Comorbid Neuropathological Features in Multiple System Atrophy

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ABSTRACT

OBJECTIVE
To elucidate the distribution of comorbid neuropathology in multiple system atrophy (MSA) and its clinical correlation.

BACKGROUND
It has been reported that multiple protein accumulations are often present in neurodegenerative diseases, such as Lewy-related pathology in Alzheimer's disease (AD) and AD pathology in Lewy body disease. However, the comorbid neuropathologies in MSA and their correlation with clinical symptoms remain poorly understood. Although a subset of MSA patients develops cognitive impairment, its cause is also not well understood.

METHODS
This study included 160 pathologically proven MSA patients in the Mayo Clinic Brain Bank. We reviewed the medical records to identify the age at onset and the presence of dementia during the clinical course. MSA patients were divided into two groups according to the age of onset: early-onset (< 60 years; n = 95, female 45%) and late-onset (≥ 60 years; n = 65, female 42%). We examined comorbid pathologies, including AD pathology, Lewy-related pathology, TDP-43 proteinopathy, argyrophilic grains (AG), cerebral amyloid angiopathy (CAA), and aging-related tau astrogliopathy (ARTAG). We defined the presence of AD pathology based on the Braak neurofibrillary tangle (NFT) staging and the Thal amyloid phase if both of them were 3 or more. We compared the frequency of each pathology and the presence of dementia between the two age groups and groups with or without dementia.

RESULTS
The Braak NFT stage and Thal amyloid phase were positively correlated with age at onset. Among co-pathologies, AD pathology, Lewy-related pathology, AG, and CAA were significantly more common in the late-onset group. The number of comorbid pathologies significantly increased with age at onset. The frequency of dementia was not significantly different between the early-onset and late-onset groups. Furthermore, there was no significant difference in the frequency of comorbid pathologies between the two groups with and without dementia.

CONCLUSIONS
Comorbid pathologies were more common with increasing age of onset in MSA. However, there was no correlation between dementia and comorbid pathologies, suggesting that MSA pathology itself may contribute to dementia in MSA rather than comorbid pathologies.

OBJECTIVES

- To determine the frequency and severity of comorbid neuropathologies in multiple system atrophy (MSA)
- To elucidate their clinicopathological association

METHODS

- We investigated **160** pathologically confirmed MSA patients in the Mayo Clinic Brain Bank.
- Age at onset (AAO) and presence of cognitive impairment (CI) were extracted from medical records.
- We divided MSA patients into two groups according to the age of onset.
  - early-onset < 60 years; n = 95
  - late-onset ≥ 60 years; n = 65
- The following pathologies were examined:
  - AD pathology (amyloid β and NFT)
  - Lewy-related pathology
  - TDP-43 pathology
  - argyrophilic grains (AG)
  - cerebral amyloid angiopathy (CAA)
  - Age-related tau astrogliopathy (ARTAG)
- We compared the frequency of each pathology between early-onset and late-onset and with CI (n = 48) and without CI (n = 112).
- The association between comorbid pathologies and disease duration was also examined.

REFERENCES

1. Robinson JL, et al. Brain. 2018
2. Dugger BN, et al. Parkinsonism Relat Disord. 2014

RESULTS

FIGURE 1 Association between AAO and AD pathology

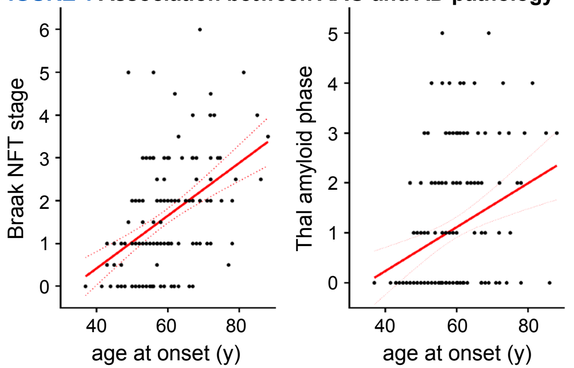


FIGURE 2 Number of co-pathologies

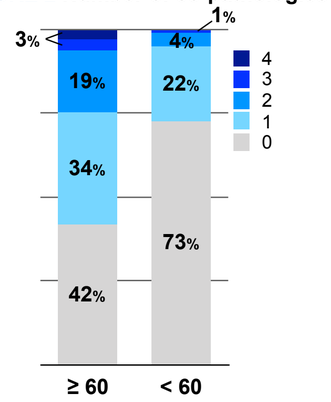
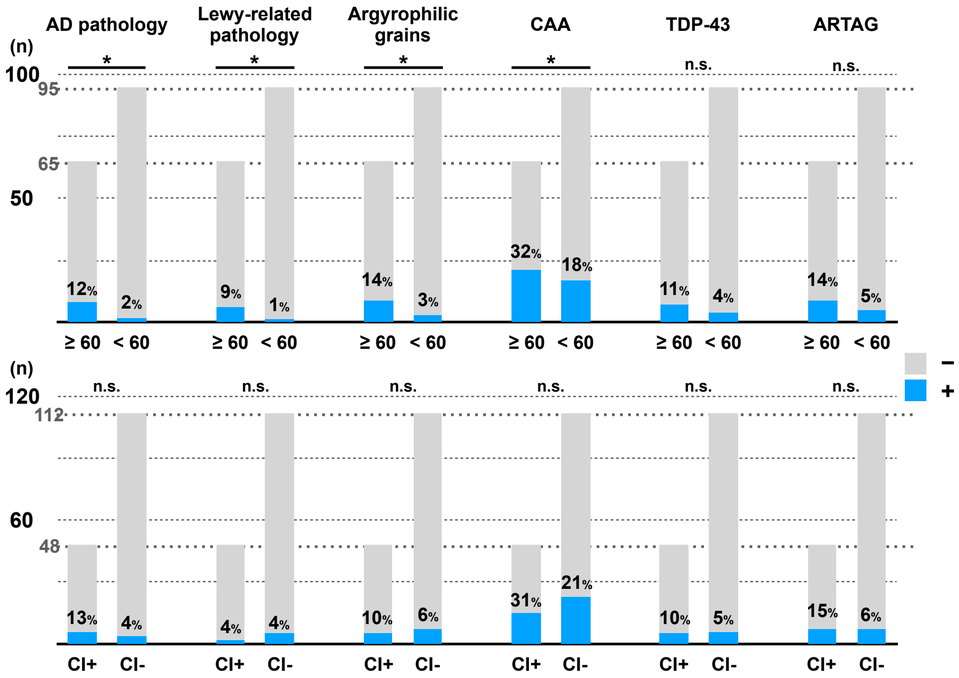


FIGURE 3 Frequency of each co-pathology



RESULT SUMMARY

- Braak NFT stage and Thal amyloid phase were associated with age at onset.
- The number of co-pathologies increased significantly in late-onset MSA.
- The frequency of AD pathology, Lewy-related pathology, argyrophilic grains, and CAA was significantly higher in late-onset MSA.
- There was no significant difference in any co-pathology between MSA patients with and without cognitive impairment.

DISCUSSION

- Diverse comorbid pathologies have been reported in neurodegenerative diseases, which may influence the clinical presentation[1].
- Previously, a small study reported there are various co-pathologies in MSA[2].
- In the present study, we confirmed a certain frequency of co-pathologies in MSA.
- Comorbid pathologies were more common with increasing age of onset in MSA.
- No correlation between dementia and comorbid pathologies, suggesting that MSA pathology itself may contribute to dementia in MSA rather than comorbid pathologies.

CONCLUSION

- We observed a certain frequency of comorbid pathologies in MSA.
- The co-pathologies increased with age at onset.
- No correlation was found between cognitive impairment and co-pathologies.