

CLINICAL RESEARCH

Acute myelopathy associated with primary infection with human immunodeficiency virus

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Abstract

A 29 year old white homosexual man presented with a two and a half week history of severe sore throat, fever, and extreme fatigue. His symptoms did not respond to antibiotics. He had mild bilateral conjunctivitis, a rash over his chest and back, and enlarged lymph nodes, but examination of the nervous system yielded normal results. He had low total white cell and platelet counts. The results of enzyme linked immunosorbent assay for human immunodeficiency virus (HIV) were equivocal when HIV IgM was detected in serum. Despite treatment with ampicillin his temperature remained high and he developed abnormal neurological signs, including a paraparesis and hyperreflexia of the arms. HIV was isolated from lymphocytes from blood and cerebrospinal fluid. Over the next six weeks the patient improved and was discharged. Two months later abnormal neurological signs persisted in his legs.

Although various neurological syndromes associated with seroconversion to HIV have been described,¹⁻³ this is probably the first report of a patient with myelopathy at the time of seroconversion.

Introduction

Acute myelopathy after primary infection with the human immunodeficiency virus (HIV) has not been reported previously. We report what we believe to be the first case.

Patient, methods, and results

A 29 year old white homosexual man presented with a two and a half week history of a severe sore throat, a painful mouth, and fever. He developed night sweats, a dry cough, and extreme fatigue and had a constant headache. Before admission he had had a single loose motion after 10 days of constipation. His symptoms did not respond to treatment with penicillin V or co-trimoxazole. A practising homosexual, he had last had sexual contact about five weeks before the onset of his symptoms. He was taking no prescribed or illegal drugs.

On initial examination his temperature was 38.5°C. He had mild bilateral conjunctivitis and a rash of discrete red macules over his chest and back. Slightly enlarged lymph nodes were palpable in the neck and left axilla. His buccal mucosa was erythematous with superimposed candida infection, and there was one small flat ulcer. His pharynx was inflamed, but the tonsils were normal and there was no exudate. His liver and spleen were just palpable, and examination of the nervous system yielded normal results.

Investigations showed a low total white cell count of $2.2 \times 10^9/l$ and thrombocytopenia (table). Alkaline phosphatase activity was increased at 177 IU/l and aspartate transaminase activity at 116 IU/l. Results of the Paul-Bunnell test were negative. A throat swab grew *Candida albicans*. Enzyme linked immunosorbent assay for HIV was equivocal (table).

He received a course of treatment with intravenous ampicillin, but his temperature remained high. On the fifth day after admission he reported that his right leg felt stiff, and his gait became increasingly unsteady. Neurological examination showed an increase in tone in both legs, especially the right, with brisk tendon reflexes and extensor plantar response bilaterally. Power and sensation were normal. Later the same day he suffered an episode of generalised shaking of the legs and experienced increasing difficulty in voiding urine. He seemed mentally slow. Full myelography and computed tomography of the brain yielded normal results. The cerebrospinal fluid contained $7 \times 10^3/l$ lymphocytes (table). No organisms were isolated. *Treponema pallidum* haemagglutination assay, IgG analysis, and electrophoresis yielded negative results. A working diagnosis of myelitis was made.

Over the next two weeks he continued to experience spasms of uncontrolled shaking of the legs. In addition, he described episodic, severe lancinating pains in his back, which he likened to electric shocks. These improved with clonazepam. He developed a paraparesis, hyperreflexibility of the arms, and a pout reflex. In view of this deterioration a repeat lumbar puncture was performed 10 days after he was admitted.

Blood and cerebrospinal fluid were cultured, and HIV was isolated from a mixture of lymphocytes from both sources (necessitated because of a fungal contamination of the culture of cerebrospinal fluid). Over the ensuing four weeks the patient's condition began to improve, and his gait began to return to normal. His white cell count rose to $6.5 \times 10^9/l$ (table). He developed an

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urticarial rash and low grade fever, which was thought to be due to clonazepam and which resolved when chlorpheniramine was given. When discharged he had an increase in tone with normal power in his legs, but his plantar responses had reverted to flexor. Two months later obvious neurological signs persisted in his legs and his walking was still unsteady.

Discussion

Dementia, myelopathy, and neuropathy in patients with long established HIV infection are well recognised.¹ In the past year neurological syndromes associated with seroconversion to HIV have been described, including examples of patients with meningitis,¹ encephalopathy,¹ neuropathy,² and radiculopathy.³ Our patient is unique, however, in having a myelopathy at the time of seroconversion. Although the primary site of damage was the spinal

immunoassay system. Intrathecal synthesis of HIV specific immunoglobulin has been shown in asymptomatic carriers of the virus⁶ and in patients with AIDS.⁷ In one patient with a chronic polyradiculopathy due to HIV sequential analysis showed a cerebrospinal fluid:blood IgG synthesis ratio of 14.7 (normal <1.4).⁷ Unfortunately, the radioimmunoassay system cannot be quantified sufficiently to compute a ratio, and the enzyme linked immunosorbent assay is more appropriate to serum (because of high globulin content) than to estimation of cerebrospinal fluid. The antibody detected in the cerebrospinal fluid may therefore represent passive transfer across the blood-brain barrier, although its detection when the concentration of antibody in the serum was so low suggests intrathecal synthesis of antibody to HIV.

The pathogenesis of the acute neurological syndromes is unclear in HIV infection. Unlike patients with the chronic syndromes, which are relentlessly progressive, at least some of the patients who

Results of various investigations in patient with HIV infection. Values in brackets are actual results of tests

Investigation	Date			
	25 June	30 June	2 July (serum)/ 4 July (cerebrospinal fluid)	7 July
Blood				
Neutrophils ($\times 10^6/l$)	1364			3445
Lymphocytes ($\times 10^6/l$)	396			2145
Platelets ($\times 10^9/l$)	144			248
HIV:				
IgM antibody capture radioimmunoassay (Macria)*	Positive (11.5)		Positive (14.8)	
Competitive enzyme linked immunosorbent assay (Wellcozyme)†	Equivocal (0.723)		Positive (0.551)	
Antiglobulin enzyme linked immunosorbent assay (Elavia)	Negative		Equivocal	
IgG antibody capture radioimmunoassay (Gacria)‡	Equivocal (2.3)		Positive (6.6)	
Cerebrospinal fluid				
Mononuclear cells ($\times 10^3/l$)		7	24	
Protein (g/l)		0.65	0.68	
Glucose (mmol/l)		3.3	6	
HIV:				
IgM antibody capture radioimmunoassay (Macria)*		Negative	Negative	
IgG antibody capture radioimmunoassay (Gacria)‡		Positive (7.2)	Positive (6.5)	
Antiglobulin enzyme linked immunosorbent assay (Elavia)		Negative	Negative	

*Ratio specific HIV IgM:non-specific IgM.

†Cut off <0.777.

‡Ratio specific HIV IgG:non-specific IgG.

Conversion: SI to traditional units—Glucose: 1 mmol/l = 18 mg/100 ml.

cord, there were subtle signs of dysfunction at a higher level (impaired mental activity and pout reflex); and cortical abnormality was also found in one of the published cases of neuropathy.² At least some of these patients thus seem to have a mild, generalised neurological disturbance, although the clinically significant dysfunction affects a limited part of the central or peripheral nervous system.

The evidence strongly supports a diagnosis of primary HIV infection. One new sexual contact five weeks before the illness would have allowed a typical incubation period.⁴ The other clinical features on admission of fever, rash, enanthem, sore throat, headache, splenomegaly, lymphadenopathy, disturbed hepatic function, and leucopenia and thrombocytopenia are characteristic, although not specific.⁴ Oral candidiasis is more typical of the acquired immune deficiency syndrome (AIDS) and suggested a diagnosis of AIDS, although candida may be isolated from the throats of most healthy subjects. The rise in titre of total antibody to HIV, together with the presence of IgM (detected by a modification of the IgG antibody capture system⁵) and resolution of the haematological abnormalities, is diagnostic of primary HIV infection. Isolation of the virus adds weight to the serological evidence.

Intrathecal antibody could be detected by a capture radio-

present with neurological dysfunction at the time of seroconversion either do not deteriorate or improve, as our patient did. Whether such patients will later develop further neurological disability is unknown.

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