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Review Article

Dementia; A Comprehensive Approach for Diagnosis and Management

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Abstract

Dementia is a disease of aging and it is one of the diseases with significant change in one's life. With an increasing aging population, the incidence and prevalence of the disease are also steadily increasing. It increases dependence on others and adds significantly to the cost of health. It is also a major stress for the children of Pakistani patients living alone while children are settled abroad. It's a slow onset and progressive disease with subtle clinical manifestation in the early stage. Also, it can be commonly confused with other health diseases and the differential diagnosis can be broad. The cost and complications of the disease increase further when there is a delay in the diagnosis and appropriate management.

This article aims to elaborate on the details of the disease, its varied manifestations and subtypes, and its management. Reversible causes of the disease are the main focus of this review article.

Keywords: Dementia, amnesia, memory loss, delirium, variants of dementia, Alzheimer's or vascular dementia

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Introduction

Dementia: Dementia is a degenerative disease, that causes loss of cognitive function including amnesia plus one of the following: affected higher mental functions, apathy, agnosia, aphasia, and/or apraxia.

What is a degenerative brain disease? Degeneration is a slow, progressive, and an irreversible process. Since it is very slow, it presents over months and evolves gradually, unlike recurrent vascular events, which present with sudden-onset add-on signs. Degeneration is the loss of neuronal cell bodies and brain volume, so atrophy is a hallmark of imaging. Degenerative disease doesn't explain any features of raised ICP (like headache, Papilledema, etc.) or neuronal irritability (seizures). Degenerative disease per se doesn't cause inflammation, so CSF is usually normal unless it's secondary to any underlying infection, immune, or paraneoplastic cause.

Degenerative diseases are more common in old age but in the case of genetic aetiology, the onset is at an earlier age and may progress rapidly. Findings for some of these diseases may initially be asymmetrical, but then they become symmetrical. Parkinson's disease is an example, as it is asymmetrical in the beginning.

At the time of diagnosis, reversible causes must be excluded, such as nutritional deficiencies including vitamin deficiencies, hypoxia, hypercapnia, thyroid disorders, metabolic causes (e.g., hypercalcemia, chronic acidotic states, hypoglycaemia or hyperglycaemia, uraemia, liver disease, etc), vascular insufficiencies, raised ICP due to any reason, infections (like TB, Neurosyphilis, HIV, fungal infections, encephalitis, CMV, Toxoplasma, neurocysticercosis etc) are reversible/treatable aetiologies which can present in a similar manner to degenerative diseases. Blood tests, CSF & MRI brain as clinically indicated will help identify reversible causes.[1,2]

A few examples of degenerative brain disease include Dementia, Parkinson's disease, Parkinson Plus Syndromes, Motor Neuron Disease & Cerebellar degenerative disease.

Pathogenesis & Clinical Manifestations of Dementia:

- **Amnesia** in isolation is loss of memory alone and without additional features does not amount to a diagnosis of dementia.
- **Delirium** is impaired consciousness with dementia-like symptoms and signs. Dementia per se doesn't explain loss or altered consciousness. Delirium is an acute process secondary to an underlying acute illness, stress or hospitalization. Delirium has fluc-

tuations and is reversible when the cause is removed. Delirium is common in patients with dementia. In such cases when delirium and dementia coexist in one patient, memory and other signs of dementia don't completely normalize after the delirium is alleviated. These symptoms and signs improve to some extent but don't completely resolve.

- **Apraxia** is inability to perform learned movements, skills or language. For example, one can't use spoon, button-unbutton shirt, etc. despite normal muscles and coordination.
- **Agnosia** is inability to interpret a sensory input. For example, one can see a spoon but is unable to say it's a spoon.
- **Apathy** is indifferent behaviour, lack of interest, and blunting of emotions.
- **Higher mental functions** are executive functions of the brain such as reasoning, judgment, personality, and language.
- **Behavioural and psychiatric symptoms** are often found in patients with dementia. These include sleep disturbances, loss of appetite, agitation, irritability, aggression, anxiety, or depression. These patients may have euphoria, frontal disinhibition, delusions, and/or hallucinations. These symptoms are prominent in Huntington's disease which usually starts in the 40s but can be part of any dementia. Lewy-Body dementia often has visual hallucinations. It's important to remember that primary schizophrenia rarely presents after the age of 30. So, the onset of psychotic symptoms in old age shouldn't be attributed to primary psychosis.[1,2,3]

Memory processing in the brain: Amnesia is memory loss, including recent (new memory, anterograde memory), and past memory. Memory loss is due to damage to structures involved in the memory circuit i.e., hippocampus, fornix, thalamus, hypothalamus, maxillary bodies, subcortical white matter, and cortex. New information (new or anterograde memory) enters the hippocampus and is run into the Papez circuit (hippocampus, fornix, thalamus, and mamillary body). The information is then circulated in the circuit for consolidation of the memory. With each subsequent repetition in the circuit, a fraction of the information is retained in subcortical and cortical memory storage neurons (mainly the frontal lobe). Memory is stored in these subcortical white matter and cortical neurons. Damage to the Hippocampus or fornix, maxillary body, or thalamus usually affects recent/new memory, but long-term memory is intact. Damage to the cortex and subcortical structures affects the long-term memory as well. The hippocampus is the most sensitive to anoxic, hypoxic, hypoglycaemic, metabolic, toxic, and nutritional insults.[1,2]

Severity of Dementia

- Severe dementia means loss of memory, impaired basic ADLs (activities of daily living), and reduced verbal expression to short sentences or single words.
- Moderate severity means further worsening of recent memory, inability to form new memories, and patients appear to be living in their past.
- Mild disease affects recent memory such as forgetting daily events, grocery lists, addresses, names, to-do lists, etc. Long-term memory, expressive language, and basic ADLs are preserved.
- MMSE score, MOCA, etc. are objective questionnaires used to document the severity of dementia.

Causes and Types of Dementia: The most common cause is Alzheimer's dementia which accounts for 60% of cases. The second most common cause after 65 years of age is vascular dementia. For people under the age of 65 years, the second most common cause is Fronto-Temporal Dementia (FTD).

Alzheimer's and FTD are not treatable or curable. Vascular dementia has some reversible risk factors which can be modified. Degeneration has a slow onset over months and years and is progressive. Vascular lesions can have rapid onset or rapid step-up of symptoms. Infections, autoimmune or malignancies can also have associated meningeal disease, and/or infectious/ inflammatory clues.

Reversible causes of dementia are uncommon, however, dementia's progression can be stopped or even reversed if the cause is identified and treated. These reversible factors include nutritional deficiencies, metabolic causes, toxins, drugs, infections and inflammation, hydrocephalus, space-occupying lesions, depression, etc.

Vascular dementia[3-7]: Dementia with focal neurological signs and imaging evidence of vascular pathology generally means probable vascular dementia if the dementia started after the vascular event(s). The presence of all these cardinal clues means probable vascular dementia. Definite vascular dementia is the presence of all these three cardinal clues plus histological exclusion of other possibilities (absent plaques, tangles, and Lewy bodies). The absence of all these cardinal clues (focal signs, imaging evidence and temporal relations of dementia with the vascular event) makes vascular dementia highly unlikely. The presence of less than three cardinal clues means possible vascular dementia. Vascular dementia is the second most common cause of dementia (almost 20% of cases in old age). It could be due to infarcts or bleeding causing brain damage. It often coexists with Alzheimer's dementia as both have common risk factors. Vascular insult can damage the brain and may unmask previously undiagnosed Alzheimer's disease.

Also, Alzheimer's is the most common dementia, and patients with Alzheimer's also have vascular risk factors due to age. It's less common to find vascular dementia in isolation.

Vascular versus Alzheimer's dementia: Ischemia damages the frontal lobe and basal ganglia more than the hippocampus, whereas Alzheimer's disease starts from the hippocampus. Therefore, executive functions are lost more in vascular than in Alzheimer's dementia. Memory is affected more in Alzheimer's than in vascular dementia. Vascular dementia often has a rapid onset, sudden step-up, new deficits, focal neurological signs (early gait issues, early incontinence, cerebellar, pyramidal, extrapyramidal, speech, cranial nerves, etc.), frontal pattern (executive and/or behavioural issues more than memory), and/or history of CVAs.

Vascular dementia patterns:

- Large vascular occlusions / ischemic stroke(s) (multi-infarct dementia) cause significant loss of brain tissue and dementia. These are large infarcts and are easily detected by brain imaging. Dementia may start within three months of a stroke. Stroke-causing dementia should be large, bilateral multiple, or at a critical location within the memory circuit. However, even a single, small infarct at a critical point in memory circuits can cause dementia. For example, a thalamus infarct can present with dementia due to loss of essential/critical neuronal connections.
- Microvascular occlusions (chronic small vessel ischemic changes) especially in deep white matter cause periventricular changes.
- Lacunar infarcts: Penetrating arterioles supply blood to deep subcortical grey nuclei such as the thalamus, basal ganglia, and subcortical white matter. These arterioles can be compromised by age, amyloid angiopathy, connective tissue disease, hypertension, arteriosclerotic disease, or CADASIL syndrome. Occlusion of these arterioles in CADASIL is due to the deposition of granular material which causes vascular occlusion. In addition, this deposition replaces the smooth muscles of blood vessels. Amyloidosis causes the narrowing of the arterioles and the replacement of smooth muscles by amyloid proteins. Amyloid vessels are fragile and bleed easily with small or large intra-parenchymal (cortex and subcortical) haemorrhages. The various causes of arteriolar occlusion cause lacunae formation or non-specific white matter changes. These lacunae are 3-20 mm round or oval areas of encephalomalacia due to strokes. The lacunae may present with stroke, TIA, or often no symptoms. Multiple lacunae or lacunae in a systemic location can cause dementia. Lacunae are usually multiple and bilateral. The presence of a minimum of two lacunae is needed to diagnose lacunar dementia. White matter changes are often around the lateral ventricle and/or in the white matter. These can be mild (punctuate) or severe (confluent, involving 25% or more of the white matter). Periventricular hyperintensities may be confused with demyelination. CADASIL or Binswanger's Disease cause multiple arteriolar infarcts in deep white matter producing empty spaces (lacunae) due to leukoencephalopathy, therefore are called multi-lacunar infarcts. CADASIL stands for cerebral autosomal dominant arteriopathy sigh subcortical infarcts and lacunae.
- Hypoperfusion causes ischemia of border zones (watershed infarcts) & mesial temporal lobe. Although the hypoperfusion is diffuse, the damage is selective due to the variable vulnerability of different areas of the brain. Hypoperfusion is caused by anoxia (shock, prolonged anaesthesia, hypotension, heart failure, etc.).
- Haemorrhagic strokes damage brain tissue and dementia may be a consequence. Pressure/mass affect and ischemia are the main mechanisms by which bleeding damages the brain.
- More than one pattern of vascular disease often coexists. Almost every case has small arteriolar disease making it the most common pattern of vascular disease leading to dementia.

The effectiveness of Acetylcholine esterase inhibitors or memantine is only mild to modest. These are not generally used for isolated vascular dementia unless associated with Alzheimer's dementia.

Alzheimer's Dementia:[7-12] Onset is usually after 65 years of age unless there is a strong genetic predisposition. Most cases are sporadic and 1% are due to autosomal dominant mutations in amyloid proteins (presenilin 1 or 2, or amyloid precursor protein). Alzheimer's dementia due to these mutations starts between the ages of 40-60, depending on the mutation and parental age at the onset of Alzheimer's. Gene mutations for Apo E4 have been implicated in sporadic cases of Alzheimer's disease. Alzheimer's dementia is also associated with many chromosomal disorders such as Down's syndrome which can present 10-20 years earlier in life. Chromosome 1, 14 and 21 have been linked with Alzheimer's disease.

Risk factors for Alzheimer's dementia:

- Heart disease, vascular diseases, and their risk factors. Age is the main risk factor as incidence is 2-5% above the age of 65 years and increases to >25-50% in those above 80 years. Aging has impaired repairing mechanisms and cumulation

of cardiovascular risk factors.

- Post-menopausal females are at higher risk of dementia than male patients. Smoking, diabetes, high cholesterol, hypertension, cardiovascular diseases, alcoholism, toxins, drug use, and nutritional deficiencies, are all predisposing risks.
- Educated people have more connections and synapses in the brain. This could be why dementia, especially Alzheimer's, is less common in educated people.
- Many cases of dementia have more than one cause. For example, patients with Alzheimer's disease and vascular dementia. This could be due to shared risk factors or multiple co-existing pathologies.

Findings in Alzheimer's dementia:

- Histologically, there are senile plaques and neurofibrillary tangles. Senile plaques are clusters of degenerating nerve endings with extracellular beta-amyloid proteins. Tangles are paired helical filaments of phosphorylated tau-proteins.
- Damage to neurons is mediated by glutamate over activity exciting neurons and promoting intracellular calcium accumulation within mitochondria leading to cell death. Physical damage due to the accumulation of plaques and tangles also damages neurons. Free radicles, aluminium deposition, and apoptosis are likely contributing factors.
- Acetylcholine is deficient in many neurons, especially in those of the neocortex and hippocampus which are the main sites affected. Serotonin and norepinephrine are also reduced especially in young age onset AD.
- These amyloid plaques can be detected by FDG-PET scan.
- MRI Brain shows atrophy of the hippocampus in the early stage. The atrophy spreads to other parts such as the cortex with the progression of the disease.

Lewy Body Dementia:[7,8,9] Lewy bodies are cross-linked alpha-synuclein proteins in the cytoplasm of the neurons. Normally, these proteins maintain neurotransmitters and the functioning of nerve terminals. Cross-linking of these proteins reduces the availability of neurotransmitters in the nerve terminals, especially acetylcholine and dopamine. These cause dysfunction and degeneration of neurons. Unlike other dementias, the occipital lobe is also involved, and patients often have visual hallucinations and visuospatial deficits, in addition to dementia. Visual hallucinations are present in 80% or more cases and aid the diagnosis of LBD. These visual hallucinations are often well-formed such as seeing humans, or animals, feeling the presence of someone, etc. Visual illusions are also present. Memory and naming are affected to a lesser degree than attention, visuospatial tasks, and executive functions.

Rapid eye movement (REM) behaviour is common and may be present earlier than other signs of dementia. That includes acting upon dreams and having vigorous limb movements that may hurt the patient or the partner. Other conditions that can cause such movements are OSA (obstructive sleep apnoea), periodic limb movements, or confused awakening of a demented patient. Sleep studies can help differentiate. Over time, the REM behaviour may settle down or decrease in intensity. REM atonia is also absent. These sleep disturbances may be reasons for daytime somnolence and fluctuations in consciousness. Fluctuations in behaviour, attention, or consciousness is common in LBD. These fluctuations in consciousness can confuse LBD with delirium or even syncopal episodes. Daytime drowsiness or staring in space (consciousness), failure to do the repeated task (attention), variable behaviours, etc. are examples of these fluctuations. Fluctuations in the early stage of dementia indicate LBD (otherwise, any advanced dementia may have these fluctuations, too).

Memory and naming are assessed by recalling events, remembering a list of items, etc.

Assessment of visuospatial abnormalities can be checked by copying complex figures, visual organization of objects, trail-making tasks / organizing blocks, visual size matching, line orientation, computerized tasks for reaction time, etc.

Parkinsonism in LBD is found in 80-85% of cases but it may not be there in the early stage. Secondly, patients don't have all classic signs of Parkinsonism (bradykinesia, rigidity, resting tremors, etc.), and usually one is enough to diagnose Parkinsonism.

Extreme sensitivity to dopamine (D2) blocking drugs is present in many cases and these medications should be avoided. This may also be a clue for diagnosis.

Additional features of LBD:

- Relatively spared or normal hippocampus on MRI (AD almost always causes atrophy of the hippocampus).
- Reduced DAT uptake is seen in LBD, Parkinson's disease, Parkinson's plus, and frontotemporal dementia. It's uncommon in Alzheimer's disease. Therefore, if Parkinson's is the only additional finding (in addition to dementia) then other causes of dementia with Parkinson's such as CBD or Parkinson's plus are also possible.
- Reduced FGD-PET uptake & slow EEG activity in the occipital lobes. Relatively normal FDG-PET uptake is seen in the cingulate gyrus (unlike

AD).

- Absent atonia during REM sleep on sleep studies (PSG, polysomnography). The presence of REM behaviour with the absence of REM atonia is very strongly suggestive of LBD, even in the absence of other clinical clues.
- Iodine MIBG scintigraphy shows reduced cardiac uptake in LBD. This uptake measures sympathetic innervation of the myocardium and is reduced in cardiac diseases (heart failure, ischemic heart disease) and autonomic neuropathies (diabetes).
- Medial temporal atrophy and reduced hippocampus FDG-PET uptake, elevated degenerative markers in CSF (tau, phospho-tau, amyloid beta), and/or tau-PET showing plaques in a patient with LBD indicate co-existing Alzheimer's disease.

FTD (Fronto-Temporal Dementia):[7,9,10,12] There is degeneration (atrophy) of the frontal and/or temporal lobe. This type of dementia starts in the younger age group of 40 to 50-year-olds. A combination of genetic and environmental factors plays a role in the pathogenesis. It affects the frontal lobe and temporal lobe. The frontal lobe is affected much earlier than the temporal. It commonly starts with personality changes (due to frontal lobe disease), behavioural problems, and language. Memory is affected late (unlike AD) and visuospatial abnormalities are not common (unlike LBD).

- Behavioural and social issues with FTD often confuse it with psychiatric diseases and delay the diagnosis. It can have a predominantly behavioural or speech variant either separate or concomitantly. With the progression of the disease, both variants overlap and combine. These behavioural and language abnormalities have a significant impact on an individual's life such as social relations, parental and family roles, work, etc. Behavioural variant FTD causes changes in character and social behaviour which explains many of these changes. The behaviour changes are also common in vascular dementia which affects the white matter of the frontal lobe. Impairments of social behaviour present with blunting of emotions, apathy, reduced social interactions, mood, temperament control, and disinhibition. These are more prominent with the atrophy of orbital and medial frontal lobes and temporal lobes.
- Personality changes such as lack of self-care, lack of self-awareness, fixed repetitive behaviour, changes in food preferences, increased food intake especially carbohydrate craving, changes in likes and dislikes, repeated unchanging actions done as if they are rituals, and feeling compelled to do, reduced cognitive flexibility, reduced attention span and easy distractibility. Amotivation and inertia are prominent. These are more with atrophy of the dorsolateral frontal lobe. The most characteristic among these features which favour FTD are changes in eating, repeated rituals (motor and/or verbal), and emotional blunting.
- Language variant affects object recognition and naming. Syntactic (grammatical) comprehension is often affected. It also affects expressive language (such as repetition of phrases and words) as well. Aphasia is progressive and can be non-fluent (Broca) or fluent (Wernicke's). Mutism (total loss of language) is the final outcome in many cases and can be confused with progressive aphasia. Motor neuron disease (MND) can have similar deficits and may be a part of MND-FTD syndrome.
- Amnesia and other higher mental functions are also gradually affected but memory loss is late, unlike AD which starts with memory issues.
- Diagnosis of FTD is mainly clinical based on language deficits, abnormal social behaviour, apathy & personality changes, changes in eating behaviour, repetitive behaviour, absence of significant amnesia, and lack of visuospatial abnormalities point toward FTD.

Dementia due to nutritional deficiencies & toxins:[13-17]

- Deficiency of vitamins B1, B6 and B12 causes neuronal damage.
- In addition to nutritional deficiencies, alcoholism can cause direct brain tissue damage.
- Hypoxia, hypoglycaemia & hyperglycaemia can damage neurons when severe, prolonged or recurrent.
- Hypothyroidism can also damage neurons by relative hypoxia, in addition to dysfunction due to the deficiency of thyroid hormones.
- Chronic poisoning (lead, mercury, arsenic, nickel, insecticides, pesticides, carbon monoxide, aluminium, drugs, etc.) also causes dementia by neuronal damage.
- Drugs include medications that can cause low blood pressure (overuse of anti-hypertensive drugs), drugs that suppress neurons (anti-epileptics, anti-psychotics), anticholinergic drugs that reduce acetylcholine activity, anti-cancer drugs (damage neurons and axons) are notorious for causing dementia-like clinical findings.

Organ failures and dementia:[13-18]

- Hepatic toxaemia and encephalopathy affect cognitive functions. Nutritional deficiencies in liver disease and alcohol also add to the insult.

- Uremic dysfunction of neurons and chemicals used in dialysis such as aluminium, etc. causes dementia in Chronic Kidney Disease (CKD). Associated vascular risk factors can cause vascular dementia as well.
- Hypoxia due to heart or lung disease, or hypoperfusion due to cardiac diseases also causes dementia.

Infectious causes of dementia:[19-20]

- HIV causes dementia in almost one-third of cases infected with the virus. Cytokines produced from the infected macrophages and glial cells can damage neurons. Subcortical structures are predominantly damaged. The use of anti-HIV drugs reduces risk and stops the progression of HIV-related dementia.
- Neurosyphilis can also cause dementia, typically after greater than 10 years from the initial infection, if left untreated. Other associated signs such as Argyl Robertson pupil (loss of light reflex due to damaged pre-rectal nuclei in midbrain, preserved accommodation reflex), posterior spinal cord ganglion involvement (tabes dorsalis), etc. often are the clues. Serology tests for Syphilis on blood and/or CSF are helpful for diagnosis, Treatment with penicillin is given.
- Chronic meningitis due to TB, fungus, Syphilis, etc. also causes dementia due to brain damage.
- Encephalitis due to any cause such as herpes simplex or many other viruses can also cause dementia.
- Creutzfeldt-Jakob Disease (CJD) is an infection caused by prions. It causes rapidly progressive dementia over months and death within a year. It causes spongiform changes in the brain. Patients have dementia, encephalopathy, and damage to pyramidal & extrapyramidal structures.

Tumors and Paraneoplastic Dementia:[19-21] Tumors can cause dementia by damaging the brain directly due to pressure effects (primary or metastatic brain disease) or by paraneoplastic mechanism (autoimmune encephalitis), biochemical changes (hypercalcemia, hormones), depression, or chemotherapy/ radiotherapy-related brain damage.

Meningioma or glioblastoma of the frontal lobe can present with dementia (pressure / mass effects). Small cell lung carcinoma often causes limbic encephalitis via antibodies. A search for malignancy as a cause is needed when clinically indicated. Clues to suspect malignancy may be smoking, weight loss, raised ICP or focal neurological signs, and/or rapid onset (weeks to months). Paraneoplastic antibodies and imaging (CT and/or PET Scan) are often needed.

Dementia due to trauma:[20-21] Severe brain injury, repeated injuries, and/or concussion can damage brain tissue. Boxers are well known for this disease.

Dementia due to depression and psychiatric causes:[22-23] Depression increases the risk for dementia, which may be due to disuse loss of neuronal connections. Depression also suppresses cortical functioning and mimics dementia without any structural damage to the brain (pseudo dementia). This pseudo-dementia often fluctuates due to fluctuations in depression and is also reversible when depression is treated. It's important to remember that dementia per se also commonly causes depression or even psychotic symptoms. Treating depression should resolve the cognitive decline completely in cases of depression leading to dementia like symptoms. Persistent cognitive deficits when depression is treated means underlying dementia.

Wilson's Disease and Dementia: Copper deposition in basal ganglia and subcortical nuclei causes extrapyramidal manifestations. Later, the spread of the copper deposition to the cortex can lead to dementia-like symptoms such as personality changes, social disinhibition, and psychiatric issues such as depression. Cognitive decline is less common.

Huntington's disease (HD) and dementia: It's a genetic disease with CAG tandem repeats. Abnormal Huntington protein is found and causes neuronal degeneration. HD presents with extrapyramidal disorder (Parkinson's, chorea, etc.), psychosis and dementia. Acetylcholine is reduced and dopamine is increased in adult-onset classic HD. This increased dopamine can explain psychosis and chorea.

Parkinson's disease and dementia: Parkinson's and its variants such as corticobasal degeneration often cause dementia. Almost, 1/3rd cases of PD may also develop into dementia due to the progression and, the spread of the degenerative process.

Normal Pressure Hydrocephalus (NPH) and Dementia: NPH commonly affects the anterior horn of lateral ventricles which are close to the medial side of the frontal lobe (which controls lower limbs) & the orbital area (which controls urinary and bowel sphincters) and the white matter of the anterior frontal lobe (cognition). Therefore, NPH commonly presents with gait apraxia (or spastic gait), incontinence, and subcortical frontal lobe dementia (causing personality changes).

Investigations for dementia:[24-28] Workup is mainly to find any reversible cause and treat it. Degenerative causes are common but not treatable. Exclusion of drugs, toxins, nutritional deficiencies, metabolic, and endocrinal causes such as hypothyroidism, and infections is important for every case. Workup for malignancies, autoimmune diseases, and rare causes is based on clinical impression.

MRI Brain is the preferred imaging modality, that excludes underlying structural and vascular causes and detects atrophy/damage to the affected part of the brain, especially the frontal and temporal lobes. Cause-specific findings often provide diagnostic help. Caudate atrophy is common in Alzheimer's. Occipital atrophy favours Lewy Body Dementia. CT Brain is not as sensitive as MRI.

FDG-PET Scan often shows abnormalities (low uptake) in the hippocampus (Alzheimer's), occipital lobe (Lewy Body Dementia), etc. FDG-PET also detects amyloid plaques favouring Alzheimer's (but can be seen in other causes such as LBD).

The severity of the dementia is assessed by various tools such as mini-mental state examination (MMSE) and/or Montreal cognitive assessment (MOCA). These are often helpful to have an objective assessment and monitor progression.

Table 1: *MMSE score and severity of dementia*

Score	25-30	21-24	10-20	<10
Severity	Normal	Mild	Moderate	Severe

Table 2: *MoCA score and severity of dementia.*

Score	>25	18-25	10-17	<10
Severity	Normal	Mild	Moderate	Severe

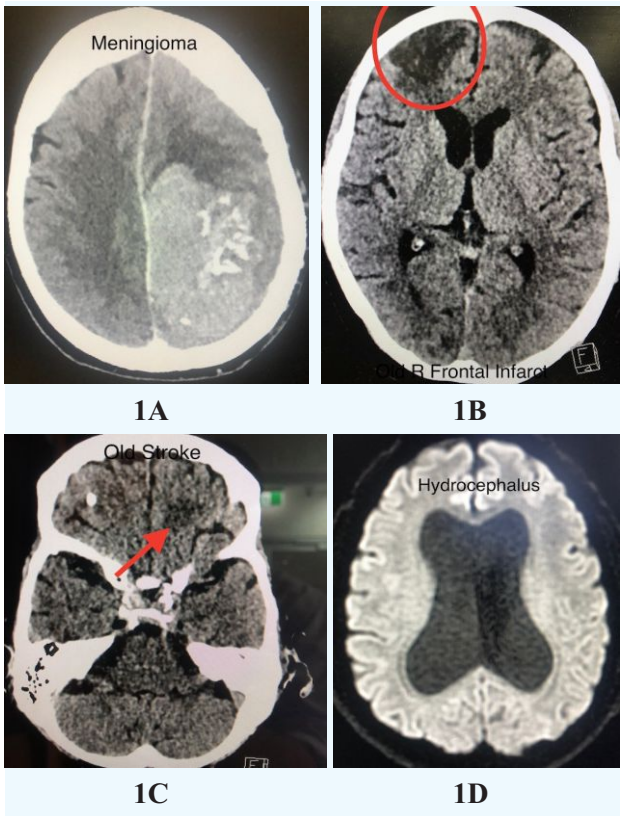

Figure 1: *1A a case of meningioma presented with amnesia & sensory changes. 1B a case of frontal dementia and CT demonstrated frontal infarct. 1C same as 1B except the CT shows a lacunar infarct in deep frontal white matter. 1D dementia and headache turned out to be hydrocephalus.*

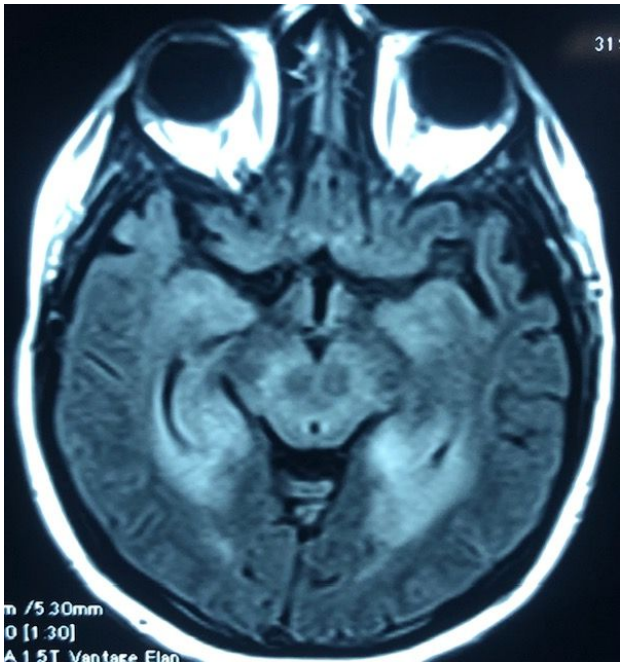

Figure 2: *Extensive GBM (Glioblastoma Multiforme) in a young patient who started with a headache, behavioural changes, and amnesia.*

Treatment of dementia:[29-34] Treatment of any reversible cause is essential, as it often stops the progression of the disease. Reversal is likely in the early stages or when structural brain damage isn't there.

- Subclinical thyroid diseases should be treated as well.
- Vascular risk factors should be treated when applicable. These risk factors are common for Alzheimer's and vascular dementia. This is one reason both these types of dementia often coexist.
- Nutritional replacement is necessary for any deficiency of vitamins.
- Hypoglycaemia should be prevented, and blood glucose control targets should be re-evaluated.
- Organ failures such as uraemia or hepatic disease, hypotension, or hypoxia/hypercapnia should be treated.
- Electrolyte abnormalities of sodium, calcium, magnesium, or acidosis should be treated.
- Treatment of surgically correctable causes such as NPH, hematoma, tumor, etc. is often helpful if the patient is fit for such procedures. NPH is managed by acetazolamide, repeated LPs, or VP shunting.

Acetylcholine-Esterase inhibitors (Donepezil, rivas-

tigmine, galantamine) are options for mild to moderate Alzheimer's or Lewy body disease if there are no contraindications such as bradycardia or heart blocks. These may help with behavioural issues in FTD but there have been reports of worsening of symptoms in some cases. These are not recommended for vascular dementia as efficacy is low to modest. These also cause cholinergic GI side effects such as diarrhea, vomiting, or pain. These are equally effective.?

Memantine is an NMDA receptor antagonist used for moderate to severe Alzheimer's and Lewy body dementia. It is not used for vascular dementia, as efficacy is low to modest. Its effect is mixed in FTD but may help with behavioural symptoms. It is used if a patient with moderate dementia is intolerant to cholinesterase inhibitors or for severe dementia.

Antidepressants are often needed for depression. It's worth noting that depression increases the risk of dementia, likely due to disuse loss of neuronal connections. Tricyclic anti-depressants (TCAs) should be avoided due to anticholinergic activity. Selective serotonin reuptake inhibitors (SSRI) & selective nor-epinephrine reuptake inhibitors (SnRI) are safer options. Depression with vascular disease is difficult to treat. SSRIs are useful for FTD as they improve behaviour, eating issues, and disinhibition.

Antipsychotics are used for psychotic symptoms but may worsen cognitive functions and cardiovascular mortality in dementia cases. Therefore, it is preferable to avoid antipsychotics in dementia if possible. Patients with LBD shouldn't be given D-2 blocker antipsychotics due to sensitivity and worsening of confusion and Parkinson's. Quetiapine or olanzapine are relatively safe. Serotonin antagonists (pimavanserin) are also effective. Atypical antipsychotics such as Aripiprazole help control psychotic symptoms in FTD.

Dopaminergic drugs for Parkinson's in LBD can worsen psychosis. Also, these are not as effective as in Parkinson's Disease. A low dose of levodopa may be used if the symptoms are severe or cause falls.

Sleep issues can be treated with Melatonin. Clonazepam can help sleep disorders but can worsen cognitive decline. Treating sleep disorders may require input from sleep specialists.

Supportive care is needed for symptom management:

- Behavioural therapy helps FTD and dementia-related behavioural issues.
- Occupational therapist (OT) assessment helps document the severity of cognitive decline by MMSE, MOCA, and other tools. It also helps modify day-to-day activities of life such as providing clues, home alterations, etc.
- Swallowing is assessed by a speech pathologist. If unsafe for swallowing, enteral feeding (PEG / PEJ tube) may be an option for patients with a short life expectancy.
- Patients may ultimately need nursing home placement when the dementia is moderate to severe.

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