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Subacute AIDS-related lumbosacral radiculopathy: a bacterial infection?

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Summary. A case of lumbosacral polyradiculitis in an HIV-1-positive man (CDC IIB) leading to a flaccid paraplegia below the level of L4 is reported. A detailed analysis of several cerebrospinal fluid samples led to the suspicion of a bacterial infection. After treatment with antibiotics and tuberculostatic agents the neuropathy improved and the patient has survived for 2 years. In contrast to similar cases that were probably caused by cytomegalovirus in terminal stages of AIDS, it is argued that an unidentified bacterial infection was the cause of the polyradiculitis in the present case.

Key words: Acquired immunodeficiency syndrome – Bacterial infection – Radiculitis

Introduction

In recent years various disorders of the peripheral nervous system have been reported in HIV-1-infected patients [5, 10, 11, 13]; among these is progressive polyradiculitis [1, 7, 12], which leads dramatically to severe destruction of the cauda equina. In some of these cases a cytomegalovirus (CMV) infection has been postulated [1, 7, 12]; by early treatment with ganciclovir a partial remission of the motor and sensory deficits was achieved in a few patients [12]. Nevertheless all of the patients, most of whom were in the final stages of AIDS, died within the first few weeks after the onset of the cauda equina syndrome, mainly due to *Pneumocystis carinii* pneumonia.

We have observed a patient with progressive polyradiculitis which became manifest in an early stage of HIV-1 infection and improved without specific anti-CMV therapy; he has survived for 2 years.

Case report

A 25-year-old homosexual man, known to be HIV-1-positive for less for than 1 year and without any sign of manifest AIDS, developed lumbar backache followed the next day by bladder and bowel disturbance; on the 3rd day he observed bilateral paresis of the lower leg muscles and paraesthesias initially confined to the S1 dermatomes. On admission (day 8) the patient had grade 3 (BMRC) strength in the L5/S1 muscles and urinary and bowel incontinence. Ankle jerks and anal reflexes were absent. There was a moderate sensory disturbance in the S1–5 dermatomes on both sides.

From the results of the first cerebrospinal fluid (CSF) examinations (see below) a bacterial infection was assumed and therapy was started with antibiotics (piperacillin/flucloxacillin/tobramycin) for 3 weeks and with tuberculostatic agents (isoniazid/rifampicin/pyrazinamide) for 3 months. Nevertheless the sensorimotor disturbances were progressive over the following 3 weeks, leading to bilateral paralysis of the L5/S1/S2 muscles and a grade 2–3 paresis of the musculature supplied by the upper lumbar roots; the knee jerks and gracilis reflexes were absent. Touch and pinprick sensation were diminished in the L1–3 dermatomes and there was anaesthesia/analgesia in the L4–S5 dermatomes. Cranial and brachial nerves remained unaffected.

Only in the first few weeks was there a slight elevation of body temperature, up to 38°C; white cell count and sedimentation rate were always normal. CD4-positive cells were reduced to 0.56/nl (lower limit of normal: 0.8/nl) initially (4 weeks after the onset of symptoms), fell below 0.4/nl only once (during the 3rd month), were still reduced to 0.46/nl in the 5th month and returned to normal (0.84/nl) after 10 months.

In the 5th week a partial remission started; at the end of the 5th month the roots L1–4 had regained their normal motor and sensory function; 1 year after the onset of the polyradiculitis a slight improvement could also be found in the proximal distribution area of the L5 and the sacral roots.

The last examination, 24 months after the onset of the neuropathy, revealed normal function of the L1–4 roots; the patient had regained control of the anal sphincter and nearly sufficient control of the vesical sphincter; even the reflexes of erection and ejaculation had partially returned. In contrast the L5/S1 muscles were still paralytic.

Electrophysiology

EMG showed partial and complete denervation in the L4 and the L5/S1 myotomes respectively. Motor nerve conduction velocity (MCV) could not be measured in the peroneal and tibial nerve owing to total denervation of the intrinsic foot muscles. MCV was normal in the femoral nerve. In spite of total anaesthesia of the foot and absence of tibial nerve somatosensory evoked potential a normal sural nerve action potential could be recorded, demonstrating the supraganglionic site of the lesion.

Neuroradiology

Thoracolumbar myelography and spinal MRI were normal.

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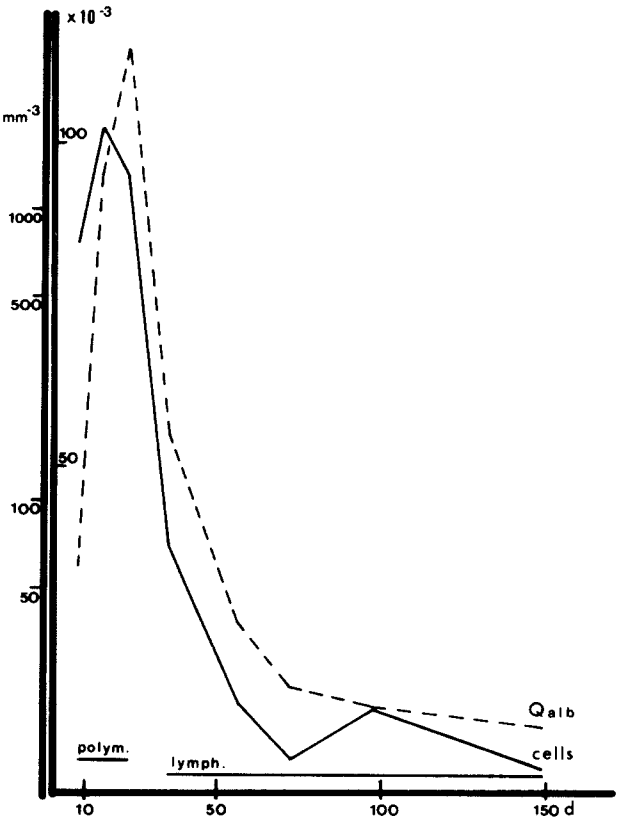

Fig. 1. Cerebrospinal fluid (CSF) findings during the course of the polyradiculitis. The *solid line* (cells, left ordinate) shows the cell count with the change from initial polymorphonuclear *(polym.)* to lymphocytic *(lymph.)* pleocytosis. The *dashed line* represents the CSF/serum albumin quotient (Q_{alb}, right ordinate)

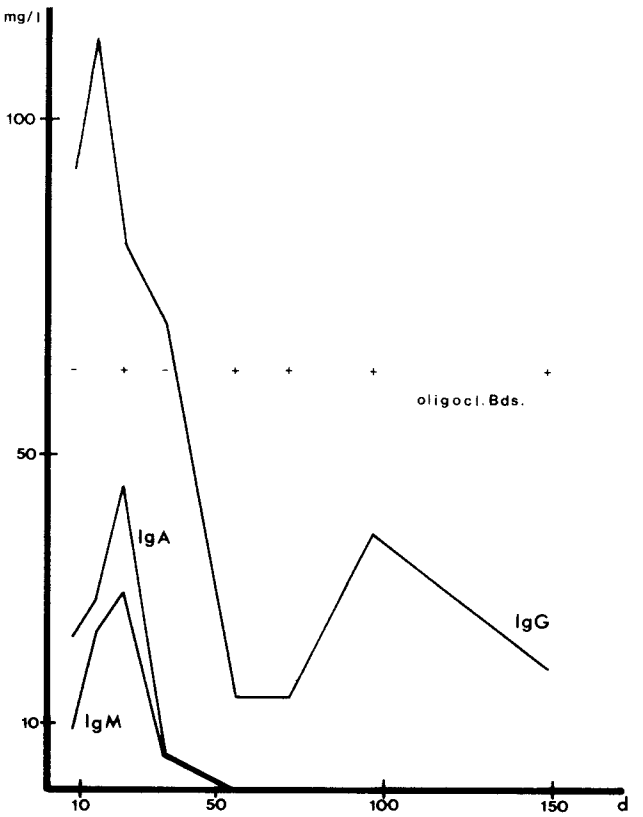

Fig. 2. Concentration of intrathecally produced immunoglobulins and demonstration of oligoclonal bands *(oligocl. Bds.)* during the course of the disease. Albumin, IgG, IgA and IgM were measured by kinetic nephelometry; the intrathecally synthesized amount of immunoglobulins was calculated according to the statistics of Reiber and Felgenhauer [15]. With one exception, oligoclonal bands were not detected until the end of the 8th week; hence the intrathecally synthesized IgG is assumed to be polyclonal in this first phase [16]

Cerebrospinal fluid

Initially the white cells were elevated up to 1900/mm^3; cytologically there was a prevalence of polymorphonuclear cells up to 80% during the first few weeks. At the end of the 5th week the cell count fell below 100, mainly lymphocytes (Fig. 1).

The CSF/serum albumin quotient (Q_{alb} [8]) was elevated up to 114×10^{-3} (upper limit: 8×10^{-3}) corresponding to an elevation of the total protein up to 6590 mg/l (Fig. 1). The concentration curves of intrathecally synthesized IgG, IgA and IgM are depicted in Fig. 2. The CSF lactate was elevated to 4.2 mmol/l (upper limit: 2.1 mmol/l). Beginning in the 3rd week the pleocytosis diminished, as did the Q_{alb} and the concentration of the immunoglobulins. The lactate level returned to normal.

Initially the CSF/serum quotient of HIV antibodies (Q_{HIV}), comparing the CSF and serum fractions of ELISA-identified HIV antibodies with CSF and serum total IgG [2], was not elevated (< 2), indicating that there was no intrathecal production of specific anti-HIV immunoglobulins; however, beginning in the 3rd month Q_{HIV} rose to 3.8.

Microbiology and serology

Several cultures for bacteria and fungi were negative, as was cryptococcal antigen. Mycobacteria could not be demonstrated in CSF/sputum/gastric juice/urine/bronchoalveolar lavage either microscopically or radiometrically or by culture. CMV in situ hybridization from blood and urine gave negative results. Serologically, antibodies against viruses (especially CMV, varicella zoster virus and herpes simplex virus), *Toxoplasma* and *Borrelia burgdorferi* could not be demonstrated.

Discussion

Since its first mention by Bredesen and Messing [4] and the first detailed description by Eidelberg et al. [7] progressive AIDS-related polyradiculopathy has been considered to be a sharply defined clinical syndrome [1, 5, 12]. Usually the neuropathy is seen in patients who are in the late stages of HIV infection [5]; in most cases *P. carinii* pneumonia precedes the neurological symptoms [5, 7]. The motor and sensory disturbance typically starts in the distribution area of the sacral and lower lumbar roots and then ascends over the next days or weeks, often leading to a flaccid total paraplegia. In some cases an extension to the upper extremities [5, 7, 12], and occasionally to the cranial nerves [7, 12], is seen. Usually the patients die within the first few weeks after the manifestation of the radiculopathy; Dalakas and Pezeshkpour [5] emphasized that the neuropathy invariably leads to death.

Electrophysiologically a widespread denervation, affecting the motor more than the sensory fibres, can be demonstrated; nerve conduction velocity is not substantially reduced. The CSF shows an inflammatory reaction

of varying intensity: cells can be absent [7], but in most cases a slight lymphocytic or a pronounced polymorphonuclear pleocytosis is found. The total protein is usually markedly elevated.

Histologically a severe inflammation of the neural structures [5, 12] and the vessels [7] can be demonstrated in the nerve roots [12] and the proximal segments of the cranial nerves [1]; the dorsal root ganglia are spared [7].

CMV is assumed to be the causative agent on the grounds of virological, serological and histological findings [1, 7, 12]. Consequently, Miller et al. [12] treated some of their patients with ganciclovir; two of them, who underwent therapy early in the course of the radiculopathy, improved. Nevertheless even these two patients died some weeks later due to pneumocystic pneumonia. Miller et al. [12] recommend an immediate clinical diagnosis followed by the rapid institution of anti-CMV therapy.

Our patient was not treated with ganciclovir. After CMV could not be demonstrated by in situ hybridization a CMV polyradiculitis was considered improbable. A further argument against this disease was the fact that our patient was in an early stage of HIV infection (CDC IIB), whereas practically all cases hitherto published had AIDS. Thus we decided to start treatment with antibiotics and tuberculostatic agents. After an initial progression the radiculopathy improved and merged into a stable defect syndrome; at the present time, the patient has survived 2 years since the onset of the neurological symptoms.

In our opinion this case raises the question whether bacterial infection may play a role besides the CMV, which has already been convincingly demonstrated.

The CSF findings especially may point to a bacterial origin of the inflammatory process:

1. A pronounced polymorphonuclear pleocytosis is rather atypical of a viral infection of the nervous system; it has not been demonstrated in cerebrospinal CMV infections of immunocompetent patients; Dorfman [6] and Fishman [9] have stated that in cases of CMV polyneuropathy "the protein level is elevated, while pleocytosis is absent". In our opinion there is no reason to assume that viral infections of the nervous system cause exceptionally marked CSF changes in HIV-positive patients; Booss and Esiri [3] emphasized that in immunocompromised patients with CMV infection the CSF is normal except for a slight protein elevation.

2. The pattern of intrathecally produced immunoglobulins as seen in our patient is rather typical of bacterial infections; according to Felgenhauer and Schädlich [8] IgA/IgG ratios above 0.2 have exclusively (with the exception of mumps) been found in bacterial diseases; in our case this ratio was nearly 0.4 (Fig. 2).

3. Finally, the marked elevation of CSF lactate up to 4.2 mmol/l has to be stressed; according to Reiber [14] values above 3.5 mmol/l suggest a bacterial infection.

We conclude that in cases of HIV-related progressive polyradiculopathy an intense search for a so far unidentified bacterial agent should be continued.

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