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Comorbidity in Dementia: Update of An Ongoing Autopsy Study

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Abstract

OBJECTIVES—To examine systemic and central nervous system (CNS) comorbidities of patients with dementia evaluated during general autopsy.

DESIGN—Retrospective cohort study.

SETTING—A large tertiary academic medical center in Los Angeles, California.

PARTICIPANTS—A cohort of 86 participants with clinically and neuropathologically diagnosed dementia who received complete autopsies and 132 participants with dementia who received partial (brain only) autopsies.

MEASUREMENTS—The causes of death as well as systemic and CNS comorbidities were obtained from autopsy reports and clinical information as available from the medical records. Findings were tabulated with respect to type of dementia, semiquantitative assessment of the severity of cerebral amyloid angiopathy, semiquantitative assessment of the severity of cerebrovascular disease, and evidence of ischemic damage in the brain.

RESULTS—Out of a total of 218 subjects with dementia, 175 (80.3%) had Alzheimer's disease (AD) either in isolation or in combination with other lesions that might contribute to cognitive impairment, such as cerebrovascular disease and diffuse Lewy body disease (DLBD), 14 (6.4%) had frontotemporal dementia (FTD), and 7 (3.2%) had isolated DLBD. The most common cause

of death among demented patients was pneumonia (57 cases, 66.3%) followed by cardiovascular disease (14 cases, 16.3%). Eighteen subjects (20.9%) had lung disease and 16 (18.6%) had evidence of old or recent myocardial infarct. Clinically undiagnosed neoplasms included colonic adenocarcinoma, metastatic pulmonary neuroendocrine carcinoma, meningioma, and Schwannoma.

CONCLUSION—Significant comorbidities were discovered at autopsy in patients with dementia. Understanding the causes of death and associated comorbidities in patients with various subtypes of dementia is important in the assessment of end of life care in these subjects.

Keywords

dementia; Alzheimer disease; comorbidity; neuropathology; autopsy

INTRODUCTION

Dementia is increasingly becoming a major healthcare challenge as the population ages worldwide, with an estimated 25 million cases of dementia globally.[1] The most common cause of dementia is Alzheimer's disease (AD) which affects approximately 5.4 million individuals in the United States alone.[2] Dementia is well known to shorten life expectancy regardless of cause of death,[3] and these individuals, including those with AD, have a two-fold increased risk of death independent of comorbid conditions.[4] This has been partially attributed to the tendency for less aggressive medical interventions in demented patients.[3,5] Previous studies have examined the causes of death, [6,7] but few have investigated the comorbid conditions associated with mortality and morbidity in demented patients.[5,8,9] The University of California, Los Angeles (UCLA) Alzheimer Disease Research Center (ADRC) obtains consents for complete autopsy examination on a significant proportion of ADRC participants, to assess the long-term medical care of patients with dementia. We have previously reported the incidence of comorbidity in autopsies of patients with dementia in which neoplasms and other potentially manageable medical conditions were discovered only at autopsy.[8]

METHODS

We evaluated the autopsy reports and clinical information available on patients whose brain specimens had been entered into the UCLA ADRC and Easton Center Brain Bank, based on a clinical diagnosis of dementia, and who also had complete autopsies performed during 2001–2010 (inclusive). We also reviewed brain only (partial) autopsies performed during 2002–2010 (inclusive) on patients entered into the UCLA ADRC and Brain Bank. For general comparison, we examined complete autopsies performed at UCLA on patients above the age of 60 years without known dementia during 2006–2010 (inclusive). The investigation was carried out in accordance with the guidelines of the Institutional Review Board of UCLA Medical Center.

For each case the type of dementia (Alzheimer, frontotemporal, etc.) and any other significant neuropathologic findings were analyzed. Standard diagnostic criteria were used to assess the neuropathologic substrates of the major types of dementia.[10,11] Gross and

microscopic examinations of the brains were performed by a Neuropathology Fellow and Neuropathologist (H.V.V., W.H.Y., or N.K.) in each case. Occasional cases were reviewed at a quarterly UCLA Neuropathology Quality Assurance Conference.

Findings were tabulated with respect to (1) type of dementia, (2) semiquantitative assessment of the severity of cerebral amyloid angiopathy (CAA), (3) semiquantitative assessment of the severity of cerebrovascular disease, and (4) evidence of ischemic damage in the brain. Ischemic damage was classified as macroinfarcts (1 cm), lacunar infarcts (grossly visible but <1 cm), microinfarcts (not visible grossly but detected in histologic brain sections), and hippocampal sclerosis (HS), which was defined as pyramidal cell loss and astrogliosis in Sommer sector or more diffusely involving the pyramidal cell layer of sectors CA1, CA3, CA4, and the prosubiculum. Assessment of the degree of atherosclerotic arterial narrowing (none; mild, <20%; moderate, 20%–50%; or severe, >50%) was based on gross and microscopic estimates of stenosis of major branches of the circle of Willis, including basilar and vertebral arteries.[11] The degree of CAA was assessed as mild (Vonsattel grade I), moderate (Vonsattel grade II), or severe (Vonsattel grade III) based on the Vonsattel criteria.[12]

Furthermore, we evaluated the cause of death and common comorbidities including coronary artery disease (CAD), lung disease such as chronic obstructive pulmonary disease (COPD), tumors, gastrointestinal ulcers, and genitourinary infections in patients with and without dementia.

RESULTS

Complete autopsies were performed on 86 patients with a clinical diagnosis of dementia, including 45 men and 41 women, with a mean age ± standard deviation (SD) of 78.5 ± 11.5 years, ranging from 50 to 100 years, and 124 patients without a clinical diagnosis of dementia, including 73 men and 51 women, with a mean age ± SD of 70.7 ± 8.2 years, ranging from 60 to 94 years. Of the demented subjects, 60 cases were also followed clinically as part of the ADRC study with demographic information in Table 1. The cause of death and presence of significant medical comorbidities are delineated in Table 2. Among patients with dementia, pneumonia was the most common cause of death (57 patients, 66.3% of total) followed by cardiovascular disease (14 patients, 16.3%) and sepsis (6 patients, 7.0%). There were 58 patients (67.4%) with pneumonia, 18 patients (20.9%) with chronic obstructive pulmonary disease (COPD) or other lung disease, 16 patients (18.6%) with evidence of old or recent myocardial infarct, and 15 (17.4%) patients with evidence of old or recent pulmonary thromboembolism. Among dementia patients, incidental findings included four gastrointestinal stromal tumors, including one measuring 10 cm that was discovered on imaging as a heterogeneous calcified mass in the abdomen during the admission shortly prior to the patient's death, three other types of gastrointestinal tumors (one gastric leiomyoma, two intestinal carcinoids), two tubular adenomas, one renal oncocytoma, one pancreatic microadenoma, and two adrenal cortical adenomas. Clinically unsuspected neoplasms included a meningioma in one and Schwannomas in two patients with AD, colonic adenocarcinoma in an AD patient, pulmonary intermediate grade

neuroendocrine carcinoma that had metastasized to the liver and inguinal lymph nodes in an AD patient, and adrenal cortical carcinoma in a patient with frontotemporal dementia (FTD).

Among patients without dementia the most common cause of death was cardiovascular disease (35 patients, 28.2% of total) followed by pneumonia (26 patients, 21.0%) and various other causes (23 patients, 18.5%), such as liver disease, hemorrhage, and stroke. There were 53 patients (42.7%) with evidence of old or recent myocardial infarct, 37 patients (29.8%) with pneumonia, 30 patients (24.2%) with COPD or other lung disease, and 25 patients (20.2%) with evidence of old or recent pulmonary thromboembolism. This is consistent with previous reports of pneumonia as the most common cause of death in demented patients while in non-demented elderly subjects cardiovascular disease was the most common cause of death.[7,13]

Furthermore, we reviewed 132 brain only autopsies of patients with dementia and combined results with those from the 86 complete dementia autopsies to evaluate central nervous system (CNS) comorbidities, as well as to compare clinical and neuropathological diagnoses; data are shown in Table 3. The majority of those with dementia (175 patients, 80.3%) had AD solely or in combination with another pathologic finding contributing to dementia, 14 (6.4%) patients had FTD, 7 (3.2%) patients had DLBD, and there was only one case of pure vascular dementia although 24 (11.0%) patients had features of AD with a significant burden of vascular disease. The "other" dementia category included Huntington disease, multiple system atrophy, corticobasal ganglionic degeneration (CBGD), one case of hereditary endotheliopathy with retinopathy, nephropathy, and stroke (HERNS), and dementia of unresolved subtype. CAA was seen in 79.7% of pure AD cases and in 61.5% of dementia patients overall. Additionally, hippocampal sclerosis (HS) was seen in 9.6% of dementia patients (5.0% unilateral, 4.6% bilateral) and in 11.4% of AD patients (5.7% unilateral, 5.7% bilateral). CAA and HS were absent in non-demented patients. Among subjects with dementia 21.6% showed evidence of microinfarcts, 6.4% had lacunar infarcts, and 7.3% had macroinfarcts with 68.3% showing evidence of cerebral atherosclerosis. Of the pure AD patients 23.6% had microinfarcts, 3.3% had lacunar infarcts, and 4.1% had macroinfarcts, with 72.4% showing some degree of cerebral atherosclerosis. Among the non-demented patients 18.5% had microinfarcts, 4.8% had lacunar infarcts, and 12.1% had macroinfarcts, with 25.0% showing some degree of cerebral atherosclerosis. Miscellaneous findings included two AD patients who had unruptured cerebral saccular aneurysms, each measuring 1.5 and 2.0 cm in size.

In one of the first studies to describe neuropathologic abnormalities seen in addition to pathologic changes of AD, Lim et al. demonstrated a higher incidence of CNS vascular lesions in their community-based cohort of subjects compared to research studies, likely due to the higher rate of medical comorbidity and older age in demented subjects in the community.[14] Similarly, we have found that in all categories of CNS comorbidity (any degree of CAA, HS, infarct, and atherosclerosis) in our subjects with dementia, the mean ages were significantly higher in those with the comorbidity (CAA n = 127, mean age ± SD = 80.2 ± 9.7; HS n = 21, 83.3 ± 9.4; infarct n = 66, 82.8 ± 8.4; atherosclerosis n = 150, 80.1 ± 9.5) compared to those without (CAA n = 91, mean age ± SD = 76.8 ± 11.4, student's t-test, P <0.05; HS n = 197, 78.3 ± 10.6, P <0.05; infarct n = 152, 77.1 ± 11.0, P <0.001;

atherosclerosis: n = 68, 75.8 ± 12.2, P <0.05). Furthermore, the mean ages were significantly higher in demented patients with any cardiac comorbidity (n = 64, 80.2 ± 10.3) compared to those without (n = 22, 74.5 ± 13.6, P <0.05) and in those with genitourinary infections (n = 15, 84.5 ± 8.3) compared to those without (n = 71, 77.5 ± 11.7, P <0.05). There was no significant difference in the ages of demented subjects with and without any lung comorbidity, tumors, or gastrointestinal ulcers.

DISCUSSION

To better understand the natural course of dementia as well as to provide optimum care for patients afflicted with the disease, it is important to be cognizant of the factors that contribute to morbidity and a shortened lifespan in dementia. In accordance with previous studies, [7–9,13,15] we found that the most common cause of death was pneumonia followed by cardiovascular disease in all types of dementia except for normal pressure hydrocephalus, in which one patient died from an acute myocardial infarction and the other from sepsis secondary to pseudomembranous colitis. Kukull et al. have shown that cause of death varied with the degree of cognitive impairment in AD. Causes related to dementia, such as pneumonia, predominated in the most severely cognitively impaired subjects and causes relatively unrelated to dementia such as cardiovascular disease and neoplasms were more common in the less cognitively impaired.[6] Furthermore, Brunnstrom and Englund reported that neoplastic diseases were an uncommon cause of death in dementia patients, accounting for only 3.8% in their study population.[7] In agreement, many in our cohort were severely demented subjects from nursing homes, with the least common causes of death being pulmonary thromboembolism and cancer (both seen in 3.5% of demented subjects).

A limitation of our study is that the unique characteristics of our population at a tertiary academic center preclude the generalizability of our findings to demented persons in the general population. Age at symptom onset in our ADRC cohort (68.6 ± 9.4) was similar to our non-ADRC group (67.5 ± 11.8) and in turn slightly older compared to research subjects in studies such as those by Tsuang et al. and Barnhart et al. in which their community cohort of AD patients were approximately 10 years older at symptom onset compared to their research cohort.[16,17] Thus our ADRC subjects may be more representative of our hospital population rather than the general population. The ethnic distribution of our ADRC subjects was similar to other studies of registry subjects in that Caucasians accounted for the majority (85% of total). Additionally, a greater proportion of our ADRC subjects had completed a high school education or beyond compared to the general population, which is commonly seen not only in research samples based at large medical centers but also in community-based samples.[14,17]

The non-demented group was approximately a decade younger in age (student's *t*-test, *P* <0.05) compared with our demented subjects. The most common cause of death was cardiovascular disease followed by pneumonia, consistent with previous studies in which the most common cause of death in non-demented elderly inpatients was cardiovascular disease followed by bronchopneumonia, and the converse was seen in demented elderly inpatients.[13] Although direct comparisons cannot be made with our demented cohort, our

results are likely to be an accurate reflection of the common causes of death and comorbidities in non-demented elderly inpatients.

While there have been several studies examining the causes of death in dementia, few have addressed the associated comorbidities. Eaker et al. have found that community dwelling demented patients had more comorbid conditions such as cardiovascular and lung disease and urinary tract infections compared to controls without dementia.[4] In our cohort of demented patients, 69.8% showed evidence of cardiovascular disease including old or recent MI, 20.9% had lung disease, and 18.6% had urinary tract infections. Furthermore, in a study by Forstl et al., both AD and vascular dementia patients had an average of approximately two medical diseases for which they had received treatment and an average of approximately four pathological medical conditions discovered postmortem.[10] Dementia patients in a psychiatric inpatient setting had an average of 5.8 medical problems which was comparable to general non-demented elderly inpatients.[18] Among the general population, the rates of clinically undiagnosed malignancies has ranged from 4% in a large study of 3118 autopsies at the Mayo Clinic to 11% of fatal undiagnosed cancers in an evaluation of 3042 autopsy cases in Sweden, in which discrepancy rates between clinical and postmortem examinations were higher in the elderly.[19,20] In our previous study, four out of 53 (7.5%) demented patients had unsuspected malignancies.[8] In the present study, six out of 86 demented patients (7.0%) had clinically undiagnosed neoplasms, including one AD patient with colonic adenocarcinoma and another AD patient with metastatic pulmonary carcinoma, both of whom were found at autopsy to have pulmonary emboli contributing to their deaths. These findings may have influenced management if known when they were alive.

In the neuropathologic evaluation of both partial and complete autopsies of demented patients, AD accounted for over half of all cases of dementia, followed by Alzheimer's in combination with other neuropathologic lesions such as combined Alzheimer's and DLBD. Despite the inherent referral bias, these results are in accordance with previous autopsy studies that have assessed dementia subtypes and found AD to account for approximately half of all dementia cases, followed by varying subtypes of dementia such as vascular dementia and DLBD.[8,21] The incidence of pure vascular dementia varies widely in both clinical community and hospital based studies as well as in autopsy studies, from rare cases to vascular dementia being the second most common subtype of dementia.[11,21,22,23] However, the coexistence of vascular pathologic lesions and AD is common.[24] The prevalence of frontotemporal dementia (FTD) in community based and autopsy studies has ranged from 2.8 to 4.7%.[21] FTD patients constituted approximately 6.4% of dementia patients in our study population. Comparison of clinical and neuropathological diagnoses shows that the diagnostic accuracy of AD (67%) is lower than that generally reported in research samples. This may partly be a reflection of the inclusion of non-ADRC subjects who presented with AD diagnosed in the community, as clinico-pathological correlation for the diagnosis of AD has been higher in research referral cases compared to community samples.[14]

Cerebral amyloid angiopathy (CAA) reflects replacement of the smooth muscle cells of the cerebral arteriolar media by fibrillar amyloid which results in weakening of the walls.[24] CAA is strongly associated with AD, found in the majority of patients with AD as well as

being most severe in AD.[11,24] A quarter of autopsy proven AD patients have been shown to demonstrate moderate to severe CAA, which is associated with a higher rate of hemorrhagic and ischemic lesions, and 83% have at least mild CAA.[12,25] In our population, CAA was exclusively present in patients with dementia, predominantly in AD by itself or in combination with another subtype of dementia. Some degree of CAA was seen in the majority of AD patients, with 56.9% demonstrating moderate to severe CAA. Furthermore, 76.3% of AD patients with evidence of infarcts showed CAA while 25.7% of AD patients with moderate to severe CAA demonstrated infarcts, consistent with a close relationship between CAA and impaired cerebral perfusion. The one case of vascular dementia showed multiple lacunar and microinfarcts as well as moderate CAA and severe atherosclerosis. However, as microinfarcts were detected incidentally in standard brain sections taken during autopsy, one limitation is sampling bias in cases in which a smaller number of sections were taken, such as in those with a clinical suspicion of Creutzfeldt-Jakob disease.

In the examination of brains from demented subjects, Lim et al. have demonstrated the concomitant presence of other pathologic abnormalities such as hippocampal sclerosis (HS) in addition to the characteristic neuropathologic substrates of dementia.[14] HS is neuron loss and gliosis usually in the subiculum and CA1 sector of the hippocampus, associated with temporal lobe epilepsy in young patients and with cognitive dysfunction and dementia, but not epilepsy, in elderly patients.[26] HS can be found in isolation in 2–4% of cases but is associated with other neurodegenerative disorders, such as AD, FTD, and vascular dementia in 12–20%; one study has shown HS to be present in more than 25% of demented patients 80 years old and above.[27,28] Symptoms are typically attributed to another dementia disorder, and HS is usually only found at autopsy.[27] Several community based studies have described the frequent finding of HS in non-AD dementia.[29,30] Hippocampal sclerosis was seen in 9.6% of dementia patients, mostly in subjects with AD solely or with concomitant ischemic lesions and was not seen in any of our non-demented patients. As the CA1 sector is vulnerable to hypoxic/ischemic injury, one mechanism underlying HS is thought to result from an ischemic insult to the brain, and HS has been associated with cardiovascular risk factors such as hyperlipidemia and myocardial infarction.[28] In our cohort, 10 out of 14 of AD patients with HS showed some degree of cerebral atherosclerosis, suggestive of ischemic insults contributing to the development of HS.

In summary, our study examining the cause of death and medical and cerebrovascular comorbidities in demented patients attest to the utility of autopsies in the assessment of terminal life care in this growing population and is important in the investigation of disease pathology in dementia.

Acknowledgments

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Table 1

Demographic Characteristics of Subjects with Dementia

	ADRC, n (%)	Non-ADRC, n (%)
Total	60	158
Sex		
male	31 (52)	72 (46)
female	29 (48)	86 (54)
Ethnicity		
Caucasian	51 (85)	102 (65)
African American	4 (7)	6 (4)
Hispanic	2 (3)	1 (1)
Asian	0	5 (3)
Other	0	1 (1)
unknown	3 (5)	43 (27)
Education		
> high school	40 (67)	45 (28)
high school	11 (18)	6 (4)
< high school	3 (5)	0
unknown	6 (10)	107 (68)
Marital status		
never married	0	5 (3)
married	33 (55)	76 (48)
widowed	17 (28)	26 (16)
divorced/separated	7 (12)	11 (7)
unknown	3 (5)	40 (25)
Age (mean years ± SD) (n)		
symptom onset	68.6 ± 9.4 (50)	67.5 ± 11.8 (86)
entry	73.0 ± 8.2 (57)	N/A
death	77.6 ± 8.9 (60)	79.1 ± 11.1 (158)
Symptom duration (mean years ± SD) (n)	8.1 ± 3.7 (50)	8.7 ± 5.0 (86)

ADRC, Alzheimer disease research center; SD, standard deviation; > high school, higher than high school education; high school, high school education; < high school, less than high school education; N/A, not applicable.

Table 2

Cause of Death and Comorbidity in Complete Autopsy Examinations

	Type of dementia											Total	No dementia
	AD	AD & Isch	AD & DLBD	AD & other	VaD	DLBD	FTD	PD	PSP	NPH	Other		
n (% of patients)	45 (52.3)	14 (16.3)	6 (7.0)	2 (2.3)	1 (1.2)	4 (4.7)	5 (5.8)	2 (2.3)	2 (2.3)	2 (2.3)	3 (3.5)	86 (100)	124
Cause of death													
PNA	31	9	3	1	1	3	2	2	2	…	3	57	26
CVD	8	4	…	…	…	…	1	…	…	1	…	14	35
PTE	2	…	1	…	…	…	…	…	…	…	…	3	1
Sepsis	2	…	2	…	…	1	…	…	…	1	…	6	22
Cancer	2	…	…	…	…	…	1	…	…	…	…	3	17
Other	…	1	…	1	…	…	1	…	…	…	…	3	23
Comorbidity													
Coronary artery dz													
MI	8	4	2	…	…	…	…	1	…	1	…	16	53
Mild	8	1	…	…	…	…	…	…	…	…	1	10	13
Mod	8	4	2	…	…	…	1	…	…	…	…	15	21
Severe or stent/CABG	16	3	2	1	…	…	2	1	…	…	1	26	39
NS	2	2	1	…	1	…	…	…	…	…	…	6	3
PNA	32	9	3	2	1	4	…	2	2	…	3	58	37
PTE	10	2	2	…	…	…	1	…	…	…	…	15	25
COPD/lung dz	9	5	…	…	…	…	1	1	…	1	1	18	30
Tumors													
Lung	1	…	…	…	…	…	…	…	…	…	…	1	5
GI	4	1	1	…	…	…	…	1	…	…	…	7	11
CNS	2	…	…	…	…	…	…	…	…	…	…	2	…
GU	2	1	…	…	1	…	1	1	…	…	…	6	10
Other	2	3	2	…	…	…	1	…	…	…	…	8	9
GU inf	9	1	3	1	…	…	1	…	…	1	…	16	7

AD, Alzheimer disease; Isch, ischemic lesions; DLBD, diffuse Lewy body disease; VaD, vascular dementia; FTD, frontotemporal dementia; PD, Parkinson disease; PSP, progressive supranuclear palsy; NPH, normal pressure hydrocephalus; CVD, cardiovascular disease; MI, myocardial infarction; Mod, moderate; CABG, coronary artery bypass graft; NS, not specified; PNA, pneumonia; PTE, pulmonary thromboembolism; COPD, chronic obstructive pulmonary disease; dz, disease; GI, gastrointestinal; CNS, central nervous system; GU, genitourinary; and inf, infection.

Table 3

Central Nervous System Comorbidity and Clinical Diagnoses in Complete and Partial (Brain Only) Autopsy Examinations

	Type of dementia												
	AD	AD & Isch	AD & DLBD	AD & other	VaD	DLBD	FTD	PD	PSP	NPH	Other	Total	No dementia
n (% of patients)	123 (56.4)	24 (11.0)	24 (11.0)	4 (1.8)	1 (0.5)	7 (3.2)	14 (6.4)	5 (2.3)	5 (2.3)	3 (1.4)	8 (3.7)	**218 (100)**	124
Cerebral amyloid angiopathy													
Mild	25	1	6	...	...	1	...	...	...	...	...	**33**	...
Mod	25	3	5	...	1	1	2	...	...	...	...	**37**	...
Sev	45	11	3	1	...	...	...	...	...	...	...	**60**	...
NS	3	...	1	...	...	...	...	...	...	...	...	**4**	...
Hippocampal sclerosis	14	3	...	...	...	1	2	1	...	...	...	**21**	...
Infarct													
Micro	29	10	4	...	1	...	...	2	...	...	1	**47**	23
Lac	4	6	...	...	1	...	1	1	...	...	1	**14**	6
Macro	5	8	2	...	...	1	...	...	...	...	...	**16**	15
Cerebral atherosclerosis													
Mild	32	2	6	1	...	2	2	...	2	...	2	**49**	11
Mod	27	7	7	...	...	1	3	1	2	...	1	**49**	7
Sev	27	9	4	...	1	...	2	2	...	...	1	**46**	13
NS	3	1	...	...	...	...	1	...	...	...	...	**5**	...
Clinical dx, n (%)													
AD	83 (67)	9 (38)	8 (33)	1 (25)	...	3 (43)	...	1 (20)	...	...	2 (25)	**107 (49)**	N/A
VaD	5 (4)	2 (8)	...	...	1	...	...	...	...	...	...	**8 (4)**	N/A
DLBD	1 (1)	1 (4)	5 (21)	...	...	1 (14)	1 (7)	...	...	...	...	**9 (4)**	N/A
FTD	6 (5)	2 (8)	1 (4)	...	...	...	10 (71)	...	...	...	...	**19 (9)**	N/A
PD	2 (2)	...	4 (17)	2 (50)	...	2 (29)	...	3 (60)	...	...	...	**13 (6)**	N/A
PSP	...	...	...	...	...	...	...	1 (20)	5	...	1 (13)	**7 (3)**	N/A
NPH	...	1 (4)	...	...	...	...	...	...	...	3	...	**4 (2)**	N/A
other	6 (5)	1 (4)	3 (13)	1 (25)	...	...	3 (21)	...	...	...	5 (63)	**19 (9)**	N/A
mixed	5 (4)	1 (4)	1 (4)	...	...	...	...	...	...	...	...	**7 (3)**	N/A
NOS	15 (12)	7 (29)	2 (8)	...	...	1 (14)	...	...	...	...	...	**25 (11)**	N/A

AD, Alzheimer disease; Isch, ischemic lesions; DLBD, diffuse Lewy body disease; VaD, vascular dementia; FTD, frontotemporal dementia; PD, Parkinson disease; PSP, progressive supranuclear palsy; NPH, normal pressure hydrocephalus; Mod, moderate; Sev, severe; NS, not specified; Micro, microscopic; Lac, lacunar; Macro, macroscopic; dx, diagnosis; mixed, mixed dementia; NOS, dementia not otherwise specified; N/A, not applicable.