^{18}fluorodeoxyglucose PET/CT as possible early diagnostic tool preceding MRI changes in Borna disease virus 1 encephalitis

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A 71-year-old woman attended our hospital with a 2-week history of fluctuating confusion.

The patient, who lived in the German state of Bavaria, close to agricultural areas, had no medical history; she was prescribed no regular medications.

On examination at admission, the patient was well and orientated; her vital signs were within typical range. Neurology examination was within normal limits.

Laboratory investigations on admission for systemic infection, liver function, and kidney function were within typical range.

A chest x-ray showed no abnormalities; an electrocardiogram showed a right bundle branch block and electroencephalography showed no epileptiform discharges.

2 days after admission, the patient rapidly became increasingly encephalopathic; she developed aphasia, atactic movements, and fluctuating vigilance resulting in a state of unresponsive wakefulness syndrome on day 16 after admission.

Brain MRIs on days 2, 5, and 14 after admission showed no abnormalities (figure 1).

Analysis of cerebrospinal fluid (CSF) on days 2, 5, and 20 after admission showed repeatedly raised total protein concentration ranging from 0·41 to 0·57 g/L (typical range 0·15–0·45); all other measurements were within normal range or unclear with regard to diagnosis (appendix; table 1).

Since MRIs and further tests were not conclusive, ^{18}fluorodeoxyglucose (^{18}F-FDG) PET/CT of the brain was done on day 8 which showed marked hypermetabolism in the basal ganglia, the temporomesial lobes, and the cerebellum; frontal and parietal lateral cortex showed distinct hypometabolism (figure 2).

On day 19 after admission, a whole-body ^{18}F-FDG PET/CT showed progression of the abnormalities found in the initial scan (figure 2).

Considering a probable autoimmune pathology, the patient was treated with high-dose glucocorticoids—increasing to a maximum of 4 g methylprednisolone after 5 days and then tapering down—and intravenous immunoglobulins (2 g/kg of bodyweight) without any clinical response.

On day 34 after admission, T2 FLAIR and diffusion-weighted MRIs showed hyperintensities in the basal ganglia and head of the caudate nucleus (figure 1) indicating possible Borna disease virus 1 (BoDV-1) encephalitis.

Retrospective analysis, done on day 37 after admission, of CSF taken on days 5 and 20 after admission using reverse-transcription quantitative polymerase-chain-reaction (RT-qPCR) was positive for BoDV-1 RNA with quantification cycle values of 34·3 and 32·5, respectively.

Testing for BoDV-1-antibodies was negative until day 35 after admission; seroconversion occurred on day 42 (indirect immunofluorescence antibody test 1:1280, line blot BoDV-1-phosphoprotein 14 arbitrary units [AU], BoDV-1-nucleoprotein 22 AU; appendix, table 2).

On day 49 after admission, the patient died. Post-mortem histology, BoDV-1-specific immuno-histochemistry (appendix, figure 2), and RT-qPCR on formalin-fixed paraffin-embedded tissue confirmed BoDV-1 encephalitis. A timeline was constructed of the patient's case (appendix, figure 1).

^{18}F-FDG PET/CT findings may aid the diagnosis of patients with unexplained encephalitis and may—as in our patient—precede MRI changes. In Rasmussen encephalitis and anti-leucine glioma-inactivated protein 1 autoimmune encephalitis, for example, brain MRI has been reported as being less sensitive when compared to ^{18}F-FDG PET/CT. In herpes simplex virus encephalitis, temporal lobe, ventral striatal, and septal abnormalities have been described on ^{18}F-FDG PET/CT. And in Creutzfeldt-Jakob disease, ^{18}F-FDG PET/CT may show hypometabolism in the basal ganglia, the occipital, frontal and parietal lobes, and in regions of the brain specifically related to clinical signs.

BoDV-1 infection is a potentially lethal zoonosis in endemic regions with reported spillover infections in

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See **Online** for appendix

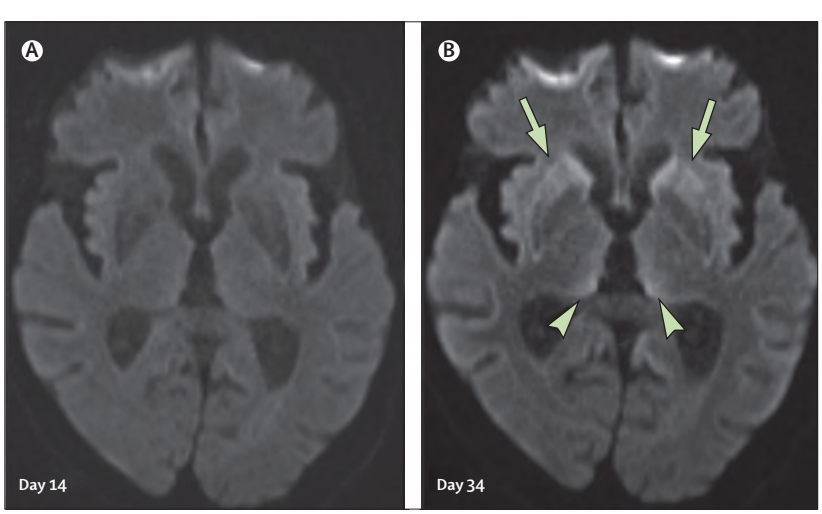

Figure 1: **MRI changes in Borna disease virus 1 encephalitis**
Diffusion-weighted MRI (A) on day 14 shows no abnormalities, but on day 34 (B) scan shows diffusion restriction in the basal ganglia (arrows) and the pulvinar (arrowheads).

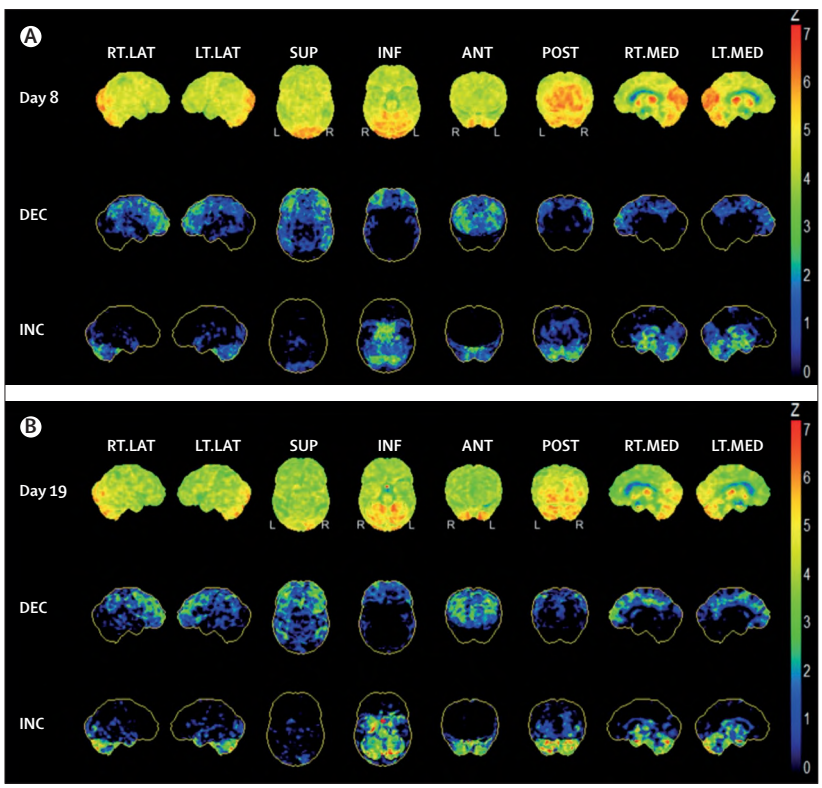

Figure 2: **^{18}fluorodeoxyglucose PET/CT changes in Borna disease virus 1 encephalitis**
^{18}fluorodeoxyglucose PET/CT scans on day 8 (A) and day 19 (B) show hypometabolism and hypermetabolism patterns; on day 8, marked hypometabolism was observed in the frontal and parietal cortices, and hypermetabolism in the basal ganglia, the temporomesial lobes, and the cerebellum. Notably, the changes progressed on day 19. RT.LAT=right lateral. LT.LAT=left lateral. SUP=superior. INF=inferior. ANT=anterior. POST=posterior. RT.MED=right medial. LT.MED=left medial. DEC=decrease. INC=increase.

horses and sheep. BoDV-1 infection can result in fatal encephalitis; all severe encephalitis cases of unknown cause should be tested for bornaviruses—especially in endemic regions.

Contributors
We were all involved in caring for the patient, acquiring data, and revising the manuscript. Written consent for publication was provided by the patient's authorised relatives.

Declaration of interests
We declare no competing interests.