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Spinal MRI in vacuolar myelopathy, and correlation with histopathological findings

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Abstract We correlated MRI features with histopathological findings in an HIV-positive patient with vacuolar myelopathy. On MRI symmetrical nonenhancing high-signal areas in the posterior columns on T2-weighted images result from extensive vacuolation visible on histological sections.

Key words Vacuolar myelopathy · Human immunodeficiency virus · Magnetic resonance imaging

Introduction

Vacuolar myelopathy is the most common pathological finding at post mortem examination in HIV-positive patients [1]. The disease is characterised by extensive vacuolation of the white matter, especially of the posterior and lateral columns [2]. Clinically, the patients present with a progressive myelopathy [2]. However, neuroradiological data of help in confirming the diagnosis are still not available; the MRI features have not yet been clearly defined in living patients. We report the MRI findings and their correlation with histopathology in a 42-year-old patient with autopsy-proven vacuolar myelopathy.

Case report

A 42-year-old HOV-positive man (stage C3, HIV infection known for 6 years) complained of a subacute, progressive, ascending weakness with walking difficulty over 6 weeks. He had bilateral paraesthesiae of the feet and hands, urge incontinence with a nocturia of 4–5 times per night and absent erection. On the day of admission the slender patient, unable to walk without crutches, showed a spastic paraparesis with hyperreflexia, an incomplete segmental sensory level at T9 and autonomic bowel dysfunction. Neuropsychological deficits with reduced attention and memory disturbance were obvious.

Except for positivity of IgG antibodies against measles and cytomegalovirus (CMV) the cerebrospinal fluid was normal. Pathological blood parameters included a pancytopenia due to long-term medication with Zidovudin and Fluconazolum with prominent reduction of CD4 lymphocytes to 7 % (normal 20–60 %) and positive IgG antibodies against CMV, measles and mumps (IgM negative). Blood values of vitamin B 12 and folic acid were normal.

MRI of brain and spine was performed on the day of admission. Brain MRI showed generalised, diffuse, but slight cerebral and cerbellar atrophy which we attributed to HIV encephalopathy. Axial and sagittal T1-weighted images before and after contrast medium and fast T2-weighted spin-echo (SE) images of the cervical and thoracic spine were obtained at 1.5 Tesla. A focal, symmetrical, triangular, well-defined, bilateral, multisegmental high-signal area was seen on T2-weighted images exactly along the cervical posterior columns with predominance in the gracile tract, without enlargement of the cord. The high signal extended from C2 to C5 (Fig. 1 a, b). The T1-weighted images were normal, and there was no pathological contrast enhancement (Fig. 1 c). The thoracic cord appeared normal.

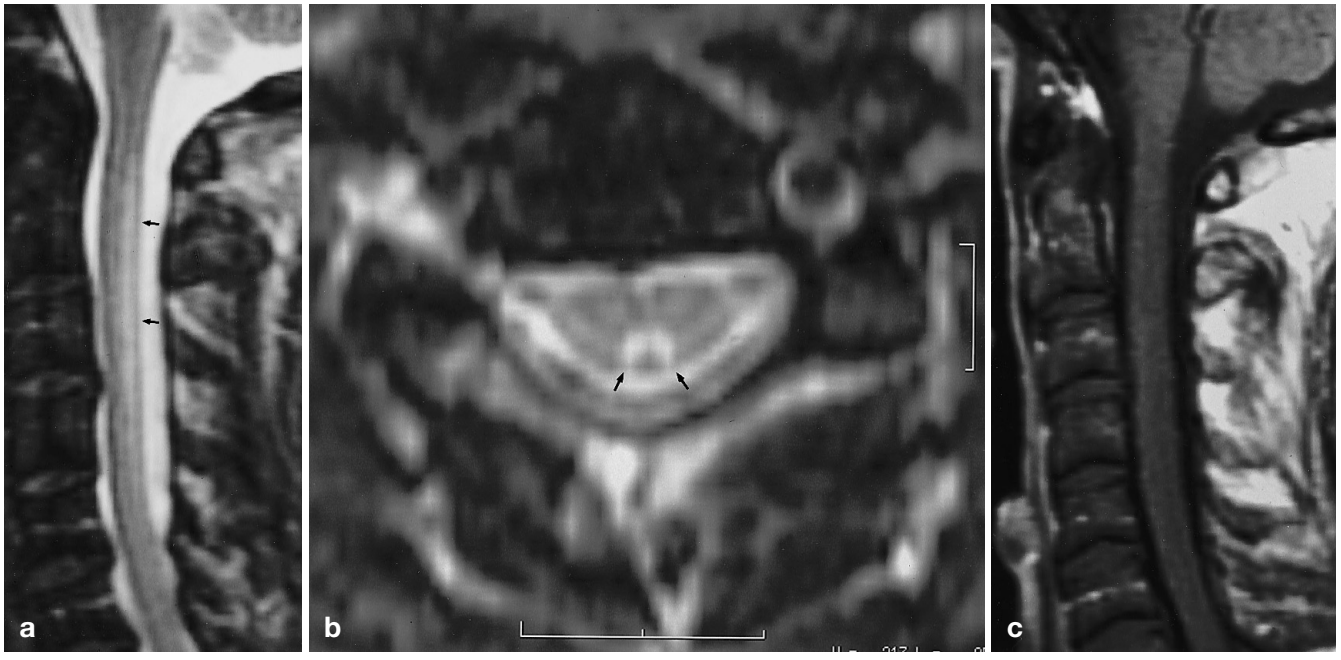

Fig. 1 T2-weighted sagittal **a** and axial **b** and sagittal contrast-enhanced T1-weighted **c** images of the cervical spinal cord; non-enhancing symmetrical triangular high-signal lesions in the posterior columns, especially in the gracile tracts *(arrows)*, without mass effect

During 10 weeks in hospital the patients spastic paraparesis worsened and increasing sensory deficits developed. The patient died of intercurrent CMV bronchitis and CMV pneumonia on the 72 nd day in hospital, 71 days after the MRI examination.

Sections from paraffin-embedded blocks of brain and spinal cord were stained using routine methods including haematoxylin and eosin, Luxol fast blue/cresyl violet for myelin and Nissl substance and Bielschowsky silver stain for axons. Immunohistochemical staining was performed on selected sections using the ABC method. Nodular cytomegalovirus encephalitis was diagnosed, not suspected on MRI. Extensive vacuolation of the cervical spinal cord was observed in the posterior and lateral columns of the white matter (Fig. 2 a) and to some extent in the ventral pyramidal tracts. No significant axonal loss was evident (Fig. 2 b). Lipid-laden macrophages were present in and adjacent to the vacuoles (Fig. 2 c).

Discussion

In 1985, Petito et al. [2] described the neuropathological findings in a previously uncharacterised progressive myelopathy in an autopsy series of 89 HIV-positive patients. It was defined microscopically as diffuse, prominent vacuolation in the spinal white matter in association with a few lipid-laden macrophages within the vacuoles or the myelin sheath. This new clinicopathological disease entity was therefore called vacuolar myelopathy (VM). Its features were confirmed by recent neuropathological investigations which describe the vacuolation as most extensive at the mid- to lower thoracic levels and in the lateral and posterior columns [2–4]; the anterior and anterolateral columns are rarely affected. The more severely the spinal cords is affected, the more symmetrical the histopathological changes are [2, 4]. The vacuoles are partly confluent and not confined to specific anatomical tracts [2]. Vacuoles are formed by an oedematous swelling within myelin, with splitting of the lamellae [2, 3] and are also found between the axon and the myelin sheath [4]. The axons are usually normal except in areas with severe vacuolation, where axonal disruption with secondary Wallerian degeneration is possible [2, 3]. HIV-antigen was shown within vacuoles and macrophages [5, 6] but macrophages immunoreactive for HIV were found in only 6 % of patients [7]. Characteristic but sparse multinucleate giant cell infiltrates can be observed, related to a productive infection [5].

VM is not specific for AIDS but is only rarely observed in non-AIDS immunocompromised patients, especially after steroid medication [3, 8–9] and very rarely in other diseases such as systemic lupus erythematosus, chronic hepaticrenal and lung disease and after toxin ingestion [8–9]. It is probably the most common myelopathy associated with HIV infection [3]. The pathogenesis of VM still remains controversial [3, 6] but three different pathogenetical mechanisms have been suggested.

First, histopathologically, VM closely resembles subacute combined degeneration in patients with B 12 de-

ficiency [5, 7, 10]. However, vitamin B 12 deficiency [7, 11] and normal serum vitamin B 12 levels [12] have been reported in patients infected by HIV and administration of vitamin B 12 does not usually improve the clinical condition. An abnormality in methyl group metabolism without evidence of B 12 deficiency results in similar histological appearances, due to a common pathway in the pathogenesis of the disease [12]. Second, the disease is related to direct HIV infection which can be isolated from the vacuoles and the multinucleate macrophages (characteristic of a productive HIV infection) in up to 6 % of patients [3, 6–7, 13]. Third, other opportunistic infections are suggested as responsible for the development of VM, especially in other immunocompromised patients [7, 14]. Other retroviruses can cause myelin vacuolation in brain or spinal cord in experimental animals [7].

Clinically, the disease is manifest as subacute spastic paraparesis of the legs, ataxia (due to loss of joint position sense), with or without sphincter incontinence and/or sensory changes [3, 14] developing over 3–16 weeks. Dementia is observed in 60 % of affected patients [3, 14] due to HIV encephalopathy.

To our knowledge, the MRI findings in patients with VM have not been reported. However, MRI findings possibly due to VM in post mortem spinal cord specimens have been described [15]: continuous, bilaterally symmetrical increased signal intensity, often diffusely affecting several white matter tracts (primarily the gracile tract, followed by the corticospinal and cuneate tracts) on proton density- and T2-weighted SE images [15]. The site of the high signal correlates with the above-mentioned histopathological description of spinal cord involvement in VM. In our patient, the sym-

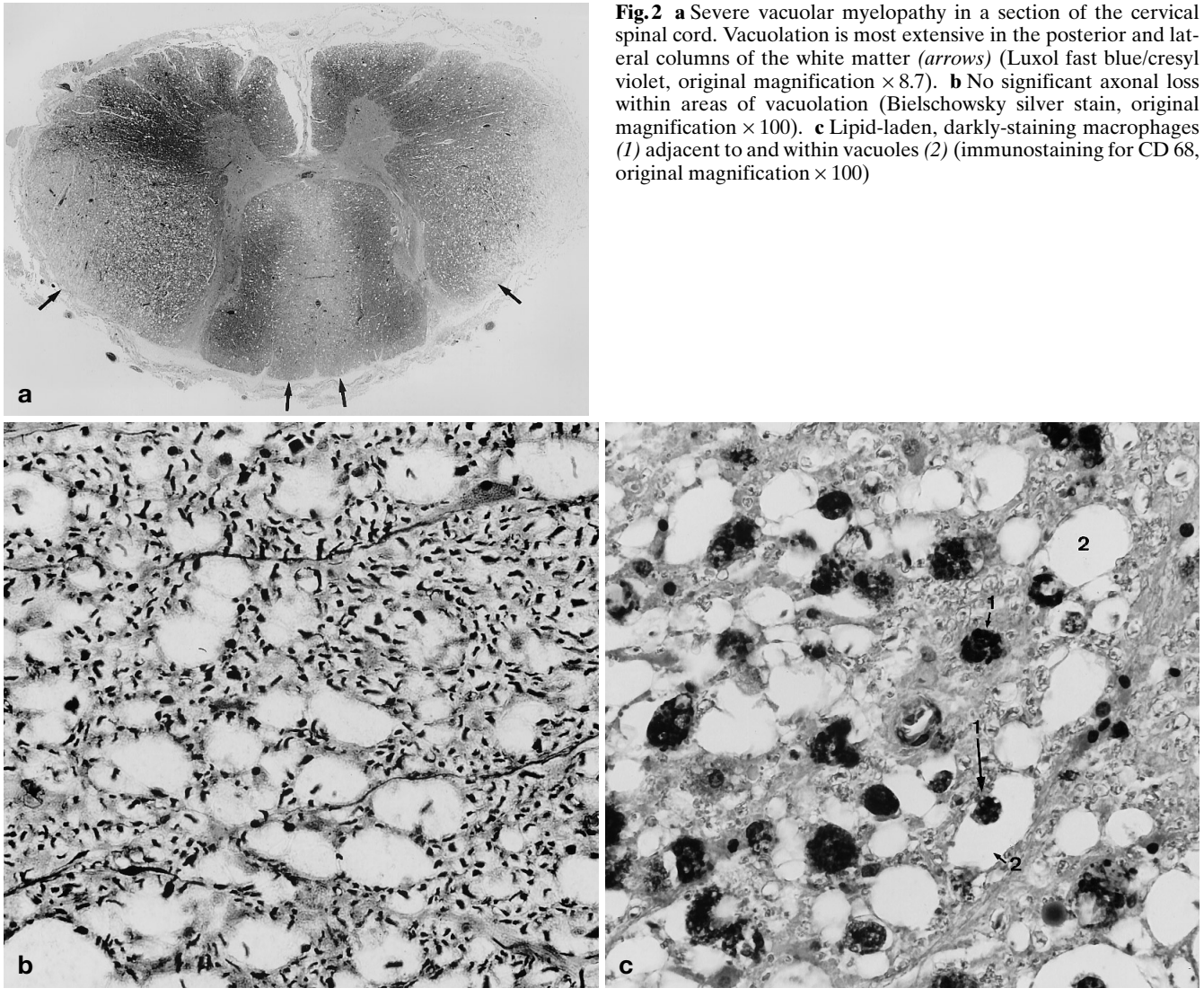

Fig. 2 **a** Severe vacuolar myelopathy in a section of the cervical spinal cord. Vacuolation is most extensive in the posterior and lateral columns of the white matter *(arrows)* (Luxol fast blue/cresyl violet, original magnification × 8.7). **b** No significant axonal loss within areas of vacuolation (Bielschowsky silver stain, original magnification × 100). **c** Lipid-laden, darkly-staining macrophages *(1)* adjacent to and within vacuoles *(2)* (immunostaining for CD 68, original magnification × 100)

metrical, triangular high-signal lesions, especially within the gracile tract over several spinal segments, correlate well with histopathological findings. The histopathologically verified involvement of the corticospinal and cuneate tracts in our patient, however, was not reliably demonstrated on MRI, probably due to less severe involvement of these tracts early in the disease, with secondary progression to these tracts after the MRI examination (corresponding to the secondary deterioration of the patient's condition).

No pathological contrast enhancement was observed. Breakdown of the blood-brain barrier (BBB) can be expected in inflammatory disease (due to chemical mediators released by inflammatory cells) or in diseases with degeneration and/or regeneration of nervous tissue [16–17]. In VM, histopathologically severe inflammatory reactive changes and axonal destruction [16–17] are absent, and there exists no obvious reason for a breakdown of the BBB.

The MRI characteristics of VM, namely the symmetrical high signal along the posterior columns, can be imitated by other conditions. Two histopathologically distinct entities commonly seen in HIV-infected patients, namely "tract pallor" (involving the gracile and corticospinal tracts) and "selective gracile tract necrosis", show similar symmetrical high signal on post mortem MRI [15] but these findings have not been demonstrated in vivo [7]. Vitamin E deficiency (in non-HIV positive patients) involves especially the gracile tract, resulting in symmetrical high signal on T2-weighted images of the posterior columns [18]. Ischemic lesions, related to vasculitis or disseminated intravascular coagulation in HIV-positive patients may also cause high-signal in the posterior columns, but often affect the anterior and lateral columns as well, and the grey matter, and do not extend over multiple segments [19, 20].

On MRI viral myelitis associated with HIV infection, caused by varicella-zoster virus and Herpes simplex virus or viral radiculomyelitis due to cytomegalovirus infection are usually easily distinguished from VM. In viral myelitis, most commonly diffuse multisegmental high signal in both grey and white matter, often in a slightly expanded spinal cord with or without diffuse or patchy contrast-enhancing areas, is observed [19, 21–23]. In viral radiculomyelitis, thickened, enhancing nerve roots, together with leptomeningeal enhancement due to spinal meningitis are seen [19, 21–22]. Parasitic infection due to toxoplasmosis or bacterial infection due to tuberculosis are rare in HIV-positive patients [20, 23] and must be differentiated from other intramedullary lesions, especially tumours or, occasionally, multiple sclerosis [20]. These lesions present as focal strongly-enhancing lesions in both grey and white matter [19–20].

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ANNOUNCEMENTS

Neuro Imaging 1998 – Head and Spine: Anatomy, Function and Pathology
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