LETTERS TO THE EDITOR

Focal neurological deficits and migraine at high altitude

The development of transient focal neurological deficits at high altitude is uncommon but well recognised.¹ In the absence of concomitant altitude illness a thromboembolic aetiology has usually been presumed. In this case transient focal neurological deficits occurred at high altitude in clear association with migraine.

A 30 year old right handed white man had lived and worked at an altitude of 3840 m in the Nepal Himalaya for two years. He had a long history of migraine, with between 20 and 30 attacks (with and without aura) each year. His attacks with aura typically included homonymous visual disturbances, with only one episode before his high altitude sojourn involving additional focal neurological features. This occurred seven years previously and incorporated subtle dysgraphia lasting 30 minutes and heaviness in the right upper limb that persisted for a few hours. He had a strong family history of migraine, including one aunt who experienced a short lived hemiplegia during one attack.

While living at high altitude his migraines did not occur more often than usual, but several attacks were associated with focal neurological features. On three occasions attacks were preceded by numbness of one arm (twice on the right, once on the left) that resolved within 30 minutes of treatment with ergotamine. All three attacks occurred at altitudes of around 3800 m and were not associated with any particular activity. The most dramatic focal event occurred while climbing on a 6100 m mountain. He had taken acetazolamide as prophylaxis for acute mountain sickness and had acclimatised well to a high camp at 5600 m. Having spent the night at this camp, he climbed for one hour to an altitude of around 5900 m when his vision started to blur. This progressed to flashing lights near the centre of vision, with half field predominance and scotomatous patchy visual loss, all typical of his migrainous aura. Ten minutes later, while informing his companions that he would be unable to ascend further, he found that he had difficulty finding the correct words. He was accompanied down to base camp (5000 m) over one hour during which time a mild left sided frontal headache developed, he became unable to speak, and moderate weakness developed in his right arm such that he had difficulty holding objects. At no stage did he have problems understanding the speech of others or difficulty walking. On further descent to 4300 m over three hours his visual symptoms had disappeared and his weakness and speech had improved considerably. At this stage he was examined by a physician who found very mild limb weakness of the right arm and a mild expressive dysphasia. Later that day he descended to 3840 m without additional problems.

Facilities for investigation at this stage were limited. On arrival at 3840 m his arterial

oxygen saturation by pulse oximeter was 87% (his normal value for this elevation) and blood pressure was 118/80; packed cell volume measured one week later was 0.60. Clumsiness in the right arm lasted another two days, while subtle word finding difficulty persisted for one week. He moved to sea level one month later and has remained well for over a year after this event, although he continues to experience regular "uncomplicated" migraine attacks as previously. Subsequent neurological review showed no residual deficits.

This case is of interest for several reasons. Firstly, the development of focal neurological features at high altitude was clearly associated with migraine. Focal neurological conditions occurring at high altitude in the absence of altitude illness have usually been attributed to thromboembolism.¹ In this case the history of migraine, the development of focal neurological features preceding headache and nausea in a typical time course, together with the complete resolution of symptoms and signs, support the diagnosis of migraine with aura. The neurological signs developed over a longer period than usual with stroke and the lack of other features of altitude illness makes high altitude cerebral oedema unlikely.

A second area of interest relates to the fact that, whereas this patient did not experience more frequent migraines while living at high altitude, his attacks incorporated more florid focal neurological features than he had previously experienced. Furthermore, the most dramatic event occurred at extreme altitude where his arterial oxygen saturation would have been only about 75%. The oxygen theory of migraine postulates that cerebral hypoxia is central to the pathophysiology of migraine attacks, and that any cause of hypoxaemia could cause migraine, including low atmospheric pressure.² Evidence suggests that migraine may result from episodes of ischaemia, possibly through triggering a spreading cortical depression.³ In the case presented here, one could also postulate that hypoxia may have an additive effect with migrainous cerebral hypoperfusion in causing prolonged neurological deficits.

Knowledge about whether migraineurs experience more severe, complicated, or frequent episodes at high altitude is incomplete. One South American study found a higher prevalence of migraine in residents living at 4328 m than in a sea level population.⁴ Susceptible low altitude sojourners have had recurrent migraine attacks triggered by ascent to certain altitudes, but these accounts are largely anecdotal. A migraine like syndrome developed repeatedly in susceptible subjects exposed to simulated altitudes of between 9000 and 11 400 m in a decompression chamber.⁵ One well documented case involved a mountaineer who experienced transient right sided sensorimotor disturbances, dysphasia, blurred vision, and nausea associated with headache while climbing above 5000 m on two separate occasions.⁶ Detailed investigations after both episodes showed no abnormalities. Although lacking a clear history of migraine, this presentation suggests the diagnosis of migraine with aura. Apart from hypobaric hypoxia, there are other potential trigger factors for migraine present at high altitude such as exercise, poor food and fluid intake, photic stimuli, cold temperatures, and sleep deprivation.

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Chickenpox and multiple sclerosis: a case report

Multiple sclerosis is a common, initially mostly relapsing-remitting, demyelinating disease of the CNS. Despite vigorous effort, the aetiology has not yet been elucidated. It is believed that, on the basis of a specific immunogenetic background, exogenous factors may trigger an immunological process that leads to focal demyelination in the CNS. Moreover, the precipitation of individual exacerbations in affected patients may probably also be triggered by exogenous factors. Viral infections have been discussed as an aetiological factor of the disease and have been shown to induce attacks.^{1,2} We report here the precipitation of an acute exacerbation of multiple sclerosis by varicella in an adult.

One week before admission, the 27 year old white male patient experienced the rapid appearance of successive crops of vesicles on skin and mucous membranes typical of varicella, accompanied by pruritus, slight fever, malaise, and anorexia. He acquired the disease from his five year old son, who had had chickenpox two weeks earlier and was in the convalescent stage at that time. The patient had not had chickenpox during childhood. Five days after the onset of the rash he felt increasing sensory impairment in both legs, unsteadiness of gait, and weakness of both legs until he was unable to walk. His medical history was unremarkable except for hypaesthesia of the right hand that resolved spontaneously one year earlier. The present medical examination disclosed only a chickenpox rash in varying stages of development and especially in the trunk, face, and scalp. On neurological examination, the cranial nerves were unremarkable except for cogwheeled pursuit movements of the eyes. There was

no neck stiffness. A distally accentuated weakness of the left arm (grade 3/5) was found. Furthermore, he presented with spastic weakness of both legs that was more pronounced on the left (grade 3/5 on the left, grade 4/5 on the right). Deep muscle reflexes were brisk in the left arm and in both legs, but pyramidal signs could not be elicited. There was decreased sensation to light touch and pinprick in the legs without a clearcut level.

Whereas visual evoked responses and nerve conduction velocity of motor and sensory nerves were normal, motor evoked potentials to the feet induced by transcutaneous magnetic stimulation of the motor cortex showed a 50% reduction of amplitude on the left and a longer latency on the right. The somatosensory evoked potentials derived from the tibial nerve showed a reduction in amplitude on the right.

T2 weighted MRI of the brain showed two hyperintense lesions with a diameter of about 1 cm, one localised in the centrum semiovale and the other one in the brain stem near the lemniscus medialis, both on the left side. After intravenous administration of contrast medium no disruption of the blood-brain barrier was detectable. Magnetic resonance imaging of the cervical and thoracic spine showed a swelling of the spinal cord at level C 2/3 and Th 2. After intravenous administration of the contrast medium an enhancement was visible in both localisations as a sign of an acute inflammatory process. Routine laboratory tests were normal except for slightly raised erythrocyte sedimentation rate and liver enzymes. Serological testing by enzyme linked immunosorbent assay (ELISA) showed antibodies against varicella zoster virus of the IgG and IgM type and also IgG antibodies against measles virus but no anti-measles IgM antibodies. All other serological tests for antibodies against neurotropic viruses, especially herpes simplex virus, cytomegalovirus, mumps virus, coxsackie viruses types B 1-5, adenoviruses, influenza, and parainfluenza viruses as well as *Borrelia burgdorferi*, were negative or did not give evidence of a recent infection.

Cerebrospinal fluid cytology disclosed a subacute inflammatory CSF cell syndrome with transformed lymphocytes and plasma cells. Whereas the albumin content was normal (18.4 mg/dl), the IgG (4.2 mg/dl) was slightly raised. The IgG index calculated according to Delpech and Lichtblau was 0.70. Oligoclonal IgG bands were present in CSF only. Repeated lumbar taps did not show major changes in the findings. Detection of varicella zoster virus DNA by the polymerase chain reaction could not be achieved in blood or CSF. Antibodies of the IgG type against varicella zoster virus and measles virus were slightly raised giving titres of 1 : 40. Differentiation of CSF antibodies by isoelectric focusing and the immunoblot technique showed that about 20% of the oligoclonal CSF IgG was directed against the nucleocapsid protein of measles virus. Autochthonous synthesis of varicella zoster virus specific antibodies could not be detected.

Suspecting an acute varicella zoster virus myelitis, we initially treated with acyclovir (30 mg/kg body weight/day in three doses). Symptoms resolved under this treatment and intensive physiotherapy. The patient was discharged with mild residual symptoms consisting of a spastic, atactic gait

after 21 days. Eight weeks after the first admission he presented with a left optic neuritis. Visual evoked potentials could not be elicited on the left whereas they were normal on the right. There were no other neurological symptoms or signs apart from the residual gait disturbance, which had greatly improved in the meantime. After one course of high dose prednisolone (1000 mg/day intravenously for five days) visual acuity returned to normal. The subsequent course was stable; repeated cranial MRI did not show any newly enhancing lesions.

According to the criteria of Poser *et al.*⁴ this patient had clinically definite, laboratory and MRI supported, multiple sclerosis. Five days before the second bout he developed acute varicella. In considering the time course, an immune mediated postinfectious encephalomyelitis is highly unlikely as it should have become symptomatic not earlier than the second week after the onset of the rash. The failure to detect varicella zoster virus DNA by polymerase chain reaction in CSF and the lack of autochthonous varicella zoster virus specific oligoclonal IgG production in CSF while oligoclonal IgG was present is strong evidence against direct viral infection of the CNS. The presence of oligoclonal IgG in the CSF directed against measles virus proteins is a common finding in patients with multiple sclerosis. The close temporal association between the hitherto more severe second bout and the varicella infection suggests precipitation of an acute exacerbation of pre-existing multiple sclerosis by varicella. No specific virus has been consistently implicated in the precipitation of exacerbations in patients with multiple sclerosis, with the exception that a significant correlation between increases in adenovirus titre associated with upper respiratory tract infections and major relapses has been shown.² It is unlikely that the precipitation of exacerbations occurs non-specifically during any infection as bacterial infections and those often affecting the urinary tract in patients with multiple sclerosis do not lead to an increased rate of episodes.¹

As a possible mechanism to explain our finding, interferon- γ has been shown to have a deleterious effect on the clinical course of multiple sclerosis in that it precipitates exacerbations.⁵ By inducing the release of cytokines such as interferon- γ , viral infections may enhance an autoreactive response to CNS antigens via upregulation of adhesion and HLA-molecule expression as well as activation of effector cells such as macrophages. Although the pathogenetic background still remains obscure, this case shows that precipitation of an exacerbation of pre-existing multiple sclerosis by chickenpox is possible.

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Interferon- α may benefit steroid unresponsive chronic inflammatory demyelinating polyneuropathy

Although controlled studies have shown the efficacy of plasma exchange, corticosteroids, and intravenous immunoglobulin (IVIg) in chronic inflammatory demyelinating polyneuropathy (CIDP), many patients do not achieve a complete and long term remission and some patients do not respond at all to these treatments.¹

We report on two patients with CIDP, unresponsive to corticosteroids, azathioprine, or cyclosporin, who showed a partial and short lived response to IVIg but made a complete and sustained recovery after treatment with interferon α -2a.

The figure summarises the clinical courses of patients. The disability was assessed on the Rankin scale.¹

Patient 1 was a 27 year old girl admitted in June 1990. In 1988 she had a progressive limb weakness that had evolved over six months. A diagnosis of CIDP was made in another neurological institute and the patient was treated with prednisone, plasma exchange, and azathioprine with poor response.

The patient showed severe, symmetric weakness of proximal and distal muscles, normal sensation, and absent tendon reflexes. Cranial nerves were unaffected. Routine haematological examinations and serum and urine immunoelectrophoresis gave normal results. Serological tests for Lyme disease and HIV were negative. The protein content of CSF was 60 mg/dl. Nerve conduction studies showed slightly reduced motor conduction velocities with multiple conduction blocks. Sural nerve biopsy was normal.

The patient was treated by plasma exchange without any effect. She was then given IVIg at a dosage of 0.4 g/kg/day for five consecutive days and showed considerable improvement. After that, six relapses occurred (the mean time between relapses was five weeks) and on each occasion reinstitution of IVIg was followed by a similar improvement.

Subsequently, we started intermittent treatment with IVIg (1 g/kg for one day every four weeks), which was successful in maintaining the maximal level of improvement. During the maintenance period additional treatments with corticosteroids, plasma exchange, and azathioprine were given, but the frequency of IVIg treatment was not altered, deterioration occurring each time we tried to prolong the interval between infusions to more than five weeks.

In January 1992 the patient noticed a