arteries and left insular artery ischaemic infarcts. (B) In addition, a brain magnetic resonance imaging (MRI) scan shows right thalamic and left internal capsule lacunes, and the initial left occipital ischaemic infarct with haemorrhage. (C) A magnetic resonance angiogram showing no flow in the right internal carotid artery.

An ECG revealed a prolonged QT interval, Q waves in II, III, and AVF leads, and signs of left ventricular hypertrophy. The laboratory studies revealed a white blood cell count of 25 600/μl with 69% neutrophils, 23% lymphocytes, 6% monocytes, 1% eosinophils, and 1% bands; haematocrit, 30%; platelets, 207 000/μl; troponin T, negative; aspartate aminotransferase (AST) and alanine aminotransferase (ALT), mildly elevated at 79 U/l and 99 U/l, respectively (a finding attributed to active hepatitis C); alkaline phosphatase 96 U/l; and the erythrocyte sedimentation rate (ESR) 26 mm/hr. Serological examination for human immunodeficiency virus (HIV) was negative.

A thoracoabdominal CT scan disclosed a 2×2 cm mass in the right subclavian and common carotid arteries and a right renal infarct. The left iliac artery was occluded. Intravenous heparin, in attempt to salvage the left leg, resulted in left parietal subarachnoid, intraparenchymal, and intraventricular haemorrhages. The causative organism was identified as *Pseudallescheria boydii* resistant to amphotericin, flucytosine, and fluconazole. On day 13 voriconazole was begun. He underwent urgent mitral valve replacement and left superior and profunda femoral, and iliac embolectomy. Heparin was discontinued, and he remained in prolonged coma. A head CT scan displayed new right frontoparietal, right anterior cerebral artery (ACA), right posterior cerebral artery (PCA) and bilateral small cerebellar infarcts (fig 1A). A follow up brain magnetic resonance imaging (MRI) scan revealed several new small left frontal and parietal haemorrhages and ischaemic infarcts of the right thalamus, ACA, and PCA along with the left insula, basal ganglia, and parietal lobe (fig 1B). The right internal carotid artery was occluded (fig 1C). The findings were attributed to infectious emboli and haemorrhaging from mycotic aneurysms.

On day 38 of hospitalisation the patient's coma resolved. He was eventually able to follow simple commands, and sit and stand, although expressive aphasia and left hemiparesis remained. His vision improved to 20/800 on the left. He was subsequently discharged to a long term care facility.

Discussion

Pseudallescheria boydii (anamorph or asexual phase: *Scedosporium apiospermum*) is a ubiquitous saprophytic fungus commonly found in soil, manure, decaying vegetation, and polluted water. Its commonest clinical presentation in the USA is as mycetoma, a chronic limited subcutaneous infection in immunocompetent individuals engendered by minor trauma, and is characterised by grain formation and local tissue destruction.[1] However, *P. boydii* has recently emerged as an agent of invasive fungal disease as well, a phenomenon linked to the increasing prevalence of immunosuppression in the community.[1–3] Although endocarditis and endophthalmitis have been described,[1] lung, bone, joint, or central nervous system (CNS) involvement is more typical of this organism.[4] Infections are classically acquired through penetrating trauma[1] or massive inoculation through inhalation, such as may occur in near drowning in stagnant or polluted water.[5] Disease subsequently results from contiguous extension and haematogenous dissemination. It is likely that our patient acquired his infection through prior intravenous drug use, resulting in endocarditis with secondary dissemination to eye, kidney, extremities, and brain.

Among the various types of invasive fungal disease attributable to *P. boydii*, survival rates