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disease and a failure to improve.3 Acute inflammatory demyelinating neuropathy in association with acute leukemia has been reported in only a few instances.1,3 However, in contrast to our patient, GBS in these cases was rapid progressive and the patients died in a few weeks without haematological remission.1,3

This case is remarkable because the associated neurological syndrome apparently did not adversely affect the therapeutic response and the prognosis of the myeloproliferative disorder. The reasons for this difference are not clear. The neuropathy in these cases is usually associated with leukemic infiltrations.1,3 However, remote effects probably related to transient immunosuppression in acute leukemia could serve as one contributing factor.5

in a trigger.

Guillain-Barré syndrome in some patients.2 The findings described in our case tend to support this view.

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Polysaturated fatty acids in peroxisomal disorders: a hypothesis and a proposal for treatment

Defects of peroxisomal β-oxidation of fatty acids are characteristic of a group of congenital disorders with severe disturbances of brain function, or of the spinal cord, such as the cerebro-hepato-renal syndrome of Zellweger, infantile Refsum’s disease, neonatal adrenoleukodystrophy, X-linked adrenoleukodystrophy and adrenoleukoneuropathy, hyperpipecolic acidemia, isolated absence of an enzyme of the β-oxidation sequence, and several variants described clinically as “Zellweger-like” and “neonatal adrenoleukodystrophy-like”.1 In all these syndromes very long chain fatty acids (C24-26) accumulate in plasma. Medical treatment at present succeeds in normalizing their level, by suppressing endogenous synthesis by glyceral trioleate and glyceral trierucate administration; but it is doubtful whether this leads to clinical improvement.

It has been shown recently that brain, retina, liver, kidney and erythrocytes of patients with several peroxisomal disorders are depleted of docosahexaenoic acid C 22:6o3 (DHA), a component which normally rises in the brain and retina during prenatal and postnatal development.6 Depletion of DHA is a hallmark of the monkey as well as in children causes disturbances of photoreceptor function (ERG, visual acuity) and peripheral neuropathy.1,3 Martinez2 orally administered 250 mg of DHA ethyl esters daily for 2 months to a child with an NALD-like syndrome. DHA erythrocyte levels normalised but in addition there was improvement of psychomotor development and visually and function.

We propose that the relationship between peroxisomal β-oxidation and DHA levels is not fortuitous, but is explained by the results of Voss et al.4 These authors have shown that in the rat synthesis of C 22:6o3 proceeds by β-oxidation of C 24:6o3. Obviously, oxidation of C 24 is impaired in patients with a peroxisomal β-oxidation defect, and this must result in shortage of DHA. The existence of the latter deficiency is confirmed by most recent, and unexpected, data from patients with schizophrenia treated with high doses of pheno- thiazines.3 These drugs are in vivo inhibitors of peroxisomal β-oxidation. The patients’ thymocytes became deficient in PUFA, especially arachidonic acid and DHA; while the ratio C 26:0/2:0:0 increased.

We propose that the patients with an impaired peroxisomal function should be assayed for PUFA levels in erythrocytes or platelets, and in biopsied liver. Brain and spinal cord will be still more informative, as their content is not necessarily reflected in blood cells. Data on X-ALD and AMN, which form the largest group of peroxisomal diseases, are still fragmentary. Although erythrocyte levels were normal in several patients, Martinez2 found the DHA in the brain of a single case to be below those of extreme neurological deprivation; the brain of a patient with adrenomyeloneuropathy had normal PUFA; b) patients with a lowered DHA should be treated by DHA supple- mmentation. Such treatments have been initiated by Dr M Martinez, under a European project “Pathogenesis, prevention and treatment of peroxisomal leukodystrophy”, in which more than 30 centres in 13 countries take part. For a correct evaluation it is necessary that objective tests (MRI, neuro-physiological and other tests) be carried out before treatment starts and that the evolution of the PUFA level be monitored.

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Hypers complex encephalitis in a patient with complex partial epilepsy: confirmation by the polymerase chain reaction with necropsy studies

Human hypers complex virus (HSV) is a relatively common and eminently treatable cause of encephalitis. Despite its moderately distinctive clinical presentation,1 the clinical diagnosis is made in few cases by positive virus cultures.2 This approach (HSV is unreliable,3 and until recently laboratory diagnosis of HSV has been unsatis- factory: isolation of the virus from CSF is rarely achieved and, although it has proved problematic, diagnosis by serology or immunoblotting must rely on the evolv- ing immune response and is therefore delayed and indirect, and brain biopsy is highly invasive. The polymerase chain reaction (PCR) is a method for the amplifica- tion of DNA with exquisite sensitivity. In cases of suspected HSV it holds out the promise of early and accurate diagnosis.

We describe a case in which the eventual diagnosis of HSV by PCR was confirmed at necropsy. It illustrates the potential diffi- culty of making this diagnosis in a patient with pre-existing epilepsy and also exempli- fies the occasional occurrence of a false neg- ative result from PCR. This implies that negative results should be assessed critically and that repeated sampling may be worth- while in equivocal cases.

A 73 year old woman was admitted “drowsy but responsive” to her District General Hospital in 1991 following “multi- ple fits”. In 1982 she had been investigated because of a 1 year history of memory loss, depersonalisation, microsia, formed visual hallucinations and, rarely, loss of conscious- ness. Successive EEGs revealed only mod- erate bitemporal abnormalities, but a CT scan demonstrated a right petrous menin- gioma with associated intracerebral oedema. The possibility of surgery was consid- ered but rejected. Her epilepsy was con- trolled by anticonvulsants and she became prone to periods of prolonged postictal confusion. On admission in 1991 she was drowsy but afebrile and there were no focal neurological signs. Her level of alertness improved over the following few days, although she remained confused, bel- ligent and possibly dysphasic. Five days after admission she had a flurry of complex partial seizures, became comatose and was treated with intravenous antibi- otics. Three days later she was transferred to our care. On arrival she was cyanosed, febrile at 40°C, and deeply unconscious. She was severely hypoxic and was ventil- ated. A chest radiograph suggested left basal consolidation. An EEG showed rhythm-
mic slow wave discharges on the right at 1–2 Hz, occasionally associated with spikes, and more clearly epileptiform activity on the left. Intravenous diazepam abolished such activity on the left, but spared that on the right. The initial diagnosis was of pneumo-
nia with complex partial status epilepticus. On the following day the EEG record was dominated by widespread, irregular, rhyth-
mic complexes with a period of approxi-
mately two seconds. Unenhanced CT scan appear-
ances had not, however, changed since 1988. A lumbar puncture was per-
fomed. The protein level had failed to improve. The CSF was under a pressure of 24
cms and contained 52x10^3/L leucocytes (93% lymphocytes) with normal CSF pro-	eins and normal glucose ratio. A fur-
ther lumbar puncture two days later showed
worsening abnormality and treatment was
started with intravenous Acyclovir, rifampicin, isoniazid and pyrazinamide. Over the following nine days her reflex
responses deteriorated and she died.

A polymerase chain reaction for the amplification of HSV-1 DNA was carried out post-mortem using the primer
scavenger oligonucleotide described by Aurelius et al., with some modifications. Reaction conditions for first and second
round PCR were as described previously. The patient’s second CSF sample and the positive control contained HSV DNA after two rounds of PCR (fg). The first
CSF sample, taken two days before, was negative. Neither oligonucleotide bands of total IgG, nor antigen specific oligonucleotide bands were detected in either CSF sample.

Viral culture and viral titres were negative in the first CSF sample; in the second sample viral culture was again negative but a weak IgG response for herpes simplex virus 1 was detected by ELISA.

Post mortem examination confirmed the presence of a right petrous meningioma. The brain was swollen and soft, with uncal and cerebellar tonsillar herniation.

Temporal and insular cortex were involved in a marked meningoencephalitis, with necrotising venulitis and perivascular infil-
tration by lymphocytes and macrophages. Immunoperoxidase staining revealed a very striking positive reaction for herpes simplex
virus antigens in neurons, macrophages, and many cells whose nature could not be identified.

This complex case emphasises the impor-
tance of prompt treatment with Acyclovir where there is clinical suspicion of the diag-
nosis of HSE. In general the diagnosis should be considered in any patient with a
fever and depression of consciousness: sus-
picion should be heightened by accompany-
ing abnormalities of behaviour, focal
seizures or signs, especially dysphasia, evi-
dence of acute temporal lobe pathology from neuroimaging or EEG, or a CSF lymp-
photysis. A number of factors conspired to reduce clinical suspicion in the present
case, in particular the patient’s long history of epilepsy with pronounced post-ictal con-
fusion and the clinical absence for a severe case of experimental pneumonia. In retrospect, the onset of encephalopathy with drowsiness, seizures, fever and new EEG disturbance was fully in
keeping with the eventual diagnosis of HSE.

It is of course always important, even in the context of a patient with a chronic disorder, to assess an acute illness on its own merits.

Although PCR is highly sensitive and specific, the negative result from the first
CSF sample reminds us that all laboratory
tests give rise to occasional false negative results: it is advisable to test more than once in difficult cases, and a negative PCR result
should not preclude the use of acyclovir
where HSE is suspected clinically.

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3 Aurelius E, Johansson B, Skoldenburg B, Staland A, Gloger H. Herpes simplex encephalitis by nested poly-
4 Wakefield AJ, Fox JD, Sawyer AM, et al. Detection of herpes virus DNA in the large intestine of patients with ulcerative colitis and Crohn’s disease using the nested poly-

MATTERS ARISING

Accuracy of clinical diagnosis of idiopathic Parkinson’s disease

I read the paper by Hughes et al in the journal with much interest and wish to compliment them for their work.

The percentage of inaccurate clinical diagnosis of idiopathic Parkinson’s disease (IPD) in their study is identical to that
which we reported last year. Their observa-
tions, however, are different from our study in several respects. For example, the largest subgroup of patients (65% of cases) which were erroneously diagnosed as having IPD by Hughes et al had progressive supranuclear palsy (PSP), in contrast, all the necropsy proven PSP cases in our study were recog-
nised before death. The reasons for that
difference are unclear. The final clinical
diagnosis in all our patients was made by
the same neurologist. Hughes et al did not indicate the number of neurologists and the
geriatricians involved in the evaluation of their patients and those contributing to the brain bank. The larger the number of clini-
cians assessing the patients, the greater would be the variability and the chance of error.

The second possibility for the misdiagno-
sis is that the patients may have been evalu-
ated during an early stage of illness, before the features characteristic of PSP were evi-
dent. The clinical data in our report were collected prospectively and we were able to assess the accuracy of the final diagnosis based on the entire period of illness which is usually longer than 12 years. Of the five patients who had had a progressive supranuclear palsy they were recognised within 5 years of onset. It is unclear in the report if they relied on initial or the final clinical diagnosis.

Another aspect that we made a note of but is not clarified in their study is the method used to assign one diagnosis to a
patient. We considered the clinical diagno-
sis correct only if it was the sole diagnosis or the pathological diagnosis was noted at the
top of the diagnostic possibilities.

Several variants of PSP, including PSP-C
were clinically and pathologically identified in the early 1960s. Those patients who were evaluated before 1960 had a large proportion of inaccurate diagnosis by current standards. Their paper does not indicate if some of the errors in diagnosis may be related to the calendar year of the study.

In addition to our paper, there is a small study by Forno et al which addressed the issue of the accuracy of clinical diagnosis in IPD. Hughes et al reported 125 cases included patients using the UK Parkinson’s Disease Society Brain Bank (PDSBB) clinical diagno-

cstic criteria. By those criteria, 11 patients did not have IPD, yet 3 of them were turned out to have Lewy body pathology. They have not discussed the reasons for this significant error. Whatever the reason, it illustrates that no diagnostic criteria are fool-proof.

I suggest a minor amendment to the PDSBB clinical criteria for consideration by the committee. Postural instability which has been recommended as one of the two major manifestations necessary for making the diagnosis of PS should be deleted if the instability is present in a large segment of normal elderly people. Most clinicians looking after elderly people consider that individuals in this age group lose balance rather easily compared, with younger age groups. Postural instabil-
ity, as evaluated in the PS, was carefully studied by Weiner et al in the elderly. When all the neurological, mechanical and other possible causes for postural reflex impairment were excluded, they noted that postural instability was an age-related phe-
nomenon. While 43% of those between age 60-69 years had impaired postural reflexes, 70% between 80-89 and 100% of those between age 90–99 years had impaired pos-
tural reflexes.

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1 Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson’s disease: A clinico-
2 Rajput AH, Rozdilsky B, Rajput Alex H. Accuracy of Clinical Diagnosis in

Figure Second round PCR products, on ethidium bromide stained gel, showing a positive control lane 3 (patients CSF) and lanes 9 and 10 (positive controls). Lane M contains molecular weight markers. pd = primer-dimer amplification products.