Letters to the Editor

937

protected disease course and a failure to improve.3 Acute inflammatory demyelinating neuropathy in association with acute leukaemia has been reported in only a few instances.1,4 However, in contrast to our patient, GBS in these cases was rapid pro-
gressive and the patients died in a few weeks without haematological remission.1,3 This case is remarkable because the associ-
ed neurological manifestation 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 attributed to leukaemic infiltrations.1,3 However, remote effects probably related to transient immunosuppression in acute leukaemia could serve as one contributory factor in triggering Guillain-Barré syndrome in some patients.2 The findings described in our case tend to support this view.

A RODRIGUES A MONTEIRO J VIANA A MACEDO F GRACA A SENA
Haematology Unit and Neurological Service, Hospital de St Antono dos Capuchos, 1100 Lisbon, Portugal.

Correspondence to: Professor Sena, Neurology Service.

1 McLeod JG, Walsh JC. Peripheral neuropathy associated with lymphomas and other retic-
2 Kendel DA, Albright RE, Graham DG. Infiltrative polyneuropathy due to acute monoblastic leukaemia in hematologic remis-
4 Bennett JM, Catesovsky D, Daniel MT, Flandrin G, Gatlon DAG, Granick H, Sultan C. Proposed revised criteria for the classifica-

Polyunsaturated fatty acids in peroxi-
somal disorders: a hypothesis and a proposal for treatment

Defects of peroxisomal β-oxidation of fatty acids are characteristic of a group of con-
genital disorders associated 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 adrenoleu-
koencephalopathy, hyperpripicolic acidosis, isola-
lated 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 (C-24, C-26) accumulate in plasma. Medical treatment at present succeeds in normalizing their level, by suppressing endogenous synthesis by glyceral trioleate and glyceral triericate administration; but it is doubtful whether this leads to clinical improvement.

It has been shown recently that brain, retin, 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.2,3 Depletion of DHA in the motor neuron as well as in children causes disturbances of photoreceptor function (ERG, visual acuity) and peripheral neuropathy.4 Martinez2 orally administered 250 mg of DHA ethyl-
hed daily for 2 years to a child with a NALD-like syndrome. DHA erythrocyte levels normalised but in addition there was improvement of psychomotor development and visually de- defines. 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 diet 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 mecha-
nism is confirmed by most recent, and unexpected, data from patients with schizo-
phrenia treated with high doses of pheno-
thiazenes.1 These drugs are in vivo inhibitors of peroxisomal β-oxidation. The patients’ thrombocytes became deficient in PUFA, especially arachidonic acid and DHA; while the ratio C 26:0/22:0 increased.

We propose that in 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 still be 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 depleted DHA in the brain of a single case to be below those of extreme nutritional deprivation; the brain of a patient with adrenoleukodystrophy had normal PUFA; b) patients with a lowered DHA should be treated by DHA supple-
mentation. Such treatments have been initi-
ated by Dr M Martinez, under a European project “Pathogenesis, prevention and treat-
ment of peroxisomal leukodystrophies”, 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. The evolution of the PUFA level should be monitored.

FRANK ROEIS
Human Anatomist and Embryologist, University of Gent, Belgium.
SVEN FISCHER
Department of Medicine II, Klinikum Großenhain, University of Berlin, Germany.
WERNER KESSLING
Department of Psychiatry, Technical University of Munich, Germany.

Correspondence to: Professor Roels, coordinator European Project of "Peroximal-Leuko-
dystrophy, Godshutienlsaan 4, 9000 Gent, Belgium.

4 Birch DG, Lees MJ, Goldman DB, Urey RD. Retinal development in very-low-birth-
6 Voss A, Reithart M, Sankerappa S, Sprecher H. The metabolism of 7,10,13,16,19-docosapentaenoic acid and 7,10,13,16-

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

Human herpes simplex virus 1 (HSV) is a relatively common and eminently treatable cause of encephalitis. Despite its moderately distinctive clinical presentation,1 the clinical diagnosis of herpes simplex encephalitis (HSE) is unreliable,2 and until recently lab-
oratory diagnosis of HSE has been unsatis-
factory: isolation of the virus from CSF is rare; achieved; antiviral therapy has proved problematic, 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 HSE it holds out the promise of early and accurate diagnosis.

We describe a case in which the eventual diag-
osis of HSE 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-
ifies 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 difficult 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 year’s history of depersonalisation, micropsia, formed visual hallucinations and, rarely, loss of conscious-
ness. Successive EEGs revealed only mod-
erate bitemporal abnormalities, but a CT scan demonstrated a persistent petrous meningioma with associated intracerebral oedema. The possibility of surgery was con-
sidered 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-
igerent and possibly dysphasic. Five days after admission she had a flurry of complex partial seizures, became afebrile 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 venti-
lated. A chest radiograph suggested left basal consolidation. An EEG showed rhyth-

Downloaded from http://jnnp.bmj.com/ on August 29, 2017 - Published by group.bmj.com
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, was continued for several days, and the patient was discharged on 100 mg/day. The EEG on discharge was normal.

On the following day the EEG record was dominated by widespread, irregular, rhythmic complexes with a period of approximately two seconds. Unenhanced CT scan appearances had not changed, however, since 1988. A lumbar puncture was performed, and cerebrospinal fluid (CSF) analysis revealed negative results. The CSF was under a pressure of 24 cm and contained 52x10^6 leukocytes (95% lymphocytes) with normal CSF protein levels and CSF glucose ratio. Further 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 set 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 (fig). 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 specific for herpes simplex virus 1 was detected by ELISA.

Post-mortem examination confirmed the presence of a right petros meningioma. The brain was swollen and soft, with uncal and cerebellar tonsillar herniation. Temporal and insular cortex were involved in a marked meningoecephalitis, with necroinflammatory and perivascular infiltration 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 importance of prompt treatment with Acyclovir where there is clinical suspicion of the diagnosis of HSE. In general the diagnosis should be considered in any patient with fever and depression of consciousness: suspicion should be heightened by accompanying abnormalities of behaviour, focal seizures or signs, especially dysphasia, evidence of acute temporal lobe pathology from neuroimaging or EEG, or a CSF lymphocytosis. 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 confusion and the absence of a severe progressive encephalopathy. 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 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.

AZI ZEMAN
K MILES
M CIARDI
S SHORKON
Institute of Neurology, Queen Square,
London, UK

Division of Virology, University College and Middlesex School of Medicine, London, UK


Figure Second round PCR products, on ethidium bromide stained gel, showing a positive DNA product in lane 3 (patient's CSF) and lanes 9 and 10 (positive controls). Lane M contains molecular weight markers. pd = primer-dimer amplification products, 139 bp = herpes simplex virus type 1 second round PCR products.
Herpes simplex encephalitis in a patient with complex partial epilepsy: confirmation by the polymerase chain reaction with necropsy studies.
A Z Zeman, K Miles, M Ciardi, J Shorvon and J D Fox

J Neurol Neurosurg Psychiatry 1993 56: 937-938
doi: 10.1136/jnnp.56.8.937-a

Updated information and services can be found at:
http://jnnp.bmj.com/content/56/8/937.2.citation

These include:

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/