Behavioural symptoms in progressive supranuclear palsy and frontotemporal dementia

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measures, on the seventh day from admission, raised ICP values (30 mm Hg) and left anosmia occurred. A new CT scan revealed progression of white-matter lesions with a 12 mm midline displacement and persistence of subfalcinal and uncal herniation. As a second-level measure for refractory high ICP, the patient underwent decompressive left hemicraniectomy.

A standard left DHC including dural opening was performed (figure 1C). Parietal white-matter biopsy and microbiology samples were obtained during the procedure. The bone flap was kept in a cryopreservation tissue bank.

After the procedure, ICP values were within the normal range (5–7 mm Hg), and pupils returned to a normal size. An elective tracheotomy was carried out on the tenth day. Twelve days after admission, sedation was stopped. The patient started autonomous ventilation in spite of a poor neurological status, only spontaneous eye opening. A T2-weighted MRI 1 week after surgery demonstrated a significant reduction in initial hypertensive lesion without a midline brain shift. The results from a CSF study showed no oligoclonal bands and immunoglobulin titres, and only mild increased protein concentration was observed. On the 17th day, the patient was discharged from the critical unit.

Biopsy revealed a loss of myelin with degradation products but preserved axons and only mild increased protein concentration was observed. On the 17th day, the patient was discharged from the critical unit.

Neuroimaging and biopsy results led to a diagnosis of acute demyelinating diseases. MS: malignant monophasic acute variant (Marburg's disease) and pseudotumoral fulminant type of acute disseminated encephalomyelitis (ADEM) were considered for differential diagnosis. Marburg's type of MS was accepted as the final diagnostic because of an absence of previous infectious disease, vaccine application and malignant progression in spite of medical intensive treatment, all of them typical features of ADEM.

Decompressive hemicraniectomy use, when maximum medical treatments have failed to control refractory raised ICP, is a controversial topic. This procedure is considered a second-level treatment option without evidence which allows recommending its use systematically. Trauma brain injury and malignant middle cerebral artery infarction represent the main indications of DHC.

Inflammatory brain diseases are a rare use of DHC. Schwab et al described six cases of acute encephalitis that required DHC to control raised ICP. All patients presented almost complete recovery. Reifai et al and Von Stuckard-Barre et al reported two cases of DHC as a successful treatment for ADEM.

With regard to Marburg's disease, few cases have been reported in the literature. The use of intravenous steroids, osmotic diuretics and immunotherapy has been investigated to control this fulminating pathology with poor results. Only Giubilei et al in 1997 reported a case successfully managed with medical therapy and excellent long-term survival. No studies have been reported on DHC use in Marburg's disease. Probably, encephalitis outcome depends on lesion life-threatening mass effect and it is not conditioned by maximum neurological deficit. Therefore, urgent lifesaving treatments could yield a good final outcome, even in dominant hemisphere disease.

In conclusion, the use of DHC in pseudotumoral inflammatory demyelinating diseases could be useful not only as a lifesaving measure but also as a treatment that allows compromised brain function to recover successfully. To the authors' knowledge, this is the first reported case of DHC applied to Marburg's disease with an excellent outcome. It would be difficult to collate a large series of patients, so multicentre series would be necessary to validate the benefits of DHC and to define the best surgical timing.

COMMENT
In our case report, the patient presented with a rapid neurological status deterioration with subacute refractory raised ICP.

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Within the spectrum of frontotemporal dementia (FTD), the behavioural variant (bvFTD) presents with prominent changes in personality, most notably disinhibition, loss of empathy, stereotypic behaviour, alteration of food preference and apathy. These features have been linked to orbitofrontal and mesial-cingulate pathology. In comparison, less is known about the behavioural changes in progressive supranuclear palsy (PSP) which remain in the shadow of the motor, oculo-motor and cognitive symptoms. In one study, PSP patients were found to be apathetic and disinhibited, while the Parkinson's disease patients had a higher frequency of hallucinations, delusions and depression. Imaging studies in PSP have demonstrated frontal-lobe atrophy that correlates with the degree of executive dysfunction and behavioural change on the frontal behavioural inventory. We compared large cohorts of patients with PSP and bvFTD using a recently validated instrument, the Cambridge Behavioural Inventory. A total of 185 patients with PSP participated (100 men, 85 women, mean age: 69.3±6.6 years). Two hundred and ten caregivers of patients with FSP were contacted by the FSP Association; 135 agreed to participate (a response rate of 64%). A further 50 patients were diagnosed in Cambridge. For those
ascertained via the PSP Association, we included a symptom checklist which was reviewed to confirm that the clinical profile was typical of PSP. Comparison of demographic features, length of history and Cambridge Behavioural Inventory (CBI) scores showed no differences between the subgroups which were, therefore, combined. The PSP cohort was subdivided according to the disease duration into four groups: 1–2 years (31 patients), 3–4 years (50 patients), 5–6 years (57 patients) and over 7 years (37 patients). The bvFTD cohort consisted of 47 patients (34 men, 13 women; mean age: 60.8 ± 6.7 years) from Cambridge. The study was approved by the Cambridge-shire Research Ethics Committee.

The CBI, available from http://www.ftdrg.org, is a care-giver-based questionnaire that has been validated against the Neuropsychiatric Inventory and distinguishes characteristic profiles in FTD, Parkinson’s disease and Alzheimer’s disease. The CBI includes questions covering: mood (depression, elation), psychotic symptoms (delusions, hallucinations), challenging behaviour and aggression, disinhibition (including sexually inappropriate behaviour), eating habits, stereotypic behaviours, sleep and motivation (loss of interests and drive, social withdrawal). Care-givers rate the frequency of each behaviour over the past month on a scale from 0 (never) to 4 (constantly). In keeping with other studies, we dichotomised the data: 0–2 were considered as low, and 3 and 4 as high endorsement. Differences in distribution were analysed using χ² tests with Bonferroni corrections.

Figure 1 illustrates the distribution of high endorsement for individual CBI subtests in both patient groups. Poor motivation (apathy) was the most prevalent feature in bvFTD (70%) and was also endorsed to a high degree in PSP (55%). The bvFTD patients scored significantly higher than the PSP group (p < 0.05) on all subtests, except psychotic symptoms and sleep disturbance. On the sleep subtest, the PSP patients were significantly more impaired, while psychotic symptoms were virtually absent in both groups. No significant relationship was found in either group between any of the subtests and either age or gender. As shown in figure 1B, the only subtests in which there was a significant relationship between disease duration and high endorsement were motivation and sleep, which both increased in a linear fashion with disease duration (p < 0.05).

The most characteristic behavioural features found in PSP, and its main similarity to bvFTD, were the high frequency and severity of the apathy, which occurred despite the relatively low scores on the mood subtest. Our results confirm, therefore, the view that the apathetic syndrome in PSP constitutes an independent entity that cannot simply be accounted for by depression.

Although the CBI correlates well with the Neuropsychiatric Inventory and appears to discern changes in motivation from mood disturbance, it remains possible that physical immobility contributes to the apparent apathy in PSP.

The most striking difference between the PSP and the bvFTD groups was the much lower frequency of disinhibition, aggression, stereotypic behaviour and alterations in eating habits in the PSP cohort. It is unlikely that this difference was related to different disease severity, as the frequency of these symptoms did not increase in PSP with disease duration, in contrast to apathy, which showed a linear increase. Positive behavioural symptoms, of the type found in bvFTD, do not seem, therefore, to be linked to the progression of the disease. This observation argues in favour of a qualitative, rather than quantitative, difference between the condition. Neither group exhibited significant psychotic symptoms. Although delusions and hallucinations have been reported in FTD, they are uncommon.

The only subtest on which the PSP patients had significantly higher endorsement than the bvFTD cohort was sleep disturbance which, like motivation, showed a linear increase with disease duration. Unfortunately, the data available did not allow us to explore the nature of the sleep disturbance in more detail.

The observed differential pattern of behavioural symptoms in PSP and bvFTD is likely to reflect differences in the distribution of pathology. The pathology of bvFTD is believed to start in the orbitofrontal and mesial region, causing deficits in social cognition, emotion recognition, moral judgement and decision-making. Apathy, by contrast, is typically associated with mesial frontal pathology. The very high rate of apathy in PSP suggests that this region is dysfunctional as a result of either direct involvement or deafferentation secondary to subcortical pathology.

The findings are of practical relevance in that care-givers can be reassured that...
the disease is unlikely to lead to aggressive, challenging, unpredictable or dangerous behaviours, which can be so distressing to those involved in care of bvFTD patients. However, the recognition of apathy as an integral, organically explainable feature of the disease, rather than a sign of rejection or disinterest, might reassure the care-givers and help them to develop better coping strategies.

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