CASE REPORT

Early-stage right temporal lobe variant of frontotemporal dementia: 3 years of follow-up observations

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SUMMARY

The right temporal lobe variant of frontotemporal dementia (FTD) is an uncommon progressive neurodegenerative disorder. We present the case of a 77-year-old right-handed man who presented with altered behaviour and problems with interpersonal relationships. He had no decline in cognitive function but brain perfusion single-photon emission CT demonstrated distinct hypoperfusion in the right temporal pole. At 2-year follow-up, he could not recognise his wife's relatives; and at 3-year follow-up, he had semantic aphasia. Decreased brain perfusion extended from the right temporal lobe into the contralateral temporal and both frontal lobes. These findings suggest that the right temporal lobe variant of FTD should be considered in elderly patients with altered behaviour and problems with interpersonal relationships, even if dementia is not suspected. The right anterior temporal lobe may play a key role in the onset of the early symptoms of this disease.

BACKGROUND

Frontotemporal dementia (FTD) is a clinical syndrome characterised by progressive impairment of behaviour and/or language and is caused by atrophy of the grey matter that selectively affects the frontal and temporal lobes.^{1,2} Research on this syndrome has revealed a distinct clinical, neuro-anatomical and pathological profile for semantic dementia (SD) or the semantic variant of primary progressive aphasia characterised by left lateralised atrophy of the anterior temporal lobe, visible on neuroimaging.^{3,4}

In contrast, several cases with the right temporal lobe variant of FTD characterised by right lateralised atrophy of the anterior temporal lobe have been reported,^{5–7} but it is an uncommon subtype and there is no consensus about its name.⁸ This may be partly because symptoms in the early stage of the disease are not recognised.

We present a case of the right temporal lobe variant of FTD where the patient had problems with interpersonal relationships in the early stages of the disease and then was followed for 3 years with cognitive function tests (Mini-Mental State Examination (MMSE), Alzheimer's Disease Assessment Scale-cognitive component-Japanese version (ADAS-Jcog), clock drawing test (CDT)), brain MRI and brain perfusion single-photon

emission CT (SPECT). We believe that the findings in this case may facilitate early diagnosis and early intervention in management of the right temporal lobe variant of FTD.

CASE PRESENTATION

A 77-year-old man presented with problems with interpersonal relationships. According to his wife, he was diligent and scrupulous about daily activities and got along with people. However, one-way conversation and self-centred behaviour had become more frequent for 2 years. As a result, he often had trouble with his wife and neighbours. During this time, he went to see his doctor with complaints of headache and appetite loss. No abnormalities were found on routine blood tests or blood chemistry. He was referred to the psychiatry department of our hospital by his primary care physician, because he complained that he was starting to worry about forgetfulness. After he graduated from university, he worked as a bank clerk until retirement at 60 years of age and then had participated in community events and had volunteered for community service. He had no significant history of medical or mental disorder except for hypertension, and no family history of dementia.

At the initial visit, he stated he was worried about dementia as well as his wife's attitude. With regard to anxiety about dementia, he said that he could not recall some words for only a moment and did not have trouble making a living. It was striking that he suddenly asked the age of examining physician (AO) while he talked about his hobby of burning his favourite music onto CD. He then offered to burn some popular songs from the time of the examining physician's youth onto CD as gifts. Five CDs were sent to the examining physician 1 week later. On initial examination, he had no neurological abnormalities such as tremor, rigidity or dysarthria. Scores on the MMSE, ADAS-Jcog and CDT did not show cognitive deficits (table 1). However, brain MRI showed atrophy of the right medial temporal and lateral temporal lobes and brain perfusion SPECT demonstrated distinct hypoperfusion in the right anterior temporal lobe (figure 1). We explained these findings to the patient and his wife but did not recommend any medication. He returned for follow-up visits every 3 months.

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Table 1 Cognitive function tests

	Score		
	77 years old	2-year follow-up	3-year follow-up
MMSE*	29/30	29/30	29/30
Clock drawing test†	15/15	15/15	15/15
ADAS-Jcog	5.4/70	9.3/70	9.7/70
Word recall task	3.7	5.3	6
Naming objects and fingers	0	1	0
Following commands	1	1	1
Constructional praxis	0	0	0
Ideational praxis	0	0	0
Orientation	0	0	0
Word recognition task	0.7	2	1.7
Remembering test directions	0	0	0
Spoken language	0	0	0
Comprehension	0	0	0
Word-finding difficulty	0	0	1

*MMSE, Mini-Mental State Examination. The maximum score is 30 and a score of 23 or lower is indicative of cognitive impairment.

†Clock drawing test. The scoring system of Freedman *et al* was used for quantitative rating. A higher score indicates preserved cognitive function; the maximum score is 15.¹⁷ ADAS-Jcog, Alzheimer's Disease Assessment Scale-cognitive component-Japanese version. Eleven subtests are combined into a composite score ranging from 0 to 70, with lower scores indicating better performance (10 or less: probability of normal or MCI). The scoring procedure of each subtest is as follows. (1) Word Recall Task: Score (0–10 points)=Mean of number of words not recalled in three trials. (2) Naming Objects and Fingers: Score (0–5 points)=Number of incorrect items. (3) Following Commands: Score (0–5 points)=Number incorrectly performed. (4) Constructional Praxis: Score (0–5 points) 0=All 4 drawings correct. (5) Ideational Praxis: Score (0–5 points)=Number of components incorrectly performed. (6) Orientation: Score (0–8 points)=Number of incorrect answers. (7) Word Recognition Task: Score (0–12 points)=Mean of number of incorrect responses in three trials. (8) Remembering Test Directions: Score (0–5 points) 0=Patient never needs extra reminders or instructions. (9) Spoken Language: Score (0–5 points) 0=No instances where it is difficult to understand the patient. (10) Comprehension: Score (0–5 points) 0=No evidence of poor comprehension. (11) Word-Finding Difficulty: Score (0–5 points) 0=No evidence of word-finding difficulty in spontaneous speech, 1=Very mild 1–2 instances, not clinically significant.^{8,18}

At 2-year follow-up, he had often had difficulty finding the right words and needed more time to find forgotten words than he did 2 years earlier. Also, he could not recognise his wife's relatives whom he had not seen for a while when he attended a funeral service for his brother-in-law. The results of cognitive functioning tests were about the same as those at age 77. Repeat brain MRI showed atrophy in the left medial temporal lobe in addition to the right medial temporal lobe. Decreased brain perfusion was seen extending from the right anterior temporal lobe into the posterior temporal, the inferior frontal lobe and the contralateral temporal and frontal lobes.

At 3-year follow-up, he could recognise his family but sometimes could not recall names and places. He made semantic errors in naming objects on the ADAS-Jcog. MRI and SPECT showed a slight increase in brain atrophy and reduction in perfusion compared with images from 1 year earlier.

INVESTIGATIONS

During a 3-year follow-up, he performed worse on the word recall and word recognition tasks on the ADAS-Jcog. Moreover, at 3-year follow-up, he had word-finding difficulty and semantic errors in naming objects. Total score of ADAS-Jcog showed the

probability of mild cognitive impairment (MCI) or another type of dementia other than Alzheimer's disease.⁹ Also, at 3-year follow-up, he scored 0 out of 3 points on the word recall task in the MMSE. On the CDT, he scored 15 out of 15 points during all 3 years of follow-up and maintained visuospatial and executive function (table 1).¹⁰

At 2-year follow-up, the patient could recognise family members in pictures but could not name and recognise his wife's relatives whom he had not seen for a while. With advancing age, brain MRI showed enlarged areas of atrophy in the right lateral temporal lobe including the temporal pole, medial temporal lobe and parahippocampal gyrus, with extension into the left temporal lobe (figure 1). There was no evidence of organic disease such as tumour.

SPECT images were obtained using a double-head rotating gamma camera (SymbaTM E; Toshiba Medical Systems, Tokyo, Japan) equipped with a parallel collimator, ~15 min after intravenous injection of 111 MBq of N-isopropyl-p-[¹²³I] iodoamphetamine (IMP). SPECT images were analysed by using a three-dimensional stereotactic surface projection (3D-SSP) programme, ISSP 5 V.1.0 (Nihon Medi-Physics, Tokyo, Japan) incorporated into the FALCON software package. Data were quantified and displayed by using the stereotactic extraction estimation (SEE) programme, SEE V.2.1 (Nihon Medi-Physics).¹¹ IMP distribution of the cortex on 3D-SSP was compared with a normal database (27 normal controls). Differences between individual data and normal data in each pixel were converted to a Z score calculated using the following formula: Z score=((control mean)–(individual value))/(control SD). The cluster of pixels with significant difference (Z score >2.0) could be identified as the target area with a reduced blood flow on Z score maps (figure 1). At age 77, the regions with a mean Z score more than 2 were the right temporal pole, the right uncus, the right parahippocampal gyrus and the right superior temporal gyrus. At 2-year follow-up, these extended to the right posterior temporal lobe, the right inferior frontal lobe and the contralateral temporal and frontal lobes. At 3-year follow-up, the left inferior frontal gyrus and the left middle temporal gyrus also had mean Z scores greater than 2 (table 2).

DIFFERENTIAL DIAGNOSIS

Autism spectrum disorder, obsessive-compulsive disorder, unspecified alcohol-related or substance-related disorder, and personality change due to another medical condition should be included in the differential diagnosis of early-stage right temporal lobe variant of FTD.

Brain MRI and brain perfusion SPECT facilitate diagnosis of early-stage right temporal lobe variant of FTD, as indicated in the case.

TREATMENT

The patient and his wife received psychoeducational intervention for the right temporal lobe variant of FTD to relieve their distress. He did not receive drug therapy during follow-up.

OUTCOME AND FOLLOW-UP

The patient continued to have problems with interpersonal relationships and spent very little time with his wife. He often had word-finding difficulty, and semantic aphasia was detected on ADAS-Jcog at 3-year follow-up. He is scheduled to return for follow-up visits once every 3 months to allow for early

Figure 1 T1-weighted MRI scans of the brain and 3D-SSP of statistical Z scores representing areas of functional reduction in the patient during 3 years of follow-up. Red arrows show the right lateral temporal lobe including the temporal pole and yellow arrows show the medial temporal lobe including the parahippocampal gyrus. A positive Z score represents a reduced regional cerebral blood flow relative to the control mean. The Z score in each Z map image is scaled from 2 to 7. ANT, anterior view; INF, inferior view; LT.LAT, left lateral view; RT.LAT, right lateral view; SPECT, single-photon emission CT; 3D-SSP, three-dimensional stereotactic surface projection.

intervention for behavioural and psychological symptoms of dementia.

DISCUSSION

The right temporal lobe variant of FTD, which bears a symmetrical relationship to the atrophy of SD, is far less common—with a prevalence one-third to one-fourth that of SD^{4 12}—and may be underdiagnosed.

We followed up this case of early-stage right temporal lobe variant of FTD with cognitive function tests, brain MRI and brain perfusion SPECT for 3 years. Our findings revealed clinical features in the early stage of disease and neuroanatomical progression. The patient presented with altered behaviour and problems with interpersonal relationships characterised by self-centred behaviour and a lack of empathy. At that time, there were no abnormal findings on cognitive function tests, but neuroimaging by brain perfusion SPECT showed hypoperfusion localised to the right anterior temporal lobe including the temporal pole. Subsequently, he showed prosopagnosia, word-finding difficulty and semantic aphasia when decreased brain perfusion extended into the posterior temporal, the inferior frontal lobe, and the contralateral temporal and frontal lobes. Regarding prosopagnosia, he did not have difficulty recognising familiar persons at a funeral or wedding, but, at 2-year follow-up, he complained, for the first time, that he could not recognise some relatives when he attended a funeral service for his brother-in-law and also could not recognise them in pictures that were taken at the funeral. This symptom may be associated with hypoperfusion in the right fusiform gyrus, which is considered to play a key role in facial recognition.¹³ Word-finding difficulty and semantic aphasia may be associated with hypoperfusion in the left temporal and frontal lobes, as well as cases in SD³

These findings suggested that his symptoms, as the disease progressed, depended on which brain regions were affected by hypoperfusion. Importantly, he initially presented with only self-centred behaviour and a lack of empathy. This clinical feature indicates a need for early diagnosis and early intervention for this disorder. Because alterations in behaviour and problems with interpersonal relationships may produce more caregiver distress than other cognitive deficits, as discussed in SD cases.¹⁴

The age at diagnosis in this case was older than commonly predicted in SD.¹⁵ As discussed above, older people may not be correctly diagnosed from symptoms in the early stage of the right temporal lobe variant of FTD such as irritability, impulsiveness or problems with interpersonal relationships, or symptoms in the early stage of the disease may not bring them to medical attention.

Another notable finding in this case is the relationship between altered behaviour and interpersonal relationships and regions of hypoperfusion, as shown by neuroimaging analysis early in the disease. Recently, increasing evidence has revealed that the extent of altered behaviour and relationship is related to the integrity of the right temporal pole in the right temporal lobe variant of FTD and SD.^{14 16} The findings in this case lend strong additional support to the relationship between the two. In the future, the right anterior temporal lobe including the temporal pole may play a key role in studies of disorders associated with socioemotional disturbances.

In summary, the findings in this case suggest that the right temporal lobe variant of FTD should be considered in elderly persons who present with altered behaviour and problems with interpersonal relationships, even if dementia is not suspected. Furthermore, the right anterior temporal lobe may play a key role in the onset of the early symptoms of this disease.

Table 2 Regions with mean Z scores greater than 2

Region/side	Mean Z score >2		
	77 years old	2- year follow-up	3-year follow-up
Frontal lobe			
Lt	#*	#	#
Rt	#	2.42 (1.97)	2.49 (2.18)
Temporal lobe			
Lt	#	2.29 (1.45)	2.89 (1.86)
Rt	2.10 (1.81)	3.47 (2.19)	3.85 (2.49)
Inferior frontal gyrus			
Lt	#	#	2.10 (1.23)
Rt	#	2.09 (1.39)	2.59 (1.32)
Medial frontal gyrus			
Lt	#	#	#
Rt	#	3.19 (1.69)	3.15 (1.85)
Orbital gyrus			
Lt	#	3.83 (0.29)	2.47 (0.19)
Rt	#	6.30 (0.38)	4.62 (0.82)
Rectal gyrus			
Lt	#	3.42 (1.52)	2.73 (1.08)
Rt	#	7.74 (1.80)	8.71 (2.89)
Subcallosal gyrus			
Lt	#	#	#
Rt	#	5.61 (1.55)	7.00 (2.41)
Postcentral gyrus			
Lt	#	#	#
Rt	#	2.43 (1.57)	2.86 (2.17)
Superior temporal gyrus			
Lt	#	2.66 (1.60)	3.41 (2.02)
Rt	2.55 (2.17)	3.84 (1.79)	4.23 (2.16)
Middle temporal gyrus			
Lt	#	#	2.87 (1.61)
Rt	#	2.63 (2.58)	3.01 (2.89)
Inferior temporal gyrus			
Lt	#	2.58 (1.12)	2.60 (1.59)
Rt	#	4.02 (2.07)	4.53 (2.47)
Transverse temporal gyrus			
Lt	#	#	#
Rt	#	2.64 (1.55)	4.96 (1.73)
Fusiform gyrus			
Lt	#	#	#
Rt	#	3.37 (1.48)	2.62 (1.41)
Parahippocampal gyrus			
Lt	#	#	#
Rt	2.34 (0.91)	5.19 (1.69)	5.75 (1.80)
Anterior cingulate			
Lt	#	2.21 (0.72)	2.12 (1.05)
Rt	#	3.56 (1.35)	3.79 (1.98)
Uncus			
Lt	#	2.50 (0.92)	4.31 (1.46)
Rt	4.25 (1.18)	4.66 (1.95)	5.58 (1.99)
Temporal pole			
Lt	#	3.21 (1.24)	4.52 (1.25)
Rt	4.78 (1.39)	5.50 (1.23)	6.35 (1.11)

Numbers in brackets are SD.

*Hash mark represents mean Z score <2.

Lt, left; Rt, right.

Learning points

- ▶ The early stage of the right temporal lobe variant of frontotemporal dementia may present in the elderly as altered behaviour and problems with interpersonal relationships, even when dementia is not suspected.
- ▶ As the right temporal lobe variant of frontotemporal dementia progresses, the pathological process may encroach on the contralateral hemisphere.
- ▶ Early diagnosis of the right temporal lobe variant of frontotemporal dementia is important, because altered behaviour and interpersonal relationship problems produce great caregiver distress.
- ▶ Brain MRI and brain perfusion single-photon emission CT are useful procedures for early diagnosis of the right temporal lobe variant of frontotemporal dementia.
- ▶ The right anterior temporal lobe including the temporal pole may play a key role in development of self-centred behaviour and lack of empathy.

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