

LETTERS

Intracranial hypotension caused by traumatic intrasacral meningocele

Cerebrospinal fluid (CSF) leakage is known to cause orthostatic headache. Spontaneous CSF leakage occurs under several conditions, such as lumbar puncture, spinal surgery, and fracture of the spine. Intrasacral meningocele is an anomaly caused by an abnormal prolongation of the meninges in the sacral spinal canal. Typical symptoms of this anomaly are low back pain, bladder dysfunction, and sciatica, possibly caused by tethered cord. We describe CSF leakage from an intrasacral meningocele without tethered cord syndrome, which caused severe orthostatic headache.

Case report

A 23 year old woman was admitted to hospital with the complaint of severe headache. She described a similar episode two years previously. There was no aura or trigger, nausea, vomiting, or fever. Non-steroidal anti-inflammatory drugs were not effective. By lying down she could get some relief from her splitting headache. Cranial magnetic resonance imaging (MRI) showed no abnormalities. On the first occasion, the headache gradually disappeared after lying down for several days.

On the day before admission, she experienced the headache again, and it was again relieved by lying down. Several days before the headache began, she had fallen on her buttock during skiing. No prominent external injury was found. Her temperature was normal. On neurological evaluation, her neck was not stiff. Kernig and Lasegus signs were negative. There was no muscular weakness or sensory disturbance. She had never experienced bladder or rectal disturbance.

Lumbar puncture yielded an opening pressure of 60 mm H₂O. The CSF contained 7 mononuclear cells/mm³; the glucose concentration was 95 mg/dl and the protein concentration was 85 mg/dl.

Cranial magnetic resonance imaging (MRI) using gadolinium (fig 1, lower right panel) did not show dural enhancement, subdural haematoma, or Chiari malformations. The cervical and thoracic regions were normal. However, a meningocele in the sacrum was found, and the caudal spinal canal was enlarged (fig 1, left). Computed tomographic (CT) myelography failed to show CSF leakage from the enlarged spinal canal (not illustrated). On the other hand, radioisotope cisternography demonstrated leakage of CSF around the meningocele. Twenty four hours after the injection, strong activity was found around the spinal canal just caudal to the most enlarged portion (fig 1, upper right panel). In the most enlarged portion of the meningocele, radioisotope accumulation was also

found, and it seemed that clearance of the CSF was impaired in comparison with the upper portion of the spinal cord. Isotope clearance around the brain was normal.

The headache gradually improved without any treatment, and none was subsequently required.

Comment

Postural headache began after a fall during skiing. An intrasacral meningocele was found, and CSF leakage from the meningocele detected. CSF pressure was low normal. Intrasacral meningoceles are now detected more commonly because of the advent of MRI scanning. Although some are truly asymptomatic, many cause pain in the low back. Pain in the buttocks and legs may be the main symptom, and this seems to be caused by root compression or tethered cord syndrome.³ In our case, headache was the principal symptom, and the patient did not complain of anything else. It was not clear whether the fall precipitated the CSF leakage from meningocele. The patient could not remember any trauma when she experienced the first attack of the headache. However, a meningocele could be vulnerable to minor injury as it is surrounded by thin bone.

In this case, however, cranial MRI did not show any abnormalities commonly associated with intracranial hypotension.⁴ CT myelography is reported to be sensitive for detecting CSF leakage along the nerve root sleeves of the spine,² but was negative in this case, although it helped establish the diagnosis. In our case it is probable that low volume but continuous CSF leakage, as demonstrated by radioisotope cisternography, was responsible for the intracranial hypotension. This case adds congenital meningocele to traumatic meningocele¹ as a cause of CSF leakage and intracranial hypotension. It has been reported that CSF leakage from a meningocele was detected in a patient with a gunshot wound.¹

T Kihara

Department of Neurology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

T Mitsuieda, K Ito, M Miyata

Japanese Red Cross Society Wakayama Medical Centre, Wakayama, Japan

Correspondence to: Dr Takeshi Kihara, Department of Neuroscience for Drug Discovery, Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida-Shimoadachi-cho, Sakyo-ku, Kyoto, 606-8501, Japan; tkihara@kuhp.kyoto-u.ac.jp

References

- Colletti PM, Siegel ME. Post-traumatic lumbar cerebrospinal fluid leak: detection by retrograde In-111-DTPA myeloscintigraphy. *Clin Nucl Med* 1981;6:403-4.
- Matsumura A, Anno I, Nose T, et al. Intracranial hypotension. *J Neurosurg* 2001;95:914-16.
- Mishra GP, Sharma RR, Lad SD, et al. Gluteal neuralgia - unusual presentation in an adult with intrasacral meningocele: a case report and review of literature. *Neurology India* 2000;48:279-81.
- Nowak DA, Rodiek SO, Zinner J, et al. Broadening the clinical spectrum: unusual presentation of spontaneous cerebrospinal fluid hypovolemia. Case report. *J Neurosurg* 2003;98:903-7.

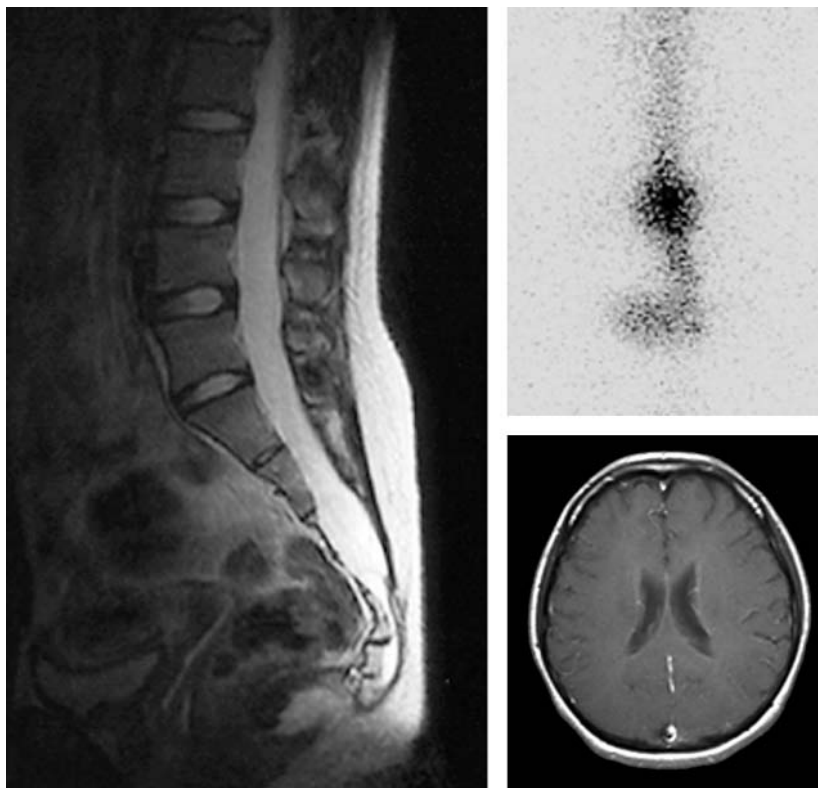


Figure 1 Left panel: magnetic resonance (MR) imaging (T2 weighted image) of lumbar and sacral region. Enlarged spinal canal demonstrated in the sacral region. Upper right panel: radioisotope cisternographic findings of the lumbosacral region. Note that leakage of the radioisotope activity was found around the region caudal to the enlarged meningocele. Lower right panel: MR imaging (gadolinium enhanced, T1 weighted image) of the cranial region. No hygroma or subdural enhancement was found.

Transient ischaemic attack preceding anterior circulation infarction is independently associated with favourable outcome

Experimental studies in various animal models have provided evidence that short episodes of global or focal ischaemia partially protect the brain against subsequent ischaemic damage. The term "ischaemic tolerance" has been established for this phenomenon, both in the cerebral circulation and in other organs (see recent review by Kirino¹). There are only a few clinical reports supporting the notion that ischaemic tolerance may also exist in stroke patients who have had a short episode of focal cerebral ischaemia—that is, a transient ischaemic attack (TIA) prior to cerebral infarction.^{2,3} The purpose of the present study was to investigate the association between the outcome of anterior circulation infarction and prior TIA in stroke patients from a large scale multicentre stroke registry.

The ASH (Arbeitsgruppe Schlaganfall Hessen) database is a prospective hospital based stroke registry for the federal state of Hesse in Germany. This registry covers all stroke units (nine neurological hospitals) in this state with the obligation to include all patients presenting with cerebral ischaemia or intracerebral haemorrhage. Thus, ~90% of stroke patients treated in these hospitals

from 1998 to 2000 are included in the ASH database with 12 571 complete datasets (2960 with TIA, 8484 with cerebral infarction, 1127 with intracerebral haemorrhage). Patients with proven anterior circulation infarction (computed tomography (CT) or magnetic resonance imaging (MRI) scan) were included in the present analysis (n = 4969); from these, those patients presenting with stupor or coma were excluded (n = 172, 4.8% with previous TIA). The characteristics of the study population are presented in table 1. In 332 (6.9%) patients a history of TIA (according to previously published guidelines⁴) preceded final infarction. Favourable outcome was defined as a Modified Rankin Scale (MRS) score of ≤1 and Barthel Index ≥90 at discharge.

On univariate logistic regression analysis (inclusion method), we found that the odds ratio (OR) for a history of TIA preceding a stroke with a favourable outcome was 1.57 (95% confidence interval (CI) 1.26 to 1.97; p<0.001). The OR remained unchanged after the adjustment for age, sex, cause of the stroke (see table 1), risk factors, time between symptom onset and hospital admission, duration of hospital stay, medical centre, and secondary prevention treatment (1.58, 1.25 to 2.02; p<0.001). The inclusion of the MRS score at hospital admission reduced the adjusted OR to 1.52 (1.10 to 2.13; p = 0.012), although it was still significant. This association was also not altered after the exclusion of all patients with severe speech

disturbances (1.77, 1.20 to 2.68; p<0.005). In a subset of patients (n = 1601), the European Stroke Scale (ESS) was determined at admission; the median ESS score was significantly higher in patients with preceding TIA (84 v 78; p<0.05, Mann-Whitney U test). On arbitrarily defining an ESS score ≥70 as a mild neurological deficit, we found an adjusted OR of 1.56 (1.05 to 2.41; p<0.029) for a history of TIA preceding a mild neurological deficit at hospital admission. Furthermore, in the group of stroke patients (n = 1520) presenting with anterior circulation TIA at hospital admission, the prevalence of preceding TIA was 15.6% (n = 237). On including the TIA patients into the regression analysis, a preceding TIA had an OR of 2.76 (2.31 to 3.38; p<0.001) for a subsequent transient neurological deficit—that is, TIA and not a stroke, after the adjustment for the above mentioned confounders.

From the present analysis we conclude that TIA preceding cerebral anterior circulation infarction is independently associated with a less severe neurological deficit at hospital admission (as quantified by the ESS), and with a higher probability of a favourable outcome after hospital treatment. Furthermore, after a TIA the probability of a subsequent TIA instead of persisting stroke is 2.75 fold higher. Our findings support previous reports. Moncayo *et al* reported an adjusted OR of 1.98 (1.27 to 3.08) for a favourable outcome in stroke patients with preceding TIA after one month from a prospective single centre database.³ In a retrospective analysis, Weih and coworkers found an OR of 3.57 (1.39 to 9.14) for an independent state in stroke patients with preceding TIA at discharge.² Thus, our data fit well within this context and support a robust association between a preceding TIA and a better outcome after subsequent cerebral ischaemia.

The main limitation of our analysis is that detailed information about the TIAs, such as the duration, the vascular territory in which the TIA occurred, and the time interval between the TIA and the final infarction was not available. Nevertheless, on the basis of the size of the database, its prospective design, and the inclusion of data from several centres, the results are reliable and make it unlikely that the positive association found (and previously described) is only due to hitherto unidentified bias.

Whether this association reflects "ischaemic tolerance" in humans could not be answered in the present study or from the literature.¹⁻³ There are at least two other mechanisms which may influence the severity of stroke in this subset of patients. Consistent with previous reports, we found a higher percentage of large vessel atherosclerosis as the presumed cause of stroke in the group with preceding TIA (see table 1).^{2,3} First, in these patients, embolus size or composition may differ significantly from emboli from other sources and may lead to more distal vessel occlusion, earlier recanalisation, and smaller infarcts.⁵ Secondly, the capacity of collateral intracranial pathways may differ in patients and may preserve brain tissue from infarction.⁶ Observational studies are unable to control for these factors and thus cannot quantify the real impact of ischaemic tolerance in stroke patients. However, one observation in the present analysis suggests a neuroprotective effect: preceding TIA was significantly associated with a 1.52 fold higher probability of

Table 1 Characteristics of stroke patients with proven anterior circulation infarction from the ASH stroke database

	Patients without history of preceding TIA (n = 4465)	Patients with history of preceding TIA (n = 332)	
Age in years (mean ± SD)	69.5 ± 12.7	69.2 ± 12.1	*
% Men	53.5	61.6	***
Hospital admission after symptom onset: <3/3-6/≥6 hrs (%)	24/22/45	19/18/55	***
Hospital stay: days (mean ± SD)	11.4 ± 9.7	13.1 ± 10.3	***
Barthel Index: <30/30-70/≥70 (%)			
Day 7	18.4/23.2/58.4	12.4/20.7/66.9	**
Discharge	17.6/22.8/59.6	12.8/14.5/72.6	***
MRS: 0-1/2-3/4-5/6 (%)			
Admission	21.9/32.0/46.0/0	30.7/33.0/36.3/0	**
Day 7	33.7/28.8/35.2/2.2	43.2/28.4/26.0/2.5	***
Discharge	36.9/27.5/32.5/3.1	49.0/23.5/23.8/3.8	***
Favourable outcome (%)†			
Day 7	24.9	33.1	***
Discharge	35.1	46.1	***
Risk factors (%)			
Arterial hypertension	71.3	69.3	*
Diabetes	28.7	28.4	*
Smoking	15.4	24.9	***
CVD	28.8	31.3	*
Stroke subtype (%)			
Large vessel atherothrombosis	22.0	28.3	***
Cardioembolic	22.7	17.5	**
Small vessel disease	26.2	25.9	*
Other determined cause	3.9	4.2	*
Undetermined	16.8	13.9	*
Secondary prevention (%)			
Aspirin	49.6	39.2	***
Other aggregation inhibitors	15.9	23.8	***
Warfarin	13.0	16.3	*

*Non-significant; **p<0.05; ***p<0.01

†Defined as having a MRS score of ≤1 and Barthel Index ≥90.

ASH, Arbeitsgruppe Schlaganfall Hessen, CVD, cardiovascular disease; MRS, Modified Rankin Scale; SD, standard deviation; TIA transient ischaemic attack

favourable short term outcome even after the correction for the degree of disability at hospital admission—that is, MRS score, suggesting improved recovery from initial neurological deficit.

In conclusion, our results support an independent association between preceding TIA and favourable outcome in subsequent cerebral ischaemia. Whether this association reflects inducible tolerance of brain tissue against ischaemic damage remains unanswered and should be elucidated in further studies taking the above mentioned considerations into account.

Appendix

The following neurological hospitals contributed to the ASH database used for the present analysis: Asklepios Neurologische Klinik Bad Salzhausen (Prof Dr von Reutern), Horst-Schmidt-Kliniken Wiesbaden (Prof Dr Weisner), Johann Wolfgang Goethe-Universität Frankfurt am Main (Prof Dr Steinmetz), Klinikum Darmstadt (Prof Dr Claus), Klinikum Fulda (Prof Dr Langohr), Klinikum Kassel (Prof Dr Ferbert), Klinikum Weilmünster (Prof Dr Hornig), Krankenhaus Nordwest Frankfurt am Main (Prof Dr Janzen), Philips Universität Marburg (Prof Dr Oertel).

M Sitzer, C Foerch, T Neumann-Haefelin, H Steinmetz

Department of Neurology, Johann Wolfgang Goethe-University, Frankfurt, Germany

B Misselwitz

Geschäftsstelle Qualitätssicherung Hessen, Eschborn, Germany

C Kugler

Institut fuer Integrative Versorgung in der Medizin (IVM), Gießen, Germany

T Back

Department of Neurology, Philipps University Marburg, Marburg, Germany

Correspondence to: Dr M Sitzer; sitzer@em.uni-frankfurt.de

References

- 1 Kirino T. Ischemic tolerance. *J Cereb Blood Flow Metab* 2002;22:1283–96.
- 2 Weih M, Kallenberg K, Bergk A, et al. Attenuated stroke severity after prodromal TIA: A role for ischemic tolerance in the brain? *Stroke* 1999;30:1851–4.
- 3 Moncayo J, de Freitas GR, Bogousslavsky J, et al. Do transient ischemic attacks have a neuroprotective effect? *Neurology* 2000;54:2089–94.
- 4 Special report from the National Institute of Neurological Disorders and Stroke. Classification of cerebrovascular diseases III. *Stroke* 1990;21:637–76.
- 5 Neumann-Haefelin T, Wittsack HJ, Fink GR, et al. Diffusion- and perfusion-weighted MRI: Influence of severe carotid artery stenosis on the DWI/PWI mismatch in acute stroke. *Stroke* 2000;31:1311–17.
- 6 Kucinski T, Koch C, Eckert B, et al. Collateral circulation is an independent radiological predictor of outcome after thrombolysis in acute ischaemic stroke. *Neuroradiology* 2003;45:11–18.

Multiple cranial neuropathy and HIV-2

The peripheral nervous system is frequently involved in different stages of HIV-1 infection.

Cranial neuropathies have already been described in HIV-1 patients, but never in HIV-2 patients. We describe the first case of multiple cranial neuropathy associated with, and presumably due to HIV-2 itself.

A 25 year old heterosexual white man was referred to our hospital for evaluation of a left facial palsy of insidious onset in the previous days. He complained of hoarseness and episodic horizontal diplopia for the previous 2 months. Past medical history was unremarkable except for an episode of hospitalisation at 3 weeks of age, when he underwent several blood transfusions.

Physical examination was normal except for diffuse tonsillar enlargement. Neurological examination disclosed anisocoria RE>LE, horizontal diplopia on left side gaze without clear evidence of oculomotor palsy, hypoesthesia of the left V3 territory, left peripheral facial palsy, left hypoacusia, bilateral decreased gag reflexes, and dysphonia.

Brain MRI (fig 1A,B) showed enlargement and gadolinium enhancement of the intracranial third (bilateral), fifth (right) and intracranial seventh and eighth (bilateral) cranial nerves. A diffuse enlargement of nasopharyngeal lymphoid tissue was apparent.

CSF examination revealed 152 mg/dl protein, 60 cells/μl (mainly mononucleated), and intrathecal IgG synthesis (CSF IgG 0.352 g/l; IgG index 0.84), without oligoclonal band, CSF VDRL, microbiological and cultural examinations were negative, and immunophenotyping of CSF lymphocytes excluded B cell monoclonality. Further investigation disclosed a positive Western blot for HIV-2, plasma viraemia by RT-PCR of 785 HIV-2

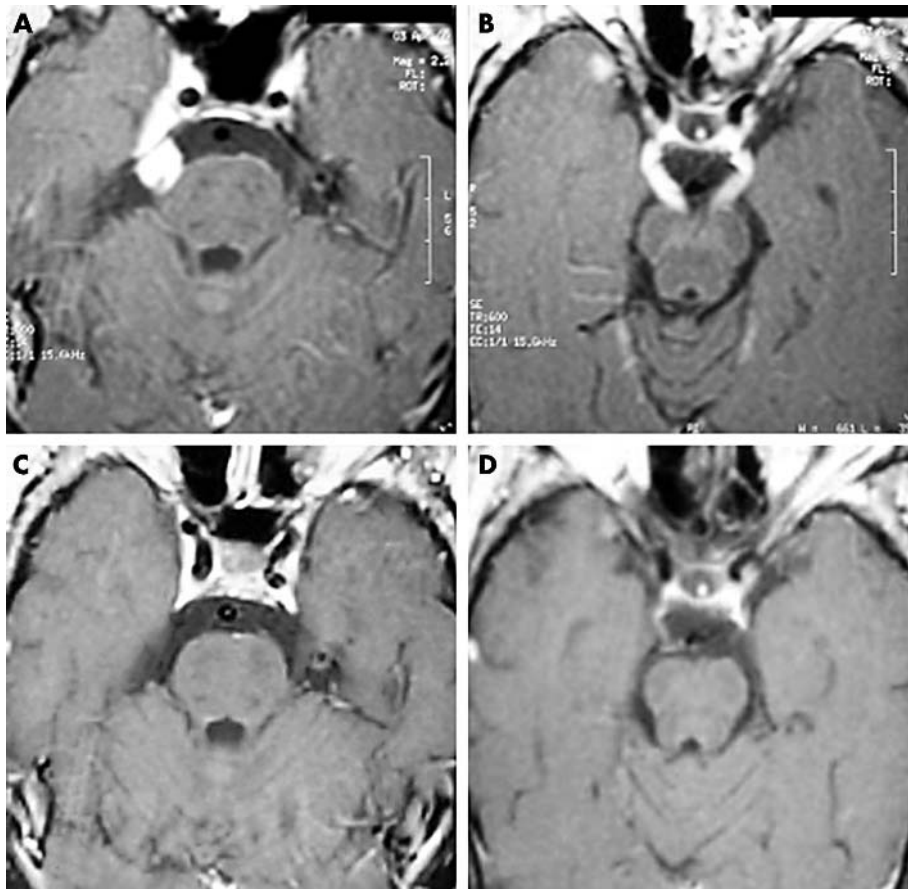


Figure 1 Brain axial T1 weighted MRI post gadolinium (Gd) administration. Post contrast images show an impressive enlargement and Gd enhancement of right cranial nerve V (cisternal and Gasser ganglion segments) (A) and of the III cranial nerves (cisternal segment) (B). Three months after starting highly active anti-retroviral therapy, there is no Gd enhancement of the V cranial nerve (C), and the right III cranial nerve shows only slight Gd enhancement (D).

RNA copies/ml (2.89 log₁₀), 198 CD4+ cells/μl, CD4/CD8 ratio of 0.3, lymphocyte count of 1074 cells/μl. Serological testing for HIV-1 and plasma viraemia (HIV-1 DNA) were negative. A nasopharyngeal lymphoid tissue biopsy revealed chronic inflammation and did not identify any specific agent. An extensive evaluation (including CSF PCR for *Mycobacterium tuberculosis*; CMV, HSV, EBV and *Toxoplasma* serologies; chest x ray; serum calcium; antineutrophil cytoplasm antibody; and antinuclear antibodies) ruled out other possible causes of multiple cranial neuropathy.

The patient was started on highly active anti-retroviral therapy (HAART) with zidovudine, lamivudine and indinavir, which gave full clinical recovery within 4 weeks. Three months later, CSF examination revealed only slight elevation of proteins (61 mg/dl), and 1 cell/μl without intrathecal IgG synthesis. Plasma HIV-2 RNA by PCR was below the threshold of detection (<500 copies/ml) and CD4 count was 243 cells/μl. Brain MRI showed only slight gadolinium enhancement of the right III nerve (fig 1C, D). At follow-up, 2 years later, neurological examination was normal.

We describe a previously unrecognised syndrome in HIV-2 infection. This case deserves further attention for additional reasons: transmission of HIV-2, presumed aetiology, and MRI imaging.

In Portugal, African communities represent a significant percentage of the population and previous studies have documented the presence of HIV-2 among both native Portuguese and immigrants, emphasising the possibility of unusually long incubation periods.¹ In our case, HIV-2 may have been acquired through blood transfusions more than 20 years ago, as the patient denied other possible ways of transmission (including sojourn in western Africa or sexual contact with people from this area).

Neurological dysfunction in HIV-2 infection has not been comprehensively studied. In HIV-1 infection, the peripheral nervous system can be involved in different ways, at different stages, with different presumed aetiopathogenic mechanisms.² Cranial neuropathies have been described mostly in association with opportunistic infections and lymphoma. Rare cases without recognised cause have been attributed to HIV-1 itself.³ In this case, the presentation of cranial neuropathy without identified aetiology, in the context of a newly diagnosed infection, suggest that HIV-2 itself may be the offending agent in our patient. Clinical improvement, associated with the reversal of CSF inflammatory characteristics and MRI findings with HAART, highlights this assumption. Of possible relevance to the latter is a case of optic neuropathy as the presenting feature of HIV-1 infection, with recovery associated with HAART.⁴ However, in our case we cannot exclude the hypothesis of an immune mediated insult to the cranial nerves or a spontaneous recovery coincident with HAART.

MRI was very useful in diagnosis and follow up, showing an impressive cranial nerve gadolinium enhancement that regressed on treatment. To a lesser extent, this finding has been described in HIV-1 patients and seems to be related to the underlying inflammatory process. However, it is not always associated with clinical dysfunction.⁵

The affinity of the HIV virus for the nervous system and the potential reversibility of associated dysfunction with HAART should be taken into account, especially when dealing with a patient with neurological symptoms of unknown aetiology. In a case of multiple cranial neuropathy, HIV-2 infection should be included in the differential diagnosis.

Acknowledgements

We thank Dr. José Vale for his helpful comments

S Calado, N Canas, M Viana-Baptista

Department of Neurology, Egas Moniz Hospital, R. Junqueira 126, 1349-019 Lisbon, Portugal

C Ribeiro

Department of Neuroradiology, Egas Moniz Hospital, Lisbon, Portugal

K Mansinho

Department of Infectious Diseases, Egas Moniz Hospital, Lisbon, Portugal

Correspondence to: Dr S Calado, Serviço de Neurologia, Hospital de Egas Moniz, R. Junqueira 126, 1349-019 Lisboa, Portugal; soficalado@netcabo.pt

Received 25 August 2003

Accepted 26 August 2003

Competing interests: none declared

References

- 1 Soriano V, Gomes P, Heneine W, *et al*. Human immunodeficiency virus type 2 (HIV-2) in Portugal: clinical spectrum, circulating subtypes, virus isolation and plasma load. *J Med Virol* 2000;61:111-16.
- 2 Simpson DM, Tagliati M. Neurologic manifestations of HIV Infection. *Ann Intern Med* 1994;121:769-85.
- 3 So YT, Olney RK. The natural history of mononeuritis multiplex and simplex in HIV infection. *Neurology* 1991;41(Suppl 1): 375.
- 4 Goldsmith P, Jones RE, Ozuzu GE, *et al*. Optic neuropathy as the presenting feature of HIV infection: recovery of vision with highly active antiretroviral therapy. *Br J Ophthalmol* 2000;84:551-3.
- 5 Sartoretti-Schefer S, Wichmann W, Valavanis A. Idiopathic, herpetic, and HIV-associated facial palsies: abnormal MR enhancement patterns. *AJNR Am J Neuroradiol* 1994;15:479-85.

Progressive encephalomyelitis with rigidity associated with anti-amphiphysin antibodies

Progressive encephalomyelitis with rigidity (PER) is a rare disorder of unknown aetiology, characterised by muscular rigidity, abnormal postures, painful muscle spasms, and myoclonus, and is caused by inflammation in the brainstem or spinal cord.^{1,2} We report a case of PER with positive anti-amphiphysin antibodies in the serum and CSF.³ This association has not been previously reported and raises the possibility that PER may have an autoimmune pathogenesis similar to that of stiff person syndrome (SPS).⁴

Case report

Clinical features

A 37 year old female presented having had symptoms of PER for about three months.

Spasms began with several minutes of paroxysmal painful muscle stiffness in the left upper limb, followed by pain and muscle spasms in the upper limbs, shoulders, neck, and back. These spasms were easily evoked by light touches, conversations, and by being startled. The patient remained bedridden and showed left dominant weakness of the limbs, with contractures in the upper limbs and difficulty in relaxing the muscles. She also developed abducent nerve palsy. Her deep tendon reflexes were absent and her plantar responses were both flexor. The serum antinuclear antibody was positive (1:160); anti-glutamic acid decarboxylase (GAD) antibody was negative. CSF testing revealed 18 white cells/mm (98% lymphocytes)³ and 160 mg/dl of protein. The MRI scan of the brain and spinal cord and the EEG were entirely normal. Surface electromyography in the arm and neck muscles showed continuous motor unit discharge elicited by passive movement of the right arm or by conversation (fig 1(A)).

The diagnosis of PER was based on the marked limb and trunk rigidity, the severe spasms provoked by sensory or emotional stimuli, and the cranial nerve palsy with mild pleocytosis as well as protein elevation in the CSF indicating inflammation of the brainstem and spinal cord. Matsuno *et al*³ also reported the clinical features of this patient.

Diazepam and baclofen were minimally beneficial; plasmapheresis had no effect on the symptoms. After treatment with intravenous injection of high dose methylprednisolone and sequential oral prednisolone, the patient showed dramatic progress. Her abducent nerve palsy was improved, and she could walk without assistance eight months after admission. She did not have any spasms or muscle pain. However, after two years, she developed a breast cancer.

Methods

Supernatants of total rat brain were prepared by homogenisation in 10 volumes of ice cold RIPA buffer, pH 7.4, containing freshly added protease inhibitors (0.1 mM PMSF, 1 μg/ml each of leupeptin, aprotinin, and pepstatin A), followed by centrifugation at 1000 g for 10 minutes at 4°C. Rat brain homogenates and immunoprecipitates were separated by SDS gel electrophoresis. The patient's sera were used at 1:1000 dilution.

Results

Western blotting and immunoprecipitation were performed as previously described.⁵ A band with an apparent molecular mass of 128 kD was recognised using the patient's serum samples (fig 1(B)). To prove that anti-amphiphysin antibodies recognised the 128 kD antigen, the patient's sera were used to immunoprecipitate the 128 kD antigen from rat brain extracts. The presence of amphiphysin in the immunoprecipitate was demonstrated by Western blotting, using mouse anti-amphiphysin antibody. The 128 kD autoantigens, which were immunoprecipitated by the patient's sera and the CSF, comigrated with amphiphysin and were recognised by an anti-amphiphysin antibody (fig 1(B)).

Discussion

As far as we are aware, this is the first reported case of PER with anti-amphiphysin antibody. Anti-amphiphysin antibodies have

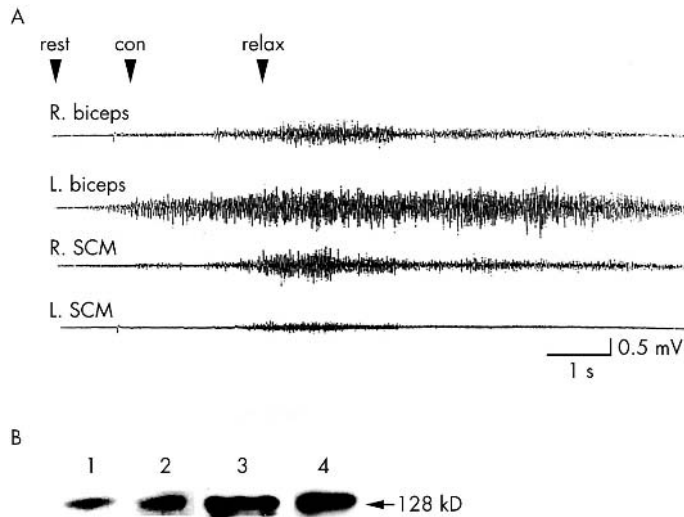


Figure 1 (A) Surface electromyography in the arm and neck muscles, with continuous motor unit discharge elicited by conversation (con). The motor unit discharge continued after she tried to relax. There was no muscle discharge at rest. SCM, sternocleidomastoid muscle. Horizontal scale, one second=8 mm; vertical scale, 0.5 mV=0.2 mm. (B) Western blot and immunoprecipitation using patient serum and CSF. The 128kD antigen is indicated by an arrow. Lane 1 was loaded with rat brain homogenate and probed by Western blotting with mouse anti-amphiphysin antibody. When tested against rat brain extracts by Western blotting, the autoantibodies of the patient reacted with an apparent electrophoretic mobility of 128kD, the same molecular weight as amphiphysin (lane 2). The serum (lane 3) and the CSF (lane 4) samples from the patient precipitated the 128 kD antigen, which was recognised by an anti-amphiphysin antibody.

been identified in several patients with paraneoplastic neurological disorders, such as encephalomyelitis, sensory neuropathy, cerebellar degeneration, opsoclonus-myoclonus, and SPS.² Although specificity of the antibodies for one type of tumour or one neurological syndrome is poor, in our patient the PER had an autoimmune basis with anti-amphiphysin antibodies.

Gouider-Khonja *et al*⁴ reported a 50 year old woman whose initial clinical presentation mimicked SPS, with later diffuse involvement of the CNS leading to a diagnosis of PER. Meinck *et al*² suggested that PER was one of the variant forms of SPS,

because of the similarity of their clinical and autoimmune features. In like manner, paraneoplastic SPS and PER have been found to be related to autoantibodies such as amphiphysin,⁵ GAD,² and gephyrin.⁶

The suggested aetiology of both SPS and PER is autoimmune disorder of the CNS directed against suprasegmental or spinal inhibitory GABAergic neurons.²⁻⁴ The differences between SPS and PER could depend on the distribution and degree of the autoimmune reaction; SPS involves the spinal interneurons, whereas PER expands to the brainstem or other areas of the CNS.²⁻⁴ More clinical and laboratory

based studies are needed to further our understanding of the pathogenesis of SPS and PER.

Acknowledgements

Part of this work was supported by Research Projects Grants in Aid for Scientific Research numbers 60180957(A H) and 80203751(N O), from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

A Ishii

Department of Neurology, Tsukuba Soai Hospital, Department of Neurology, University of Tsukuba, Tsukuba, Japan

A Hayashi

Department of Neurology and Rehabilitation, Juntendo University, Tokyo, Japan

N Ohkoshi, S Matsuno, S Shoji

Department of Neurology, University of Tsukuba, Tsukuba, Japan

Correspondence to: A Hayashi, Clinical Pathology, Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan; hayashi@med.juntendo.ac.jp

Reference

- 1 Whiteley AM, Awash M, Urich H. Progressive encephalomyelitis with rigidity. Its relation to 'subacute myoclonic spinal neuronitis' and to the 'stiff man syndrome'. *Brain* 1976;**99**:27-42.
- 2 Meinck HM, Thompson PD. Stiff man syndrome and related conditions. *Mov Disord* 2002;**17**:853-66.
- 3 Matsuno S, Ohkoshi N, Hayashi A, *et al*. A case report of steroid-responsive progressive encephalomyelitis with rigidity showing muscle stiffness limited to the upper body. *Clin Neurol* 1998;**38**:680-2.
- 4 Gouider-Khouja N, Mekaouer A, Lamaout A, *et al*. Progressive encephalomyelitis with rigidity presenting as a stiff-person syndrome. *Parkinsonism Relat Disord* 2002;**8**:285-8.
- 5 De Camilli P, Thomas A, Cofield R, *et al*. The synaptic vesicle-associated protein amphiphysin is the 128-kd autoantigen of stiff-man syndrome with breast cancer. *J Exp Med* 1993;**178**:2219-23.
- 6 Butler MH, Hayashi A, Ohkoshi N, *et al*. Autoimmunity to gephyrin in stiff-man syndrome. *Neuron* 2000;**26**:207-312.