QUESTION 71

An 86yo woman with moderate Alzheimer’s disease, including difficulty with language, is increasingly agitated and believes there are people living in her ceiling, despite ongoing reassurance to the contrary. The patient lives with her son who seeks your advice regarding management of these delusions.

Which of the following would be most beneficial?

A. Commence a benzodiazepine
B. Find alternative accommodation
C. Isolate and rest the patient in her room
D. Address factors in the home that exacerbate the delusion
E. Commence respite in a day care centre

Answer = D

Dementia = an acquired deterioration in cognitive abilities that impairs the successful performance of ADLs. Impairment in memory plus language, visuospatial ability, calculation, judgement or problem solving.

CAUSES OF DEMENTIA

Table 350–1. Differential Diagnosis of Dementia

<table>
<thead>
<tr>
<th>MOST COMMON CAUSES OF DEMENTIA</th>
<th>LESS COMMON CAUSES OF DEMENTIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's disease</td>
<td>Toxic disorders</td>
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<tr>
<td>Vascular dementia</td>
<td>- Drug, medication, and narcotic poisoning</td>
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<tr>
<td>Multi-infarct</td>
<td>- Heavy metal intoxication</td>
</tr>
<tr>
<td>Diffuse white matter disease</td>
<td>- Dialysis dementia (aluminum)</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>- Organic toxins</td>
</tr>
<tr>
<td>Parkinson's disease (20% develop dementia)</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>Drug/medication intoxication</td>
<td>- Depression (pseudodementia)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>- Schizophrenia</td>
</tr>
<tr>
<td>Adrenal insufficiency and Cushing’s syndrome</td>
<td>- Conversion reaction</td>
</tr>
<tr>
<td>Hypo- and hyperparathyroidism</td>
<td>Degenerative disorders</td>
</tr>
<tr>
<td>Renal failure</td>
<td>- Huntington's disease</td>
</tr>
<tr>
<td>Liver failure</td>
<td>- Pick's disease</td>
</tr>
<tr>
<td>Pulmonary failure</td>
<td>- Dementia with Lewy bodies</td>
</tr>
<tr>
<td>Chronic infections</td>
<td>- Progressive supranuclear palsy (Steel-Richardson syndrome)</td>
</tr>
<tr>
<td>HIV</td>
<td>- Multisystem degeneration (Shy-Drager syndrome)</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>- Hereditary ataxias (some forms)</td>
</tr>
<tr>
<td>Papovavirus (progressive multifocal leukoencephalopathy)</td>
<td>- Motor neuron disease [amyotrophic lateral sclerosis (ALS); some forms]</td>
</tr>
<tr>
<td>Prion (Creutzfeldt-Jakob and Gerstmann-Sträussler-Scheinker diseases)</td>
<td>- Frontotemporal dementia</td>
</tr>
<tr>
<td>Endocrine and other organ failure:</td>
<td>- Cortical basal degeneration</td>
</tr>
</tbody>
</table>
- Tuberculosis, fungal, and protozoal
- Sarcoidosis
- Whipple's disease
- Head trauma and diffuse brain damage
  - Dementia pugilistica
  - Chronic subdural hematoma
  - Postanoxia
  - Postencephalitis
  - Normal-pressure hydrocephalus
- Neoplastic
  - Primary brain tumor
  - Metastatic brain tumor
  - Paraneoplastic limbic encephalitis

- Multiple sclerosis
- Adult Down's syndrome with Alzheimer's
- ALS—Parkinson's—Dementia complex of Guam
- Miscellaneous
  - Vasculitis
  - CADASIL
  - Acute intermittent porphyria
  - Recurrent nonconvulsive seizures
- Additional conditions in children or adolescents
  - Hallervorden-Spatz disease
  - Subacute sclerosing panencephalitis
  - Metabolic disorders (e.g., Wilson's and Leigh's diseases, leukodystrophies, lipid storage diseases, mitochondrial mutations)

- Potentially reversible dementia.

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### Table 350-3. Clinical Differentiation of the Major Dementias

<table>
<thead>
<tr>
<th>Disease</th>
<th>Initial Symptom</th>
<th>Mental Status</th>
<th>Neuropsychiatry</th>
<th>Neurology</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>Memory loss</td>
<td>Episodic memory loss</td>
<td>Initially normal</td>
<td>Initially normal</td>
<td>Entorhinal and hippocampal atrophy</td>
</tr>
<tr>
<td>Vascul</td>
<td>Often sudden; variable initial symptoms; apathy, falls, focal weakness</td>
<td>Frontal/executive cognitive slowing; can spare memory</td>
<td>Apathy, delusions, anxiety</td>
<td>Usually motor slowing, spasticity; can be normal</td>
<td>Cortical and/or subcortical infarctions, confluent white matter disease</td>
</tr>
<tr>
<td>FTD</td>
<td>Apathy; reduced judgment/insight/speech/language; hyperorality</td>
<td>Frontal/executive, language; spares drawing</td>
<td>Apathy, disinhibition, hyperorality, euphoria, depression</td>
<td>Vertical gaze palsy, axial rigidity, dystonia, alien hand (due to PSP/CBD overlap)</td>
<td>Frontal and/or temporal atrophy; spares posterior parietal lobe</td>
</tr>
<tr>
<td>DLB</td>
<td>Visual hallucinations, REM-sleep disorder, delirium, Capgras syndrome, parkinsonism</td>
<td>Drawing and frontal/executive; spares memory; delirium prone</td>
<td>Visual hallucinations, depression, sleep disorder, delusions</td>
<td>Parkinsonism</td>
<td>Posterior parietal; hippocampi larger than in AD</td>
</tr>
<tr>
<td>Prion</td>
<td>Dementia, mood changes, anxiety, movement disorder</td>
<td>Variable, frontal/executive, focal cortical, memory</td>
<td>Depression, anxiety</td>
<td>Myoclonus, rigidity, parkinsonism</td>
<td>Cortical ribboning and basal ganglia hyperintensit</td>
</tr>
</tbody>
</table>
Note: AD, Alzheimer’s disease; FTD, frontotemporal dementia; PSP, progressive supranuclear palsy; CBD, cortical basal degeneration; DLB, dementia with Lewy bodies; MRI, magnetic resonance imaging.

ALZHEIMER’S DEMENTIA

Clinical Manifestations

- Characterised with insidious onset memory loss progressing over time to include dyspraxia, dysphasia and personality change
- 20% of patients do not present with memory complaints but with other problems such as word-finding, organisational or navigational difficulties
- In end-stage AD, patients may become rigid, mute, incontinent and bedridden
- Typical duration 8 to 10 years (ranges from 1to 25 years)

Diagnosis

- Imaging may be normal early in disease
- Late in disease, diffuse cortical atrophy and hippocampal atrophy on MRI
- Laboratory tests should be essentially normal

Epidemiology

- Major risk factors are age and family history
- 20-40% of population over 85yrs affected

Pathology

- Most severe in hippocampus, temporal cortex and nucleus basalis of Meynert
- Neuritic (senile) plaques and NFTs accumulate in small numbers in normal aging but in excess in AD
- Neuritic plaques contain a central core that includes amyloid, proteoglycans, apo E4, alpha-1, antichymotrypsin and other proteins
- Plaque core surrounded by debris of degenerating neurons, microglia and macrophages
- Amyloid angiopathy = accumulation of amyloid in cerebral arterioles – can lead to cerebral lobar haemorrhages
- NFTs are twisted neurofilaments that represent abnormally phosphorylated tau protein

Genetics

- Some cases of AD are related to certain genes (eg: point mutations in APP gene on chm 21 causes early-onset AD)
- Adults with trisomy 21 who survive beyond age 40 consistently develop progressive dementia typical of AD
- A couple of other genes have been identified which are associated with early onset AD
- ApoE (especially ApoE4) on chm 19 associated with late-onset familial and sporadic forms of AD – may be involved in the clearance of amyloid

**Treatment**

- Avoid cholinesterase inhibitors where possible
- Non-pharmacological treatment is most important
- **Cholinesterase inhibitors** offer modest benefits in mild to moderate AD – slow decline
- Donepezil is usually first choice as once daily and fewer side effects
- No clear evidence to suggest that switching agents will produce a better response
- Side effects include GI upset, insomnia, vivid dreams, asthma, bradyarrhythmias, cramps and dizziness
- **Memantine** is an antagonist of NMDA and is for moderate to severe AD – may slow deterioration

**Treating Behavioural Disturbances**

- Avoid typical antipsychotics in patients with suspected DLB or Parkinson’s disease
- To control hallucinations, delusions or seriously disturbed behaviour use risperidone, olanzapine or haloperidol
- To relieve symptoms of anxiety or agitation give oxazepam 15mg once to 4 times a day (for short time only)

**VASCULAR DEMENTIA**

- Can be divided into multi-infarct dementia and diffuse white matter disease
- Often step-wise decline but can be gradual with diffuse white matter disease (due to multiple lacunar infarcts)
- Tau may play a role in familial forms
- CADASIL is a form of dominantly inherited diffuse white matter disease = cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
- Progressive dementia in the 5th to 7th decades in multiple family members who may also have a history of migraine and recurrent stroke without HT
- Due to mutations in notch 3 gene which can be tested for
- No treatment

**FRONTOTEMPORAL DEMENTIA**

- Begins between 50 and 70 yrs
- Behaviour symptoms, predominate early, memory typically spared
- Planning, judgement and language commonly affected
- Can sometimes have motor abnormalities early
- Poor insight
- Late in disease, apathy and withdrawal
- Marked atrophy of temporal and/or frontal lobes, can be asymmetrical
- Tau plays a role
- Large overlap with PSP, CBD and MND
- Pick’s disease usually refers to a subset of FTD patients with certain pathological findings
- Symptomatic treatment only
PROGRESSIVE SUPRANUCLEAR PALSY

- Begins with falls and a vertical supranuclear gaze paresis
- Progresses to symmetric rigidity and dementia
- Stiff posture, hyperextension of the neck, slow gait, frequent falls
- Limited voluntary eye movements but oculocephalic reflexes (doll’s head manoeuvre) retained therefore supranuclear
- Dementia similar to FTD

CORTICAL BASAL DEGENERATION

- Slowly progressive dementia
- Typically presents with unilateral onset with rigidity, dystonia and apraxia of one arm and hand ("alien hand")
- Eventually becomes bilateral and includes dysarthria, slow gait, action tremor and dementia

DEMENTIA WITH LEWY BODIES

- Visual hallucinations, parkinsonism, fluctuating alertness and falls
- Dementia may precede or follow parkinsonism
- Fluctuating pattern
- Usually better memory but worse visuospatial deficits than AD
- Lewy bodies are intraneuronal cytoplasmic inclusions, found in cortex, amygdala, cingulated cortex and substantia nigra
- Anticholinergics may help
- Dx on MRI or SPECT