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Pathological findings correlated with MRI in HIV infection

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Abstract. MRI forms an important part of the assessment of patients with HIV-related disease presenting with cerebral smyptoms. Eleven formalin-fixed brains were studied at 0.5 T using T2- and T1-weighted sequences. In two cases of progressive multifocal leucoencephalopathy and one case each of toxoplasmosis and lymphoma, the extent of white matter abnormality seen on MRI corresponded broadly with that on pathological examination. In general, however, histological changes were more frequent than lesions on MRI. Cases in which abnormalities were not seen with standard MRI included those with multiple tuberculous granulomata, multinucleate giant cells, microglial nodules, perivascular cuffing and cytomegalovirus inclusions. A common finding on MRI was punctate or patchy high signal in the basal ganglia on T2-weighted scans, seen in six cases. Corresponding histological changes included calcification of vessels with widened perivascular spaces, and mineralised neurones.

Key words: HIV – MRI – Basal ganglia – postmortem examinations

HIV-related disease has now to be considered in the differential diagnosis of patients presenting with a wide range of neurological complaints. MRI forms an important part of the assessment when patients present with cerebral symptoms [1–4], but in theory the subdued inflammatory response in these immunosuppressed patients may make MRI relatively insensitive to pathological changes. Several studies have demonstrated that the extent of pathological change found post mortem has exceeded that of abnormality shown by MRI performed close to the time of death [5–7]. However, a more exact comparison of MRI with macroscopic appearances and histological changes can be made only in a post-mortem study [8]. We have compared post-mortem MRI findings with detailed pathological examination.

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Materials and Methods

Eleven formalin-fixed brains of individuals known to have HIV infection, dying at 31–59 years of age, were obtained. Seven had been homosexuals and four haemophiliacs. The interval between known HIV positivity and time of death varied from less than 1 week, in cases first investigated during the terminal illness, to 7 years. MRI was performed at 0.5 T: using a T2-weighted sequence (SE 4000/80) contiguous slices, 5 mm thick, were obtained in the coronal plane, and T2-weighted (SE 2600/80) and T1-weighted (IR4000/150/40, STIR) images in the transverse plane. The coronal plane chosen for MRI was perpendicular to the body of the corpus callosum and the brains were subsequently sliced in the same plane. Slices of particular interest were studied further by MRI prior to photography and histological examination. In all cases a standard set of 5-mm-thick blocks, selected to include representative samples of the cortex, basal ganglia, brain stem and cerebellum, together with blocks taken from identified abnormalities, was examined histologically. The blocks were processed through paraffin wax using standard histological techniques.

Results

In two cases progressive multifocal leucoencephalopathy was seen on MRI and pathologically (Fig. 1). High signal was observed on both T2- and T1-weighted images and the extent of white matter abnormality at MRI corresponded broadly with that at pathological examination. In both cases there was extensive demyelination with phagocytosis of the products of myelin breakdown by macrophages, and local oedema. Characteristic bizarre astrocytosis was present and inclusion bodies were seen in the nuclei of oligodendrocytes. In two further cases the MRI showed focal high signal on T2-weighted sequences (Fig. 2). Histological sections in one case showed toxoplasmosis with confluent necrosis of the central white matter and adjacent cortical grey matter, and a prominent acute inflammatory reaction; many toxoplasma bradyzoites and some cysts were seen.

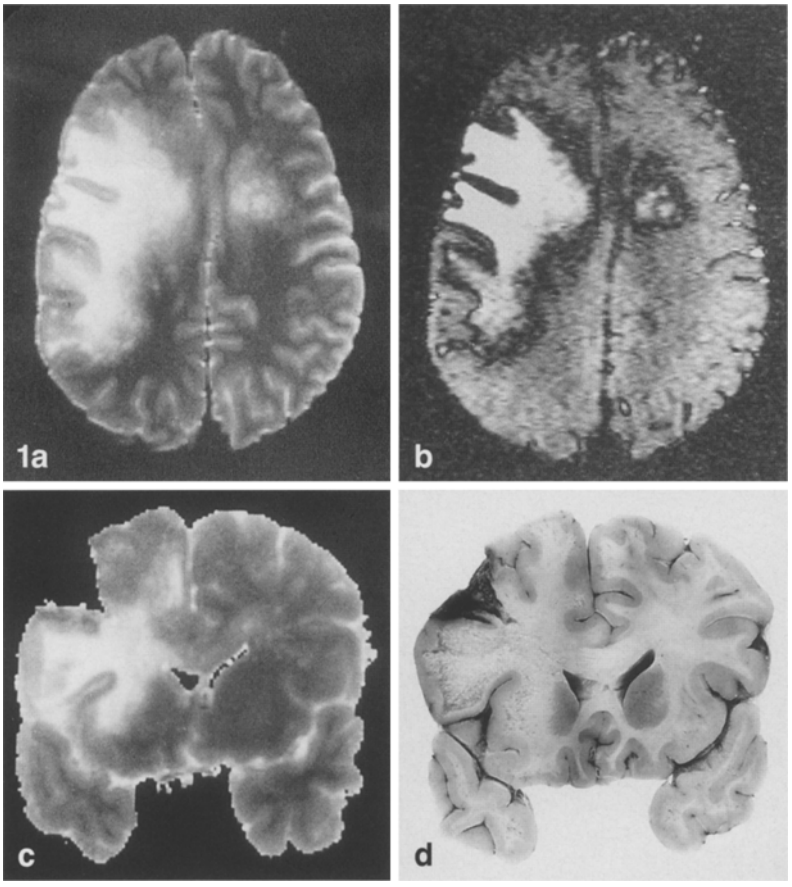


Fig. 1. **a** Axial T2-weighted and
b STIR images of a case of progressive multifocal leucoencephalopathy. The T1-weighted sequence (**b**) shows striking low signal at the periphery of the lesion, probably indicating the presence of free lipid from myelin breakdown.
c T2-weighted coronal image showing a large region of abnormal signal in the right hemisphere.
d Corresponding pathological slice demonstrating the extent of white matter abnormality

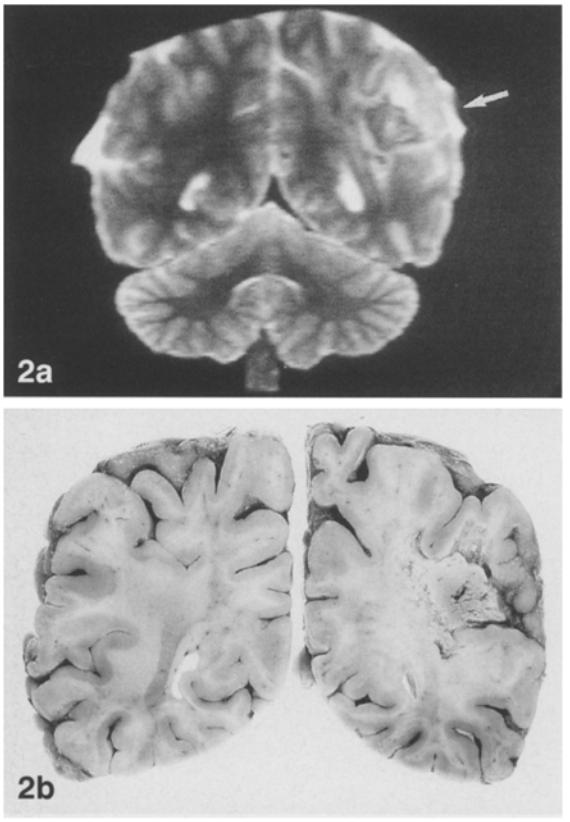


Fig. 2. **a** T2-weighted coronal image of a case of toxoplasmosis showing abnormal signal in the left hemisphere *(arrow)*.
b Corresponding pathological slice with necrotic tissue clearly visible

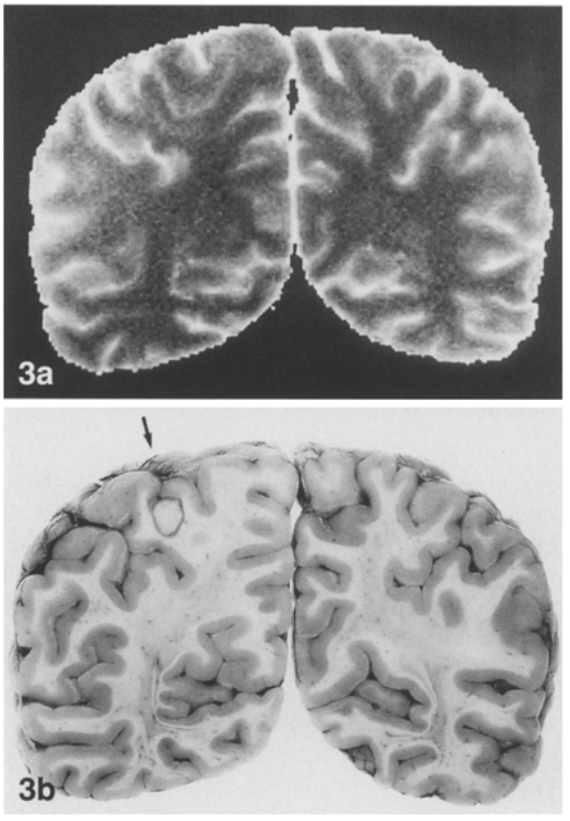
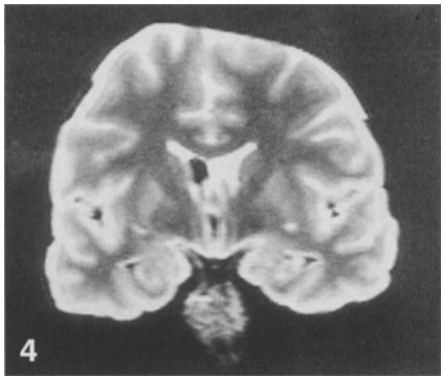


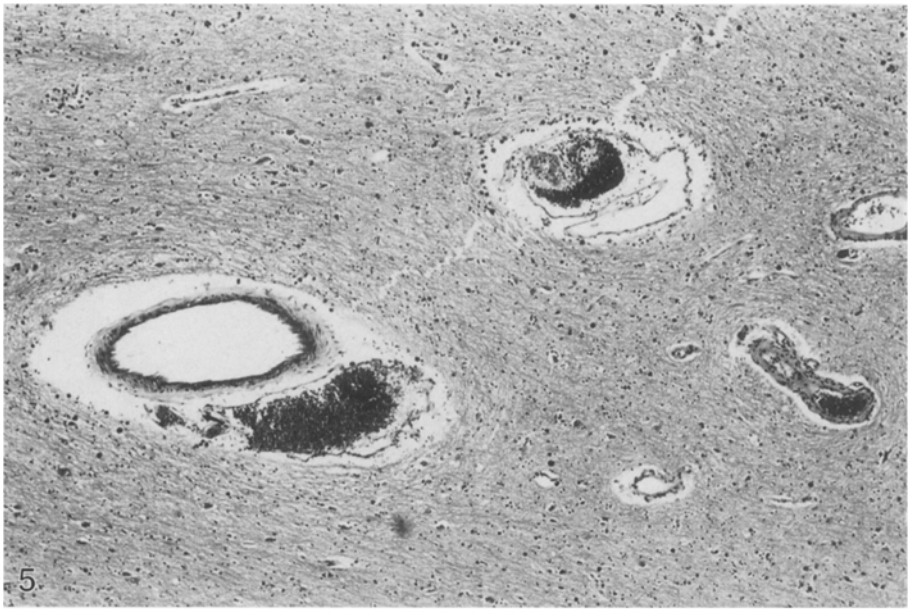
Fig. 3. **a** Normal T2-weighted coronal image.
b Corresponding pathological slice showing tuberculous granuloma *(arrow)*

The other case proved to be a high-grade B-cell malignant lymphoma with much tumour necrosis. In both cases the extent of MRI abnormality broadly corresponded with that seen pathologically.

In general, however, histological changes were seen more frequently than lesions detected by MRI. Multiple tuberculous granulomata up to 1 cm in diameter were found in one patient when standard T2- and T1-weighted MRI of the uncut brain and individual slices was normal (Fig. 3). The granulomata were atypical: many mycobacteria were present within macrophages, but Langhans giant cells were absent, and while there was extensive individual cell necrosis, caseation was not seen. A case of cryptococcal meningitis was also found to have normal MRI.

A common MRI finding, present in six cases, was punctate or patchy high signal in the basal ganglia, particularly the lentiform nuclei on T2-weighted images (Fig. 4). Corresponding histological changes were variable, and included calcification of vessels with widened perivascular spaces in two cases (Fig. 5), mineralised neurones (two





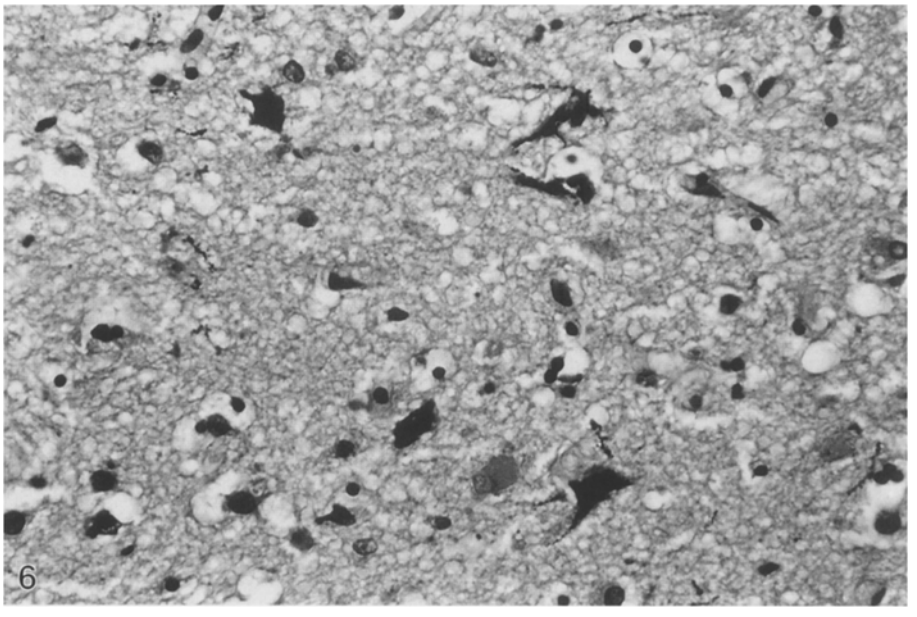


Fig. 4. T2-weighted coronal image demonstrating high signal in the basal ganglia, particularly the lentiform nuclei

Fig. 5. Histological section from the basal ganglia showing widened perivascular spaces. Haematoxylin and eosin, ×12

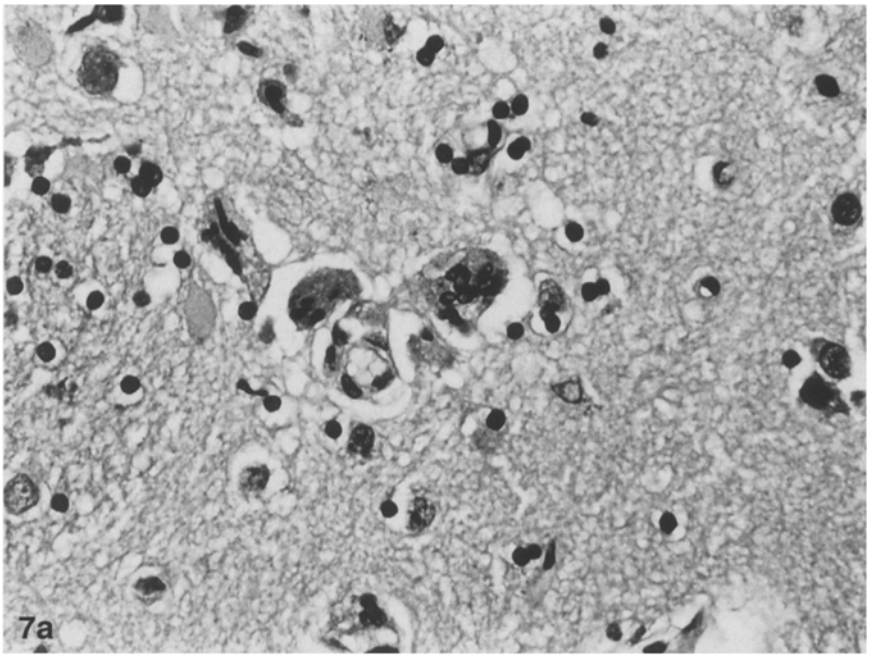
Fig. 6. Histological section from the basal ganglia showing mineralised neurones. Haematoxylin and eosin, ×75

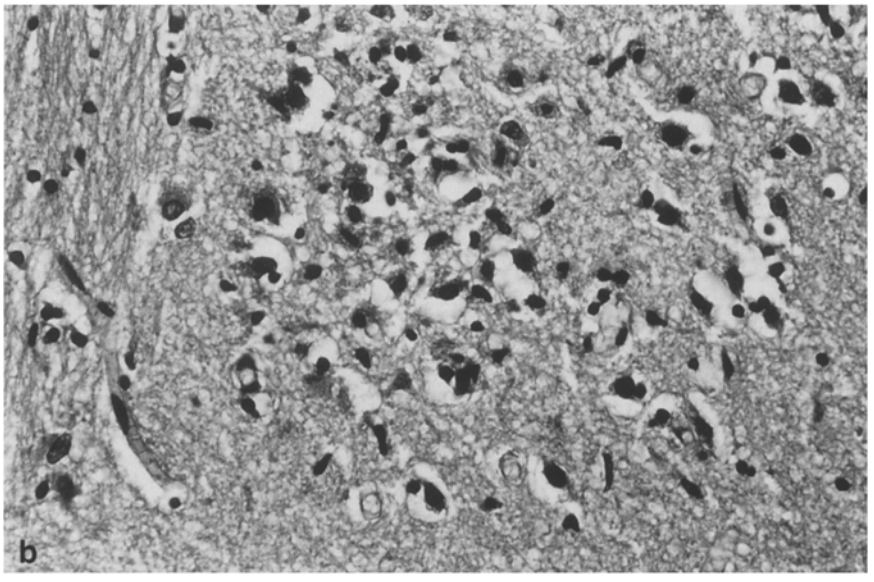
cases) (Fig. 6) and multinucleate giant cells (MNGC) and microglial nodules (MGN) (two cases). MNGC and MGN extended throughout the cerebrum and brain stem in one case without MRI abnormality (Fig. 7), and MGN were seen in the brain stem and cerebellum in three cases with no accompanying MRI changes. Perivascular mononuclear cell cuffing in one case (Fig. 8) and cytomegalovirus (CMV) inclusions in the cerebellum and subependymal region in two cases were not detected by MRI.

Discussion

We found that major abnormalities seen with MRI in HIV-related disease correlated broadly with pathological changes. However MRI was insensitive to a number of histological changes including MNGC, MGN, perivascular cuffing and CMV inclusions. Grafe et al. [8] similarly found no MRI abnormalitiy in regions where MGN were seen histologically. All these changes are probably associated with an increase in cellularity and would be expected to lead to a minor increase in the T1 or T2 relaxation times [9], although of course, the area of histological abnormality is generally smaller than the standard MRI pixel and much smaller in relation to slice thickness, here 5 mm, and the average signal change may therefore not be great enough to be visible even when the changes are diffuse. It is likely that similar findings would be obtained in vivo, although were perivascular cuffing to be associated with increased permeability of the blood-brain barrier, it might be detectable by gadolinium-DTPA enhancement [10], a possibility which could not be tested in fixed post-mortem brains. It has recently been shown that proton MR spectroscopy can detect abnormalities in the white matter when imaging is normal [11].

A striking finding was the frequent occurrence of MRI abnormalities in the basal ganglia. Histological findings





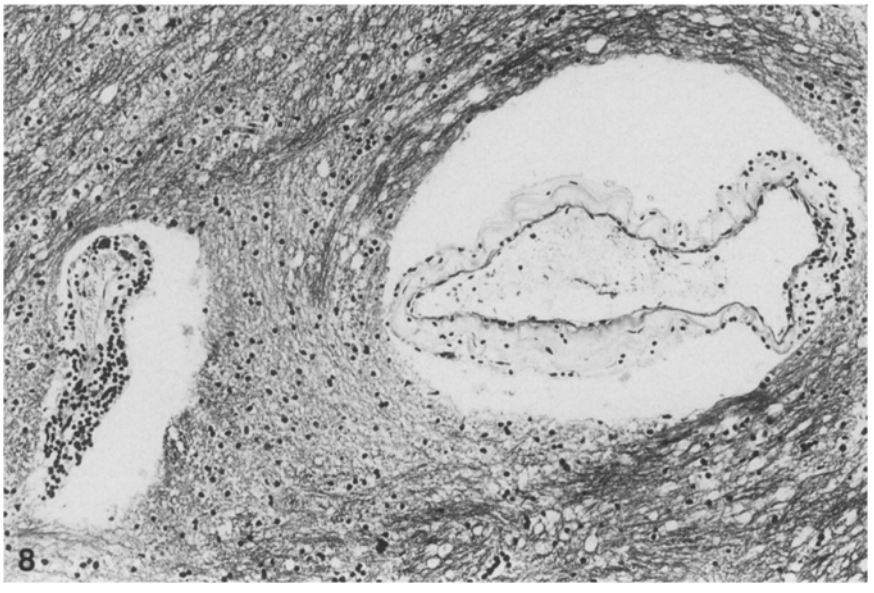


Fig. 7. Haematoxylin and eosin-stained histological sections from the cerebrum showing
a A multinucleate giant cells (× 100)
b microglial nodules (× 75)

Fig. 8. Histological section from the cerebrum showing perivascular mononuclear cells. Haematoxylin and eosin, × 30

corresponding to the abnormal signal included calcification of vessels, with dilated perivascular spaces, and mineralised neurones. The origin of the abnormal MRI signal is probably an increase in the extracellular water content as a result of enlargement of the perivascular spaces. Basal ganglia abnormalities were observed on in vivo MRI, although usually in the later stages of the disease, by Arendt et al. [12], who stressed the frequent occurrence of minor extrapyramidal motor abnormalities in patients with early HIV infection, suggesting that basal ganglia abnormalities, both clinically and on MRI, may be more common than previously recognised. It has been suggested that high signal in the basal ganglia on T2-weighted sequences may represent dilated perivascular spaces in the early stages of cryptococcal meningitis [13]; in our study only one case had this infection and no abnormality was seen on MRI, although a post-mortem study may be less sensitive than an in vivo one in detecting extracerebral disease. Whether the basal ganglia are a common site of initial brain infection by HIV is unclear and deserves further study.

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