



# Coexistence of multiple sclerosis and Alzheimer's disease



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## INTRODUCTION

- People with multiple sclerosis (MS) are living longer than ever (1, 2) and will likely face the same age-related diseases as other seniors.
- Little is known about the coexistence of MS with Alzheimer's disease (AD), the most common form of dementia worldwide (3).

## OBJECTIVES

1. To determine if MS and AD can coexist in the same patient.
2. To identify the clinical and neuropathological features of an individual with both MS and AD.

### Approach:

Step 1: A literature review

Step 2: Create original case-series of AD/ MS

## METHODS

### Step 1: Focused literature review

- We searched PubMed (to May, 2017) to find published articles reporting coexisting cases of MS and AD.
- Of 2216 possible articles, 6 reported both MS and AD.
- Of the 6 included articles, 1 was an abstract from an observational self-report survey, 3 were case reports, and 2 were case series.

### Step 2: Create original case-series using a pathology database search

- The Vancouver Coastal Health Authority, Canada, anatomical pathological database was searched for possible cases of coexisting MS and AD (January, 1980 – May, 2017).
- Of 14,007 total autopsy reports, 8 were retrieved and 4 included; i.e. had sufficient information to confirm existence of AD & MS.
- Post-mortem pathological (autopsy) reports were extracted and linked to medical records.

## STEP 1: FOCUSED LITERATURE REVIEW

Authors, year, country, (citation)	Number of cases; sex; age‡; MS disease course	Study design	Summary
Weber & Ulrich, 1976, Switzerland, (4)	N=1; F; 63 years; N/R	Case report, included autopsy	Clinical history of progressive dementia. Autopsy revealed MS, encephalitis, and AD.
Barkhof et al., 1993, The Netherlands, (5)	N=1; M; 73 years; 'clinically silent'	Case report, included autopsy	Clinical diagnosis of 'probable' AD. Pre-mortem MRI: periventricular white matter lesion. Autopsy confirmed AD diagnosis and inactive MS lesion. MS lesion also found in the cervical spinal cord.
Dal Bianco et al., 2007, Austria, (6)	N=8; N/R; >64 years; 'progressive'	Case series, autopsies only	Archival autopsy material from 45 patients with MS examined. 8 'probable AD' cases; criteria: Consortium to Establish AD Registry.
Frischer et al., 2009, Austria, (7)	N=11; N/R; N/R; RRMS, SPMS, PPMS, & 'benign'	Case series, autopsies only	Archival autopsy material from 67 MS patients. 11 had evidence of AD - cortical lesions containing amyloid plaques and neurofibrillary tangles fulfilling same criteria as above.
Stewart et al., 2011, USA, (8)	N=10; N/R; N/R; N/R	Self-report online survey	USA's National Health and Wellness online Survey: 549 MS cases compared to 74,451 controls. MS cases more likely to report coexisting AD vs. controls (10 [1.9%] vs. 77 [0.1%], respectively, p<0.001).
Flanagan et al., 2014, USA, (9)	N=3; 2F & 1M; 53-56 years; suggestive of PPMS	Case report, included one autopsy	All 3 had progressive dementia. 1 case had post-mortem diagnosis of MS and AD. 2 cases diagnosed premortem by decreased CSF amyloid-β <sub>1-42</sub> /tau index, MRI, and 18F-fluorodeoxyglucose-PET patterns.

F = female; M = male; MRI = magnetic resonance imaging; N/R = not reported; PET = positron emission tomography; PPMS = primary progressive multiple sclerosis; RRMS = relapsing remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis. ‡Age or age range at death.

## STEP 2: PATHOLOGY DATABASE SEARCH

Case ID	Sex; Race	Year birth-death (age); Cause of death	MS disease course	AD disease course	MS & AD pathology
1	Female; N/R	1922-1997 (74 years); Pneumonia and empyema.	SPMS Onset symptoms: Diplopia, reduced visual acuity, fatigue, weakness & loss of sensation, unstable gait, and urinary incontinence.	At age 70: cognitive dysfunction and decreased responsiveness. Visual hallucinations, memory impairment, speech problems.	Multiple areas of demyelination in brain and spinal cord. Moderate number of neuritic plaques in the neocortex.
2	Female; Caucasian	1935-2013 (77 years); Disseminate adenocarcinoma	SPMS Onset symptoms: Optic neuritis, truncal ataxia, weakness & sensory loss, disequilibrium, and urinary incontinence.	At age 59: 'Mental changes'; cognitive slowing, memory impairment, and impairment reading and writing.	Multiple demyelinated areas. Occasional to moderate neuritic plaques in the neocortex.
3	Female; Caucasian	1950-2010 (60 years); Not determined – autopsy limited to head and spinal cord.	MRI, age 56: multiple foci of demyelination. No pre-mortem MS diagnosis ('clinical symptoms not consistent with MS').	At age 56: cognitive impairment, decreased memory, orientation deficits. Worsening motor weakness, language deficits, rigidity & myoclonic jerks.	Multiple areas of demyelination consistent with MS. Frequent neuritic plaques and neurofibrillary tangles.
4	Male; N/R	1911-1986 (75 years); Ischemic heart disease	N/R	N/R	Multiple demyelinated areas in brain & spinal cord. AD-like changes of cerebral degeneration.

## CONCLUSION

- We highlight a critical gap in our understanding of two relatively common, challenging neurological conditions.
- As populations age, it is increasingly important to recognize and understand how to manage individuals living with both complex neurological conditions – MS and AD.

## DISCLOSURES

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