Abnormal cortical amyloid deposition in ^{18}F-Florbetapir PET/CT: General paresis of the insane mimicking early-onset Alzheimer's disease

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Abstract

General paresis (GP) is a type of neurosyphilis characterized by progressive memory impairment and mental disorders. It exhibits clinical, neuroimaging, and pathological similarities to Alzheimer's disease (AD). Here, we report a 37-year-old male with memory impairment and emotional disorders, who was clinically diagnosed with neurosyphilis, specifically GP. The fluorine-18 (18F)-Florbetapir positron emission tomography/computed tomography (PET/CT) of the patient showed mild diffuse amyloid deposition in both the cerebral and cerebellar cortex. Moreover, hypermetabolism in the left hippocampal region was revealed on 18F-fluorodeoxyglucose (^{18}F-FDG) PET/CT. The patient's cerebrospinal fluid (CSF) test and genotyping results further excluded coexistent genetic AD. This case highlights the significance of considering neurosyphilis as a possible differential diagnosis in dementia patients with atypical positive amyloid PET findings. The mechanisms underlying aberrant amyloid deposition in neurosyphilis require further investigation.

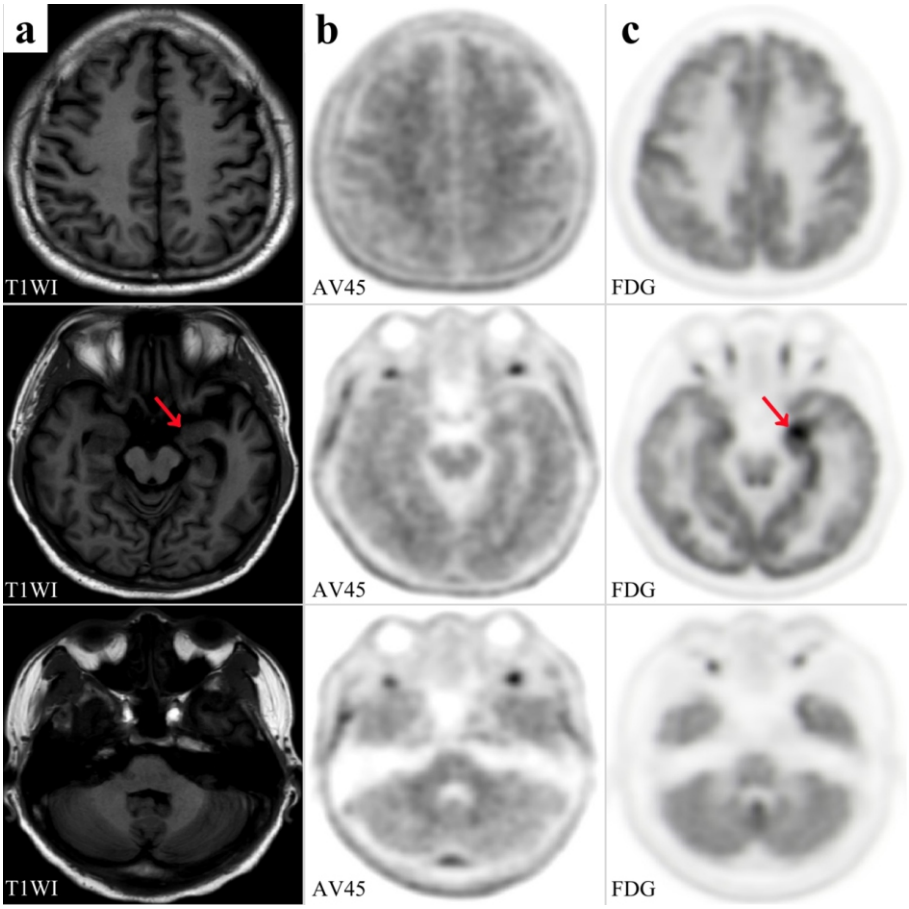

Figure 1. A 37-year-old male with memory loss for 3 years, aggravated for 1 month accompanied by mood and mental behavioral abnormalities, had scores of 21/30 on the Montreal Cognitive Assessment (MoCA). On admission, the patient's serological tests were positive for *Treponema pallidum* particle agglutination test (TPPA) and toluidine red unheated serum test (TRUST); cerebrospinal fluid (CSF) showed elevated white blood cells and protein, and positive venereal disease research laboratory (VDRL) and TPPA tests. Brain magnetic resonance imaging (MRI) showed diffuse white matter hypointensity, mild cerebral atrophy, with more pronounced atrophy of the left hippocampus (a, arrow). Furthermore, the patient's CSF Aβ1-42 decreased and T-Tau increased, while Aβ1-42/Aβ1-40 and P-Tau were in the normal range. Subsequently, brain fluorine-18 (^{18}F)-Florbetapir positron emission tomography/computed tomography (PET/CT) scan was performed, which showed reduced contrast and blurred borders in the grey and white matter of the cerebrum and cerebellum, i.e. weakly positive for amyloid deposits in the cerebral and cerebellar cortex (b). And brain ^{18}F-fluorodeoxyglucose (FDG) PET/CT showed hypermetabolism in the left hippocampal region (c, arrow). Besides, apolipoprotein E (APOE) genotyping revealed the ε2/ε3 genotype, and whole-exome sequencing excluded mutations in APP, PS1 and PS2, arguing against coexistent genetic Alzheimer's disease (AD). Finally, the patient was diagnosed with neurosyphilis related dementia i.e. general paresis of the insane (GPI). After 4 weeks of penicillin treatment and follow-up, the patient complained of improved memory and mood, with MoCA scored 23/30.

General paresis (GP) is a type of neurosyphilis that manifests progressive dementia, psychiatric symptoms, and executive dysfunction, which resemble the clinical features of AD [1]. The neuroimaging characteristics of GP can also simulate those observed in AD, including cortical atrophy, hippocampus atrophy, and hippocampus metabolism abnormality [2]. In addition, it has been reported that GP shares pathological similarities with AD, such as neuronal loss, fibrillary alterations, and local amyloid-β (Aβ) deposition [3]. Compared to the typical amyloid deposition pattern of AD, which showed moderate to high levels of cerebral amyloid deposition in two or more brain areas but no cerebellar amyloid deposition [4, 5], in this case of GP, we observed mild diffuse amyloid deposits in both cerebral and cerebellar cortex on ^{18}F-Florbetapir PET/CT. The mechanism of cortical amyloid deposition in neurosyphilis remains unclear. One potential explanation is that the production and deposition of amyloid precursor protein are triggered by the chronic inflammatory response induced by the Treponema pallidum infection. An alternative hypothesis is that Treponema pallidum directly affects amyloid metabolism, resulting in amyloid deposition [6-9]. Moreover, the hypermetabolism in the left hippocampus of the patient seen on ^{18}F-FDG PET may indicate local inflammation induced by the infection. This case highlights the significance of considering neurosyphilis as a possible differential diagnosis in cognitive impairment patients with an atypical weak positive finding on amyloid PET imaging. Further research is required to determine the mechanism underlying aberrant amyloid deposition in neurosyphilis and the potential clinical applicability of amyloid PET imaging in this condition.

The authors declare that they have no conflicts of interest.

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