diagnosed within this period.[1] Our study confirmed the validity of this choice as only 6% of tumours developed between 3 and 6 years from the onset of PNS. When we analysed the subgroup of 11 Hu-ab-positive patients without cancer with a follow-up of more than 6 years, we found no clinical feature predicting this course.

The onset of PNS in patients over 40 years of age and with a history of smoking are both considered to be clinical clues for underlying cancer. Our study, however, shows that these variables are imperfect predictors. More than 80% of our Hu-ab-positive patients without cancer were smokers. Although three of four Hu-ab-positive patients under 40 did not develop cancer, one of them did. These data emphasise that young age may help predict the absence of cancer, but it cannot be taken as a definite predictor.

The youngest patient in our series of patients without cancer was 28 years old and had an associated SLE.[2] The presence of a systemic autoimmune disorder in a patient with Hu-abs, however, should be evaluated with caution. In a previous study, 2 of 173 patients with primary Sjögren's syndrome or SLE had Hu-abs and one of them developed small-cell lung carcinoma.[3] In patients with the Lambert–Eaton myasthenic syndrome, the incidence of autoimmune diseases in patients with cancer was 11%.[4] Thus, the presence of a systemic autoimmune disorder in a patient with Hu-abs does not rule out the possibility of a concomitant neoplasm.

In about 70% of our patients without cancer, the disability caused by PNS was mild or moderate (Rankin score <4). This proportion is considerably higher than that reported in previous studies on Hu-abs-positive patients and probably represents a selection bias.[1] Patients without cancer and with severe PNS are more likely to die from PNS within 3 years.

Anecdotal case reports suggest that the Hu-mediated immune response may destroy an underlying cancer.[5] If this hypothesis is correct, one would predict that the cytotoxic immune response would be more effective when the tumour is at the microscopic stage and therefore undetectable by even the most sensitive imaging techniques. The absence of distinguishing clinical features between Hu-ab-positive patients without cancer and those who develop cancer supports the possibility that these patients developed an effective Hu—probably a T cell-mediated—immune response that eliminated the tumour at an early stage of its development.

In conclusion, our study confirms that all patients with Hu-abs require regular examinations for underlying malignancy whatever their clinical features, including age, smoking habit and history of systemic autoimmune disease.

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Niemann–Pick type C disease in a 68-year-old patient

Niemann–Pick disease type C (NPC) is an autosomal recessive neurovisceral lipid storage disease resulting from mutations of either the NPC1 (95% of families) or the NPC2 gene, showing a wide spectrum of clinical phenotypes and a highly variable age at diagnosis.[1 2]

We report NPC1 in the oldest patient affected with the disease so far. This 68-year-old woman presented with a 15-year history of depression and fluctuating mood, and was treated several times in psychiatric departments during the previous years. At the age of 54 she was unable to work further. In the past 4 years she had developed a fluctuating, progressive dementia with reduced impulse, affective instability, dysphagia, cramped hands and dyskinesia. A percutaneous endoscopic gastrostomy was initiated owing to the loss of considerable body weight in the previous months. Initial examination, 4 years ago, showed blepharospasm, a vertical gaze palsy and choreiform oral-buccal movements in the patient. She was bedridden and was not able to communicate, was only intermittently groaning and followed simple requests inconstantly. Her hands were held in a dystonic, flectional position and her upper extremities were moved stereotypically. A positive bilateral Babinski sign was found. Cerebral MRI showed a mild cerebellar atrophy and some isolated periventricular signal intensities in the T2/TIRM. Protein was slightly enhanced (73.7 mg/dl) in CSF, without pleocytosis. Initial electroencephalography showed only a mild slowing. CT of the abdomen showed a mild splenomegaly (14 cm), which was unknown before, and a hepatic steatosis.

Owing to the combination of a slowly progredient neurodegenerative disorder with splenomegaly and vertical gaze palsy, NPC was suspected and confirmed in skin fibroblasts, where filipin staining showed a clear-cut pattern of the variant biochemical subtype.[1]

The NPC1 gene, mapped to chromosome 18q11–q12, spans 56 kb and contains 25 exons. It encodes a 1278-amino-acid integral membrane protein with 13 transmembrane domains.[1 2] Molecular genetic analysis showed a new frameshift mutation of the NPC1 gene, K1206fs, on one allele in our patient. By cDNA sequencing, the second allele remained so far unidentified, a not uncommon situation for patients with NPC1.[1] Neuroimaging of fluorodeoxyglucose (FDG)-PET labelled with fluorine-18 showed remarkable hypometabolism bilateral in thalamic and parietooccipital cortical regions (fig 1), in good agreement with the recent observation that diminished thalamic metabolism is a shared feature on FDG-PET in patients with NPC.[3]

After discontinuation of drug treatment for neuroleptic and Parkinson's disease, the cognitive functions of the patient improved without relevant drugs. Interestingly, during a period of 2 weeks, the patient communicated only in English, a language spoken temporarily during early primary school. Finally, she was able to eat and to communicate in a simplified fashion. At present, 4 years later, the patient lives in a nursing home and still displays fluctuating daily abilities.

Conclusion

NPC represents an autosomal recessive disorder with a major biochemical, molecular and clinical variability. We report on the oldest patient with NPC, which highlights this important, although rare, diagnosis of which neurologists and psychiatrists need to be aware and which, hopefully, might be treated in the near future. Ongoing research suggests that substrate reduction treatment may be able to halt or slow progression of the disease, particularly in milder cases such as the one presented.[4] At present, clinical trials with an inhibitor of glycosphingolipid biosynthesis (miglustat) are under way in patients with NPC.[5]

To enable such treatment, however, the organic cause also has to be identified early in patients with psychiatric presentations. Thus, there is need for a thorough physical and

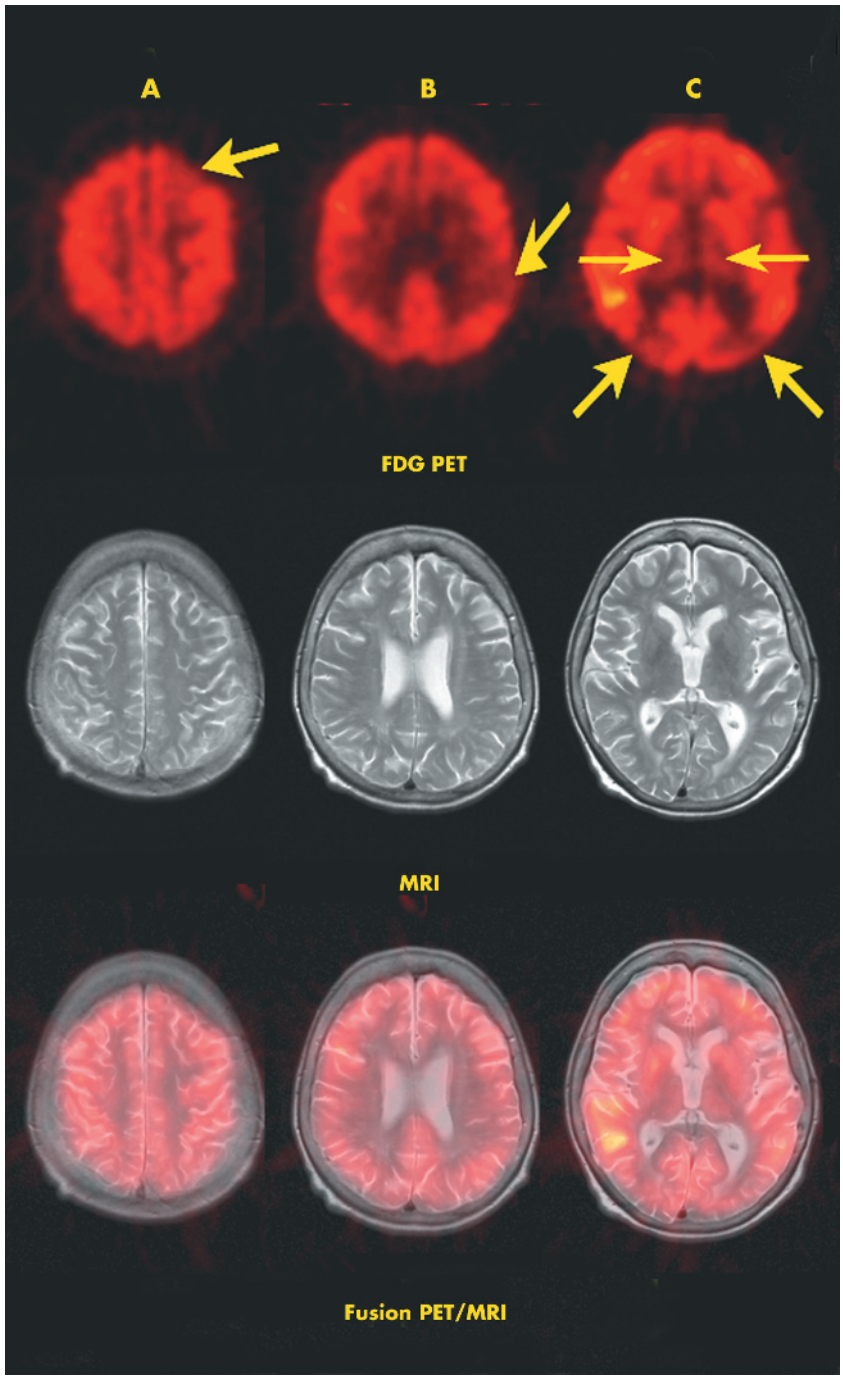

Figure 1 Image fusion of transversal slices each of positron emission tomography (PET) and T2-weighted magnetic resonance imaging (MRI). Decreased uptake of ^{18}F fluorodeoxy-glucose (^{18}F FDG; upper row) in the left frontal cortex (A, arrow), left parietal cortex (B, arrow), left and right parietooccipital cortex (C, thick arrows) and both thalami (C, thin arrows).

biochemical assessment in such patients to avoid missing these sorts of diagnosis.

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Late recovery from permanent traumatic vegetative state heralded by event-related potentials

A post-traumatic vegetative state that holds for more than 12 months is defined as ''permanent'', implying a very low probability of regaining consciousness. Here we report on a patient who emerged from a traumatic vegetative state after 20 months. Beginning from the 6th month, we observed an improvement in the event-related potentials (ERPs) of his brain to complex sensory and verbal stimulation, although the clinical examinations remained unchanged. The possible role of ERPs as predictors of regaining consciousness after a vegetative state is discussed.

The vegetative state is a most severe neurological syndrome and includes the loss of all kinds of conscious behaviour despite preserved wakefulness.[1] In patients with traumatic head injury, a vegetative state that holds for more than 1 year is considered to be ''permanent'', which implies irreversibility. In fact, even minimal improvement after this period is extremely improbable. From time to time, however, cases of late emergence are reported,[2 3] sometimes even 5 years after the incident.[4] The statement ''The available data are insufficient to provide a trustworthy estimate of the incidence of late improvement'' (Childs and Merger,[3] p 24) is still valid; figures varying as broadly as from 1.6% to 14% have been reported.[1 3]

Given the rarity of such cases, the slightest hint that such an unexpected improvement may occur would be useful. Here we describe a patient in whom cognitive components of cortical ERPs were consistently obtained for more than 1 year before clinical recovery.

A 28-year-old man was admitted to an intensive care unit with a Glasgow Coma Scale score of 3 after a severe car accident. After 5 days, he regained vigilance but had diminished gaze fixation and could not follow even the simplest commands. Intensive stimulation resulted in generalised flexor responses. Three months after the incident, he was transferred to the rehabilitation hospital with a Disability Rating Scale score of 24 (ie, 29, most severe vegetative