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Chapter 13

Other Dementias

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Additional information is available at the end of the chapter

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1. Introduction

The non-Alzheimer dementias (NAD) are a group of disorders that account for approximately 30 to 40 per cent of dementias worldwide [1-3]. Some of the common types of NAD are listed in Table 1.

2. Vascular dementia

The term vascular dementia (VaD) deals with cognitive impairment affecting daily activities required for living of vascular origin (ischemia, haemorrhage). However, VaD as a concept and disease entity is undergoing regular transformation. The term 'vascular cognitive impairment' (VCI) introduced in 1995 [4] is used to include any cognitive impairment from cerebrovascular disease (CVD) except major stroke. It was then proposed that the term VCI should include all forms of cognitive impairment associated with CVD [5] (Table 2). This term would include not only VaD but also mild cognitive impairment (MCI) with no dementia and dementia of mixed origin (Alzheimer's and vascular dementia) (see [6]). It has been argued that this classification does not fit the purpose of clinical differentiation and that this term should be restricted to MCI without dementia due to vascular cause [7]. However, some scholars are of the opinion that VCI is a research terminology and that clinicians should identify the condition and deal with the associated risk factors thereby avoiding progression to VaD [8].

The diagnostic criteria that characterise cognitive syndromes associated with vascular disease are usually based on two factors: demonstration of presence of a cognitive disorder by neuropsychological testing and history of clinical stroke or presence of vascular disease by

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neuroimaging that suggests a link between the cognitive disorder and vascular disease. The term VCI is not used for patients who have an active diagnosis of drug or alcohol dependence or for patients with delirium [9].

2.1. Epidemiology

VaD is considered to be the second most prevalent type of dementia worldwide accounting for about 15 to 20 % of the dementia cases [10]. Prevalence of VaD in Japan has been reported to be as high as 47 % [11]. 16 % of all cases of late-onset dementia (65 years or after) [12] and 18 % of all cases of early-onset dementia (below 65 years) [13] was found to be VaD. However, it must be kept in mind that establishing the exact epidemiology of VaD is not an easy task mainly due to difficulty in diagnosing clinically [14] and overlap of AD neuropathology (see [15]).

Some of the risk factors for developing VaD are hypertension [16] and metabolic factors like diabetes and obesity. Males are considered to be at a significantly higher risk of developing VaD [17]. The incidence rate of VaD was found to be two times higher than Alzheimer's disease for males in Japan [18]. The risk factors have been classified [19] and are listed in Table 3. Some of the protective factors found in the Canadian Study of Health and Aging include eating shellfish and regular exercise for women [20]. Antioxidants, which include vitamin E and C and also intake of fatty fish have been found to be protective against VCI [21].

a. Vascular dementia
• Vascular dementia of acute onset (post-stroke)
• Multi-infarct dementia
• Subcortical vascular dementia (Binswanger's disease)
• Mixed cortical and subcortical vascular dementia
• Other vascular dementia (CADASIL, vasculitis, post-cardiac arrest)
b. Dementia with Lewy Bodies
c. Frontotemporal dementia
d. Dementia in other diseases
• Pick's disease
• Creutzfeldt-Jakob disease
• Huntington's disease
• Parkinson's disease
• Human immunodeficiency virus (HIV) disease
e. Treatable or reversible dementias
• Normal pressure hydrocephalus
• Alcohol-related
• Neoplasia (glioma, meningioma, secondaries)
• Vitamin deficiencies (B12, folate, thiamine, nicotinic acid)
• Metabolic and endocrine (liver disease, hypothyroidism)

Table 1. Types of non-Alzheimer dementia

• VCI-no dementia
• Vascular dementia
• Mixed Alzheimer's disease and vascular dementia

Table 2. Vascular cognitive impairment (VCI)

1. Demographic
Age
Male sex
Lower educational level
2. Atherosclerosis
Hypertension
Cigarette smoking
Myocardial infarction
Diabetes mellitus
Hyperlipidemia
3. Genetic
CADASIL
Apolipoprotein E
4. Stroke-related
Volume of cerebral tissue loss
Bilateral cerebral infarction
Strategic infarction (thalamic, angular gyrus)
White matter disease

Table 3. Risk factors for vascular dementia according to reference [18]

2.2. Clinical features and pathophysiology

Firstly, to diagnose dementia, there should be a decline in memory and a decline in at least two cognitive skills such as orientation, social behaviour, verbal skills, attention, motor control, praxis, emotional control and executive functions (goal-directed behaviour and problem-solving skills). In VaD, the onset may be sudden or gradual, with stepwise progression. Since vascular component is involved, there may be focal neurological deficits such as hemiparesis or swallowing disturbances and dysarthria (pseudobulbar lesion symptoms). A history of transient ischaemic attacks is common. Depending on the site of the lesion, features such as motor aphasia, dyspraxia (due to left anterior cerebral artery ischemia) or psychosis (right middle cerebral artery) or amnesia and visual disturbances (posterior cerebral artery) may be seen. Other important associated features include gait disturbance which may be associated with a history of unsteadiness as well as frequent falls. It is vital to distinguish dementia of vascular origin from degenerative form of dementia. This is because VaD, when diagnosed at an early stage provides for chances to prevent or delay progression. Thus, treatment strategies may vary. For this purpose, clinicians use a scoring system called Ha-

chinski ischaemic score [22]. A score of above six signifies dementia due to vascular cause. Some of the clinical criteria developed to assist in diagnosing VaD include State of California Alzheimer Disease Diagnostic and Treatment Centers (ADDTC) criteria [23], International Classification of Diseases (ICD-10) criteria [24], National Institute of Neurological Disorders and Stroke (NINDS)-Association Internationale pour la Recherche et l'Enseignement en Neurosciences (AIREN) criteria [25] and Diagnostic and Statistical Manual for Mental Disorders (DSM-IV) criteria [26].

The most widely followed or accepted criteria for diagnosis of VaD is the NINDS-AIREN criteria. According to this, both clinical and radiological criteria must be fulfilled. Clinical criteria include presence of dementia and CVD as well as a relation between the two features i.e. dementia should develop after and within 3 months of the stroke. Radiological criteria are based on topography and severity of vascular lesions. There should be either a large vessel stroke or multiple lacunar infarcts in basal ganglia or white matter lesions in periventricular regions. Large vessel lesions should be present in dominant hemisphere or in both the hemispheres while white matter lesions must involve at least 25 % of the cerebral white matter. However it was found that the neuroimaging criteria listed above does not always differentiate between stroke patients with and without dementia [27]. Definite vascular dementia is diagnosed by fulfilling the above mentioned criteria with histopathological evidence from brain biopsy or autopsy. Absence of other causes of dementia must be ruled out.

2.2.1. Post-stroke dementia

Post-stroke dementia (PSD) is the type of VaD developing after a stroke. Among patients who have experienced a first stroke, the prevalence of poststroke dementia (PSD) varies in relation to the interval after stroke, definition of dementia, location and size of the infarct. This includes a large-vessel lesion or single strategic lesion (thalamus or midbrain) (Figure 1). The cause of stroke may be haemorrhagic, or ischemic. The rate of dementia in people with stroke was found to be two times respect people without stroke [28]. Increasing age is significantly associated with PSD [29,30]. The severity of cognitive decline after a stroke is associated with increased risk of PSD [31]. Long-term mortality is 2 to 6 times higher in patients with PSD after adjustment for demographic factors, associated cardiac diseases, stroke severity, and stroke recurrence (for review, see [32]). Silent cerebral infarcts, white matter changes, and global and medial temporal lobe atrophy are associated with increased risk of PSD [32]. Dementia is severe in lesions involving thalamus or midbrain. After stroke, recovery of patient involving both physical and cognitive functions is variable.

2.2.2. Multi-infarct dementia

As the name suggests, there are multiple strokes occurring in the same patient (Figure 2). Sometimes these may even go undetected and may be noticed only after a major stroke. This causes the characteristic step-wise progression of the disease where there may be deterioration in cognitive abilities but also there may be periods of stability or even improvement of the patient. The severity of dementia increases with each stroke. The type of vessel involved

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may be either large or small vessels or both. It is thought that the reason for multiple infarcts is due to underlying predisposing factors associated with VaD.

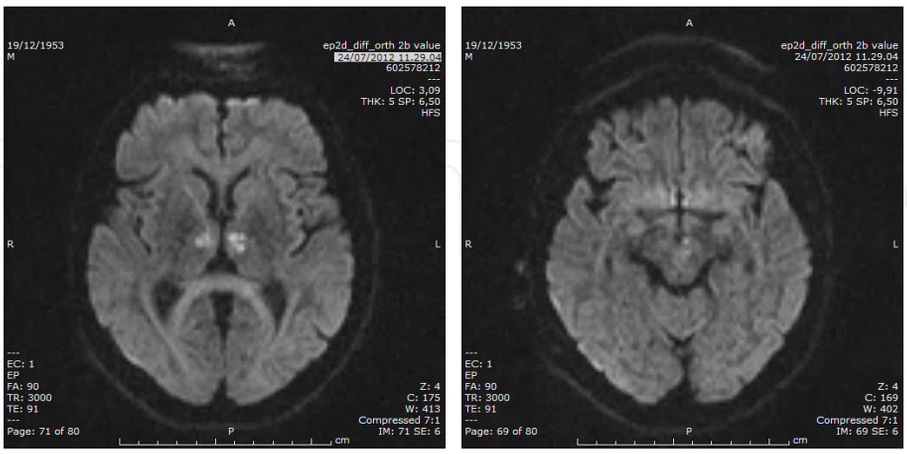


Figure 1. Brain MRI scan (DWI sequences) of a 59 years old man presenting with an acute onset of confusion, ideative and motor slowness and apathy with memory loss. A marked cognitive and motor slowness and apathy remained after 15 days from onset. MRI scan showed ischemic lesions in the medial part of both thalami and in the midbrain (top of the basilar syndrome).

2.2.3. Binswanger's disease

It is a type of subcortical ischaemic VaD. It is a progressive small vessel disease. Occlusion of small arteries (arterioles) leads to hypoperfusion and this in turn leads to white matter lacunes and necrosis [33]. Clinical features vary slightly where the patients develop a slowly progressing dementia. Brain imaging studies reveal increased white matter and periventricular lesions (Figure 3).

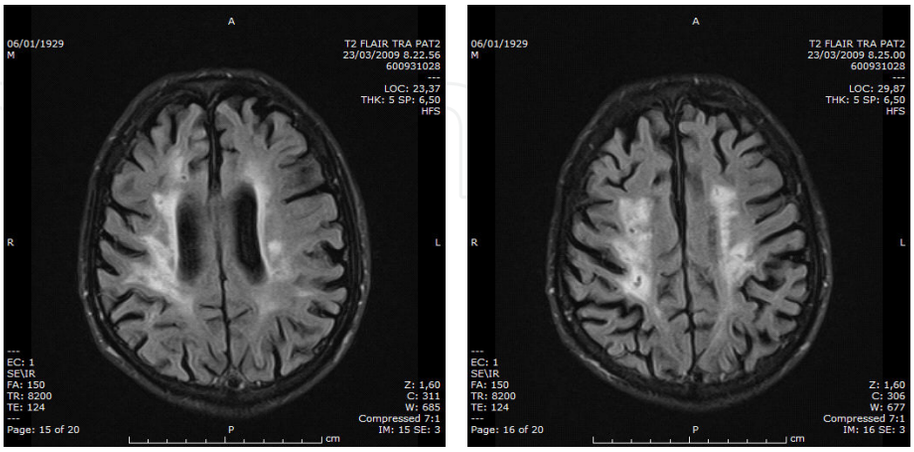


Figure 2. Brain MRI (FLAIR sequences) of a 80 years old man with a multi-infarct progressive dementia with bulbar symptoms. Multiple cortical and subcortical infarct are seen together with periventricular white matter changes and corticola atrophy.

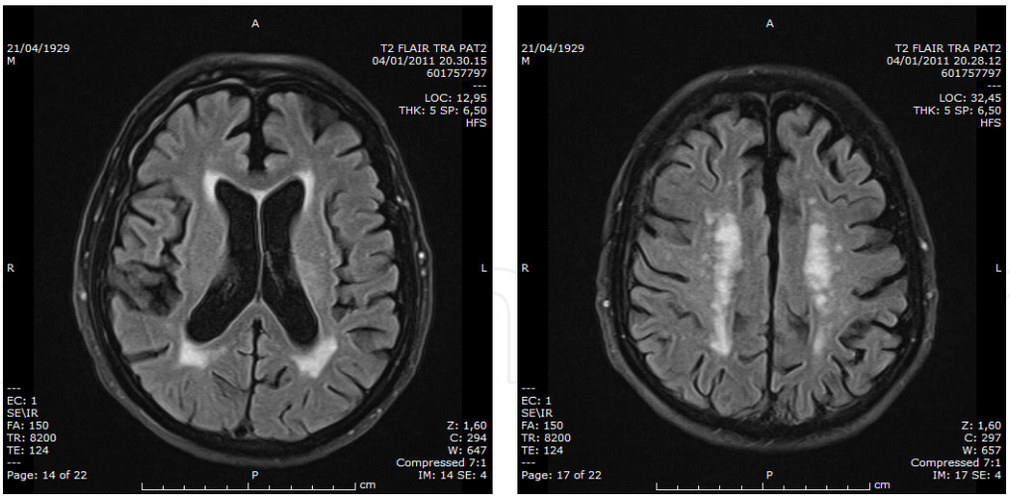


Figure 3. White matter changes and periventricular lesions observed in a 82 years old man with loss of memory and slowly progressive cognitive impairment. Brain atrophy is also present (mixed dementia)

2.2.4. Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL)

CADASIL is a familial form of vascular dementia. It is associated with migraine and is a subcortical ischaemic type of dementia. It is due to mutation in the *NOTCH3* gene on chromosome 19. It is the most common genetic form of VaD. The disease has an autosomal dominant type of inheritance. From the pathological point of view vascular lesions occur not only in vessels of the brain but also other organs. Hence, it can be diagnosed by skin biopsy and confirmed by immunohistochemistry with *NOTCH3* monoclonal antibody [34]. Brain imaging shows white matter lesions of necrosis and lacunae. A recessive form has also been described and mutations in the HTRA1 gene identified [35,36].

2.3. Neuropathology

The types of lesions seen in VaD are mainly infarctions. The infarctions may be present in the cortex and subcortical regions (complete infarctions) as well as the white matter and basal ganglia (lacunar infarctions). Cerebral amyloid angiopathy may be observed. Atrophy and sclerosis of hippocampus are also common [37]. A study was conducted on 135 post-mortem brains with dementia to conceptualize the natural history of cerebrovascular lesions (CVL) and operationalize it into a cerebrovascular staging system [38]. The authors rated the following CVL; in the frontal and temporal lobes: arteriosclerosis, amyloid angiopathy, perivascular hemosiderin leakage, perivascular spaces dilatation in deep and juxtacortical white matter, myelin loss and cortical infarcts; in the hippocampus: neuronal loss, perivascular spaces dilatation and presence of micro- and large infarcts; in the basal ganglia: arteriosclerosis, perivascular spaces dilatation, density of micro- and large infarcts, either lacunar or territorial.

2.4. Management

2.4.1. Investigations

Routine blood investigations and biochemistry including lipid and glucose levels as well as liver enzymes must be done in order to rule out treatable causes of dementia and identify risk factors such as hyperlipidemia and diabetes. The Mini-Mental State Examination is a brief but good way of screening for dementia. Executive function may be tested by Clock-Drawing Task. A proper history from the patient and/or informant must be obtained and should include history for unprovoked falls, TIA and urinary incontinence also. Computed tomography (CT) and Magnetic Resonance Imaging (MRI) are useful investigations to check for both large and small infarcts and white matter lesions. Other imaging techniques like Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) may be done to assess blood flow. Population MRI studies have revealed high prevalence of overt small-vessel disease in the elderly population (23 % for silent lacunes and 95 % for incidental hyperintensities). These lesions are associated with an increased risk for stroke and dementia [39]. A thorough and complete neurological examination must be done to confirm signs of stroke. It is extremely important to conduct a good cardiovascular examination including measuring blood pressure and examining for presence of murmurs. Electrocardiogram to look for presence of fibrillation is essential.

2.4.2. Treatment

Since there are several risk factors associated with developing VaD, it is important to treat them or keep them in check. In people at risk for VCI, smoking cessation is mandatory. Lifestyle modification such as eating a low-fat diet, moderation in alcohol intake and regular exercise are reasonably effective. Hypertension, hyperglycemia and hypercholesterolaemia must be treated. Antiplatelet therapy is used and is effective in preventing further strokes. Primary prevention with antihypertensive drugs perindopril and indapamide has been shown to be effective in reducing risk of dementia and cognitive decline in patients with recurrent stroke [40]. Treatment of VaD is usually symptomatic. No specific drug has yet been recommended. Cholinesterase inhibitors (ChEI) such as donepezil have been found to be beneficial in improving cognition [41] but other ChEI such as galantamine[42] and rivastigmine [43] have been found to be ineffective. N-methyl-D-aspartate antagonist like memantine has been tried in trials but was also found to be ineffective [44].

2.5. Prognosis

The prognosis of VaD is generally poor. Most patients die within few years from onset. Death may be due to CVD or complications of dementia. Since there is no specific treatment recommended, it is very important to diagnose the disease at an early stage and stop it from progressing further. Preventive measures are also vital.

3. Dementia with lewy bodies

Dementia with Lewy Bodies (DLB) is a degenerative type of dementia (like AD). It is the second most common type of degenerative dementia (after AD). Lewy Bodies are inclusion bodies present in the cytoplasm containing a protein called ubiquitin. The first cases of DLB with cortical involvement were reported in 1961 [45]. The Lewy Body was seen in autopsy by neuropathological staining only as far as 1989 [46]. Over the years, DLB has been given several terminologies, namely diffuse Lewy body Disease [47], Lewy body dementia [48], Lewy body variant of AD [49], senile dementia of Lewy body type [50] and dementia associated with cortical Lewy bodies [51].

3.1. Epidemiology

The prevalence of DLB is about 0.1 to 5 % in the general population and about 10 to 20 % of all dementia cases [52-54]. The incidence is about 0.1 % a year in the general population and about 3 % a year of all new dementia diagnosed cases [55]. A French cohort study found that the incidence of DLB increases with age [56].

3.2. Clinical features and pathophysiology

The main feature is the presence of dementia which means impairment of cognition affecting normal day to day and social activities. Guidelines [57] suggest the core features as being fluctuation in level of cognition, detailed visual hallucinations that are recurrent and parkinsonism that is spontaneous. Any two of these core features indicate probable DLB while the presence of only one of the core features indicates possible DLB. Other psychiatric features may include depression, anxiety or apathy. There may also be a history of repeated falls given by the carers. Another interesting feature is the presence of Rapid Eye Movement sleep behaviour disorder (RBD) [58, 59]. RBD is a sleep disorder and is characterized by loss of muscle atonia during rapid eye movement as well as movement of limbs, with or without vocalization and dreaming. Carers often give a history that it is as though the patient is acting out his or her dreams. A recent study [60] found that inclusion of RBD as a core feature may help improve diagnosis of DLB.

On pathological examination, LB contain ubiquitin which is examined by immunohistochemistry. Increased presence of LB in the parahippocampus has been linked to increase in the severity of dementia [61]. DLB patholgy has been shown to be related to plaques in hippocampus and amygdala [62]. Another biomarker for diagnosis is α-synuclein (AS) immunohistochemistry [63]. Genetic mutation of AS has also been associated with DLB [64]. Diagnosis with AS staining was found to be more sensitive and more specific than ubiquitin staining [65]. Presence of LB in the temporal lobe has been shown to be related to visual hallucinations [66].

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3.3. Management

3.3.1. Investigations

Clinically, dementia must be diagnosed. Other neuropsychiatric features such as depression, hallucinations and sleep disturbances must be identified. Proper history from carer or family member must be obtained. A complete psychiatric and neurological evaluation must be carried out. There are no specific diagnostic tests. MRI may show preservation of medial temporal lobe [67] or reduced amygdala volume [62]. SPECT may show hypoperfusion in occipital lobe [68]. Using SPECT with dopamine transporter imaging is turning out to be promising [69,70]. Imaging and findings of global amyloid deposition may also give a clue in diagnosis of LBD [71].

3.3.2. Treatment

Drugs used in treatment include levodopa viz. usually used to treat Parkinson's disease. A one year follow-up study has shown it to be acutely effective [72] but its use is debatable as it also lead to adverse effects most notably being hallucinations [73]. Another promising drug is memantine which was also found to be well tolerated [74]. A Cochrane review found cholinesterase inhibitors to be not useful in patients with DLB [75]. Other measures include education of carers and also reality orientation of patients.

3.4. Prognosis

The prognosis in DLB can be variable. Initial health and well-being may play a role in deciding the prognosis. When compared to AD, the prognosis has been found to be similar [76] as well as more severe [77]. No single factor have been identified that may dictate the outcome of disease progression [78].

4. Frontotemporal dementia

Frontotemporal dementia (FTD) is considered to be the second most common type of early-onset (before the age of 65) dementia. There is pathological involvement of frontal and temporal lobes of the brain. FTD consists of a behavioural variant (bvFTD) and a language variant. The language variant can be further divided into semantic dementia (SD) and progressive non-fluent aphasia (PNFA). Overlap of FTD with motor neuron disease (MND) is also seen clinically, pathologically and genetically [79]. The whole clinico-pathological spectrum is often referred to as frontotemporal lobar degeneration.

4.1. Epidemiology

The prevalence of FTD was found to be about 15 in 100,000 in UK involving age groups 45-64 years [80] while in the Netherlands it was found to be 9.4 per 100,000 in the age group 60-69 years [81]. The prevalence of early-onset AD and FTD was (be consistent between past

and present verbs) found to be similar [80,82]. The incidence was found to be about 3.5 cases per 100000 person-years [83]. Average age of onset is around 50-60 years [80,81].

4.2. Clinical Features and pathophysiology

The core features are an insidious onset, decline in personal and social conduct as well as early emotional blunting and loss of insight [84]. The most common presenting symptoms are then changes in behaviour. Decrease in cognitive functions involving executive functions and speech is also observed. bvFTD is the most common of the subtypes [85] and is considered to be the most typical of FTD. It is associated with degeneration of frontal and temporal lobes [86] Other important features include behavioural disinhibition, apathy and loss of empathy [87]. SD is characterised by loss of ability to name and recognise words, objects and faces. It is associated with atrophy of left temporal lobe [88]. However, at least initially, speech in SD may be unhampered, fluent and grammatically correct [89]. In PNFA, speech is hampered and is grammatically incorrect but usually comprehension is preserved. This is associated with problems in language expression [89] and also with left temporal lobe atrophy and Broca's area degeneration [84,90]. FTD associated with MND has similar clinical presentations involving areas of language, memory and behavioural changes[91]. Genetic studies involving families where some members have FTD and others have MND have shown a repeat of hexanucleotide sequence GGGGCC in chromosome 9 open reading frame 72 region (*C9ORF72*) [92,93].

FTLD shows atrophy or degeneration of frontal and/or temporal lobes along with microvacuolation and neuronal loss in the cerebral cortex [94]. By the use of immunohistochemistry, FTLD is associated with the accumulation of microtubule-associated protein tau and transactive response DNA-binding protein 43 (TDP-43). It can also be divided into two types (1) FTLD with tau-positive inclusions (FLTD-tau) and (2) FTLD with ubiquitin-positive and TDP-43-positive but tau-negative inclusions (FLTD-TDP) [95]. FLTD-tau mainly present as PNFA and overlap with Pick's disease while FLTD-TDP present mainly as SD and is associated with MND. Patients with bvFTD can show either of the two types of pathology [96,97]. Apart from TDP-43 involvement in MND, another protein called fused in sarcoma (FUS) is also associated with familial cases of dementia and MND [98].

4.3. Management

4.3.1. Investigations

MRI is the most useful investigation. Features of lobar atrophy may be observed. In bvFTD, there is involvement of frontal, temporal, cortical and subcortical areas (Figure 4). Hypoperfusion of these areas is also seen with SPECT and hypometabolism with PET. In the language variant, left temporal grey matter involvement is observed. Orbitofrontal cortex involvement is associated with behavioural changes in these patients. Also, cortical and subcortical hyoperfusion is found to be more marked on the left side [99]. A complete neuropsychological battery is necessary to fully characterise clinically these patients.

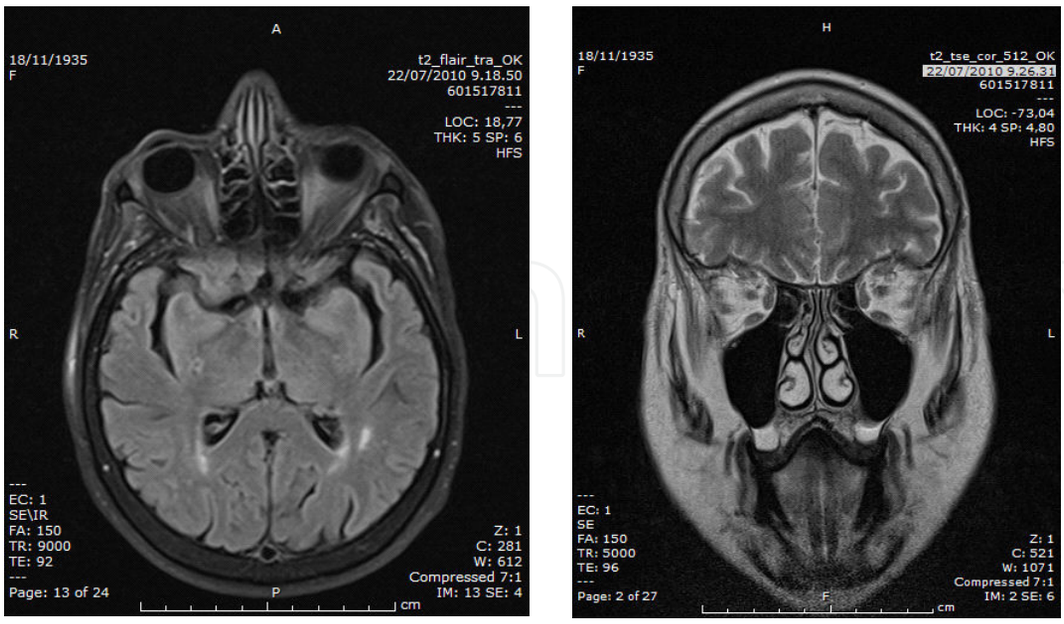


Figure 4. MRI brain scan (FLAIR and T2 sequences) of a 75 old woman with progressive FTD with mainly behavioural disturbances showing frontal and temporal lobe atrophy along with minor periventricular hyperintensities. She had deficit in executive and attention functions, aggressive behaviour and obsessive-compulsive disorder.

4.3.2. Treatment

No known or effective treatment exists for FTD. Treatment is mainly supportive or palliative. Multi-disciplinary management involving psychiatrist, physician, clinical psychologist and specialist nurse may be an effective way to treat patients with FTD.

4.4. Prognosis

The prognosis varies and to some extent depends on the type of FTD. The severity of the disease is more and clinical progression is faster in bvFTD [100]. In the language variant, the disease progression is slow with mainly impairment of language component for several years [89].

5. Dementia in other diseases

5.1. Dementia in Pick's disease

Pick's disease (PD) is a neurodegenerative disease. From the clinical point of view it overlaps with FTD but it is characterised by the presence of Pick bodies. These Pick bodies are argyrophilic, intraneuronal, cytoplasmic inclusions made up of three-repeat tau. Other fea-

tures include circumscribed atrophy of frontal and temporal lobes, gliosis and loss of neurons [101] as it has seen in FTD. Clinically, patients present with symptoms similar to FTD such as those of bvFTD, PNFA and SD as mentioned previously. Therefore, it is difficult to distinguish FTD from PD clinically. Post-mortem clinical correlation studies have shown that PD is associated more closely with behavioural and language associated symptoms and not with motor disturbances [102]. The age of onset is around 45 to 65 years [103, 104]. There are no known risk factors associated with PD. 'Knife-edge' atrophy is observed pathologically in the cortex which implies sharp, circumscribed degeneration (also referred to as 'dried walnut' appearance) [105]. There may also be the presence of swollen, ballooned neurons in the cortex called as Pick cells although they are not always present. No specific treatment is available at present for PD.

5.2. Dementia in Creutzfeldt-Jakob disease

Creutzfeldt-Jakob disease (CJD) is a subacute fatal neurodegenerative disease. It is the most common of the prion diseases to affect humans. Prion proteins are infectious-like agents that cause diseases termed as transmissible spongiform encephalopathies. Prion proteins are found normally in the cells of central nervous system and immune system [106]. However, a misfolded form of this protein is considered to be pathologic. CJD occurs as sporadic, genetic, iatrogenic or juvenile variant forms. Clinical features associated with CJD are a rapidly progressive encephalopathy with dementia, cerebellar ataxia and myoclonus [107]. It progresses to stupor and coma in few months. The sporadic form of CJD (sCJD) accounts for about 85 % of all CJD cases [108, 109]. The average age of onset is around 60 years. Median time to death is about 5 months and 85-90 % of patients die within 1 year of onset [110-112]. In the familial form, mutations in the gene *PNRP* that encodes the prion protein are seen. Autosomal dominant inheritance is observed. Disease progression is slower than sCJD. Iatrogenic form of CJD occurs accidently during surgical or medical procedures. In the juvenile variant form of CJD (vCJD), the age of onset is around 30 years. Other features include early psychiatric features (depression, anxiety, apathy), delay in dementia and duration of illness of more than 6 months [113,114]. Pathologically all cases of CJD have features of neuronal loss, spongiform changes (vacuolation in grey matter) and astrogliosis [107]. Pathological prion proteins can be observed via immunohistochemistry [113].

5.3. Dementia in Huntington's disease

Huntington's disease (HD) is a genetic cause of dementia. It is inherited as an autosomal-dominant trait. The mutation in the *huntingtin* gene (chromosome 4) producing the disease was identified in 1993 [115]. Mutant protein called huntingtin has an abnormal CAG repeats (at least 36) on the coding sequence of this gene. HD is characterised by chorea (involuntary, jerky movement of limbs spreading to all muscles of body), behavioural and psychiatric changes (mainly psychoses and depression) along with dementia. The onset is around middle age (about 40 years). Cognitive changes mainly slowing of intellectual capabilities and decline of executive functions occur and may sometimes be detected even before onset of motor symptoms [116, 117]. Dementia is progressive and increases as the course of the dis-

ease advances. Pathological features include neostriatal (caudate and putamen) atrophy in early stages of disease [118] and presence of intranuclear inclusions of mutant huntingtin in neurons of the striatum region of the brain [119]. Management includes genetic counselling, regular neurological and neuropsychiatric evaluation. Treatment is mainly symptomatic.

5.4. Dementia in Parkinson's disease

Parkinson's disease (PD) is a neurodegenerative disease mainly associated with motor symptoms. However, dementia develops in about 40 % of the sufferers [120,121]. Dementia developing after diagnosis of PD is termed as Parkinson's disease dementia (PDD). The prevalence of PDD in PD after 8-10 years has been found to be nearly 75 % [122,123]. Risk factors for developing early dementia are old age and severity of motor symptoms [123]. Clinical diagnostic features associated with PDD are impairment in attention, executive functions and memory. Other behavioural features are apathy, hallucinations and delusions [124]. Sleep disorders like RBD may be present and has been found to be associated with increased risk of developing PDD [125]. There are no investigations to diagnose PDD but there is association with hippocampal and medial temporal lobe atrophy [126]. SPECT studies have found abnormalities in dopamine transporter and occipital region hypoperfusion [127]. Cholinergic deficits are also observed and treatment with cholinesterase inhibitors has been found to be useful in PDD [128]. Treatment is otherwise symptomatic. Prognosis varies but PDD sufferers have been found to have increased risk of mortality [129].

5.5. Dementia in HIV disease

The HIV-1 virus is known to cause AIDS and also other neurological disorders. These neurological disorders are known as HIV-associated neurocognitive disorders (HAND). The most severe form of HAND is HIV-associated dementia (HAD) [130]. The annual incidence of HAD in 1990's was 7 % [131]. However, with the advent of highly active antiretroviral therapy (HAART), the incidence has decreased by more than half to about 2 to 4% [132-134]. The clinical features as part of the diagnostic criteriae include dementia, no evidence for presence of delirium nor any other cause for dementia [130]. Neuroinflammation in brain is observed. Viral proteins that are released from infected glial cells activate uninfected microglial cells and astrocytes to secrete cytokines and neurotoxins. This causes neuronal cell death i.e. neurodegeneration [135,136]. To help in detecting HAD, a rating scale has been developed which tests timed fingertapping, alternating hand sequence test and recall of four items at 2 minutes [137]. HAART is used as treatment of HAD. The aim is to suppress the virus and its replication in plasma and CNS [138]. Some of the drugs used in HAART regimen are a combination of efavirenz, lamivudine and zidovudine. Other medications like memantine, valproic acid and selegiline listed under adjunctive therapies have not been found to be useful in HAD [139]. HAD is associated with increased mortality with median survival time after dementia found to be 6 months [131].

6. Conclusions

The NAD or other dementias form a vital part of the fight against dementia and its consequences. Even though AD forms the bulk of dementia cases, knowledge and understanding of NAD might play an important role in the much needed quest for cure or prevention of dementia. More cutting-edge research into these diseases and their pathogenesis will help combat the spread and probably even onset of dementia.

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