Case Report

FDG-PET findings in fronto-temporal dementia: A case report and review of literature

Chidambaram Natrajan Balasubramanian Harisankar, Bhagwant Rai Mittal, Kanhaiya Lal Agrawal, Mohammed Labeeb Abrar, Anish Bhattacharya, Baljinder Singh, Manish Modi[1]

Departments of Nuclear Medicine and PET and [1]Neurology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

ABSTRACT

Fronto-temporal lobar degeneration (FTLD) is a clinically and pathologically heterogeneous syndrome, characterized by progressive decline in behavior or language associated with degeneration of the frontal and anterior temporal lobes. Three distinct clinical variants of FTLD have been described. Despite the difficulties, accurate diagnosis is critical because the clinical management differs for Alzheimer's disease (AD) and FTLD. Positron emission tomography with fluro-deoxy-glucose (FDG-PET) typically shows sufficient abnormalities that can be used to improve the accuracy of distinguishing AD from FTLD in individual cases. Though temporo-parietal hypometabolism is sensitive in diagnosis of AD, it is less specific. The importance of evaluating the cingulate and anterior temporal cortices for arriving at a diagnosis of FTLD is stressed.

Keywords: Alzheimer's disease, F-18 FDG, fronto-temporal lobar degeneration, PET/CT

INTRODUCTION

Fronto-temporal lobar degeneration (FTLD) is the third most common degenerative dementia, behind Alzheimer's disease (AD) and dementia with Lewy bodies. It is a heterogeneous disorder[1] with at least three recognized clinical presentations. Despite the existence of consensus clinical diagnostic criteria, patients with FTLD are commonly misdiagnosed as having AD or a psychiatric illness. These mistakes are understandable, given the insidious, progressive nature of both FTLD and AD and their shared symptoms. Both discussed illnesses may have prominent behavioral changes, which can overlap symptoms typically seen in psychiatric disorders. Distinguishing FTLD from AD is important as the treatment is different. Anti-cholinesterases used in treatment for AD may worsen the symptoms of FTLD. We report the fluoro-deoxyglucose positron emission tomography (FDG-PET) findings in a case of progressive aphasia and dementia. The importance of identifying hypometabolism in the anterior cingulated and anterior temporal cortices, in spite of presence of temporo-pariteal hypometabolism, in arriving at a diagnosis of FTLD is stressed.

Access this article online

Quick Response Code:

Website: www.ijnm.in

DOI: 10.4103/0972-3919.90261

CASE REPORT

A 50-year-old female presented with history of behavioral disturbance, diminished spontaneity, and interaction. She also had decreased speech output for previous three years. She developed mutism and diminished self care since the last six months. Biochemical evaluation was unremarkable and thyroid functions were within normal limits. Magnetic resonance imaging (MRI) of the brain showed cerebral atrophy predominantly involving the frontal and temporal lobes. However, the perisylvian area was relatively preserved. Patient was subjected to F-18 FDG PET/CT which showed significantly reduced metabolism involving the bilateral frontal, posterior temporo-parietal, right anterior temporal, anterior cingulated and right perisylvian cortices [Figure 1]. There was preserved metabolism in the sensori-motor cortices, posterior cingulate, occipital cortices, basal ganglia and thalami. Considering the involvement of the anterior cingulate, anterior temporal cortices, diagnosis of FTLD was favored over AD. Understanding the moderate specificity of temporo-parietal hypometabolism for AD and the relatively high specificity and positive likelihood ratio of anterior cingulate and anterior temporal hypometabolism for FTLD may improve FDG-PET scan interpretation and therefore maximize the positive effect of these studies on diagnostic accuracy.

DISCUSSION

FTLD is a clinically and pathologically heterogeneous syndrome,

Address for correspondence:
Dr. Bhagwant Rai Mittal, Department of Nuclear Medicine, PGIMER, Chandigarh - 160 012, India. E-mail: brmittal@yahoo.com

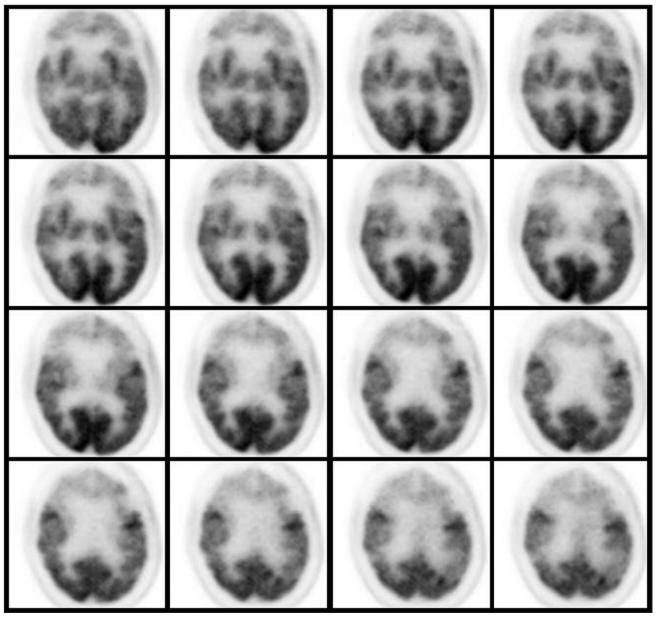

Figure 1: F-18 FDG PET/CT transaxial slices of the brain show hypometabolism in bilateral frontal, temporal, parieto-occipital cortices and anterior cingulated cortices. Adequate metabolism is noted in the posterior cingulated and precuneus. A diagnosis of fronto-temporal dementia was favored considering hypometabolism in the anterior cingulate and anterior temporal. Normal FDG uptake in precuneus and posterior cingulated ruled out AD

characterized by progressive decline in behavior or language associated with degeneration of the frontal and anterior temporal lobes.[1] FTLD has only recently been appreciated as a leading cause of dementia, particularly in patients presenting before the age of 65 years. Three distinct clinical variants of FTLD have been described: (i) behavioral-variant fronto-temporal dementia, characterized by changes in behavior and personality in association with frontal-predominant cortical degeneration; (ii) semantic dementia, a syndrome of progressive loss of knowledge about words and objects associated with anterior temporal neuronal loss; and (iii) progressive non-fluent aphasia, characterized by effortful language output, loss of grammar and motor speech deficits in the setting of left perisylvian cortical atrophy. The original cases described by Arnold Pick and Alois Alzheimer[2] demonstrated neuronal inclusions that were later shown to be tau-positive at histopathology. The link between tau and FTLD was further strengthened by the discovery that mutations in the microtubule associated protein tau (MAPT) gene cause familial FTLD.[3] The TAR DNA-binding protein 43 (TDP-43) was identified as the major ubiquitinated protein associated with tau-negative FTLD,[4] and mutations in the progranulin (PGRN) gene were shown to be responsible for the majority of familial tau-negative cases.[5]

Autopsy studies based on consecutive, unselected cases have demonstrated that FTLD accounts for roughly 5% of all pathologic diagnoses in patients with dementia.[6] However, this is likely to represent an underestimate of the true prevalence, since many of the autopsies reported in these series predated the modern molecular techniques currently used to diagnose FTLD. Taken together, these epidemiologic data suggest that FTLD is a common cause of early onset (age <65 years) dementia, with an incidence and prevalence similar to AD, and is likely to be an underappreciated cause of dementia in older individuals. Median survival in FTLD has been estimated at 6–11 years from symptom onset and 3–4 years from diagnosis.[7] Survival is shorter and cognitive and functional decline are more rapid in FTLD than in AD.[8]

Patients with behavioral variant FTLD (bv-FTLD) clinical variant present with marked changes in personality and behavior, and often display a mixture of apathy and disinhibition. Cognitive decline is typically less dramatic than the behavioral disturbance. Attention and working memory may be impaired, while episodic memory is variably spared. Amyotrophic lateral sclerosis (ALS) can co-occur with any of the FTLD clinical variants, but is most commonly associated with bvFTLD.[9] Semantic dementia (SD), also referred to as the temporal-variant of FTLD, is characterized by a fluent, anomic aphasia and behavioral changes in the setting of marked, often asymmetric degeneration of the anterior temporal lobes. Progressive non-fluent aphasia (PNFA) is a progressive disorder of language expression and motor speech associated with left perisylvian atrophy. Apraxia of speech, defined as difficulty initiating speech, a slow rate of speech or incorrect sequencing or omission of phonemes, is highly characteristic of PNFA.[10]

Despite the difficulties, accurate diagnosis is critical because the clinical management differs for AD and FTLD. The US Food and Drug Administration (USFDA) currently has approved five drugs for the treatment of AD. In contrast, no drugs have been shown to be effective in FTLD, although serotonin reuptake inhibitors are often used. Cholinesterase inhibitors can worsen behavioral symptoms in patients with FTLD and are generally avoided.[11]

Brain imaging provides an independent, objective, and quantitative measure of disease that complements clinical information and can aid in distinguishing FTLD and AD. Voxel-based morphometric analysis of structural magnetic resonance imaging can detect differences in regional atrophy between groups of patients with FTLD, FTLD subtypes, and AD and controls.[12] However, visual interpretation of individual magnetic resonance imaging scans, while helpful, can be misleading. Positron emission tomography with F-18 FDG-PET typically shows sufficient abnormalities that can be used to improve the accuracy of distinguishing AD from FTLD in individual cases.[13,14] Patients with AD characteristically have reduced activity most prominently in the posterior temporo-parietal and posterior cingulated cortices.[15] By contrast, the FDG PET scans of patients with FTLD have hypometabolism that is most prominent in the frontal, anterior temporal, and anterior cingulate cortices.[16] Metabolic abnormalities are not limited to these regions, however. As the severity of dementia increases, the severity and topographic extent of hypometabolism also increase and begin to involve other regions.

Womack and colleagues[17] stated that hypometabolism in the anterior cingulate and anterior temporal regions should carry at

least as much weight for a diagnosis of FTLD as temporo-parietal hypometabolism carries for a diagnosis of AD, even when this is seen in the presence of temporo-parietal hypometabolism. They found that the presence of temporo-parietal hypometabolism on FDG-PET imaging was a common finding in pathologically diagnosed FTLD cases. They found that the sensitivity of temporo-parietal abnormalities to be quite good for AD (93.6%), the specificity was only 50%. This reduced specificity had consequences because temporo-parietal hypometabolism had a disproportionate effect on interpretation errors for patients with FTLD. While posterior temporo-parietal hypometabolism had more sensitivity, involvement of posterior cingulate was more specific for AD. Atrophy of the paralimbic fronto-insular-striatal network, of which the anterior cingulate cortex is a part, distinguishes FTLD from AD, while atrophy of the dorsolateral frontal cortex does not.[18] These findings in turn mirror the distribution of the von Economo neurons. These neurons are found in the anterior cingulated and anterior insular cortices and are absent from the dorsolateral frontal lobes. They are preferentially and severely affected early in the course of FTLD and may underlie this specific distribution of hypometabolism and atrophy.[19,20] Womack showed that relying more on anterior temporal and especially anterior cingulate hypometabolism for a diagnosis of FTLD would improve the accuracy of scan interpretation.[17] Our index case also showed hypometabolism in the anterior cingulated and anterior temporal cortices favoring a diagnosis of FTLD.

REFERENCES

1. Rabinovici GD, Miller BL. Frontotemporal lobar degeneration: Epidemiology, pathophysiology, diagnosis and management. CNS Drugs 2010;24:375-98.
2. Alzheimer A. Uber eigenartige Krankheitsfalle des sparteren Alters. Psychiatr Nervenkr Z Gesamte Neurol Psychiatr 1911;4:356-85.
3. Hutton M, Lendon CL, Rizzu P, Baker M, Froelich S, Houlden H, *et al.* Association of missense and 5'-splice-site mutations in tau with the inherited dementia FTDP-17. Nature 1998;393:702-5.
4. Neumann M, Sampathu DM, Kwong LK, Truax AC, Micsenyi MC, Chou TT, *et al.* Ubiquitinated TDP-43 in frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Science 2006;314:130-3.
5. Gass J, Cannon A, Mackenzie IR, Boeve B, Baker M, Adamson J, *et al.* Mutations in progranulin are a major cause of ubiquitin-positive frontotemporal lobar degeneration. Hum Mol Genet 2006;15:2988-3001.
6. Brunnström H, Gustafson L, Passant U, Englund E. Prevalence of dementia subtypes: A 30-year retrospective survey of neuropathological reports. Arch Gerontol Geriatr 2009;49:146-9.
7. Kertesz A, Blair M, McMonagle P, Munoz DG. The diagnosis and course of frontotemporal dementia. Alzheimer Dis Assoc Disord 2007;21:155-63.
8. Rascovsky K, Salmon DP, Lipton AM, Leverenz JB, DeCarli C, Jagust WJ, *et al.* Rate of progression differs in frontotemporal dementia and Alzheimer disease. Neurology 2005;65:397-403.
9. Lomen-Hoerth C. Characterization of amyotrophic lateral sclerosis and frontotemporal dementia. Dement Geriatr Cogn Disord 2004;17:337-41.
10. Gorno-Tempini ML, Dronkers NF, Rankin KP, Ogar JM, Phengrasamy L, Rosen HJ, *et al.* Cognition and anatomy in three variants of primary progressive aphasia. Ann Neurol 2004;55:335-46.
11. Di Lazzaro V, Pilato F, Dileone M, Saturno E, Oliviero A, Marra C, *et al. In vivo* cholinergic circuit evaluation in frontotemporal and Alzheimer dementias. Neurology 2006;66:1111-3.
12. Short RA, Broderick DF, Patton A, Arvanitakis Z, Graff-Radford NR. Different patterns of magnetic resonance imaging atrophy for frontotemporal lobar degeneration syndromes. Arch Neurol 2005;62:1106-10.
13. Panegyres PK, Rogers JM, McCarthy M, Campbell A, Wu JS. Fluorodeoxyglucose-positron emission tomography in the differential diagnosis of early-onset dementia: A prospective, community-based study. BMC Neurol 2009;9:41.
14. Foster NL, Heidebrink JL, Clark CM, Jagust WJ, Arnold SE, Barbas NR, *et al.* FDG-PET improves accuracy in distinguishing frontotemporal dementia and Alzheimer's disease. Brain 2007;130:2616-35.
15. Minoshima S, Giordani B, Berent S, Frey KA, Foster NL, Kuhl DE. Metabolic reduction in the posterior cingulate cortex in very early Alzheimer's disease. Ann Neurol 1997;42:85-94.
16. Ishii K, Sakamoto S, Sasaki M, Kitagaki H, Yamaji S, Hashimoto M, *et al.* Cerebral glucose metabolism in patients with frontotemporal dementia. J Nucl Med 1998;39:1875-8.
17. Womack KB, Diaz-Arrastia R, Aizenstein HJ, Arnold SE, Barbas NR, Boeve BF, *et al.* Temporo-parietal Hypometabolism in Frontotemporal Lobar Degeneration and Associated Imaging Diagnostic Errors. Arch Neurol 2011;68:329-37.
18. Rabinovici GD, Seeley WW, Kim EJ, Gorno-Tempini ML, Rascovsky K, Pagliaro TA, *et al.* Distinct MRI atrophy patterns in autopsy-proven Alzheimer's disease and frontotemporal lobar degeneration. Am J Alzheimers Dis Other Demen 2007;22:474-88.
19. Seeley WW, Carlin DA, Allman JM, Macedo MN, Bush C, Miller BL, *et al.* Early frontotemporal dementia targets neurons unique to apes and humans. Ann Neurol 2006;60:660-7.
20. Seeley WW, Crawford R, Rascovsky K, Kramer JH, Weiner M, Miller BL, *et al.* Frontal paralimbic network atrophy in very mild behavioral variant frontotemporal dementia. Arch Neurol 2008;65:249-55.

How to cite this article: Harisankar CB, Mittal BR, Agrawal KL, Abrar ML, Bhattacharya A, Singh B, *et al.* FDG-PET findings in fronto-temporal dementia: A case report and review of literature. Indian J Nucl Med 2011;26:96-8.

Source of Support: Nil. **Conflict of Interest:** None declared.