Conduction block in the forearm associated with acute varicella zoster virus infection

We report the case of an adult patient with neurophysiological evidence of persisting conduction block in the forearm segment of the left median nerve and absent responses from the sensory branch of the musculocutaneous nerve (MCN), which had developed during an episode of acute generalised varicella zoster virus (VZV) infection. Clinical manifestations of motor involvement in herpes zoster (HZ) are generally rare and usually due to central nervous system involvement. Motor peripheral nervous system manifestations do exist and have been ascribed to nerve root degeneration due to lymphocytic inflammation and vasculitis with possible spread into the spinal cord. Recently, conduction block has been identified for the first time as the cause of weakness in an immunocompromised patient with HZ, with evidence of extension of VZV infection along the median nerve on magnetic resonance imaging, but persisting conduction block has up to now not been described as a complication of acute VZV infection.

Case report

A 29 year old Caucasian electrician was seen for neurophysiological assessment with weakness of his left hand and numbness along the lateral aspect of his left forearm of 9 months’ duration. The numbness had developed 9 days into a severe primary attack of chickenpox, which required hospitalisation. The weakness remained unnoticed by the patient until detection during routine follow up. Oral aciclovir had been commenced 3 days after the onset of the acute illness. No intravenous access had been used in the patient’s left arm. The past medical history included an anecdotal first primary illness. The patient had been treated with aciclovir for an episode of varicella zoster virus infection 9 years before the current illness. There was no history of diabetes or other primary neurological conditions.

Motor nerve conduction studies revealed partial conduction block in the forearm segment of the left median nerve. The sensory nerve action potential for the left sensory branch of MCN was absent with normal amplitudes and velocities from the right. Nerve conduction studies were normal for the right median as well as the ulnar and radial nerves bilaterally. Needle electromyography showed normal motor units with a reduced interference pattern and single fasciculation potentials in left APB and was normal in left first dorsal interosseous, flexor pollicis longus, biceps, and extensor digitorum communis.

Comment

Conduction block in acute VZV infection has, to the best of our knowledge, never been described before. Partial infraction of a mixed nerve in vasculitic mononeuritis multiplex can cause conduction block by selectively damaging Schwann cells, although axonotmesis with axonal damage and sensory-motor symptoms in the affected nerve would be more typical and should have been apparent during neurophysiological testing. Both the median nerve and the sensory branch of MCN share fibre supply from cervical nerve roots which later form the lateral cord, and they are often in close anatomical proximity in the arm due to frequent anatomical variations. The simultaneous involvement of the median nerve and the sensory branch of MCN might thus indicate a direct spread of the virus between the two nerves. Alternatively, indirect spread from the purely sensory branch of MCN via the spinal cord might have occurred. Autopsies of nervous tissue from HZ patients have shown VZV DNA and antigen to be present in damaged nerve fibres including motor neurons, suggestive of neuronal spread. Recently, conduction block in the forearm segment of the median nerve in a case of HZ has speculatively been attributed to local damage of Schwann cells of the motor nerves by direct local invasion or remote allergic mechanisms, although the exact pathophysiology in these cases remains to be established.

The patient was found to have fasciculation potentials but no other forms of spontaneous activity in APB, but in none of the other muscles tested. The observed fasciculation potentials most likely represent axonal hyperexcitability at the site of the conduction block in analogy to the presumed mechanism responsible for the occurrence of single and grouped fasciculation potentials in other neuropathies characterised by persistent conduction block.

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Written confirmation from the Local Research and Ethics Committee in Cardiff was obtained confirming that formal ethical approval was not needed for this case study.

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Competing interests: none declared

References


Figure 1 Left median compound muscle action potentials recorded from abductor pollicis brevis muscle of a patient with previous varicella zoster virus infection and weakness in left median nerve innervated hand muscles. Stimulation sites at wrist and elbow (A) and 1.0, 2.5, 3.7, 5.3, 7.2, 9.1, and 11.1 cm above the proximal wrist crease (B). Gain 5 mV per division, sweep duration 20 ms (A) and 30 ms (B), respectively. Slowing of motor fibres and partial conduction block between 9.1 and 11.1 cm above the proximal wrist crease is demonstrated.
Toscana virus causing severe meningoencephalitis in an elderly traveller

Toscana virus (TOSV) is classified in the sandfly fever virus group of arboviruses (family Bunyaviridae, genus Phlebovirus) along with Sicilian (SFSV) and Neapolitan (SFNV) causative agents. The disease coincides with Sicilian (SFSV) and Neapolitan (SFNV) endemics. TOSV has been identified as a cause of mild acute aseptic meningitis. In endemic regions TOSV has been identified as a significant cause of sandfly fever virus group of arboviruses. Toscana virus (TOSV) is classified in the family Bunyaviridae, genus Phlebovirus, species Phlebotomus perniciosus. Phlebotomus perniciosus is endemic to the Mediterranean, Middle East, Western Asia, North Africa and the mountainous areas of southern Europe. The disease coincides with the seasonal life cycle of insect vectors.

Laboratory confirmation of clinically suspected cases can be carried out by detection of TOSV IgG or IgM antibodies in blood and cerebrospinal fluid (CSF) using different techniques. Direct detection of virus is possible by cell culture or reverse transcriptase polymerase chain reaction (RT-PCR) but will often fail because of the short term nature of the viraemia.

Throughout the last decades there have been increasing numbers of cases of TOSV infection imported into northern Europe from endemic areas. Among other causes, it therefore now has to be considered in the differential diagnosis of acute aseptic meningitis.1

Case report

Four days after having returned from Malaga, Spain, in July 2004 an 80 year old woman was admitted to hospital with a state of deteriorated consciousness. There was enuresis and encopresis, probably as a result of an epileptic fit. Apart from adult onset diabetes mellitus the patient's medical history was unremarkable. On admission to hospital, the patient was confused and agitated, with a body temperature of 39.5°C. There was neck rigidity but neurological examination showed no other abnormalities.

Routine clinical chemistry analyses on admission showed slight increases in liver enzymes (aspartate aminotransferase 50 U/l; alanine aminotransferase 87 U/l), erythrocyte sedimentation rate (18 mm/h), and glycated haemoglobin (HbA1c; 7.6%).

Examination of CSF revealed lymphocytic pleocytosis (265 cells/mm³) and raised protein (47 mg/dl) and lactate (4.3 mmol/l) (table 1). PCR for herpes simplex virus 1 RNA was negative. Infection of the CNS was confirmed by virus RNA detection using PCR in serum and cerebrospinal fluid (CSF).

Serum and CSF samples collected on days 2, 6, 13, and 27 after admission were examined for the presence of anti-TOSV, anti-SFSV, and anti-SFNV IgG and IgM antibodies. In contrast, IgG and IgM IFA revealed positive results for both TOSV (strain ISS.Phl.3 1971) and SFNV (strain Sabin 1985), but anti-SFSV (strain Sabin 1985) antibodies were not found in either serum or CSF samples.

Case report

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Table 1

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<thead>
<tr>
<th>Reference range</th>
<th>WBC count (cells/mm³)</th>
<th>Lactate (mmol/l)</th>
<th>Glucose (mmol/l)</th>
<th>Total protein (mg/dl)</th>
<th>Oligoclonal bands</th>
<th>Tau protein (μg/ml)</th>
<th>Neurone specific enolase</th>
<th>S-100 protein (μg/ml)</th>
<th>Anti-TOSV antibodies in serum</th>
<th>Anti-TOSV antibodies in CSF</th>
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</thead>
<tbody>
<tr>
<td>Day 2</td>
<td>0 to 5</td>
<td>1.1 to 2.2</td>
<td>2.78 to 4.16</td>
<td>15.45</td>
<td>Negative</td>
<td>&lt;350</td>
<td>&lt;2</td>
<td>&lt;12.5</td>
<td>&lt;1:10</td>
<td>&lt;1:10</td>
</tr>
<tr>
<td>Day 6</td>
<td>265</td>
<td>4.3</td>
<td>7.33</td>
<td>47</td>
<td>Negative</td>
<td>94</td>
<td>NA</td>
<td>8.2</td>
<td>&lt;1:10</td>
<td>&lt;1:10</td>
</tr>
<tr>
<td>Day 13</td>
<td>60</td>
<td>3.1</td>
<td>6.16</td>
<td>32</td>
<td>Negative</td>
<td>NA</td>
<td>NA</td>
<td>7.5</td>
<td>&lt;1:10</td>
<td>&lt;1:10</td>
</tr>
<tr>
<td>Day 27</td>
<td>30</td>
<td>2.5</td>
<td>4.88</td>
<td>25</td>
<td>Negative</td>
<td>NA</td>
<td>NA</td>
<td>5.3</td>
<td>&lt;1:10</td>
<td>&lt;1:10</td>
</tr>
</tbody>
</table>

CSF, cerebrospinal fluid; EIA, enzyme immunosorbent assay; IFA, immunofluorescence assay; NA, not assessed; WBC, white blood cell; EIA, enzyme immunoassay; IFA, immunofluorescence assay; NA, not assessed.

Anti-TOSV IgG titres ranged from 1:640 to 1:10240 in serum and 1:20 to 1:5120 in CSF. IgG levels for SFNV ranged from 1:320 to 1:2560 and from 1:20 to 1:1280. IFA IgM titres could only be detected in serum, ranging from 1:80 to 1:160 for TOSV and from 1:40 to 1:80 for SFNV.

The presence of a pattern of cross reactivity typical of TOSV infection supported a preliminary diagnosis of acute TOSV encephalitis. For confirmation, the specificity of antibodies was demonstrated by a commercially available TOSV IgG/IgM enzyme immunosorbent assay (EIA) using recombinant antigen (Diesse Diagnostica, Milan, Italy). The CSF showed a consistent result (EIA 1:400 for both TOSV and SFNV).

Comment

Besides Rift Valley fever virus, TOSV is the only member of the Phlebovirus group causing aseptic meningitis. Previously, severe neurological manifestations have been described only occasionally. Within three to six days after infection symptoms such as fever, myalgia, headache, vomiting, and neck rigidity do occur, but a less severe degree of encephalitis has generally been reported. As in other viral meningitides, symptoms of aseptic meningitis related to TOSV infection disappear completely within a few days. Asymptomatic infections and infections without CNS involvement also occur.

The brain involvement in this case caused a severe, long lasting impairment of consciousness, seizures as an unusual clinical manifestation, and a prolonged convalescence period. Seldom reported before, raised liver enzymes can be interpreted as a sign of a systemic infection with involvement of the liver.

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<td>25</td>
</tr>
<tr>
<td>Oligoclonal bands</td>
<td>Negative</td>
<td>Negative</td>
<td>One band</td>
<td>Negative</td>
</tr>
<tr>
<td>Tau protein (μg/ml)</td>
<td>&lt;350</td>
<td>94</td>
<td>NA</td>
<td>191</td>
</tr>
<tr>
<td>Neurone specific enolase</td>
<td>&lt;2</td>
<td>NA</td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td>S-100 protein (μg/ml)</td>
<td>&lt;12.5</td>
<td>8.2</td>
<td>7.5</td>
<td>5.3</td>
</tr>
<tr>
<td>Anti-TOSV antibodies in serum</td>
<td>&lt;2300</td>
<td>NA</td>
<td>1030</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Table 1: Results of cerebrospinal fluid and serum sample analysis after admission (as far as we know this is the first time that markers of cell damage and immune reaction have been measured in a patient with acute toscana virus meningoencephalitis).**
Owing to the large variety of pathogens causing acute aseptic meningitis, clinicians rely on rapid laboratory confirmation of suspected cases by standard methods such as RT-PCR or the plaque reduction neutralisation test (PRNT). Nowadays, PRNT is rarely used owing to its complexity and time-consuming nature, while RT-PCR appears inadequate because of the short duration of the viraemia. Recently developed EIA formats can establish the presence of infection by detecting specific IgM in acute phase samples and were able to confirm TOSV infection in this case. With millions of travellers and increasing TOSV infections around the Mediterranean basin, commercially available EIA methods will be of growing importance. In addition to other severe travel related diseases, TOSV infections now need to be considered by physicians.

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References

Intracerebral haemorrhage in CADASIL
Cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL) is a rare hereditary disease characterised by recurrent transient ischaemic attacks, strokes, and vascular dementia. Pathological studies reveal multiple small infarcts and diffuse white matter changes as well as vascular alterations most prominent in small arteries.1 The presence of granular osmiophilic material in arterial walls on ultrastructural examination is pathognomonic. Mutations in the notch3 gene located on chromosome 19 are associated with the disease.4 Here we report a patient with an unusual clinical course with recurrent intracerebral haemorrhage.

Case report
A 47 year old woman was admitted after a fall at home, followed by several minutes of unconsciousness. Her past medical history was uneventful. In particular, there was no history of migraine or depression, and she was not taking any drugs. On admission, her husband reported memory deficits for several weeks. Initially, the patient complained about headaches and mild dysarthria. Moderate left sided hemiataxia and pronation of the left arm were present. Blood pressure was raised to 220/120 mm Hg.
without a known history of arterial hypertension. Neurpsychological deficits were prominent in impaired semantic, visual-spatial, and episodic memory, and in deterioration in cognitive speed. Concentration and mathematical problem solving were also reduced, indicating severe cognitive impairment. Initial cranial computed tomography revealed a haemorrhage of 20 mm diameter in the left cerebellar hemisphere. Subsequent magnetic resonance imaging (MRI) with T2* gradient echo (GE) showed more than 25 small haemorrhages distributed over the entire brain. T2-weighted scans showed white matter lesions with periventricular emphasis (fig 1). Serum markers for vasculitis and coagulation indices were normal, as was the cerebrospinal fluid. An ophthalmological examination showed hypertensive changes. Ultrasound sonography of the extracranial and intracranial vessels revealed arterio-sclerotic vessel walls but no stenosis. Electronmicroscopic examination of a skin biopsy showed granular osmiophilic material (GOM) in the basal lamina of small arterioles, establishing the diagnosis of CADASIL. Direct bidirectional sequencing of all exons coding for epidermal growth factor (EGF)-like repeat domains (exons 2 to 24) of notch3 did not reveal any mutation.

After stepwise normalisation of arterial blood pressure, the patient gradually improved over the following weeks. Hesitation and dysarthria resolved gradually, but severe neuropsychological deficits remained, rendering her unable to take care for herself. A follow up examination three months after discharge showed further amelioration of gait without any other focal neurological symptoms. The neuropsychological deficits had improved slightly, but there were still severe memory deficits. The patient was aware of these deficits and she reacted in a depressive manner. Activities of daily life were moderately impaired. Follow up MRI showed no new lesions.

Comment

The clinical course of this case with intracerebral bleeding in combination with excessive blood pressure values was consistent with hypertensive intracerebral haemorrhage. Although there was no history of known arterial hypertension, the changes of the retina supported this diagnosis. Hypertension is the most common cause of intracerebral haemorrhage, accounting for 50–70% of cases. Hypertensive bleeding into the cerebellum, however, is relatively rare (<10%). The finding of numerous cerebral microbleeds on T2* GE MRI led to the suspicion of amyloid angiopathy, a common cause of intracerebral haemorrhage in the elderly. On the other hand, the relatively young age of the patient and the family history (mother and two sisters suffering from migraine; father died at 47 years of unknown cause) was compatible with an autosomal dominantly inherited condition, for example, CADASIL. The finding of GOM in the basal lamina of small vessels is pathognomonic of this disease, and confirmed the diagnosis. Mutations in exons 2 to 24 of the notch3 gene are found in approximately 95% of patients, but were not detected in this case.

While transient ischaemic attacks and ischaemic strokes, along with the development of vascular dementia, are common, major intracerebral haemorrhages are not a common feature of CADASIL. There have been sporadic reports of intracerebral haemorrhages, but the significance of these observations remains unclear, given the absence of intracerebral haemorrhage in large patient series. In a recent study with GE T2* weighted scans, microbleeds (up to 22 in a single subject) ranging from 2 to 10 mm in diameter were present in 69% of CADASIL patients examined, but no major ICH was found. Another study found microbleeds in 31% of all CADASIL patients examined, and an increased risk of intracerebral haemorrhage was predicted. The presence of microbleeds correlated with age and the use of antiplatelet drugs. CADASIL leads to degeneration of small arterioles, thus increasing the probability of vessel rupture in arterial hypertension. While the white matter pathology in our patient may appear relatively spare, lesions in the external capsule and the temporal lobe typical of CADASIL were present.

We conclude that CADASIL should be considered in patients with cerebral haemorrhage, and careful blood pressure management is particularly important in CADASIL patients, as the risk of vessel rupture and subsequent intracerebral haemorrhage appears to be further increased compared with patients with arterial hypertension alone. While there is no effective treatment for CADASIL, control of arterial hypertension could at least slow the rate of deterioration in this disabling and demening disorder.

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References


Catastrophic primary antiphospholipid syndrome presenting as status epilepticus

Antiphospholipid syndrome (APS) is defined as the occurrence of arterial or venous thrombosis or recurrent miscarriage, with raised titres of antiphospholipid antibodies, namely lupus anticoagulant (LA) or anti-β2-glycoprotein antibodies (aCL). Classic form of APS is catastrophic antiphospholipid syndrome (CAPS) or Asherson’s syndrome. Proposed diagnostic criteria for definite CAPS are: multiorgan failure, development of manifestations within 1 week, presence of antiphospholipid antibodies and histopathological evidence of microthrombosis (positive predictive value 99.4%). Precipitants include infection, surgery, and childbirth. Patients typically develop widespread microthrombosis and coagulopathy with marked thrombotocytopaenia. Clinically apparent cerebral infarction occurs much less frequently than in un complicated APS but the major pathological manifestation of CAPS is cerebral microthrombosis at postmortem examination.

CASE REPORT

A 30 year old woman delivered her first child following a full term uncomplicated pregnancy. Three weeks later, she developed headache and transient hemiparesis. The following day she had an episode of speech arrest, bit her tongue, and held both arms stiffly in the air for about 1 minute. On admission to hospital, she was pyrexial and developed generalised tonic clonic seizures. There was no relevant previous medical history and she was not taking any medication. Blood tests, including erythrocyte sedimentation rate (ESR) and C reactive protein (CRP), were normal. Computed tomography scan of the brain and analysis of the cerebrospinal fluid (CSF) were normal. Gynaecological examination showed no retained products of conception. The seizures proved refractory to treatment with intravenous lorazepam. She was transferred to a specialist neurological centre that day.

On arrival she was agitated, disorientated and pyrexial (38°C). Generalised tonic clonic convulsions continued. Neurological examination was normal except that all limb reflexes were pathologically brisk and plantar responses were extensor. General examination was unremarkable. Despite being given “loading” doses of phenytoin, phenobarbitone and magnesium sulphate, the seizures continued. She was anaesthetised and intubated, and mechanical ventilation was introduced.

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Treatment with high dose intravenous aciclovir for presumed viral encephalitis was commenced.

Investigations revealed a normal full blood count and film with a platelet count of 267 x 10^9/L. ESR and CRP were mildly raised at 46 mm/h (normal 1–20) and 28.7 mg/l (normal 0–3). Serial measurements of platelet count, ESR, and CRP did not show any significant change throughout the illness. All other blood tests including coagulation screen were normal or negative.

Magnetic resonance imaging of the brain was normal with no evidence of venous sinus thrombosis, cerebral infarction or haemorrhage. A second lumbar puncture revealed an opening pressure of 30 cm H2O. CSF analysis showed clear colourless fluid with 4 lymphocytes/mm³, a red cell count of <1/mm³, total protein of 0.36 g/l and a CSF:plasma glucose ratio of 4.4:8.9 mmol/l. CSF and serum oligoclonal bands were negative. MEEG confirmed a diffuse encephalopathic process with unequivocal epileptiform activity over the frontal regions bilaterally with some periodic complexes more prominent on the left. A thrombophilia screen was performed during her illness but results were not available until after her death, and revealed she was suffering from APS. The postmortem laboratory investigations and postmortem examination revealed she was suffering from late-onset APS. The alternative postpartum TMA diagnosis of thrombotic thrombocytopenic purpura was excluded by the fibrin nature of the thrombi and the normal fibrinogen.

CAPS occurs in <1% of patients with APS. However, it is vital to be aware of the diagnosis as patients rapidly develop severe multisystem failure. A review of the pathogenesis of 80 cases of CAPS noted an excess of women (79%) with an average age at onset of 37 years. The majority with multiorgan failure had secondary APS, mostly associated with systemic lupus erythematosus. Obstetric complications are recognised precipitants of CAPS, probably because of increases in levels of natural clotting factors. Two cases of CAPS occurring in the postpartum period have been reported, both following fetal loss.

Cerebral involvement has been reported in around 60% of cases of CAPS. However, there are no previous reports of primary antiphospholipid syndrome presenting with status epilepticus. The case was unusual in several other respects. There was no previous diagnosis of APS and no history of miscarriages or thrombotic events. The patient presented with isolated neurological symptoms with no evidence of other organ involvement until 7 days later. Daily blood tests did not raise the suspicion of thrombophilia or blood dyscrasia and, in contrast to a series of 80 patients in whom 98% had high aCL titres, this patient had negative aCL.

The optimal treatment for CAPS is uncertain but the rationale is to prevent ongoing thrombosis with anticoagulation and to prevent production of mediators that generate the hypercoagulable state by immunosuppression. A review of data from the international CAPS registry found that patients who received the combination of anticoagulation plus steroids plus plasma exchange or intra-venous immunoglobulin had the best survival rate (63%).

This case emphasises that CAPS may present as an apparently isolated cerebral disorder. It is important to maintain a high degree of suspicion of antiphospholipid syndrome in critically ill patients, particularly with known precipitating factors for CAPS such as during the postpartum period. Early treatment with anticoagulation and immunosuppression gives the best chance of improving the >50% mortality rate of the condition.

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References

Use of mirror dystonia as guidance for injection of botulin toxin in writing dysfunction

The successful application of botulinum toxin (BTX) injections in the treatment of focal hand dystonia is largely dependent on careful evaluation and selection of muscles to be injected. It has been suggested that patients should be examined for abnormal postures at rest and while carrying out the affected task in question as well as other tasks (such as using a cup or a comb) as simple techniques such as the localisation of subjective pain and fatigue accompanied by palpation of the area of discomfort can also be used.

Mirror dystonia consists of dystonic postures and movements of the dominant hand while writing or performing other tasks with the non-dominant hand. We present a series of six patients who were successfully injected with BTX using mirror dystonia as an additional tool for muscle evaluation.

We carried out a retrospective review of the case records of consecutive patients with writing dysfunction (writng tremor) who had been injected with BTX type A (Botox®, Allergan Pharmaceuticals, Irvine, California, USA) between November 2000 and October 2002 at our movement disorders clinic. Our study was limited to patients with writing dysfunction who displayed mirror dystonia while writing with their non-dominant hand. We specifically examined patients for mirror dystonia by asking them to write with their non-dominant hand while resting the dominant hand on the ulnar side of the forearm (unaware of our focus on the detection of mirror dystonia of the resting limbs). Patients were injected under EMG guidance, using an Allergan® EMG needle. We recorded the muscles injected and the dose each muscle received. Peak effect was defined as the maximum improvement obtained from the injection. It was rated on a 0 to 3 global impression scale (0 = no effect; 1 = mild improvement; 2 = moderate improvement; 3 = marked improvement).

The presence and severity of adverse events was also recorded. We also looked at the concordance between observation of the dominant limb in the action of writing and

Figure 1 Cerebral white matter small vessel showing necrosis and perivascular microgliaosis following occlusion by thrombus.
observation of the mirror dystonia movements of the same limb while writing with the non-dominant hand. The formulation and preparation of BTX was carried out using standard methods. Overviews of the demographic, clinical, and treatment variables are presented in table 1. We identified six patients with writing dysfunction (M/F: 1/5, mean age 46 years (range 30 to 75), mean duration of disease 7.16 years (range 2 to 13)). Four patients (cases 1, 2, 3, and 6) had writer’s cramp and two (cases 3 and 4) had features overlapping writing tremor with writer’s cramp. Three patients reported marked improvement (cases 1, 2, and 3), two moderate (cases 3 and 4), and one mild improvement (case 6). We further identified two subgroups: four patients where mirror dystonia consisted of any combination of extension/abduction of the thumb, fingers, and wrist (subgroup A: cases 2, 3, 4, and 5) and two patients where mirror dystonia consisted of hyperflexion of wrist or thumb and fingers (subgroup B: cases 1 and 6). In subgroup A two patients experienced marked improvement and two had moderate improvement following injections. Two of these four patients did not show mirror dystonia movements when seen 15–17 weeks later at the time they were due for repeat injections. In subgroup B one patient experienced marked improvement and one mild improvement. None of our patients had evidence of mirror dystonia in the non-dominant hand when writing with the dominant hand. Regarding adverse events, transient weakness was experienced by four patients (for one to four weeks). No other adverse events were reported.

Concordance in the action of writing and observation of the mirror dystonia movements in the same limb was found in four patients. In three there was enrichment of the observation in that additional muscles could be shown to be active. The two discordant patients had writing tremor with no overt deviation noted when the dominant hand wrote.

The importance of recognition of mirror dystonia in patients with writing dysfunction has been previously highlighted by Jedynak et al. They reported that 29 of 65 patients with writer’s cramp had evidence of mirror dystonia and suggested that mirror dystonia may be useful in muscle selection (it may help in the differentiation between primary and compensatory movements). Borgohain et al also reported on the subject; however, that work has only been published in abstract form. The investigators proposed that mirror dystonia used as a guide for muscle selection for BTX injections may reduce the difference in outcome between extensor and flexor writer’s cramp and suggested that mirror dystonia was a superior method for muscle selection compared with compensatory movements.

Although the mechanism of mirror dystonia remains unclear it has been suggested that it is likely to be related to the metabolic abnormalities shown to involve the primary sensorimotor and supplementary motor cortices in patients with focal hand dystonia. Magnetic cortical stimulation has confirmed that corticocortical inhibition is reduced over both hemispheres. Jedynak et al suggested that mirror dystonia is the consequence of abnormal cortical inhibition and decreased selectivity of muscle patterns for highly skilled manual tasks.

We conclude that analysis of the pattern of dystonic posturing displayed in mirror dystonia when examining patients with writing dysfunction is a useful guide for selection of muscles to be injected with BTX. A prospective trial of BTX injections in muscles selected through analysis of mirror dystonia could provide further information about the therapeutic results of this method.

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References
Drug induced pseudolymphoma secondary to ethosuximide

Ethosuximide is an antiepileptic succinimide, widely used in the treatment of absence seizures. Haemopoietic complications associated with the administration of this drug have included leukopenia, agranulocytosis, pancytopenia with or without bone marrow suppression, and eosinophilia. We report a patient with pseudolymphoma induced by ethosuximide, a complication never reported previously.

Case report

A 12 year old boy presented with a two months history of fever, weight loss (3 kg), and non-painful swellings on the neck, axillae, and inguinal regions. The patient had been on ethosuximide for three months for childhood absence epilepsy. It was being given at a dose of 30 mg/kg/day, in three divided doses, and the seizures had been under reasonable control.

Physical examination on presentation revealed enlarged lymph nodes on the both sides of the neck, axillae, and inguinal regions. All the nodes were non-tender, firm, measuring 1 to 2 cm in diameter, and freely mobile. The liver and spleen were not palpable and all other systems were normal. A full blood count revealed a leucocenia of $3.6 \times 10^9/\mu l$ (48% neutrophils, 3% eosinophils, 40% lymphocytes, and 9% monocytes) and a decreased platelet count of $119.0 \times 10^9/\mu l$. Studies for serological markers revealed no acute or chronic infection with cytomegalovirus, Epstein–Barr virus, herpes simplex virus, or toxoplasmosis.

An excisional biopsy of a 2 cm cervical node was done. Frozen section diagnosis was consistent with lymphoma. Permanent sections showed a diffuse polymorphic lymphoid hyperplasia with effacement of the normal architecture; there was an admixture of lymphoid cells, including small and large lymphocytes and plasma cells (fig 1). Leucocyte phenotyping, using the ABC immunohistochemical method, showed heterogenous T cell and B cell populations: T cell subsets included CD45RO and CD30. B lymphocyte markers included CD20. One day after ethosuximide discontinuation the fever disappeared. The lymph nodes were noticed to have decreased in size on the second week and completely resolved on the end of the second month. The leucocyte and platelet counts normalised after two weeks of ethosuximide withdrawal. Positive rechallenge resulted in drug induced fever and enlargement of the lymph nodes after one week of ethosuximide administration.

Comment

Lymphadenopathy has been recognised as a complication of drug treatment, particularly with antiepileptic drugs, since the first report of phenytoin-induced pseudolymphoma in 1940. Since then, this idiosyncratic reaction has also been described with carbamazepine, lamotrigine, nifedipine, thioridazine, atenol, amiloride/hydrochlorothiazide, meixetine, penicillamine, captropil,enalapril, and methotrexate. Most of these are associated with cutaneous pseudolymphomas, but the antiepileptic drugs are more likely to precipitate cervical lymphadenopathy.

Pathologically, the term “pseudolymphoma” has been used to describe lymphoid cell proliferation with effacement of nodal architecture, so that there is a false appearance of a reactive process. Although the precise pathogenesis of this drug reaction is unknown, pseudolymphoma may develop as a hypersensitivity reaction when a drug or one of its structural ligands acts as an antigen, triggering an immune reaction. Alternatively, the drug in question may promote a dysregulated immune response to another drug or non-pharmacological antigen.

Ethosuximide is widely used in the treatment of absence seizures. On the basis of more than a decade of studies on its cellular effects, the mechanisms of action are thought to include blockade of the low threshold, T-type Ca$^{2+}$ current and an activation in both the non-inactivating Na$^+$ current and the Ca$^{2+}$ activated K$^+$ current in thalamic and cortical neurones. The most common dose related side effects are gastrointestinal complaints (nausea, vomiting, and anorexia) and central nervous system (CNS) effects (drowsiness, lethargy, euphoria, dizziness, headache, and hiccup). Some tolerance to these effects develops. Parkinson-like symptoms have also been reported. Urticaria and other skin reactions, including Stevens–Johnson syndrome, as well as systemic lupus erythematosus, eosinophilia, leucopenia, thrombocytopenia, pancytopenia, hepatic dysfunction, and aplastic anaemia, also have been attributed to ethosuximide.

In this case, the disappearance of lymphadenopathy with the withdrawal of the drug, and its prompt reappearance when the drug was reintroduced, suggests a strong cause–effect association between ethosuximide and lymphadenopathy. To our knowledge, this is the first case report of ethosuximide induced pseudolymphoma and the second to report lymphadenopathy as an adverse effect of ethosuximide.

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BOOK REVIEW

Imitators of Epilepsy, Second Edition


This 300 page hardcover work encompasses four sections: one on general considerations relevant to the topic with specific focus to epileptic versus non-epileptic diagnostic dilemmas; the second section presents different types of non-epileptic spells according to age of presentation; the third section describes other disorders that resemble epileptic seizures such as migraine, vestibular problems, movement disorders, hyperekplexia, and startle disorders; and the fourth section focuses on encephalopathies, neuro-endo-crine, metabolic and toxic conditions imitating epilepsy. Paroxysmias, sleep disorders and narcolepsy as well as cerebral vascular imitators of epilepsy are also well described. The last section is relevant to psychological psychiatric imitators of epilepsy such as hyperventilation syndrome, psychogenic non-epileptic seizures, and panic attacks. Most chapters contain a review of the basic definitions and physiology of the respective differential diagnoses imitating epilepsy followed by the clinical characteristics and case vignettes. Some authors of this co-authored work provide a personal perspective regarding diagnosis and treatment. This book is of particular interest to any clinician working with epilepsy patients as it is to medical students on one side and general neurologists and specialised epileptologists on the other side. The fact that imitators of epilepsy are frequently encountered in non-neurological populations or patients presenting outside neurological services makes this book a useful addition to libraries of non-neurologists as well.

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P A J M Boon
Catastrophic primary antiphospholipid syndrome presenting as status epilepticus

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