Polymicrobial central nervous system infection in the acquired immunodeficiency syndrome

Sir: More than 40% of AIDS patients have central nervous system (CNS) complications. These complications may be infectious, neoplastic or vasculitic. In some cases CNS involvement may go undiagnosed ante-mortem. Neurological disorder is the presenting manifestation of AIDS in as many as 20% of the patients. AIDS patients are characterised by a high incidence of opportunistic infections both systemic and in the central nervous system. Many patients are infected by fungi and protozoa such as Cryptococcus neoformans, Candida spp. and Toxoplasma gondii as well as atypical mycobacteria and cytomegalovirus (CMV). The aetiological agent HIV itself is neurotropic.

We describe the case of a man with AIDS diagnosed by CDC criteria who had documented CNS infection by Cryptococcus neoformans, candida and CMV as well as HIV itself.

In 1985 a 38 year old man who had had episodic contact with prostitutes in New York was diagnosed as suffering from AIDS. He had 2 proven episodes of Pneumocystis carinii infection which responded to antimicrobial therapy. He was seropositive for HIV and had an inverse ratio of helper T cells to suppressor T cells. In August 1986 he was hospitalised for fever (38°C), frontal headache, dizziness, nausia and vomiting. His neck was supple with mild evidence of meningeal irritation and there was a slight right central facial palsy. The retina was without evidence of CMV retinitis or candidal infection. In addition a slight memory loss was noted. The leucocyte count was 3300/mm³. Serology for CMV and Epstein-Barr virus (EBV) was negative. Radiographs of the frontal and maxillary sinuses were normal. Computed tomography of the brain was normal. Glucose and protein in the CSF were within normal limits and no cells were found. Gram stain was positive for candida. India ink smear was negative for cryptococcus but a positive antigen titre for cryptococcus (1:512) was found. CSF culture grew out candida. Antifungal therapy with amphotericin B and flucytosine (5-fluorocytosine) was begun. A week after commencement of therapy the CSF cryptococcal antigen titre was 1:256 and after 2 months of therapy it was 1:16. At this time CSF culture was negative for candida. In December 1986 the patient was again infected with Pneumocystis carinii proven by biopsy. His general condition deteriorated. Lumbar puncture was unremarkable. Cryptococcal antigen in CSF was again 1:16 and CT demonstrated brain atrophy without other pathological findings. Convulsions developed and the patient died shortly thereafter.

At necropsy the brain weighed 1380 grams. There were a number of necrotic lesions in particular in the cerebellum, the dentate nucleus and the cerebellar cortex. Numerous cells with CMV inclusion bodies were seen in the necrotic areas and within microglial nodules of the brain as well as in the lungs. Cryptococcal lesions were seen in the brain substance, in the Virchow-Robin space and in the meninges. Cryptococcus was found in the brain substance itself and within histiocytes. Other than this no inflammatory response was seen. Electron microscopy demonstrated typical HIV virus near and within lymphocytes. No other brain pathology was found.

In the pre-AIDS period Cryptococcus neoformans and Candida albicans were both known as major CNS pathogens while toxoplasma and CMV were relatively rare. The AIDS epidemic has increased the incidence severalfold. Some patients with cryptococcal CNS infection are totally lacking in neurological signs and symptoms. Lumbar puncture is often non-diagnostic. A prolonged course of antifungal therapy is warranted and maintenance therapy is necessary to prevent relapse. Nevertheless evidence of cryptococcal infection has been found at necropsy in patients who received prolonged maintenance therapy.

Other infective agents such as Toxoplasma gondii, Mycobacterium avium intracellulare and CMV which were very rare in the pre-AIDS period are a diagnostic and therapeutic challenge today. Recently HIV itself was shown to cause many neurological syndromes.

Polymicrobial infection of the CNS in immunosuppressed patients has been reported before and during the AIDS era but these cases are relatively rare. In a review of 366 neurologically symptomatic patients only three were found to have proven coexisting CNS infection by two organisms.

Despite the fact that our patient had only minimal neurological symptoms two CNS infections were diagnosed early: cryptococcus by CSF antigen titre and candida by Gram stain and CSF culture. Anti-fungal therapy led to clinical and laboratory improvement; however, necropsy revealed that therapy eradicated the candidal infection only.

Necropsy also revealed two other CNS infections: CMV and HIV. The former was not suspected as blood and CSF serology were negative, no evidence of retinitis was found and inclusion bodies were not seen on lung biopsy. We did suspect CNS infection by HIV because of brain atrophy seen on CT, progressive dementia and convulsions.

To our knowledge this is the first published case of an AIDS patient with four concomitant CNS infections. The following points are emphasised: (1) Polymicrobial CNS infections may occur in AIDS patients with minimal or absent neurologic symptoms. (2) Even when the aetiological agent is identified and antimicrobial therapy is optimal treatment failure often occurs. (3) Failure of treatment may be due to an occult concurrent CNS infection undiagnosed before death.

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References

Letters


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Magnetic resonance imaging in an HTLV-I antibody positive patient with tropical spastic paraparesis

Sir: Recently interest has been shown in the magnetic resonance imaging of patients with HTLV-I antibody positive tropical spastic paraparesis (TSP). The MRI changes in TSP may only be mild and with the sensitivity of MRI in detecting lesions these may be fortuitous rather than disease associated. We describe below the case of a young West Indian woman with a spastic paraparesis in whom there were extensive white matter lesions on MRI with an oligoclonal pattern to the CSF electrophoresis and circulating HTLV-I antibodies.

A 36 year old woman who had lived all her life in Grenada, presented with a 3 year history of dragging the left leg progressing to stiffness in both legs and unsteadiness when walking. In 1979, she had pulmonary tuberculosis, treated medically. There was no suggestion of a vasculopathy and she was a non-smoker. General physical examination was normal, except for a spastic paraparesis with bilateral extensor plantar responses. There was reduced vibration sense below the costal margins and position sense was impaired in the feet.

Routine blood tests were normal, as was full myelography. The CSF contained 2 white cells, 0.4 g/l protein and 3.2 mmol/l of glucose. Oligoclonal bands were present in the CSF but not in the serum. Serum angiotensin converting enzyme was 35 (16–53 mmol/minute/ml). Visual evoked potentials were normal. The CT brain scan revealed low attenuation lesions in the white matter, particularly in the periventricular region. MRI (fig.) showed multiple areas of abnormally increased signal in the white matter of both hemispheres and brain stem.

The clinical and laboratory findings in our patient would have suggested a diagnosis of multiple sclerosis but that she had lived her life in the West Indies where the disease is rare. The finding of HTLV-I antibodies in the blood is consistent with a clinical diagnosis of tropical spastic paraparesis. The clinical similarity of the two diseases has been dealt with elsewhere but the pathology is quite different with an inflammatory meningeal process with mononuclear cell infiltration predominating in TSP. The extent of the white matter changes on MRI of our patient is unlikely to be fortuitous, age related or due to ischaemic or granulomatous pathology. It may well be that the degree of white matter involvement depends on the stage of the illness and the suggestion that the lesions in TSP are more sparse than in multiple sclerosis is not supported by this case.

As the pathological changes are so different in the two conditions, it is disappointing that the MRI findings are similar. This case, like others, demonstrates the need for full investigation of patients with spinal cord symptomatology and negative myelography. We are grateful to Dr A Dalgleish and Dr K Cruickshank for performing the HTLV-I antibody screen on our patient.

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Parkinsonism as first manifestation of lymphomatoid granulomatosis

Sir: Lymphomatoid granulomatosis (LCP), as first described in 1972 by Liebow et al, is an angiocentric and angiodestructive lymphoreticular and proliferative disorder of the lungs. LC may be distinguished from lymphoma by frequent involvement of lung, skin, renal interstitium and central nervous system. Although initially described as a vasculitis, it is now considered that LC is a lymphoproliferative lesion composed predominantly by T-lymphocytes. Two-thirds of the patients die with a median survival of 14 months despite therapy, and a definable lymphoma is found to have developed in 12% of the patients. The time interval between initial diagnosis and lymphoma ranges from weeks to several years.

CNS dysfunction has been reported in 20% and peripheral neuropathies in 15% of patients. However, extrapyramidal involvement has been rarely described. We report a case of a woman with pulmonary LC and extrapyramidal manifestations.

In December 1986, a 67 year old woman was admitted to hospital because of cough, fever, weight loss and inability to walk. In August 1984 she had developed a mood disorder and she was treated with tricyclic compounds without any improvement. In April 1985, the