Part II – Neurological Disorders

CHAPTER 17
DEMENTIA

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NEUROLOGY IN AFRICA

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CHAPTER 17

DEMENTIA

Dementia is a general term for any disorder in which there is progressive loss of higher cortical functions. These higher functions include memory, language production and understanding, visuospatial function, and "executive" or frontal lobe function e.g. planning and judgement. Dementia is not a diagnosis in itself, it is simply a consequence of a wide variety of underlying conditions, such as: degenerative brain disease e.g. Alzheimer's disease (AD), cerebrovascular disease, cerebral infections e.g. HIV infection, deficiency states e.g. B-12, metabolic disorders e.g. hypothyroidism and substance misuse e.g. alcohol. The core features of dementia are impairment in at least two areas of higher cortical function, usually memory plus one other. There is a decline from a previous level of functioning severe enough to interfere with activities of daily living such as work, family or social activities and there is a progression over time. The aim of this chapter is to present a brief overview of dementia. The student should aim for an overall understanding of dementia including definition, aetiology, main clinical features, diagnosis and management.

Key points

- dementia is a loss of memory & at least one other cognitive function
- loss is sufficient to interfere with the activities of daily living
- loss of higher cortical functions is progressive
- need to exclude treatable causes of dementia

EPIDEMIOLOGY

Dementia affects >2% of the population in high income countries at the age of 65 years, with the prevalence doubling every five years thereafter. Thus by the age of 85 years approximately one third of the population there have a dementia of some type. However because of population distribution most persons with dementia now live in low or middle income countries and as life expectancy lengthens that burden is set to increase. There are few studies on dementia from Africa, but age adjusted studies from there in whole populations aged 65 years and over suggest a lower overall burden of 1-3%, this is in comparison to rates of 5-10% in similar age groups in other low and middle income parts of the world. However, the current HIV epidemic in Africa is increasing the overall burden of dementia there but in a mainly younger population.

AETIOLOGY

The main causes of dementia are Alzheimer's disease, cerebrovascular disease and HIV disease. Less common degenerative causes include frontotemporal dementia (FTD) or Pick's disease, dementia with Lewy bodies (DLB), Parkinson's disease with dementia (PDD) and Huntington's disease (Table 17.1). Treatable causes of dementia include HIV, B-12 deficiency, hypothyroidism, alcoholism and rarely syphilis. The differential diagnosis of dementia in Africa includes chronic confusional and psychiatric states, chronic brain disorders, tumours and subdural haematoma.

Main causes of dementia in Africa

- Alzheimer's disease
- cerebrovascular disease
- HIV
- alcohol

Risk factors

The main known risk factors are old age, genetic predisposition (e.g. APO-E genotype) and vascular risk factors such as hypertension, hypercholesterolaemia and diabetes. Diet, lifestyle and lower level of education may also be risk factors. At present there are no known specific preventatives or curative measures for most forms of dementia.

Table 17.1 Classification and main features of dementia

Dementia type	Frequency*	Overall %	Main clinical features
Dementia (all causes)	2 % @ 65 yrs 33% >85 yrs	100%	progressive loss of two or more intellectual functions (e.g. memory, language), sufficient to disrupt daily life
Alzheimer's disease	1.5% @ 65 yrs commonest cause of dementia in later life	60%	core feature is usually poor day-to-day memory, language and visuospatial function
Vascular dementia	0.5% @ 65 yrs	20-30%	usually a history of stroke with physical signs such as limb weakness & dysarthria: cognitive impairment may take many forms
Frontotemporal dementia	less common than AD but an important cause of young-onset dementia: accounts for up to 20% of patients with dementia aged 45-65 years (HIV excluded)	<10%	***frontal:*** insidious changes in personality and behaviour, other domains often intact ***temporal:*** progressive aphasia, fluent or non-fluent
HIV associated dementia	10-20% of patients with advanced HIV	not-known	non-specific: generalised cognitive and motor slowing with poor day-to-day memory
Dementia with Lewy bodies	less common	<1%	parkinsonism, fluctuations, visual hallucinations

** based on high income countries*

General course and prognosis in dementia

By definition, dementia is a progressive disorder. Consciousness is not altered, but with time impairments of higher function extend into all cognitive areas (see appendix 1). The level

of functioning declines until patients are entirely dependent on others for their care. Death follows either directly from the failure of core brain systems or more often as a secondary consequence of complications such as pneumonia, untreated pressure sores and venous thrombosis. The duration and course of dementia depends on the cause but typically lasts for years. Life expectancy in Alzheimer's disease is about 6-7 years from onset in high income countries.

ALZHEIMER'S DISEASE

Alzheimer's disease is the commonest cause of dementia worldwide (Table 17.1). It is reported to be less common in Africa as compared to similar aged populations in high income countries, including Afro-Americans. However studies from Africa suggest that it still accounts for >60% of all cases of dementia there. Its main cause is unknown. It is rare under 45 years of age but thereafter its prevalence rises exponentially with age and increasingly after 65 years of age. It is associated with a positive family history of dementia and affects females more than males.

Genetics

Alzheimer's is usually a sporadic disease, but can occasionally be familial when it is autosomal dominant, due to mutations in the genes for presenilin 1 & 2 (PS1 & 2) or amyloid precursor protein (APP) on chromosome 21.The majority of familial AD is caused by mutations in PS1, which usually results in very early onset disease (under 45 years) with rapid progression and additional physical signs. Apolipoprotein E (APOE e4), a lipid transport protein which has been identified as an independent risk factor for AD appears not to influence AD progression in SSA.

Pathophysiology

It is due to loss of neurones from the cerebral cortex and is associated with characteristic deposition of beta-amyloid plaques and neurofibrillary tangles in the neurones. This results in decreased acetylcholine synthesis in the brain.

Clinical features

The clinical features range from mild cognitive impairment with an isolated difficulty in day-to-day memory or forgetfulness, followed by slow progression over years to a severe loss of other cognitive functions, including recognition, language and visuospatial awareness. Loss of memory for recent events and recent personal experiences are typical. Behaviour and personality are often well preserved to begin with, and the diagnosis can be overlooked in the early stages. Physical signs appear later in the disease, when patients may develop parkinsonism, myoclonus and incontinence.

Diagnosis

The diagnosis is made by a careful history from the patient and an informant, supported by objective evidence of cognitive impairment on bedside tests. A Mini Mental State Examination (MMSE) (see appendix 2) score of 24/30 or less is supportive of a diagnosis of dementia, having excluded other secondary causes of dementia with appropriate blood tests and brain imaging.

Investigations

The main investigations in dementia are outlined in Table 17.2. The main aim is to exclude a treatable cause e.g. B-12 deficiency or HIV.

Table 17.2 Main investigations in dementia

Investigation	Aetiology
Haematology	
FBC & ESR	all causes
Chemistry	
blood sugar	
renal & liver function tests	metabolic causes
serum calcium	
Serology & others	
HIV, VDRL, TPHA	infection: HIV, syphilis, hypothyroidism,
T4	vitamin deficiencies,
B-12	neurodegenerative
CSF examination	
X-rays	
chest	CVD, infection, TB, malignancy
CT head	brain atrophy, stroke, vascular changes, infection, tumours, subdural haematoma
Others	
EEG, genetic testing	CJD, APO-E genotype

Management

There is no cure at present for Alzheimer's disease. Non drug interventions are the mainstay of management. This includes the provision of information and support for the carer's family and the community. One aspect of the disease is a deficiency of acetylcholine synthesis in the brain, and centrally acting cholinesterase inhibitors that raise levels of acetylcholine in the brain may result in temporary symptomatic benefit. In high income countries, the cholinesterase inhibitors are recommended for patients with mild to moderate dementia (MMSE range 12-24/30). Patients may derive some limited benefit in cognitive function for 1-2 years but there is no effect on the eventual progression of the disease. These are stopped if the MMSE score is <12/30.

Drug options include the cholinesterase inhibitors donepezil 5-10 mg daily or rivastigmine 1.5–3 mg bid, or galantamine 4-6 mg bd. The main side effects are related to increased peripheral cholinergic activity and include nausea, abdominal colic and diarrhoea. However the high cost of the regular use of these drugs prohibits their widespread use in AD in Africa. For behavioural and psychiatric disorders, it may be necessary to use an antipsychotic medication. These include haloperidol 0.5-1.5 mg twice daily. Alternatives include risperidone 0.5 mg or olanzapine 2.5 mg/po daily initially. Valproic acid may decrease agitation and help as a mood stabilizer and be better tolerated than the antipsychotics. It is wise to start with low doses and adjust any increases in dosages slowly.

Key points

- Alzheimer's is the most common form of dementia worldwide and in Africa
- associated with increasing age >65 yrs & a positive family history
- first symptom is often forgetfulness
- progresses to involve language, recognition, self-care & continence
- there is no cure & death occurs after approximately 6-7 years

VASCULAR DEMENTIA

Cerebrovascular disease is considered to be the second most common cause of dementia worldwide accounting for 20-30% of all cases. Patients are usually >40 years and have a known risk factor for vascular disease including hypertension, diabetes, atrial fibrillation, hyperlipidaemia and smoking.

Clinical features

Vascular disease may cause cognitive impairment by different mechanisms. Firstly, a small (strategic) stroke in an eloquent area or secondly by the cumulative effects of repeated large-vessel strokes. This is associated with the classical "step-wise" deterioration of vascular dementia. Thirdly, due to hypertension affecting the small penetrating arteries supplying the sub cortical white matter, causing multiple lacunar infarcts. This leads to a more insidiously progressive sub cortical dementia with motor findings. Clinically there will usually be physical signs including pyramidal tract signs and often gait disturbance or pseudo-parkinsonism and frequently urinary incontinence.

Diagnosis and management

Neuroimaging of the brain, in particular MRI shows widespread white matter changes particularly around the ventricles or areas of frank infarction. The management is unsatisfactory but involves the reduction and treatment of the usual vascular risk factors.

FRONTOTEMPORAL DEMENTIA

Frontotemporal dementia (FTD), or Pick's disease, is a neurodegenerative disorder characterised by progressive deterioration of behaviour, personality and language abilities together with prominent atrophy of the frontal and temporal lobes. It accounts for <10% of cases of dementia in high income countries and also occurs in Africa but its frequency there is not known. FTD is typically of younger onset, with age of onset between 45 and 65 years, although cases with older onset are well recognised.

Genetics

Up to 40% of patients with FTD have a positive family history of early-onset dementia with an autosomal dominant inheritance pattern. A number of causative genes on chromosome 17 have been identified, including tau & progranulin.

Clinical features

In the frontal or behavioural variant of FTD, typical presenting problems include disinhibition, loss of empathy, changes in eating patterns, ritualized or stereotypical behaviours and apathy. In the language variants of FTD problems include loss of word meaning (semantic dementia) or nonfluent speech (progressive non-fluent aphasia). However, it must be emphasized that there is a good deal of overlap between these variants of FTD. Patients with a predominantly frontal presentation may also show language impairments, and equally patients with a predominantly language presentation may show behavioural disturbance. Physical signs are not usual but there is an overlap with motor neurone disease. A core feature is a lack of insight and patients with behavioural disturbance can be very challenging to manage. Eventually all patients progress to a global dementia.

Diagnosis and management

Neuroimaging reveals a very characteristic selective atrophy of frontal and temporal lobes (Fig 17.1). There is no specific treatment.

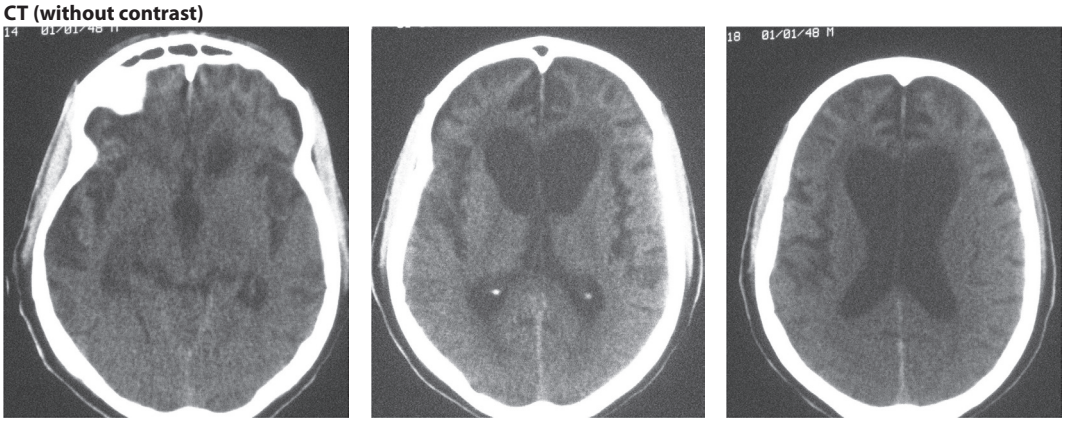

Figure 17.1 Frontotemporal Dementia

HIV-ASSOCIATED DEMENTIA (HAD)

Chronic HIV infection of the brain leads to a dementia in at least 10-20% of patients in Africa, affecting a younger population than is usual for dementia (Chapter 8). HAD occurs increasingly with advancing levels of immunosuppression and in particular with CD4 counts <100/cm^3. HAD presents with abnormalities of cognition, memory and motor function. The dementia is characterized early on by apathy, disinterest and loss of attention with a characteristic slowing of both mental and motor function (HIV associated neurocognitive dysfunction or HAND). Later, it leads to a global loss of cognitive function, with immobility and incontinence in end stage disease. However, most patients in Africa never reach this advanced stage, dying beforehand mainly of opportunistic processes, mostly infections. Associated neurological findings include frontal lobe release signs (FLRSs), absent ankle reflexes (distal sensory neuropathy) and frequently isolated brisk knee reflexes and extensor plantar responses (vacuolar myelopathy). The FLRSs, the snout reflex and the palmomental reflex, (Chapter 8), are found in the majority (70-90%) of patients with HAD. CT of the head usually demonstrates cerebral atrophy and excludes other confounding causes. The frequency of HAD has been shown in Africa to decrease significantly six months after starting ART.

DEMENTIA WITH LEWY BODIES

This occurs most commonly in the elderly and without a positive family history. This is a degenerative disorder characterized by the presence of Lewy bodies in the neurones of the cerebral cortex, brain atrophy and loss of pigment in the substantia nigra. Clinically, patients present with a dementia, coupled with mild dopamine sensitive parkinsonism, visual hallucinations, delusions and fluctuating cognition. CT of head reveals mild generalised brain atrophy. Patients may benefit from the cholinesterase inhibitors, perhaps even more so than patients with AD. However, caution should be taken with antipsychotic drugs as they may

cause a dramatic worsening of the parkinsonism and precipitate the neuroleptic malignant syndrome. Patients with Parkinson's disease may develop a similar dementia later in the course of their illness and the situations are probably just two ends of a spectrum.

Key points

- main causes of dementia are Alzheimer's disease, cerebrovascular disease & HIV disease
- there is no treatment that reverses the decline in Alzheimer's & cerebrovascular disease dementia management involves care of patient in general & treatment of specific symptoms
- care involves practical advice & support to patients, carers & families
- drug treatment generally involves use of anticholinesterases & neuroleptics

APPENDIX 1 SUMMARY BEDSIDE COGNITIVE TESTING*

Higher cerebral function	Clinical testing method	Measurement
Alertness	level of wakefulness	record level e.g. fully awake
Orientation	time, person and place	score out of 10
Attention and concentration	count back from 20 or repeat string of increasing numbers (max 6)	record best result after two trials
Memory		
Antegrade /short term	fictitious name/address or four to seven numbers	assess immediate recall and again after 5 min noting mistakes
Retrograde/long-term	dates/places of schooling, work or marriage or country events	assess accuracy of recall (check with relatives)
Executive function (frontal lobe)		
Word fluency	name as many animals or fruits in one minute	>20 normal <10 abnormal
Abstract thought	proverb interpretation e.g. "a rolling stone catches no moss"	interpretation
Cognitive estimates	how many people in Tanzania	accuracy
Alternating hand movements	open and close right and left fists alternatively	ability to replicate examiner
Dominant hemisphere function		
Aphasia	speech content understanding expression reading/writing	assess spontaneous speech for fluency, content and errors. to simple commands to naming objects to read/write a sentence
Calculation	arithmetic	simple addition/subtraction
Praxia	"wave goodbye" or "hammer a nail"	ability to follow instruction or replicate examiner
Non dominant hemispheric function		
Neglect	ignores all stimuli from one side hemispatial neglect	ignores stimulus on neglected side when bilateral stimuli presented (extinction) when drawing clock face one side is left out

** done only on a patient who is awake and cooperative*

APPENDIX 2 THE MINI MENTAL STATE EXAMINATION

The Mini-Mental state examination (MMSE)	Maximum test score
Orientation time, date, day, month, year ward, hospital, district, town, country *(score one point for each correct answer)*	 5 5
Registration examiner names three familiar objects (e.g. ball, pen, key) patient asked to repeat the three names *(score one point for each correct answer)*	3
Attention and calculation ask patient to subtract 7 from 100, stop after five subtractions, 93, 86, 79, 72, 65 *or* spell a five letter word backwards e.g. world *(score one point for each correct answer)*	5
Recall ask patient to name the three objects that you previously named *(score one point for each correct answer)*	3
Language naming: point to two objects e.g. watch and pen and ask the patient to name them *(score one point for each correct answer)*	2
Repetition ask patient to repeat sentence ("no ifs, ands or buts") no repeated attempt *(score one point for correct answer)*	1
3-Stage command e.g. "take this piece of paper in your right hand, fold it in half, and place it on the table *(score one point for each stage done correctly)*	3
Reading ask patient to read and obey a written command on a piece of paper e.g. close your eyes *(score one point)*	1
Writing ask patient to write a sentence sentence should be sensible and contain a noun and a verb *(score one point)*	1
Copying ask patient to copy picture of two intersecting pentagons *(score one point if all ten angles are present and the two must intersect)*	1
Total	30

Score: > 24/30 = normal, < 24/30 = cognitive impairment

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