^{18}F-FDG PET/CT findings in a case of a semantic variant of primary progressive aphasia

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Abstract
Progressive speech and language disorders are commonly referred to as primary progressive aphasia (PPA), which is a clinical syndrome eroding both speech and language. Functional imaging may reveal the cause of this disorder even if structural imaging is absent. Fluorine-18- fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) allows the assessment of neuronal activity by semi-quantitatively measuring glucose metabolism in the brain. In medical literature, ^{18}F-FDG PET/CT studies show hypometabolic areas in different regions of the brain which are special clues for differentiating the subgroups of PPA. **Conclusion**: This case was reported to demonstrate the characteristic ^{18}F-FDG PET CT findings for a semantic variant of PPA.

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Introduction

Aphasia, which is most commonly caused by stroke, is an acquired language disorder ranging from having difficulty in remembering words to losing the ability to speak, read, or write, but does not affect cognitive functions. On the other hand, the term primary progressive aphasia (PPA) describes the clinical findings of a group of frontotemporal lobar degeneration spectrum disorders in which major cognitive disorder is a progressive language impairment that remains relatively isolated at the initial stages while other cognitive domains are preserved [1-3]. Although, neurodegenerative aphasias share the same language impairment features such as impaired naming, word choice, repetition, word comprehension, spelling, and syntax with classic stroke-related aphasias, PPA usually causes different patterns of aphasia. Although, there are no community-based surveys documenting the frequency of PPA in the population, autopsy-based studies suggest prevalence for PPA of 1.1-6 per 100,000 and an incidence of about 0.88-1.4 per 100,000 patients with fronto-temporal lobar degeneration and additional cases with Alzheimer's dementia [4].

Primary progressive aphasia can be classified into 3 well-defined clinical syndromes: progressive non-fluent aphasia (PNFA), semantic dementia (SD), and logopenic aphasia (LPA), but the exact number and types of syndromes within the PPA spectrum are still debated [5-8] since, a consensus on PPA classification has not yet been established [8]. The first two variants of PPA are closely related to frontotemporal dementia, affecting similar regions of the brain, while the LPA variant is closely related to Alzheimer's disease [3]. All PPA variants show dysfunction of the language network, which is usually located in the left hemisphere but there are case reports available describing right hemisphere involvements in left-handed patients with PPA [9, 10]. Patients with PPA and their families have higher incidence of language disabilities, suggesting a familial tendency to developmental and degenerative language disorders [11]. Age of onset ranges from 40 to 80 years and is characteristically much earlier than the age of typical Alzheimer's type dementia [3].

This case reports the fluorine-18-fluoro-2-deoxyglucose ^{18}F-FDG positron emission tomography and computed tomography (PET/CT) findings of a patient with semantic variant of PPA.

Case report

A 62 years old male patient with progressive worsening of his language functions over

the last 3 years was examined by his neurologist for the first time and he was referred to our department with the diagnosis of primary progressive aphasia for a ^{18}F-FDG PET/CT study. He had no prior medical history related to his complaints or prior cognitive impairment. He didn't have hypertension. Neurological and neuropsychological examination revealed mild memory loss and speech difficulties. He had word-finding problems, naming difficulties and deficits during repetition of long words. His long-term attention was minimally reduced. His motor and sensory examination was normal. At the time his non-fluent dysphasia had begun, 3 years ago, he also stated having difficulties in understanding the meaning of words which is the principal symptom in semantic subtype of PPA. His Mini-Mental Status Examination score was 27 out of 30. He had optical stimuli evoked potentials in his electroencephalogram. Cerebrospinal fluid analysis was normal. Besides, other biochemical, hematologic parameters and systemic examination of the patient were also reported to be normal.

Imaging of brain glucose metabolism by brain ^{18}F-FDG PET/CT scan (Discovery 690, GE, Milwaukee, WI, USA) revealed asymmetrically decreased ^{18}F-FDG uptake predominantly in the anterior part of the left temporal lobe, while CT images showed left temporal lobe atrophy (Figure 1). Additionally, an automated analysis programme of 3-dimensional stereotactic surface projections was used to interpret the ^{18}F-FDG-PET scan images, and a metabolic map of the brain was produced by this analysis programme. The software package (Cortex ID, GE Healthcare, USA) that we used to evaluate the PET/CT scan is commercially available. Stereotactic surface projection maps also demonstrated hypometabolism in left temporal lobe of the patient (Figure 2).

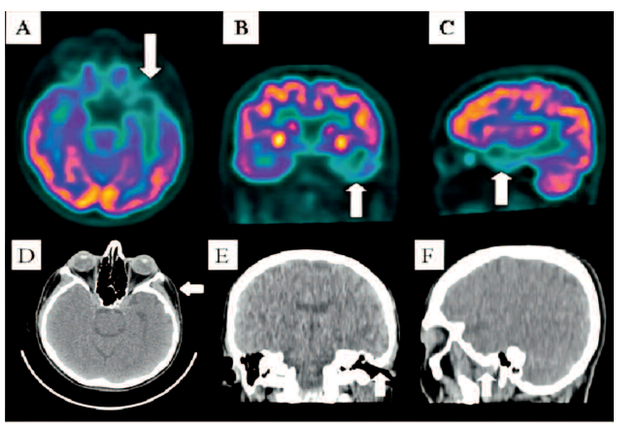

Figure 1. A. axial, B. coronal and C. sagittal images of ^{18}F-FDG PET/CT scan demonstrating the marked hypometabolism in the left temporal lobe and D. axial, E. coronal and F. sagittal images of CT scan demonstrating gyral atrophy in the left temporal lobe.

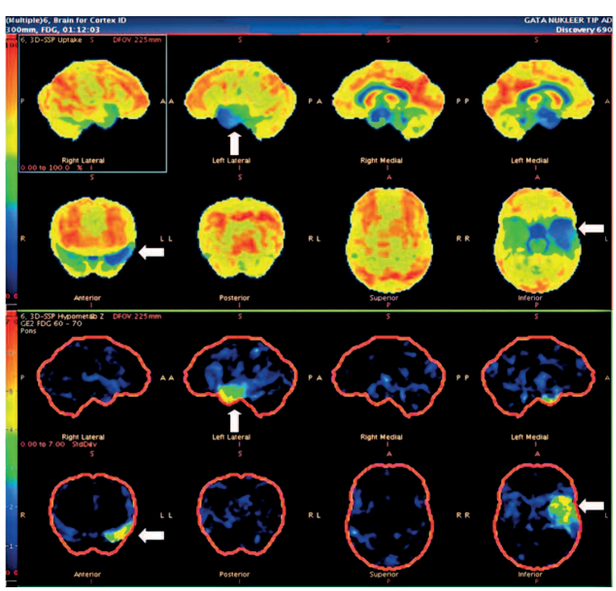

Figure 2. Statistical stereotactic surface projection maps showing hypometabolism in the left temporal lobe. Score values are color coded as indicated in the color scale (0=normal; 7=most abnormal). The score in the left temporal lobe of our patient was changing from 3 to 7 (up to 2 scale number is normal).

Discussion

There is no single type of language dysfunction that may be pathognomonic for PPA. As mentioned before, it's a clinical spectrum extending from the classical type of non-fluent aphasia to a fluent variant that is characterized by normal articulation, grammatically correct speech and pronounced verbal comprehension deficits [7, 12]. Besides, speech and language deficits differ between the subtypes of PPA. Since our patient in the last 3 years had progressive speech difficulties, articulation problems and anomia, his neurological findings were considered to be consistent with the clinical features of the semantic variant of PPA. Semantic aphasia is associated with left anterior temporal lobe disease. SD is a multimodal disorder of meaning and patients no longer understand the meaning of words, faces, objects and other sensory stimuli, which they perceive normally. Although, patients presenting with problems in the verbal domain, naming and word comprehension, typically show more marked left temporal atrophy, the patients with visual problems, in recognising familiar faces and objects, show more marked right-sided atrophy [13, 14].

The diagnosis of PPA is supported by magnetic resonance imaging (MRI) showing patterns of atrophy and by functional ^{18}F-FDG PET/CT studies demonstrating hypometabolism. In our patient, both structural and functional imaging studies showed similar findings of affecting mainly the temporal parts of the language network including Wernicke's area which is located in the posterior third of the upper temporal convolution of the left hemisphere of the brain [7, 15]. Although, anatomical imaging may be normal at early disease stages, specific atrophy patterns are detected in late stages. With disease progression, there is more posterior temporal involvement as well as left inferior frontal, orbitofrontal, cingulate, and right temporal lobe disease [3, 16]. In our case, the left temporal lobe hypometabolism affecting predominantly the anterior and inferior parts was detected.

Each of the subgroups of PPA has different neuroanatomical and neurometabolic patterns [12]. Logopenic aphasia is

associated with posterior-superior temporal and inferior-parietal involvement. On the other hand, PNFA is associated with other brain centers involvement. Fluorine-18-FDG PET/CT scan can reveal decreased metabolism in the affected areas prior to structurally noticeable atrophy. Therefore, left frontal lobe hypometabolism in the non-fluent subgroup, left anterior temporal lobe hypometabolism in the semantic subgroup and left temporoparietal hypometabolism in the logopenic subgroup are expected findings on ^{18}F-FDG PET/CT scans of patients with PPA [3].

Fluorine-18-FDG PET/CT is sensitive to show decreased metabolism in the affected areas prior to structurally noticeable atrophy [16, 17]. Besides, it can show subclinical metabolic deterioration in PPA cases [18].

Aphasic patients can also show considerable variability according to lesion localization and extent [19]. For example, aphasia secondary to cerebellar injuries has been known to be due to crossed cerebral-cerebellar diaschisis which is a metabolic depression of the cerebellum, contralateral to a cortical injury. The opposite phenomenon, i.e. left cortical dysfunction secondary to contralateral cerebellar injuries was also observed [20]. Since, the subcortical lesion can create diaschisis secondary to cortical dysfunction, language impairment can be linked to the hypoperfusion of these subcortical structures [21]. In our patient no hypometabolic region indicating diaschisis was detected. The left temporal hypometabolism, which is characteristic the semantic variant of PPA, accompanied by the left temporal cortical atrophy were only findings which helped us to differentiate from those reported in patients with PNFA affecting mainly the posterior part of the temporal and parietal lobes.

Diagnostic criteria and description of variants of PPA are mentioned by Galiano Blancart RF et al. (2011) [17] and recently by laccarino L. et al. (2015) [22].

Since the extent and severity of language im¬pairment is significantly correlated with brain glucose metabolism, the data provided by ^{18}F-FDG PET CT in patients with PPA can show: a) decreased metabolism in the affected areas prior to structurally noticeable atrophy and therefore, it can be helpful for anticipation of subclinical metabolic deterioration which occurs before the clinical diagnosis of PPA. b) Can demonstrate the metabolic activity in unexpected lesions of cerebellum and subcortical structures causing aphasia due to diaschisis and c) ^{18}F-FDG PET/CT can show decreased metabolism in the affected areas prior to structurally noticeable atrophy and therefore, to provide earlier diagnostic information than the anatomical imaging modalities.

In conclusion, prominent left temporal hypometabolism in our patient with progressive worsening of his language functions over the previous 3 years was detected by the ^{18}F-FDG PET/CT scan, consistent with findings seen in semantic dementia.

The authors declare that they have no conflicts of interest.

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