ABC of AIDS

C A CARNE

NEUROLOGICAL MANIFESTATIONS

Causes of neurological manifestations

Opportunistic Infections

Tumours

Primary effects of HIV

About 10% of patients with the acquired immune deficiency syndrome (AIDS) present because of neurological problems, but as many as 75% have evidence of disease of the central nervous system at necropsy. The neurological manifestations of AIDS may be caused by opportunistic infections, by tumours, and by the primary neurological effects of the human immunodeficiency virus (HIV). HIV may also, infrequently, cause neurological symptoms in immunocompetent people with HIV infection.

The disorders of the nervous system most commonly seen in patients with AIDS are encephalitis, meningitis, cerebral space occupying lesions, demyelination, retinitis, myelopathy, and peripheral neuropathy.

Encephalitis

Clinical features of subacute encephalitis

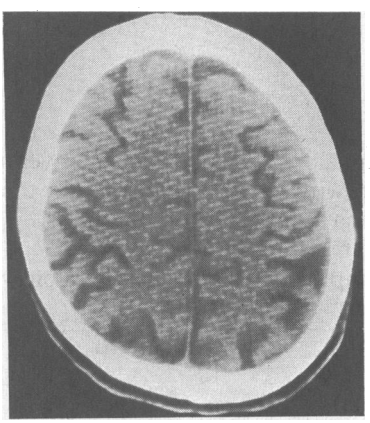
Forgetfulness

Loss of concentration

Lethargy

Loss of balance

Deterioration in handwriting



About one third of patients with AIDS develop subacute encephalitis. It occurs predominantly among those who have had opportunistic infections rather than those who have Kaposi's sarcoma alone. It usually starts with subtle cognitive changes, although it is sometimes first noticed as an acute confusional state precipitated by fever or mild metabolic derangement. Major cognitive symptoms comprise forgetfulness, loss of concentration, and slowness of thought. Common motor symptoms are loss of balance, leg weakness, and deterioration in handwriting. Lethargy, loss of libido, and withdrawal may occur, mimicking psychological depression. Bedside testing of mental state may reveal slowness of verbal responses, blunting of affect, difficulty in performing serial 7s, and impaired performance in tests of recent memory. The most common finding in the remainder of the neurological examination is gait ataxia. Motor signs, including generalised hyperreflexia and weakness of the legs, may be seen. The illness may progress to severe dementia over several weeks or months, the patient eventually becoming bedridden and incontinent.

Computed tomography usually shows dilated ventricles and prominent cortical sulci indicative of cortical atrophy. Electroencephalography commonly shows diffuse bilateral slowing. Examination of cerebrospinal fluid often shows a mild lymphocytic pleocytosis and a rise in protein concentration or lowered glucose concentration, or both. This clinical picture most commonly results from a direct effect of HIV on the brain. Less commonly encephalitis may be caused by cytomegalovirus; occasionally by herpes simplex virus, atypical mycobacteria, or diffuse lymphomatous infiltration; and rarely by varicella zoster.

Meningitis

Clinical features of cryptococcal meningitis

Fatigue/fever/weight loss

Headache

Nausea and/or vomiting

(Photophobia)

(Neck stiffness)

(Focal signs)

Meningitis in patients with AIDS is most commonly caused by the fungus *Cryptococcus neoformans*. Headache is almost universal among patients with this condition, about half have nausea or vomiting, and some experience photophobia. These symptoms are often preceded by non-specific symptoms, such as fatigue, fever, or weight loss. Physical examination sometimes reveals neck stiffness, and less commonly there are focal neurological abnormalities. The organism may also be disseminated in the lungs, kidneys, skin, fundi, and other organs. Examination of cerebrospinal fluid usually shows a mild pleocytosis, lowered glucose, and raised protein, though all of these may be normal. The diagnosis may be made by India ink staining or culture of cerebrospinal fluid or cryptococcal antigen detection in serum or cerebrospinal fluid. Computed tomography usually shows nothing abnormal.

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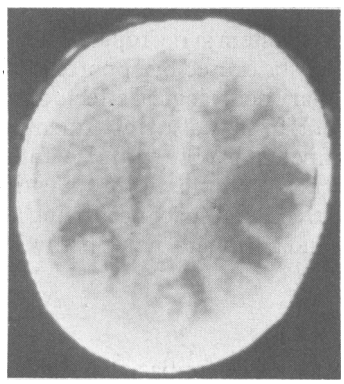
Space occupying lesions

Cerebral space occupying lesions

Caused by: Opportunistic infections
Tumours

Symptoms: Lethargy and/or confusion
Focal deficit
(Fitting)

Space occupying lesions may be caused by either opportunistic infections or tumours resulting in focal neurological deficit or fits. These are often preceded by lethargy or confusion for days or weeks. This presentation is most commonly caused by infection with the protozoon *Toxoplasma gondii*, causing intracerebral abscesses.



The symptoms of cerebral toxoplasmosis most often evolve over one to two weeks. Headache is often a major complaint. Characteristically it is bilateral, severe, and persistent and often wakes the patient at night. Patients are commonly also confused and lethargic, but this may result from coexistent HIV encephalitis. A focal neurological deficit or, less commonly, fitting is the dominant symptom in other cases. On examination almost all these patients have signs of a focal deficit, most commonly a mild hemiparesis. Less often there are signs of cerebellar or brainstem dysfunction, such as ataxia or a cranial nerve palsy. In most cases computed tomography shows the presence of mass lesions, which usually show ring enhancement after the injection of contrast medium. The same scan appearance may be caused by abscesses resulting from infection with *Candida albicans* or *Mycobacterium tuberculosis* and sometimes by primary cerebral lymphoma. Serological findings in toxoplasmosis are difficult to interpret owing to the pertubation of the immune system. Some authorities recommend a one to two week trial of antitoxoplasma chemotherapy in patients whose computed tomogram shows ring enhancing lesions and whose toxoplasma serology (indirect immunofluorescence) is positive at a serum dilution of 1/2 or greater. If this trial of treatment fails to produce an improvement a brain biopsy is performed. Others recommend brain biopsy in all cases.

Causes of ring enhancing lesions on CT scans

Toxoplasma
Candida
Mycobacterium tuberculosis
Primary cerebral lymphoma
Cytomegalovirus

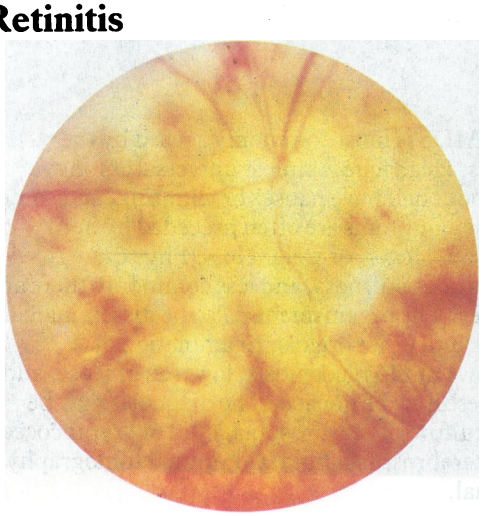
Demyelination

Progressive multifocal leucoencephalopathy

Aphasia
Blindness
Ataxia
Hemiparesis

Progressive multifocal leucoencephalopathy, an unusual demyelinating disease, is sometimes seen in patients with AIDS. It appears to be the result of infection with a papovavirus and may cause aphasia, blindness, hemiparesis, and ataxia. The disability progresses until death. Characteristically computed tomography shows low density lesions without contrast enhancement.

Retinitis



The most common cause of impaired visual acuity in patients with AIDS is a retinitis caused by cytomegalovirus. The diagnosis is made clinically. The earliest findings are of irregularity and narrowing of the lumen of the retinal vessels. Vascular occlusion follows with the appearance of perivascular exudates and haemorrhage before infarction of the affected area of retina. Without treatment the infection will often progress to cause bilateral blindness. Chorioretinitis caused by toxoplasma has also been seen.

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Myelopathy and peripheral neuropathy

Vacuolar myelopathy

Symptoms: paraesthesiae
leg weakness

Signs: paraparesis
±spasticity
±ataxia

Peripheral neuropathy

Distal
Symmetrical
Dysaethesiae
±weakness
±distal atrophy

As many as a quarter of patients with AIDS may suffer from a condition known as vacuolar myelopathy. Patients may complain of motor or sensory symptoms or both, which include bilateral or, less commonly, unilateral weakness of the legs, possibly coinciding with paraesthesiae. Examination shows a paraparesis, often accompanied by spasticity or ataxia (or both). In severe cases the condition continues to evolve over several weeks to months with the development of urinary incontinence. It is often seen in association with subacute encephalopathy and is widely believed to be a direct effect of HIV on the spinal cord.

The peripheral neuropathy most commonly seen in patients with AIDS is a symmetrical sensorimotor neuropathy with painful dysaesthesiae and less commonly with weakness and distal atrophy. This appears to be the direct effect of HIV on peripheral nerves and often occurs in association with subacute encephalitis.

Neurological manifestations of HIV infection before the development of AIDS

Neurotropic effects of HIV

At seroconversion

Acute Encephalitis
Meningitis
Myelopathy
Neuropathy

In chronic HIV infection

Subacute/chronic Encephalitis
Meningitis
Vacuolar myelopathy
Peripheral neuropathy

Uncommonly HIV may cause neurological dysfunction in people who have not developed and may never develop AIDS as currently defined.

Acute manifestations may occur at the time when patients first develop antibodies to HIV, generally within three months of exposure to the virus. These may take the form of encephalitis, myelopathy, acute neuropathy, or meningitis. The acute encephalitis may comprise fever, general malaise, mood change, changes in the level of consciousness, and fits. Recovery is almost complete after one week, and there do not appear to be long term neurological sequelae. The acute neuropathy may be manifest as a facial palsy which recovers over the course of a few months. Acute meningitis may be seen at the time of seroconversion for HIV.

An atypical aseptic meningitis may also occur in people infected with HIV before AIDS develops. These patients present with headache, fever, and meningeal signs but often also have atypical features, such as recurrence, chronicity, cranial nerve disease, and long tract signs. The fifth, seventh, and eighth cranial nerves are the most commonly affected. Peripheral neuropathy, as seen in some patients with AIDS, may occur in people before they develop AIDS. However, mononeuritis multiplex is said to be more common at this stage. Finally subacute encephalitis may occur in people with HIV infection who have not developed AIDS.

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A mentally handicapped woman in her 30s developed a small smooth goitre while being treated for depression and was found to have mild hypothyroidism. She has been treated with thyroxine and feels better. Her thyroid function test results are now normal but her goitre remains. Is it advisable to arrange for a thyroid scan?

The development of a smooth symmetrical goitre in a woman in her 30s is most suggestive of a lymphadenoid goitre, and the presence of thyroid antibodies would confirm this diagnosis. The fact that the thyroxine concentration and free thyroxine index are at the lower limits of normal and the thyroid stimulating hormone concentration is raised is diagnostic of preclinical myxoedema. It is stated that she is mentally handicapped and receiving treatment for depression but the treatment is not specified. If she is taking lithium this would be relevant. Lithium inhibits thyroid hormone release in both thyrotoxic and euthyroid subjects[1] and is often associated with the development of goitre and hypothyroidism.[2] If the mental handicap is due to Down's syndrome this could also be relevant as there is an increased frequency of autoimmune thyroid disease in these patients. Indeed, evidence of thyroid autoimmunity or hypothyroidism may be present in as many as 30% of patients with Down's syndrome.[3] A scan is unlikely to be helpful in these patients, and as she is taking thyroxine the uptake of isotope by the gland will be suppressed. Isotope scans are of particular application in nodular goitres and in thyrotoxic patients when it is necessary to differentiate Graves' disease from painless thyroiditis. It is not surprising that the goitre is still present after three months' treatment with 50 μg thyroxine, as the dose of thyroxine is small and many lymphadenoid goitres take several months to resolve. It would be advisable to increase the dose of thyroxine to 0·1 mg or even 0·15 mg daily and combat any side effects of thyroxine with β blockade.—C W H HAVARD, consultant physician and endocrinologist, London.

1 Spalding SW, Burrow GN, Bermudez F, Himmelhock JM. The inhibitory effect of lithium on thyroid hormone release in both euthyroid and thyrotoxic patients. *J Clin Endocrinol* 1972;35:905.
2 Brownlie EW, Chambers ST, Sadler WA, Donald RA. A report of 14 cases of hypothyroidism and four cases of thyrotoxicosis. *Aust NZ J Med* 1976;6:223-9.
3 Lobo EA, Khan M, Tew S. Community study of hypothyroidism in Down's syndrome. *Br Med J* 1980;280:1253.

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