FDG-PET findings in three cases of Mills’ syndrome

Primary lateral sclerosis (PLS) is a rare subtype of motor neuron disease that exclusively affects upper motor neurons, usually beginning in the lower limbs and, less frequently in the bulbar region or the upper limbs. In contrast to amyotrophic lateral sclerosis (ALS), PLS typically has a symmetrical presentation and this characteristic was part of the initially proposed PLS criteria. We report 18-fluorodeoxyglucose-positron-emission tomography (FDG-PET) findings in three cases with an asymmetrical subtype of PLS, more commonly known as Mills’ syndrome. There is no universally accepted definition of Mills’ syndrome, but it is mostly referred to as a slowly progressive motor syndrome with unilateral or asymmetrical pyramidal signs. In this syndrome, the disease process remains more or less restricted to the motor areas contralateral to the affected side, as suggested by a study visualising microglial activation using 11C-(R)-PK11195 PET.

Three female patients presented with an asymmetrical form of pure upper motor neuron dysfunction, starting in the right arm (patient 1 and 2) and the right leg (patient 3). The asymmetrical presentation correlated with clear regions of hypometabolism on FDG-PET in the contralateral Rolandic and peri-Rolandic areas, as can be seen in ALS or PLS (figure 1). MRI of the brain was unrevealing in all three patients. Extensive investigations did not reveal other underlying pathologies. Mutations in C9orf72, SOD1, FUS and TARDBP were excluded in all three patients. There was a concordance in limb dominance and site of onset, as all three patients were right handed.

No clinical or electrodiagnostic signs of lower motor neuron involvement were noted up to 8 (patient 1), 4 (patient 2) and 2 years (patient 3) after disease onset. Over this period of time, the disease spread from the right arm to the right leg and, to a lesser degree, to the contralateral side (patient 1), remained restricted to the right arm (patient 2) and spread from the right leg to the right arm (patient 3). This suggests a disease propagation by contiguous spread, as opposed to a network-spreading pattern through the corpus callosum in typical PLS.

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Figure 1  T2-weighted MRI (upper row) and stereotactic surface projections of the brain 18-fluorodeoxyglucose-positron-emission tomography (FDG-PET; middle row, cranial view) with corresponding Z-score images (comparing patient to healthy volunteers; lower row). No lesions on MRI that could explain the hypometabolism on FDG-PET were noted.
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