Central pontine myelinolysis temporally related to hypophosphataemia

Central pontine myelinolysis (CPM) is known to be associated with the rapid correction of severe hyponatraemia. However, there have been case reports of CPM occurring in normonatraemic patients. Here we describe two patients in whom chronic alcohol abuse led to profound hypophosphataemia that was closely temporally related to the development of CPM.

Case 1

A 44 year old woman was admitted with a seven days of difficulty in walking, and three day history of progressive dysarthria, and subjective sen-}

tation. She had consumed 100–140 units of alcohol a week for several months before presentation. On admission she was fully oriented with normal from the onset of symptoms to the time of death.

Case 2

A 44 year old woman was admitted with a seven days of difficulty in walking, and three day history of progressive dysarthria, and subjective sen-}

tation. She had consumed 100–140 units of alcohol a week for several months before presentation. On admission she was fully oriented with normal from the onset of symptoms to the time of death.

The two patients presented here showed acose temporal association between severe hypophosphataemia and the development of CPM. Both patients abused alcohol, and the first patient had moderate hyponatraemia with hypokalaemia. They may therefore have been particularly susceptible in CPM for a variety of reasons. It is possible, however, that severe hypophosphataemia adversely affected the Na+/K+-ATPase pump and finally triggered an apoptosis and CPM. The temporal association of neurological deterioration with the rapid correction of profound hypophosphataemia in case 1 is unlikely to relate to osmotic stress in view of the small contribu-

tion. However, whether or not a new concept could accommodate less widespread or incomplete apoptosis.

There are useful practical conclusions to be drawn from the observed association of CPM with hypophosphataemia. First, one must suspect the diagnosis of CPM even in patients even without “typical” electrolyte abnormalities. Second, as severe hypophos-
phataemia in itself has been correlated with increased mortality it would seem prudent to check and treat low serum phosphate concen-

trations in susceptible patients. This particularly refers to alcohol abusers or malnourished patients treated with intravenous glucose, diuretics, and steroids which may lower serum phosphate concentrations.

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Spastic movement disorder: what is the impact of research on clinical practice?

One expects that convincing research results would have an impact on clinical practice. However, whether or not a new concept becomes transferred to an application in clinical practice is dependent on the medical
which should determine the therapeutic
has to be separated from functional testing,
examination required for diagnostic purposes
movement, essential reflex mechanisms are
action (which impairs the patient). During
bedside examination are an epiphenomenon
physical signs obtained during the clinical
formance of functional movements.
by these drugs could be associated with an
orientation
articles in journals with a practical
established scientifically in journals with a
Facts and consequences

Over many years it was widely accepted that
spasticity consists of muscle hypertonia (that
is, medically described resistance to movement
called to stretch") caused by exaggerated re-
exues, leading to the spastic movement
disorder.' This concept was based on animal
observations (for example, the decretebrate
cat') and on the physical signs evident on
clinical examination at the bedside. Conse-
quently, the aim of any treatment was to
reduce reflex activity by antispastic drugs.
Possible differences in pathophysiology be-
tween the clinical signs of spasticity and the
spastic movement disorder which hampers the
patient were not considered.

The new concept
Early clinical observations1 and studies in the
1980s on spastic movement disorders clearly
failed to support the traditional concept. In
the subsequent 20 years an increasing
number of studies using different technologi-
ical approaches with electromyographic (EMG)
and clinical approaches with electromyographic
(EMG) and biomechanical recordings focused
the subsequent 20 years an increasing
consequences

The old concept was simple to understand and
had a clear therapeutic consequence: the
prescription of antispastic drugs. It is
seemingly logical that exaggerated reflexes
cause muscle hypertonia. The new concept
is more complex. Its implications—that
antispastic drugs should not generally be
used—make the doctor somewhat re-
sources.

It is not rewarding for a neurologist to take
care of patients after a stroke and to have to
explain that there are limited therapeutic
options (the drug treatment is impossible to
restore normal function, and that physical
exercises will be more helpful than drug
treatment).

It is, of course of no interest for companies
producing antispastic drugs to support
graduate medical education in this new
concept, with its limited opportunities for
treatment.

The consequences of this experience should be
as follows. First, scientific research results
should be translated into an understandable
and pragmatic format, to convince doctors
and patients of the superiority of the new
concept. Second, such a novel concept should
initiate the development of new forms of
treatment (for example, in the field of active
physiotherapy); at very least it should be
associated with provision of a structured
physical treatment programme which allows the
doc-
tor to become involved. Third, the concept
should emphasise that immobilised patients
may benefit from the use of antispastic
drugs (for example, in the management of spasms
and for easier nursing); this would make the
concept more acceptable to the drug
companies. Finally, the concept should include
perspectives and limitations of any possible
achievements.

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Intracranial hypotension after
chiropractic manipulation of the
cervical spine

The aetiology of intracranial hypotension is
not fully understood, but CSF leakage from
spinal meningeal divertica or dural tears
may be involved. In the majority of patients
without a history of mechanical opening of
the dura the cause of intracranial hypotension
is unknown and the syndrome is termed
“spontaneous” intracranial hypotension. We
report a case of intracranial hypotension ensuing
after a spinal chiropractic manipu-
lation leading to CSF isodense effusion in the
upper cervical spine.

Case report
A 40 year old woman underwent a spinal chiro-
practic manipulation. The chiropractor
grasped the head of the supine patient and
exerted axial tension while rotating the head.
During this manoeuvre the patient complained
of a sudden sharp pain in her upper neck, and
the procedure had to be stopped immediately.
Subsequently she complained of headaches
and after 24 hours she developed nausea and
vomiting. Her headaches worsened, and lying
down gave the only measure of limited relief.
On the sixth day she developed double vision
and presented to the neurology department of
a community hospital.
She had a right abducens palsy and pachy-
meningeal gadolinium enhancement on mag-
netic resonance imaging (MRI). The first

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working diagnosis was encephalomyelitis and steroids were given. Six days later a repeat lumbar puncture showed 60 cells per mm³ and raised lactate. The second working diagnosis was basal tuberculous meningitis and treatment with a antituberculous regimen was started. Another MRI was performed, and now showed bilateral subdural effusions. At this point blood leucocytosis was found and a subdural empyema was postulated as the third working diagnosis. The patient was referred to our neurosurgical university hospital for surgical evacuation and leptomeningeal biopsy.

On examination there were no signs of meningitis and apart from an incomplete right sixth nerve palsy the cranial nerves were intact. Neuropsychologically she was fully oriented but with slowed reactions. On general examination she showed no signs of a connective tissue disorder. All blood tests were within normal limits.

The diagnosis of intracranial hypotension was established by the typical clinical and radiological findings and treatment was started. On MRI a suspected CSF leak at the level of C1–C2 could be identified, with a CSF isodense fluid accumulation in the paravertebral soft tissue and musculature (fig 1). MRI of the spine was demonstrated radiographically. Furthermore MRI of the spinal dural thecal sac with subse-
dual interspace after spinal chiropractic manipulation. There is marked CSF isointense fluid accumulation (arrows) in the dorsal perivertebral space around the dural sac. The subarachnoid space around the myelon is flattened. The level of maximum extradural CSF isointense fluid accumulation was at C1/C2; no other site of spinal CSF leakage could be detected.

Clinical and electrophysiological improvement of adrenomyeloneuropathy with steroid treatment

The two most common phenotypes of X-linked adrenoleucodystrophy are the childhood cerebral form and adrenomyeloneuropathy, which occurs mainly in adults and affects the long tracts in the spinal cord most severely. Most patients with the cerebral forms have an inflammatory demyelinating process, while the principal pathology of adrenomyeloneuropathy is a non-inflammatory distal axonopathy. Although 30% of patients with adrenomyeloneuropathy also develop some degree of inflammatory brain pathology, all forms of X-linked adrenoleucodystrophy are caused by a defect in the gene ABCD1 which codes for the peroxisomal membrane protein ALDP and is associated with the abnormal accumulation of very long chain fatty acids. Most patients with X-linked adrenoleucodystrophy have primary adrenocortical insufficiency. Although adrenal hormone treatment is considered mandatory and may be life saving, most investigators have expressed the opinion that it does not alter neurological status. We report a patient with a variant of adrenomyeloneuropathy in whom adrenal hormone replacement therapy improved neurophysiological function and clinical status.

Case report

A 39 year old man was evaluated for adrenoleucodystrophy at the Kennedy–Krieger Institute (KKI) in 1985, because his nephew had been diagnosed with childhood onset adrenoleucodystrophy. The nephew died aged nine years and had necropsy confirmation of the diagnosis. Our patient had no neurological symptoms at that time. In 1996, he returned to KKI with complaints of “leg stiffness” and “being off balance.” His plasma adrenocorticotropic hormone (ACTH) level and serum very long chain fatty acids were both raised. Brain magnetic resonance imaging (MRI) showed “subtle white matter changes in the posterior periventricular region that were either at the upper limit of normal or severely abnormally” (not shown).

In July 2000, he presented to the Buffalo VA Medical Center with complaints of leg stiffness and balance problems. Physical examination showed mild hyperpigmentation, especially in the palmar skinfolds. On neurological examination he was ataxic and had proprioceptive and vibratory sensory loss in the lower limbs. Deep tendon reflexes were increased and bilaterally active. There were palmar and plantar fasciculations. The patient was unable to stand on his toes. The clinical diagnosis was adrenoleucodystrophy (ADL).

figure 1

In a series of 30 patients with intracranial hypotension, Chung et al reported one who had also undergone spinal chiropractic manipulation. A spinal CSF leak could not, however, be identified. In their study, thorough history taking in all the patients revealed risk factors for a possible traumatic origin of spinal hypovolaemia in seven of the 30 patients, including playing golf, vigorous physical activity, swimming, yoga exercise, and upper respiratory infections with severe cough.

Trauma, even if mild, may be a risk factor and may account for a substantial proportion of patients with “spontaneous” intracranial hypotension. Our case shows that spinal chiropractic manipulation can lead to intracranial hypotension. History taking should include a thorough inquiry about trauma, with special emphasis on chiropractic manoeuvres and mild traumatic events. The syndrome of intracranial hypotension must be added to the list of differential diagnoses in cases of subdural effusion or meningeal enhancement because of the favourable outcome with conservative treatment. A substantial number of unhelpful meningeal biopsies and empiric intravenous courses of antibiotic drugs may be avoided by considering this syndrome in the differential diagnosis.

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examination there was increased tone and decreased vibratory and positional sensation in the lower extremities only. His gait was spastic, with hyperactive deep tendon reflexes and extensor plantar responses.

Before steroid treatment was begun, brain MRI and evoked potential testing were undertaken, as follows:

- **visual** evoked response: OS/OD, P100 = 166.0/159.6 ms
  - brain stem auditory evoked response:
    - A wave, 1.20 ms; II–V absent; AD, wave I, 1.94 ms; II, 2.88 ms, III–V absent;
    - peroneal nerve somatosensory evoked response: left/right, L3 = 8.64/9.44 ms, P27 = 54.60 ms (delayed)/absent;
    - median somatosensory evoked response and upper and lower extremity peripheral nerve conduction velocities: normal.

Brain MRI showed mild to moderate confluent hyperintense lesions on T2 weighted and fluid attenuated inversion recovery images (FLAIR) in the posterior periventricular white matter (not shown).

After six months of oral prednisone, 20 mg twice daily, the patient had significant improvement in his leg stiffness and gait. Reflexes became normal, but the sensory deficits were unchanged. ACTH levels declined from 3122 to 26 pg/ml. On visual evoked response testing, P100 latencies became normal (OS/OD, P100 = 106.6/110.0 ms; fig 1). Brain stem auditory evoked responses showed improvement by the appearance of wave II and III in the left side, but no change in the right side. The left peroneal somatosensory evoked response became nearly normal, with a P27 latency of 35.5 ms; the right P27 peak appeared at a latency of 44.8 ms. Median somatosensory evoked response and peripheral nerve conduction velocities were unchanged. The improved evoked response and brain stem auditory evoked response findings were sustained at the 15 month follow up study (not shown).

**Comment**

The neurological findings and history in this patient are typical of adrenomyeloneuropathy, and this diagnosis was confirmed by the abnormally high plasma levels of very long chain fatty acids. In addition, brain MRI studies showed the presence of moderately severe cerebral inflammatory involvement, as occurs in approximately 30% of patients with adrenomyeloneuropathy. The demyelinating or inflammatory lesions affecting the spinal cord and brain stem long tracts that are characteristic of this disorder are the likely causes of the gait disturbance, the prolonged interpeak latencies of the peroneal somatosensory evoked response, and the abnormalities of brain stem auditory evoked response before prednisone treatment. The posterior periventricular lesion noted on MRI indicates that the patient had inflammation or demyelination in the visual radiations, which probably correlates with the initially abnormal visual evoked response. Adrenocorticosteroid replacement therapy restored the plasma ACTH level to normal, improved the gait disturbance, and completely corrected the visual evoked response latencies.

Prolonged interpeak latencies of the somatosensory evoked response and the brain stem auditory evoked response, with nearly normal or normal amplitudes, reflect demyelination. The reduced interpeak latencies from the brain stem auditory evoked response and the peroneal somatosensory evoked response after treatment indicate remyelination. 1 No patients with X-linked adrenoleukodystrophy appear to have spontaneous remissions. 1 Therefore the clinical and evoked response improvement is likely to be attributable to prednisone treatment. Although two male patients with adrenomyeloneuropathy showed neurological improvement after starting on prednisone, neither patient had simultaneous improvement in their evoked responses and MRI. 1 13 Our findings are thus consistent with the hypothesis that steroid replacement therapy ameliorated the inflammation or demyelination in our patient. His improvement with prednisone replacement therapy suggests that a more systematic analysis of the neurological effects of corticosteroid treatment in X-linked adrenoleukodystrophy is warranted.

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**Acute anterior radiculitis associated with West Nile virus infection**

Our knowledge of neurological syndromes associated with West Nile virus (WNV) infection continues to evolve. Recent reports during the 1999 outbreak in New York City have most commonly described an encephalitis and aseptic meningitis associated with the infection, but muscle weakness was also found to be an unexpected but prominent feature. 2 Although electrophysiologic testing in some cases revealed a predominantly axonal polyneuropathy, the mechanism of this weakness remains unclear. The first attempt to account for WNV associated weakness was described in a 1979 case report, suggesting acute anterior myelitis as the aetiology. 3 More recently, involvement of the anterior horn cell was implicated in several cases of WNV poliomyelitis, as localised by electrophysiologic studies. 4 14 We present the first known case of a WNV poliomyelitis-like syndrome with associated magnetic resonance imaging (MRI) findings, and propose an alternate explanation for the associated weakness.

**Case report**

A 29 year old right handed man with no significant past medical history reported...
symptoms of fever, myalgia, nausea, vomiting, and neck stiffness several days after a fishing trip in the Chicago metropolitan area in August 2002. Simultaneously with these symptoms, he described dull, non-radiating left hip pain. On the following day he began to experience weakness of his left leg, which caused him some difficulty in walking. However, he consistently denied back pain or sensory symptoms. Within three days, his constitutional symptoms resolved, but the hip pain and leg weakness persisted. There was no relevant social history. Of note, he reported multiple insect bites while on that fishing trip.

On examination, he was afebrile, alert, and fully cognisant. General examination was unremarkable. Straight leg raising did not produce pain, and there was a full range of motion in the left hip. Neurological examination revealed a flaccid monoparesis (MRC grade 2–3) of the left leg, involving both proximal and distal muscles. Deep tendon reflexes were absent in the left lower extremity. Sensory examination was normal. He had an antalgic gait, with associated left foot drop and a hip thrust to compensate for significant hip flexor weakness. The remainder of the examination was unremarkable.

Laboratory evaluation included the following normal tests: complete blood counts, metabolic panel, antineural antibody, serum immunoelectrophoresis, and HIV-1 western blot. Cerebrospinal fluid (CSF) analysis showed 22 white cells per mm$^3$ (80% lymphocytes), glucose 53 mg/dl, and protein 63 mg/dl. Electrodiagnostic studies of the affected limb were obtained 11 days after the onset of symptoms. These showed motor amplitudes reduced by 79–95% in the left lower extremity when compared with the right. Conduction velocities and sensory amplitudes were normal. Needle examination revealed fibrillations and positive sharp waves in the left tibialis anterior and medial gastrocnemius muscles. There was decreased recruitment and increased firing rate in these muscles, as well as the left quadriceps muscle. Needle examination of the left and right paraspinal muscles was normal. MRI of the lumbosacral spine showed intradural nerve root enhancement greater on the left, affecting L1–S1 (fig 1). Serum tested positive for WNV IgM antibody by enzyme immunoassay, and CSF results were reported as equivocal (exact titres are not provided by the Illinois Department of Public Health).

Suspected aetiologies before the results of WNV testing included an infectious or postinfectious radiculitis, plexitis, or anterior myelitis. He was treated with three days of intravenous methylprednisolone. During his hospital course, he had complete resolution of his hip pain and mild improvement in strength. Deep tendon reflexes returned within two days, and he was discharged home.

**Comment**

Decreased muscle strength can occur in up to one third of patients infected with WNV, and complete flaccid paralysis is seen in up to 10%. In the cases described, however, weakness was usually associated with an encephalitis or aseptic meningitis, and the pathology appeared to be localised to the peripheral nerve. Recent reports, including ours, describe an isolated acute flaccid monoparesis in which the electrodiagnostic findings are consistent with either motor axon or anterior horn cell pathology. Our report is further differentiated by radiographic evidence which confirmed asymmetrical nerve root involvement with good clinical correlation. The absence of sensory findings can be explained by relative sparing of the dorsal roots on both electrodiagnostic testing and MRI. Finally, the simultaneous onset of constitutional symptoms, hip pain, and leg weakness in our case suggests that the WNV infection can cause motor weakness during the initial viraemia, rather than there being a postviral autoimmune aetiology for the weakness.

The mechanism of weakness associated with WNV infection continues to be unclear. It has been hypothesised that it is similar to poliovirus, causing an acute flaccid paralysis in humans by attacking motor neurones directly. This theory has been supported pathologically, as WNV has been isolated in the spinal cords of birds and horses, causing a similar paralytic syndrome. However, MRI studies of acute poliovirus infection have shown increased signal in the anterior horn, whereas the most recent cases of WNV associated weakness have not had any of these MRI

![Figure 1](http://jnnp.bmj.com/)

**Figure 1** Magnetic resonance imaging of T1 weighted pre- (A1, B1) and post- (A2, B2) gadolinium axial sections of the lumbar cord. Levels L1–2 (A1, A2) and L2–3 (B1, B2) are pictured, showing greater enhancement of nerve roots on the left (arrows).
abnormalities. Further, the EMG findings in all reported cases do not differentiate between a motor axonopathy and anterior horn cell pathology, making either location possible as a cause of weakness.

To our knowledge, this is the first case to present MR findings supporting ventral root involvement in a case of faccical paralysis associated with WNV. We propose that anterior radiculopathy should be considered in addition to motor neurone pathology when assessing pure motor weakness caused by WNV.

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A case of possible autoimmune bilateral vestibulopathy treated with steroids

Bilateral vestibulopathy can have various causes: ototoxicity (mainly caused by aminoglycosides), meningitis, bilateral tumours, neuropathies, bilateral sequential vestibular neuritis, or Menière’s disease. Some types of bilateral vestibulopathy seem to arise from systemic autoimmune processes—for example, systemic lupus erythematosus, poly- chondritis, Cogan’s syndrome, or rheumatoid arthritis. About 20% of cases of bilateral vestibulopathy, however, remain “idiopathic” despite extensive diagnostic workup. Prompted by studies on immune mediated sensorineural hearing loss, we previously demonstrated IgG antibodies against the membrana vestibuli, afferent nerve, and utricle in sera of eight of 12 patients with “idiopathic” bilateral vestibulopathy, compared with one of 22 healthy controls. The patients had systolic blood pressure of less than five seconds. An audiogram was normal. High resolution magnetic resonance imaging of the brain and computed tomography of the temporal bones were also normal. Testing for serum autoantibodies (determined as described previously) against the inner ear structures, the semicircular canals, and otolith organs was positive (titre >1:100). No antinuclear, anticentiplastom, or antineuronal antibodies were detected.

On the assumption that an immune dysregulation caused the bilateral vestibular dysfunction, the patient was treated with steroids for six weeks, beginning with 100 mg/day methylprednisolone, and tapering the dose every third day by 20 mg/day until the patient was receiving only 20 mg/day for a duration of four weeks. Follow up examination at the end of this treatment showed that vestibular function had improved on both sides, with a peak slow phase velocity of 14°/s after caloric irrigation with 30°C water and 12°/s on the right and 10°/s on the left with cold water (30°C). At that time serum autoantibodies remained positive.

Two years later, the patient was seen again for follow up examination. The head impulse test was normal. Caloric vestibular testing showed a complete recovery of vestibular function with a peak slow phase velocity of >25°/s (30°C) on both sides. Per- and postrotatory nystagmus were longer than 50°/s (30°C/44°C) on both sides. Per- and postrotatory nystagmus lasted less than five seconds. An audiogram was normal. High resolution magnetic resonance imaging of the brain stem and computed tomography of the temporal bones were also normal. Testing for serum autoantibodies (determined as described previously) against the inner ear structures, the semicircular canals, and otolith organs was positive (titre >1:100). No antinuclear, anticentiplastom, or antineuronal antibodies were detected.

Comment

Immune mediated inner ear disease is characterised by sensorineural hearing loss that is most often rapidly progressive and bilateral, and may be accompanied by vestibular symptoms. Diagnosis of autoimmune inner ear disorders, however, is problematic as there is no universally accepted set of diagnostic criteria. Diagnosis is only considered when other causes of hearing loss have been ruled out. In this patient, there was no evidence of any other cause of hearing loss, and no other autoimmune disorders were present. The patient had normal serum autoantibodies against the inner ear structures, the semicircular canals, and otolith organs. The patient had a positive family history of autoimmune inner ear disorders. The patient was treated with systemic corticosteroids, and there was a complete recovery of vestibular function.

We had hypothesised in our earlier study that some of the so called idiopathic vestibulopaties might be caused by autoimmune inner ear disorders. From the clinical course and response of this patient, we conclude that idiopathic cases of vestibular disorders might be due to autoimmune inner ear disorders. Therefore, we recommend that inner ear autoantibodies be determined in bilateral vestibular disorders. If there is evidence of an autoimmune disorder and vestibular failure is not complete, a short term treatment trial should be started to preserve or even improve vestibular function. This, however, needs to be further evaluated in a prospective study on a large group of patients.
extremities started to occur, with radiological evidence of multiple cystic lesions in the distal bones. At the age of 30 she began to have insidious personality changes, depression of mood with suicidal ideas, and loss of social inhibition and judgment. Aged 40, psychological assessment suggested frontal dysfunction, and neurological examination showed the presence of primitive reflexes, mild apraxia, dyscalculia, and spatial and temporal disorientation. An EEG showed theta and delta activity dominating in the frontal areas, and brain CT showed a marked and diffuse cerebral atrophy with calcification in the basal ganglia. The disease progressed, with marked worsening of cognitive and motor functions, cerebral ictal events and epileptic seizures, leading finally to a vegetative state.

The affected sister (II,2) is 35 years old. At the age of 30 she began showing progressive loss of judgment, depressed mood, changes of personality, and uninhibited attitudes. No pathological fractures occurred, but x ray imaging showed cystic bone lesions in the metatarsal bones. Neuropsychological assessment revealed deterioration of intellectual function with frontal signs, dyscalculia, and dysgraphia. Cerebral MRI showed severe diffuse cerebral atrophy with basal ganglia calcification.

Neither cystic bone alterations nor pathological cerebral signs were found in the relatives.

Genetic analyses

Sequencing analyses did not detect any mutation in the five exons and in the intron–exon boundaries of TYROBP gene. Microsatellite analysis was undertaken with molecular markers spanning 120 kb of the genomic region containing the TYROBP gene. Although only marker D19S610 was fully informative, the linkage analysis excluded any association between the presence of the disease in our family and the PLOSL locus on chromosome 19.

In the two affected sisters, sequencing analysis identified a homozygous C to T mutation at position 191 (191 C→T) in exon 2 of the TREM2 gene. The mutation changes glutamine 33 to a stop codon (Q33X). To screen the family members for the identified mutation, we investigated a possible change in enzymatic restriction sites introduced by the mutation. The mutation abolished a Pst I site. This allowed us to propose a simple test to screen the family members: the parents (I,1; I,2), the proposita’s daughter (III,1), and the brother (II,4) were found to be heterozygous carriers of the mutated allele, while the other sister (II,3) was homozygous for the wild type allele (fig 1).

Comment

The clinical features of our cases are typical of PLOSL, but this family presents a novel homozygous mutation in exon 2 of TREM2. This mutation generates a premature stop codon and it is unlikely to be a polymorphism. Our findings confirm that PLOSL is characterised by a remarkable genetic heterogeneity, showing that mutations in different components of a single signalling pathway may lead to the same clinical condition.

In conclusion, in Italy PLOSL is explained by two different mutations in TREM2 gene. Its prevalence is underestimated because the disease is likely to go unrecognised. We believe that if physicians were more aware of this disease and were able to identify more cases, this would lead to a better clinical and genetic understanding of the condition.

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Acute anterior radiculitis associated with West Nile virus infection

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