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).

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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 intracanalicular 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

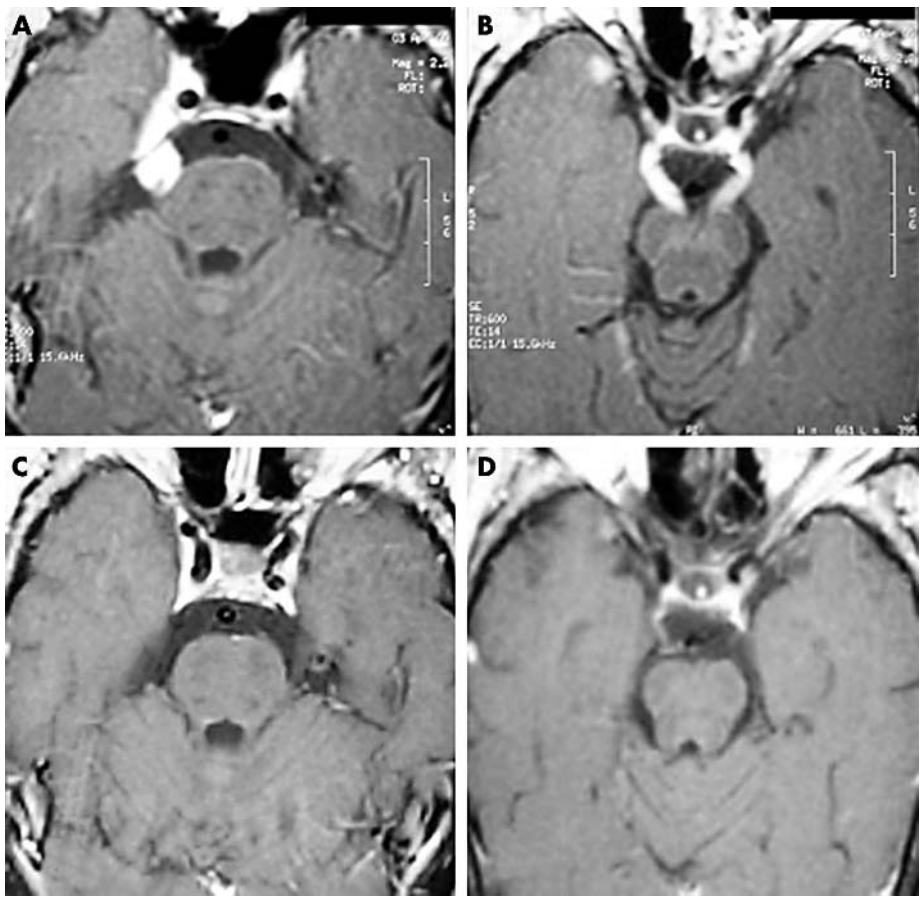

Figure 1 Brain axial T1 weighted MRI post gadolinium (Gd) administration. Post contrast images show an impressive enlargement and Gd enhancement of right cranial nerve V (cisternal and Gasser ganglion segments) (A) and of the III cranial nerves (cisternal segment) (B). Three months after starting highly 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 $\log_{10}$), 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.

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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