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UPDATE

Dementia and imaging: the basics

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Abstract
Dementia is becoming more common as the population ages. We review the prevalence of different causes of dementia. Alzheimer's disease heads the list, followed by vascular dementia, Lewy body dementia, and frontotemporal lobar degeneration. Although these are distinct entities, their symptoms overlap and they have many comorbid conditions in common. We review the importance of recognizing the early symptoms and signs of dementia and point out the key differences between different types of dementia. We illustrate the fundamental importance of differentiating between reversible and irreversible disease on imaging and of establishing the follow-up of patients with irreversible conditions.

PALABRAS CLAVE
Demencia;
Resonancia magnética;
Tomografía computarizada;
Enfermedad de Alzheimer;
Demencia vascular

Demencias e imagen: lo básico

Resumen
La demencia es una enfermedad cada vez más frecuente en la población que envejece. Se revisa su prevalencia, encabezada por la enfermedad de Alzheimer, seguida por la demencia vascular, la demencia de cuerpos de Lewy y la degeneración lobar frontotemporal. Aunque son entidades distintas, presentan síntomas
superponibles y comorbilidades frecuentes. Se revisa la importancia de reconocer los síntomas y signos precoces de la demencia y de advertir las diferencias claves entre ellas. Se ilustra, desde el punto de vista radiológico, lo fundamental que es diferenciar las que son reversibles y establecer la forma de seguimiento de las no reversibles.

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We are what we remember
Italo Calvino

Introduction

The term dementia refers to the syndrome of intellectual deterioration manifested by persistent intellectual impairment of the memory, as the cardinal finding, in addition to other cognitive and personality disorders. The vast majority are progressive, and only 15% of cases are reversible (table 1), meaninga specific-treatment aetiology. However, it does not imply a full recovering of patient's prior cognitive status.[1] Dementia is a serious health problem and is the sixth leading cause of death in Spain.[2] Of the four million elderly people in Spain over 80 years old, 170,000 of them get sick each year (85%) in the midst of increasing life expectancy. Given this high prevalence, radiologists need to know the main features of these diseases.

There is no single pathophysiological mechanism that produces all types of dementia, but the end result in all cases is the loss of neurons (or their connections) in one or more of the multimodal association cortical regions (prefrontal cortex, parietal lobe and limbic system). Although the aetiology of the majority of cases is unknown, risk factors include age, low educational level and stroke.[3] Cardiovascular disease aggravates the course of dementia. At midlife,the population attributable risk of dementia was highest for hypertension, Later in life diabetes conveys the highest risk of dementia.[4] While dementia is indeed a complex group of diseases that is difficult to classify, they tend to be classified based on their immunohistochemistry, especially by the type of protein that accumulates in relation to cerebral damage.[5] Thus, Alzheimer's disease (AD) has β amyloid protein deposits, while frontotemporal lobar degeneration (FTLD) comprises the group of tauopathies with tau protein inclusions. Lewy body dementia belongs to the group of progressive neuronal synucleinopathies characterised by the formation of Lewy bodies and neurites (immunoreactive with α-synuclein), while Creutzfeldt-Jakob disease (CJD) is caused by an accumulation of the nonviral infectious proteinaceous particles called prions.[5]

Clinical manifestations

Most patients with dementia develop intelligent quotient (IQ) loss, which typically begins with memory loss. They exhibit difficulty in learning new information and develop subtle aphasia and apraxia, which then worsens. Regardless of the type of dementia, the stages of impairment are graded between 0 and 3 according to the Clinical Dementia Rating (CDR) scale, as well as between 0 and 7 according to the Global Dementia Scale (GDS).[6]

Mild cognitive impairment (MCI), classified as a score of 0.5 on the CDR scale, is the term used to describe the early signs and symptoms of dementia.[5] MCI refers to patients with only subjective memory impairment, which is confirmed by the informant and memory tests taken by the patient that are at least 1.5 standard deviations below the

Table 1 Treatable causes of dementia: cognitive deficits are not necessarily reversible

Treatable causes	Diagnoses to be identified
Vascular	Multi-infarct disease, silent brain infarction, chronic subdural hematoma, parenchymal hematoma, primary vasculitis of the central nervous system and secondary vasculitis (e.g., Collagen diseases)
Metabolic endocrine	Thyroid disease, parathyroid, liver, Cushing's syndrome, Addison's disease, hypopituitarism, renal failure, liver failure, porphyria, vitamin B12 deficiency, folate deficiency, pellagra, thiamin deficiency, Wilson's disease, hypo- or hypermagnesemia, hypo- or hypercalcemia, dehydration, dialysis-induced encephalopathy, hyperlipidemia, insulinoma
Toxic	Drugs (anticholinergics, antihistamines, neuroleptics), alcohol, heavy metals (arsenic, lead, mercury), manganese
Infectious	Neurosyphilis, ringworm, Lyme disease, AIDS dementia complex, herpes encephalitis, bacterial meningitis, other viral encephalitises, Whipple disease, progressive multifocal leukoencephalopathy
Neoplastic	Primary and metastatic tumours, paraneoplastic syndromes
Traumatic	Hygromas, hematomas, hemorrhagic contusion, anoxic chemical damage
Hydrocephalus	Noncommunicating versus communicating, chronic adult
Neuropsychiatric	Depression, delirium, bipolar disorder
Autoimmune	Sarcoidosis, lupus erythematosus, Sjögren syndrome, Behçet's disease, temporal arthritis, systemic vasculitis, thrombotic thrombocytopenic purpura
Various	Multiple sclerosis, idiopathic hypereosinophilic syndrome, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, congestive heart failure, radiation-induced dementia
Mixed	Combination of the above

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normal range for the patient's age and education. The long-term study of individuals with MCI shows that 4%per year develop dementia, compared with 1%of age-matched controls.[7] The first pathological changes affect projection neurons of the parahippocampal gyrus. This translates into changes in the entorhinal cortex and hippocampus that may be viewed with magnetic resonance imaging (MRI). The rate of "normal" brain aging to the preclinical phase of dementia occurs slowly, and there is still no evidence that this change is detectable. At present, episodic memory tests are the best neuropsychological predictors of conversion from preclinical dementia to dementia.[8,9] When evaluating this population, it is always appropriate to keep in mind the changes that occur in normal neurological aging by means of neuroimaging studies:

- Loss of cortical volume after 40 years of age, with increased subarachnoid spaces.[10] The annual volume loss for a normal subject is 0.45%per year, compared with a patient with dementia who could lose 1%annually.[10] There is a gradient in volume loss from the front to the back of the body; the associated cortex area is affected more and the primary areas less.[10,11]
- Hyperintensities of the periventricular white matter (on halo) (white matter hyperintensities, WMH) and non-confluent subcortical punctiform lesions.[12] They present a periatrial to frontal gradient, with a loss of white matter volume rate of 0.23%a year.[10]
- Lacunar strokes (≥ 3 mm) in the fifth decade of life in up to 10%of the population. This frequency increases with age, reaching 35%in the ninth decade.[11] The greater the number of infarctions and white matter lesions, the more frequent the subclinical cognitive impairments.[13]

Prevalence

Alzheimer's dementia is most common in our environment, followed by vascular dementia (VD) and Lewy body dementia[14] (fig. 1).

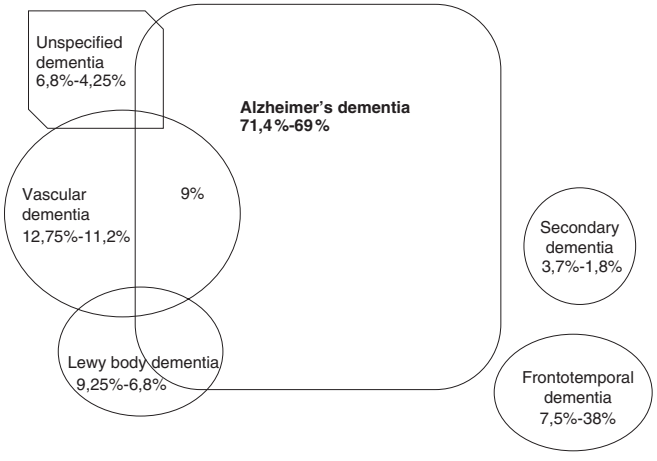

Figure 1 Outline of the current prevalences of different types of dementia with strict criteria (not restrictive) in Spain, based on data from references 3 and 14. Lewy body dementia also includes dementia associated with parkinsonism in general.[3]

Depending on the ethnic groups, the second leading type of dementia is Lewy body dementia, and the third is the FTLD, especially in areas of European ancestry.[15]

Disease aetiologies differ in early-onset dementia, which occurs in patients younger than 65 years of age. In these cases, AD decreases, and dementia subtypes associated with trauma, alcohol and human immunodeficiency virus (HIV) are more prevalent.[16]

Benefits and problems of early diagnosis

The benefits of early investigation and diagnosis include identification of treatable physical and psychiatric causes, treatment of comorbid conditions, initiation of psychosocial support, and instigation of pharmacological symptomatic treatments. Pharmacotherapy is more effective in the early stages when aetiological treatment is lacking. However, diagnoses are usually made late due to the insidious variable onset of the syndrome, which lacks a clear demarcation until the later stages, among other reasons. Patients, families, and general practitioners may all bereluctant to diagnose dementia because it is such a serious and largely unmodifiable disease that still carries a huge burden of stigma.[8]

Diagnosis of dementia

Diagnosis is mainly clinical, based on the triad of medical history, information from an informant and cognitive study.[8,9]

The use of structural imaging is widely accepted and is recommended by both the Spanish Society of Neurology and the American Academy of Neurology.[17,18] There is no evidence to support the superiority of any particular imaging technique. Computed tomography (CT) is the most available modality and is useful for dismissing most reversible causes of dementia. MRI is usuallytthee technique of choice for VD, due to its superior sensitivity to vascular changes.[19,20] Table 2 presents an MRI scanning protocol.

There is evidence that structural imaging influences patient treatment during the initial evaluation of dementia.[19,20] In patients younger than 65 years old, the presence of focal signs and the short duration of the development of cognitive impairment (less than one year) are signs that probably make brain imaging studies more useful.[1,16] In this patient group, the images can detect lesions in white matter, the vascular system and bones, and they can assess disease aetiologies such as infectious or post-traumatic, which are not so common in the oldest group.[1]

However, the diagnostic accuracy of structural imaging is not greater with volume measurements than with visual assessment of atrophy, especially in mild cases. The accuracy is still comparable to clinical examinations, and there are studies in which visual assessment exceeds volumetric analysis.[19] It is noteworthy that many of the findings in the images do not have pathological confirmation and, therefore, represent the clinical syndrome and not the pathology.[11]

Table 2 Imaging protocols for dementia studies

Computed Tomography	Magnetic Resonance Imaging
Generally to rule out treatable dementias Follow-up+. Slices oriented with the temporal lobe plane with thickness of 2-3 mm	Sagital T1 Axial PD and T2 (or at least T2) Coronal FLAIR/STIR Axial diffusion-enhanced B0 / B 1000 s/mm^2 Axial gradient echo T2-weighted* ++ 3D gradient echo T1 weighted. Voxel size 0.86 mm × 0.86 mm × 1.6 mm ++ Spectroscopy with PRESS sequence, 128 replications. Two echo times (TE, 31 and 136 ms) and the same repetition time (TR) 2,000 ms

+Follow-up: patients who could not be scanned by MRI; ++: volumetric studies; +++: spectroscopy. At least short echo time (TE) and posterior cingulate location.
*Technical sequence parameters dependent on each scanner.

Objectives of imaging

— To exclude a potentially reversible cause of dementia. In our setting, only between 1%and 15%of dementia cases are treatable.[1]
— To assess the specific subtype of dementia, particularly to differentiate AD from VD and FTLD.
— Future objectives of imaging, which cannot yet be given, include:
  — Quantifying the stage of the disease for initiation of a specific treatment response.
  — Identifying individuals who may respond to treatment.

Alzheimer's Disease

AD is a progressive neurodegenerative dementia with late presentation; only 10%of cases occur in people under 65 years old. Its defining pathological characteristic is the accumulation of neurofibrillary tangles and senile plaques. Most cases are sporadic, and the primary susceptibility gene associated with these cases is the apolipoprotein (Apo) ε. The most prevalent allele in the general population is ε3, at approximately 80%. The ε4 form is associated with an increased risk of AD, reaching a probability of 50-90% in homozygotes, compared with 20%in the general population.[6]

This disease involves cognitive dysfunction due to loss of neurons and synapses. It begins in the limbic cortex and, as the disease progresses, it extends to the neocortex. In addition to the temporal lobe, there are functional and morphological changes in other regions such as the posterior cingulated gyrus. Positron emission tomography (PET) identifies this area as the functional region of the brain affected earliest, both in patients with early AD and in asymptomatic carriers of the ApoE ε4 allele.[21] Besides histopathological changes, there is a gradual loss of cholinergic function,. main stay of cholinesterase inhibitor treatment. As cholinesterase is the enzyme that breaks down the neurotransmitter acetylcholine. Its inhibition, achieves a higher level of neuronal interconnection, delaying cognitive decline.[22] Vascular lesions often coexist with AD, and it is currently supposed that AD and VD may act synergistically. Furthermore, there is mounting evidence of a common pathogenesis.[23]

Epidemiology

AD is the most common cause of dementia, and its prevalence increases with age. In Spain, the prevalence of dementia in people over 65 years old is 9.2%, higher in women (11.1%) than in males (6.5%). This prevalence increases with age until the nineties, where it stabilises at a 25-54%.[2,3,14]

Diagnosis

The diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R), the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) are all valid, although the latter criteria set is preferred.[20] However, they present limitations that may vary with the severity of the disease and with clinical expertise.[19] Definitive diagnosis of AD cannot be only clinical and requires histological confirmation. With clinical data alone, it is only possible to reach a diagnosis of possible or probable AD. The most recent recommendations for post-mortem diagnosis of AD define the disease as a clinicopathological entity and emphasise the clinical impression for the pathological diagnosis.

Fundamental radiological imaging findings

The characteristic findings of AD are not easily perceived in the initial stages, where there is diffuse loss of cortical volume. As the disease progresses, an accelerated loss of focal volume is shown in the medial temporal lobes (particularly the hippocampus), the parahippocampal

circumvolution, the entorhinal cortex and the amygdale. In clinical practice, the width of the lateral ventricle horn is the most reproducible measure to evaluate this atrophy (fig. 2). Computed tomography is a valid technique and is usually the first test performed, especially if there are contraindications for MRI. On CT scans obtained of the orbitomeatal plane, the most appropriate measure to distinguish the disease is the temporal horn of the lateral ventricle width. With these planes, a ratio is obtained of the radial width of the temporal horn respect to the biparietal diameter (fig. 2A). Thus, the volume loss is adjusted for head diameter, which is more useful for tracking individual and intergroup differences. Normal subjects, patients with AD and patients with AD with extensive white matter lesions have mean ratios of 0.025, 0.038 and 0.044, respectively.[24]

On MR images (fig. 2B), the best view is the coronal plane, which should always be evaluated at the same level (e.g., mammillary bodies) to check atrophy progress. A scale of five degrees can achieve an adequate diagnostic accuracy between 83 and 96%(table 3, fig. 3).[25] An MRI study of the Italian population for more than 60 years has estimated that for mild AD, the temporal horn measures 6.5 mm, and for advanced AD, it measures 7.2 mm. Maintaining a specificity of 95%for both cases, the sensitivity is 74%for mild AD and 82%for moderate AD.[26]

A

B

Figure 2 A) Measurement of temporal lobe atrophy in computed tomography (CT). Temporal lobe angulationhe on axial CT image, where the the width of the temporal horn of the lateral ventricle measurement is shown with respect to the biparietal diameter. B) Temporal lobe atrophy on MRI image. FLAIR weighted coronal image showing the method of measurement of the width of the temporal horn of the lateral ventricle (double arrow) as well as that of the choroidal fissure (thick arrow).

Other techniques

Imaging techniques values, as intermediate markers for therapeutic efficacy for AD, has not been positively proven in a clinical trial with a drug to modify the disease. Therefore, the evidence is insufficient to recommend imaging diagnostic modalities in clinical practice.[19]

Regarding voxel-based morphometry (VBM), the rate of change in hippocampal volume in consecutive MRI studies has proven to be the most specific volume marker for the identification of early-onset AD.[27]

However, medial temporal lobe atrophy is not specific to AD and is seen in other types of dementia, which limits its usefulness as a diagnostic marker.[19]

Although it presents early, MCI and AD overlapping is too large to be of value in individual patients. There is recent evidence that automatic VBV of the whole brain classifies as well as clinical diagnosis.[28]

The diagnostic accuracies of 1H MR spectroscopy (H1ERM), single photon emission computed tomography (SPECT) and PET are not greater than those of the clinical criteria in AD—moderate evidence for recommendation—.[19]

Still, these last two functional techniques appear adequate for differentiate FTLD and Lewy body dementia from AD.[19] The H^1ERM shows a decrease in N-acetylaspartate and an increase in myo-inositol in AD patients with respect to healthy subjects, measured in the posterior parietal. Functional MRIs show decreased activation in several regions, including the temporal lobe in memory tasks in these patients compared with control subjects.[24,29] PET shows abnormal patterns of low uptake of ^{18}F-fluorodeoxyglucose in the posterior cingulate, precuneus, temporoparietal and frontal cortex regions in patients with AD. Similar hypoperfusion patterns have been identified with SPECT and with contrast-enhanced perfusion MRI,[30] although PET is better to differentiate AD fromcontrol patients. There is moderate evidence that PET, in early dementia, can increase the accuracy of clinical diagnosis without increasing the overall cost.[19] Higher accuracy (90%) is expected with GDP-PET with a specific ligand for the β-amyloid protein.[30] These functional and spectroscopic techniques are not currently cost-effective for the diagnosis of AD, assuming the minimum current pharmacological effectiveness (moderate evidence). If a drug that significantly changed the course of the disease were to be discovered, the cost-effectiveness of diagnostic tests would be changed.[19]

Table 3 Criteria of Scheltens et al. for the assessment of temporal lobe atrophy

Grade	Width of choroidal fissure	Width of temporal horn	Height of the hippocampal formation
0	N	N	N
1	↑	N	N
2	↑↑	↑	↓
3	↑↑↑	↑↑	↓↓
4	↑↑↑	↑↑↑	↓↓↓

↑: increase; ↓: decrease; N: normal.

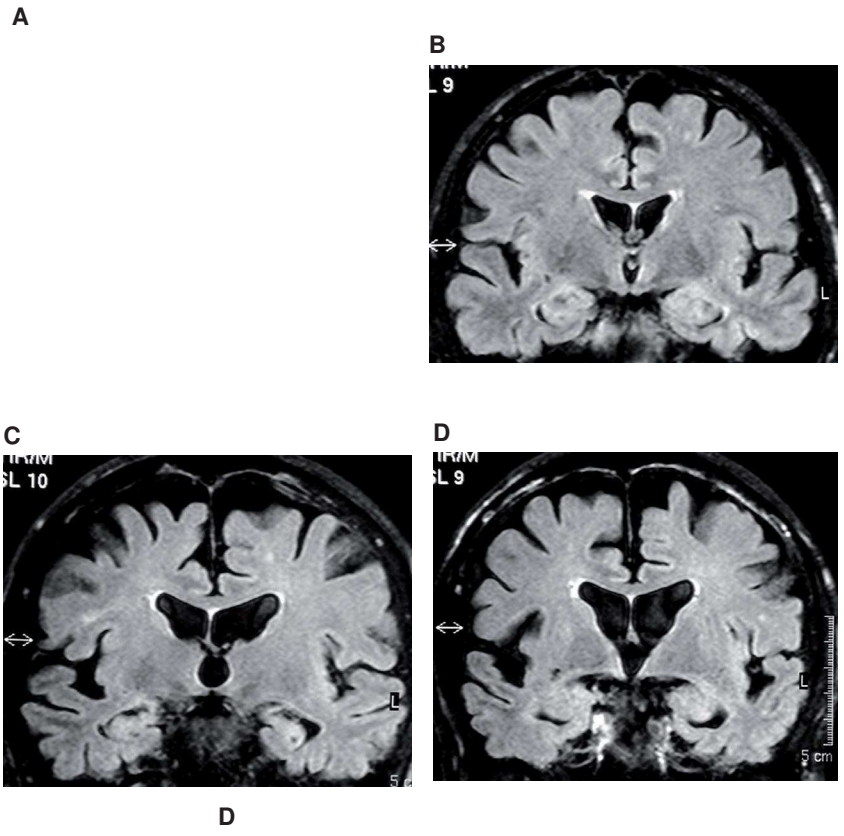

Figure 3 Alzheimer's dementia. FLAIR coronal images showing the evolution of temporal cortical volume loss from a normal stage, grade 0 (A); mild cognitive impairment, grade 1 (B); mild dementia, grade 2 (C); and advanced, stage 4 (D).

Vascular dementia

Pathology, clinical and general data

Vascular dementia is the second most common form of dementia. No specific pattern of cognitive impairment can distinguish vascular dementia from AD, although dysexecutive symptoms are predominant.[7] Imaging tests are essential for diagnosis, but there is no evidence on diagnosis outcomes. The most commonly diagnosis criteriare from *National Institute of Neurologic Disorders and Stroke - Association Internationale pour la Recherche et l'Enseignement en Neurosciences* rules (NINDS-AIREN)[20,31] (table 4). Howere, they show poor sensitivity (50%) and high specificity (85%).[17] That is, if a patient fulfills them, it is almost sure to be a case of VD. These criteria are difficult to implement because in addition to the topography of infarction, severity is required,[32] and there are more variables than in AD (e.g., infarction of the posterior cerebral artery must be bilateral) (fig. 4A). Also, there are four strategic locations where an infarct, by itself, may be responsible for cognitive impairment: the hippocampus, the medial thalamus, the caudate nucleus and the right parietal lobe[32] (fig. 4B).

In descending order of importance, the best predictors of a diagnosis of VD are: a) temporal relation between stroke and dementia onset, b) bilateral strokes of gray matter (frontal, temporal, parietal, basal ganglia and thalami) and c) symptoms or signs of previous stroke.

To overcome these difficulties in diagnosis, there are more functional criteria that can be applied in clinical practice (table 5), but a greater effectiveness with the NINDS-AIREN criteria has been documented.[33] VD may be the result of a

Table 4 Vascular dementia. Criteria for gradation of the NINDS-AIREN criteria

I. Topography	Injuries associated with dementia, including any of the following or their combination	A. Stroke of large vessels in the following territories	Bilateral anterior cerebral artery (ACA) Posterior cerebral artery (PCA), including paramedian thalamus, inferior temporal lobe Middle cerebral artery (MCA) including parietotemporal, occipitotemporal and angular gyrus Carotid territory bordering: bilateral superior frontal, parietooccipital and/or superficial and deep MCA
		B. Microvascular disease	Lacune in white matter or basal ganglia (should be two or more lacune in basal ganglia and two or more lacune in frontal white matter) Extensive white matter lesions Bilateral thalamic lesions
II. Severity	Besides the above, relevant radiological lesions associated with dementia include:	A. Injuries of large vessels in the dominant hemisphere B. Bilateral large-vessel stroke C. Leukoencephalopathy involving > 25% of total white matter (beginning to be confluent in four regions, e.g., bilateral frontal and bilateral parietal)	

A lesion is considered confluent when it measures more than 20 mm and comprises two or more smaller lesions.

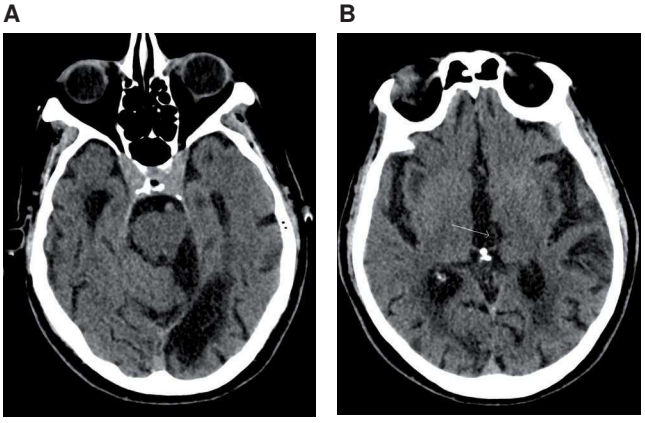

Figure 4 Vascular dementia. A) Axial image showing a stroke in the left posterior cerebral artery. B) Axial CT scan that shows an infarct in the medial thalamus (arrow). This lesion by itself is responsible for clinical cognitive impairment.

single strategic infarct, multiple cortical or lacunar infarcts or microvascular injury in which there are no symptoms of stroke or heart attack in the image. However, brain imaging cannot reliably confirm the chronology of injuries or clinically report the relative contributions of the degenerative and/or ischemic processes.[34,35] Given the low sensitivity of the NINDS-AIREN criteria in identifying these patients and comorbid risk factors (more than half the cases of vascular dementia are mixed with AD), a new classification model of cognitive decline and dementia has been proposed[35] (fig. 5). There is a form of dementia of vascular origin that affects young patients, called CADASIL syndrome (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy). It is a newly recognised hereditary disease characterised by transient ischemic attacks, strokes, progressive subcortical dementia, migraines and mood swings.[31]

Fundamental radiological imaging findings

MRIs are the ideal imaging modalities to show lesions.[20,33] The characteristic findings are cortical and lacunar infarcts and large white matter lesions, also known as leukoaraiosis. The images always have to have a T2 sequence, given the insensitivity of FLAIR (fluid attenuated inversion recovery) to thalamic infarcts (fig. 6).[36] The lesions present with CADASIL are primarily subcortical in the anterior temporal and frontal lobes with involvement of U fibers, while the cortex is preserved.

Of all dementias, this is the type where micro-bleeding occurs with the highest frequency, at 65%. With AD, micro-bleeding is only observed in 18% of cases.[37] In cerebral amyloid angiopathy, the characteristic finding is the presence of lobar haemorrhages in different stages. They are located, in descending frequency, in the frontal, parietal, temporal and occipital lobes. Cortical/subcortical haemorrhagic lesions are clinically silent and are best detected with T2-weighted gradient echo sequences (fig. 7).

Attribution of white matter hyperintensities to VD, and hence the patient's diagnosis to VD on that basis, in the absence of more specific features for VD is one of the most common mistakes in dementia diagnosis.[32]

more extensive the white matter lesions, the more likely it is that the patient has risk factors for stroke, cognitive impairment and cognitive deterioration. To assess these injuries, there are visual scales or quantification of these injuries with special software. In the absence of quantification, a validated scale is recommended for gradation.[38] It is important to remember the hyperintensities present in normal aging (see above). However, confluent lesions are

Table 5 Criteria for vascular dementia (VD) diagnosis in clinical practice

Low probability of VD	Supportivemoderate probability of VD	Strongly supportive-high probability of VD
No history of stroke	Any stroke above midbrain by history, without subsequent impact on cognition	Stroke temporally related to the onset of dementia or worsening of cognition
0-1 focal sign (e.g., asymmetry of reflexes)	2-3 neurologic signs suggestive of cerebrovascular origin in the absence of history of stroke	Multiple (> 3) neurological signs suggestive of cerebrovascular origin in the absence of history of stroke
White matter hyperintensities, none or minimal	White matter hyperintensities, mild to moderate	White matter hyperintensities, severe
01 lacune	2-3 lacunes	≥ 4Lacunes
No cortical infarcts or only 1 small one (single-gyrus)	Cortical infarction, single, only in noncritical region	Cortical infarcts, multiple, large
No infarcts in critical regions (hippocampus, caudate, thalamus, parietal cortex)	Lacunar or small infarct only in critical regions	Infarcts larger than lacune in hippocampus, caudate, thalamus, parietal cortex

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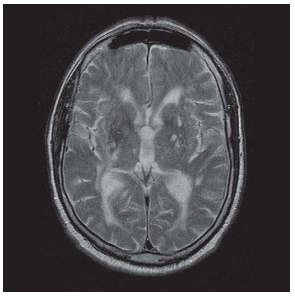

Figure 6 Vascular dementia. A) FLAIR weighted coronal image showing white matter lesions and probable lesions in both thalami with predominance on the left. B) T2-weighted axial image showing lacune infarcts in both thalami much more clearly than in the FLAIR image.

Figure 5 Outline of the proposed classifications of dementia and vascular cognitive impairment (VCI), taking into account the common risk factors. SD-DCV: VCI without dementia; AD: Alzheimer's dementia. Adapted from reference 35. Copyright Elsevier.

due to arteriolar disease.[12] Small vessel disease is the most frequently seen cause of a diagnosis of VD in radiological findings; the disease is found in 74%of the cases.[39] This shows white matter hyperintensities that comprises t more than 25%of total white matter and/or white matter lesions with lacunars infarcts.[39] There is cortical atrophy, though not at the same stageas there is with AD, which occurs without a specific pattern and also contributes to cognitive degeneration.[40]

Lewy Body Dementia

Pathological, clinical and general data

This designation is used for patients with spontaneous parkinsonism (not induced by drugs), dementia and persistent visual hallucinations. The epidemiology is poorly understood, although it is similar to AD, with no precise definitions of age and sex distributions and potential risk factors. Pathologically, many patients with Lewy body dementia also have AD, which alters the clinical presentation, although cognitive impairment is more pronounced than with AD. The clinical criteria for consensus of a Lewy body dementia diagnosis are specific but insensitive.[41] The final method of diagnosis is histochemical staining to detect Lewy bodies (pale eosinophilic inclusions), which can be measured semiquantitatively.[41]

The distinction between this type of dementia and other, neurodegenerative forms is important. So Lewy body

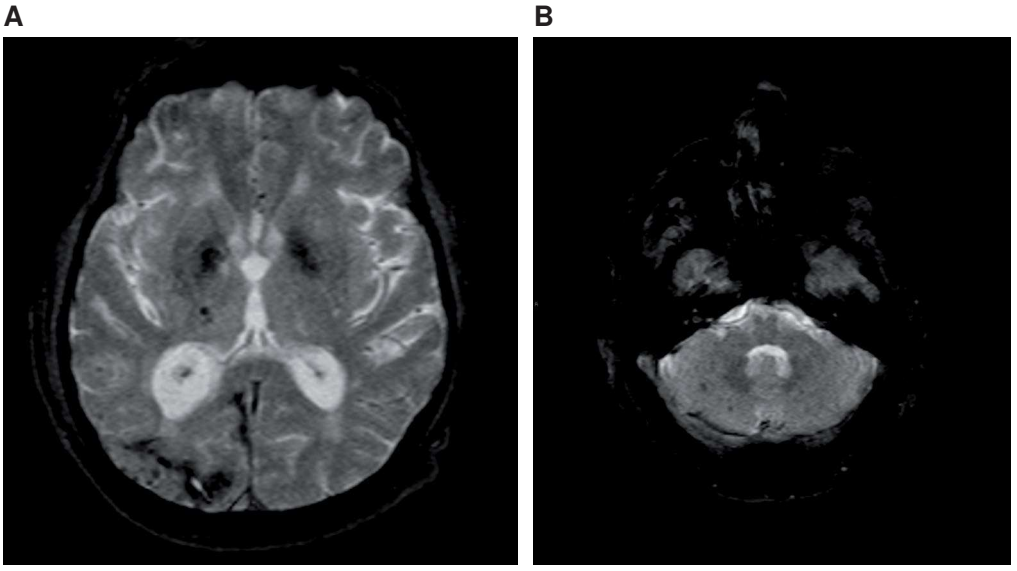

Figure 7 Amyloid angiopathy. A) T2* weighted axial image showing a corticosubocrtical right posterior parietal hemorrhage. Another hemorrhagic focus is also seen in the internal capsule. B) Lower level where other subcortical hemorrhagic foci are observed in the cerebellum.

patients may develop irreversible extrapyramidal symptoms with the standard antidopaminergic and anticholinergic treatment used to treat psychosis associated with dementia. They may also develop sensitivity to neuroleptics, a potentially fatal reaction, which is thought to be mediated by acute blockade of D2

receptors. These complications can occur in up to half of the patients with this disease.[27] This entity is confused with Parkinson's disease because many Parkinsonian patients have dementia. For diagnosis of Lewy body dementia, a year rule is used to separate them: if the patient's dementia begins in the first year after the onset of parkinsonian symptoms, it is classified as Lewy body dementia, whereas dementia that begins more than one year after onset of Parkinsonian symptoms is classified as a case of Parkinson's disease (insufficient evidence).[20]

Fundamental imaging findings

Imaging tests have a mere supporting role in diagnosis while MRI and CT findings are nonspecific, showing discrete diffuse cortical atrophy.[27] There is greater atrophy of the midbrain and less impairment of the hippocampus in comparison to AD cases, which as of yet is only detectable with quantitative studies using VBM.[42] SPECT tests show less hypoperfusion of the occipital lobe than with AD cases. In patients where diagnostic doubt exists, performing a FP-CIT SPECT test is recommended. This shows low uptake of dopamine transporters, which is normal with AD.[30]

Fronto-temporal Lobe Degeneration (FTD)

Pathological, clinical and general data

This disease, formerly called fronto-temporal dementia, comprises a diverse group of entities such as corticobasal degeneration and progressive supranuclear palsy.[37] Pathologically, there is atrophy, spongiosis and gliosis, and the clinical phenotypes of these diseases are not reliably differentiated.[5,43] Recent criteria classify them according to their positivity for tau protein and, among these cases, according to protein isoforms.[44] From a practical clinical point of view, these pathologies are usually divided into syndromic variants that show different, even though overlapping, patterns of atrophy. The forms are behavioural, semantic and progressive nonfluent aphasia. In the behavioural variety, the most common presentation is profound changes in personality and social behaviour, including a loss of manners and social habits. For the other two forms, disease presentation includes alteration of language, usually as progressive nonfluent aphasia. The behavioural variant of FTD (FTDb) is exhibited with early behavioural abnormalities and is associated with greater loss of frontal lobe volume.

Patients with semantic dementia show a well defined pattern of atrophy that more predominantly affects the anterior temporal lobes. Progression to death is much faster than in AD, with averages of 4.2 years and 6 years, respectively.

Fundamental radiological ilmaging findings

MRI tests of patients with FTD often show asymmetric atrophy of the frontal and temporal lobes, usually with left predominance[27] (fig. 8). The larger gradient of antero-posterior atrophy in patients with FTD may help distinguish FTD from AD, which shows a posterior and more symmetrical bias. Functional studies (PET or SPECT) show premature asymmetric anomalies in the ventromedial frontal cortex. Longitudinal PET studies show that the initial stage of FTD is limited to the frontal lobe and in later stages passes to the temporal and parietal cortices.[45]

Creutzfeldt-Jakob Disease (CJD)

Pathological, clinical and general data

Currently, it is estimated that MRI testing is more useful for prion disease than for any other form of dementia.[46]

CJD is a rare cause of rapidly progressive dementia, which occurs with an incidence of approximately one case per million annually. The majority of cases are sporadic, and clinical presentation includes cognitive impairment, often with psychosis and delirium. It exhibits rapid development with motor symptoms (myoclonus) and finally coma. There are several types of CJD, including sporadic (most common), familial, iatrogenic (caused by contaminated tissue receptors, hormone administration or contaminated surgical instruments) and the variant of CJD that has been associated with the ingestion of meat products contaminated with prions.[46]

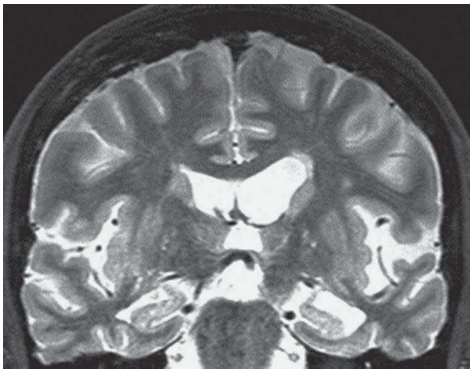

Figure 8 Frontotemporal lobar degeneration, aphasic form. STIR weighted coronal image that shows marked cortical atrophy of left frontotemporal predominance. Note the contralateral asymmetry, especially with respect to the lateral fissure, choroidal fissure and lateral ventricle temporal horn.

Fundamental radiological imaging findings

Diffusion-weighted images are the most sensitive and are the earliest to detect abnormalities in the early stages of the disease, before abnormalities appear in FLAIR-weighted images and finally in T2 (fig. 9).[46] This causes a characteristic decrease of the symmetrical signal of the basal ganglia. One can also observe a decrease in the less symmetrical distribution of the thalami and asymmetric cortical involvement. The restriction of diffusion reflects the reduction of water movement within the vacuoles, typical of spongiform degeneration.[46] Measurements of the apparent diffusion coefficients may be useful for detecting changes in this sequence, before changes in the image signal due to diffusion are detected.[46]

The variant form of CJD has a characteristic appearance in conventional MRI sequences (called the pulvinar sign), with symmetrical high signal intensity in the posterior thalamus on T2- and FLAIR-weighted images.[27]

Subsequently, rapid diffuse atrophy develops, which may include the cerebellum. It should be emphasised that an

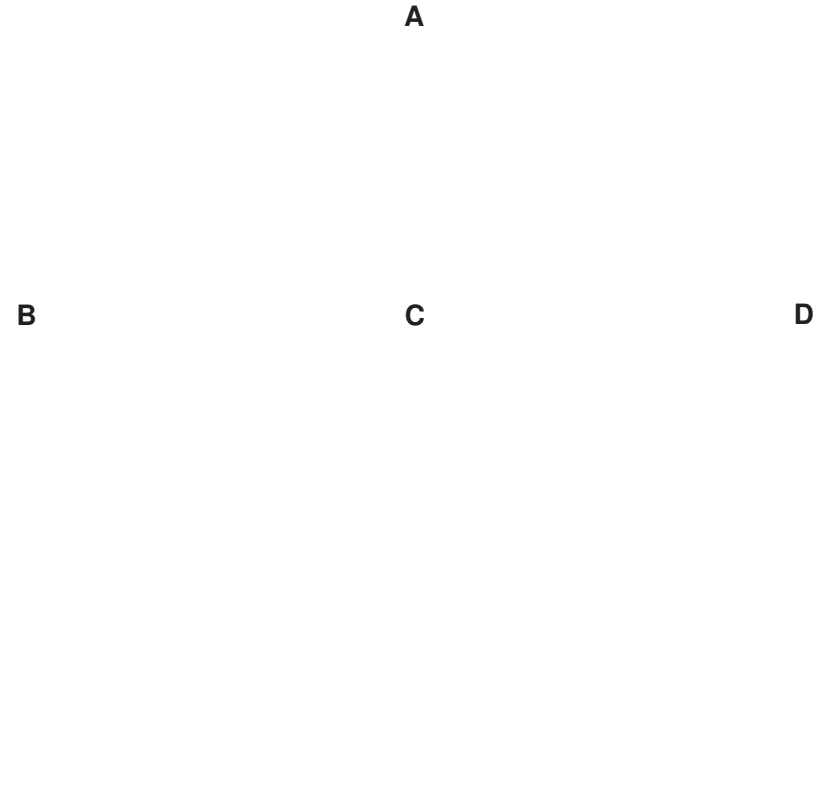

Figure 9 Creutzfeldt-Jakob disease. A) Diffusion-weighted images (B 1000 s/mm^2) where signal hyperintensity of basal ganglia is observed. B) On the apparent diffusion coefficient (ADC) image, a signal decrease is observed of the caudate nuclei and the putamen. FLAIR weighted (C) and T2-weighted image (D). These changes are less visible and appear later than those in the preceding images. Courtesy of Dr. A. Rovira, Barcelona.

initial normal MRI does not exclude CJD in a middle-aged or elderly patient with rapid onset dementia.

Dementia caused by human immunodeficiency virus

Human immunodeficiency virus (HIV) dementia, also known as the AIDS dementia complex, is thought to be due to direct infection of the macrophages and microglia of the central nervous system by the HIV retrovirus.[27] Before the development of highly active anti-virals, up to 20 % of patients infected with HIV developed dementia. Similarly, HIV dementia is the defining illness for AIDS in approximately 5% of HIV carriers. However, in patients in whom treatment fails, there is severe leukoencephalopathy. It is characterised pathologically by marked infiltration of perivascular spaces by monocytes and macrophages infected with HIV.

Fundamental radiological ilmaging findings

The most frequent finding in AIDS dementia is generalised cortical atrophy. This is identified as an increased cerebral sulci disproportionate to the patient's age.[21,47] There is also symmetrical involvement, patchy or confluent, of the ventricular and deep adjacent white matter that is visible with both CT and MRI scans. There is a frontal predominance, which may affect corpus callosum genuhe. No mass effect or contrast enhancement is produced, and if any of this is seen, another diagnosis should be considered.[47]

Adult chronic hydrocephalus

Adult chronic hydrocephalus (ACH) is the most common cause of reversible dementia and classically manifests itself with the triad of non-pathognomonic dementia, early-onset gait apraxia and urinary incontinence. It is a complex syndrome with a little known physiopathology and natural history, which begins insidiously with cognitive symptoms.[48] The name "adult chronic hydrocephalus" is preferred to normal pressure hydrocephalus because there are pressure gradients and no "normal" exists. Additionally, the name does not imply a specific physiopathology, as does the "normal pressure" term.[49] Definitive diagnosis is made by clinical examination, and the condition may improve with a ventriculoperitoneal shunt.

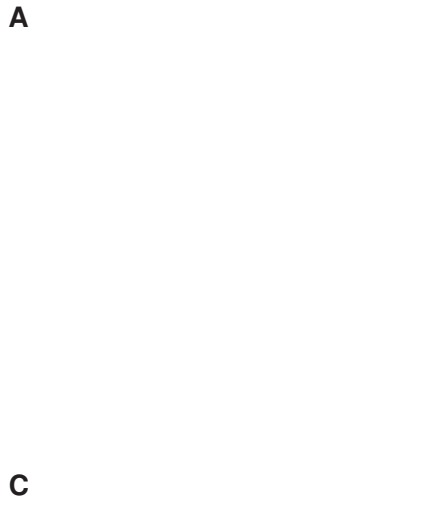

Figure 10 Adult chronic hydrocephalus (normal pressured hydrocephalus. A) Coronal FLAIR weighted image. For a discrete enlargement of the lateral ventricles. B) T2-weighted axial image, where a collapse of the sulci in the vertex is observed. C) Coronal FLAIR weighted image. Another patient with Alzheimer's disease with similar dilatated ventricles and sulci with cerebrospinal fluid in convexity. D) T2-weighted axial image of the last patient, showing the prominence of the sulci relative to B.

Table 6 Main findings of structural imaging of the most common dementias

Dementia	Main imaging finding	Role of image / diagnostic criteria
Alzheimer's disease	Cortical atrophy with parietotemporal gradient, especially valuable in hippocampal formation	Recommended. NINCDS-ADRDA / DSM-IIIR[20]
Vascular dementia	Multiple lacunar infarcts of large vessels. Extensive white matter lesions, greater than those of normal aging	Indispensable NINDS-AIREN[31]
Lewy body dementia	Nonspecific atrophy	Recommended. LBD Consortium[41]
Frontotemporal lobar degeneration (frontotemporal dementia)	Asymmetric atrophy of frontal lobes (behavioural variety) or of the anterior portion of temporal lobes (semantic / aphasic varieties)	Recommended. FTD Consortium[44]
Creutzfeldt-Jakob disease	First: restriction of diffusion in the basal ganglia, then in cortical areas. Second: T2 and FLAIR hyperintensities in these areas	Recommended, MRI especially useful. WHO[51]
HIV dementia	Disproportionated cortical atrophy and periventricular white matter hyperintensities unusual for the patient's age	Recommended. Criteria of American Academy of Neurology[52]
Adult chronic hydrocephalus	Dilation of the ventricular system, especially lateral ventricles, disproportionate to cortical sulci	Indispensable. Relkin et al.[48]

MRI: Magnetic Resonance Imaging, HIV: human immunodeficiency virus.

Radiological Imaging Findings

The main radiological finding in ACH cases is dilatation of the ventricular system, particularly of the anterior horns of the lateral ventricles, disproportionate to the appearance of cortical sulci.[49] The Evans index (marker of ventricular dilation: width of the frontal horns divided by the biparietal diameter of the atria), is pathologically greater than 0.30, but this does not work isolated for clinical diagnosis. This dilation of the anterior ventricular horns and third ventricle with spherical morphology are indicative of adult hydrocephalus.[48] What helps most to distinguish patients with similar ventricular sizes are axial images near convexity.[27] In such images from patients with ACH, there is hardly any cerebrospinal fluid in the sulci, while cerebrospinal fluid remains in the sulci in images from AD patients (fig. 10). White matter lesions can coexist with other forms of dementia.[49] Phase-contrast MRI studies, which are used to demonstrate hyperdynamic spinal fluid, have not proven useful in predicting which patients will respond to treatment.[50]

Table 6 summarises the conclusions of the main imaging findings.

Declaration of conflict of interest

The author declares to not have any conflict of interest.

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