Coexisting Multiple Sclerosis and Huntington's Disease:
Reflections on the Immune Theory in Neurodegenerative Disorders

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Background

Variable disease associations have been described with multiple sclerosis (MS), including other immune-mediated and neurodegenerative disorders. Coexisting MS and Huntington's disease (HD) has not been previously described. This association raises questions on the interactions between immune dysfunction, neurodegeneration, and genetics.

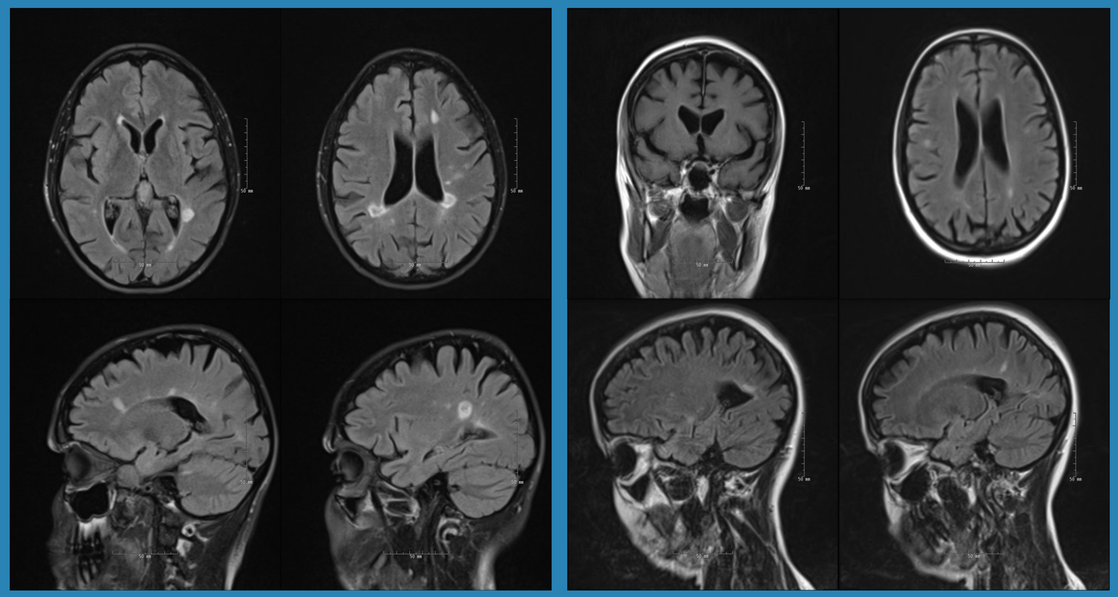
Case Reports

Case 1 is a 44-year-old female who developed diplopia and ataxia at the age of 31. Brain MRI showed supratentorial and brainstem T2 lesions with morphology typical of MS. CSF showed elevated IgG index and positive oligoclonal bands (OCBs). Symptoms resolved spontaneously. She was started on interferon β1-a (IFNb1a) two years later because of new enhancing MRI lesions. She subsequently developed gradual cognitive decline and abnormal movements of the face and limbs. Family history was positive for a paternal grandmother with HD. Her father had early dementia but was never tested for HD prior to his death at the age of 60 from heart disease. Exam showed generalized chorea and hyperreflexia with a UHDRS of 15 and EDSS of 3.0. HD was confirmed by genetic testing showing 38 CAG repeats.

Case 2 is a 45-year-old female who at the age of 43 developed progressive abnormal movements of the face and limbs with gradual cognitive decline. She had no family history of HD. Initial workup showed periventricular T2 lesions and a CSF positive for high IgG index and OCB's. She was diagnosed with MS and started on IFNb1a. She kept getting worse despite treatment. At the time of her initial evaluation at our institution, she exhibited generalized chorea with a UHDRS of 56. Genetic testing came back positive for 45 CAG repeats. She was diagnosed with de novo HD and radiologically-isolated syndrome.

FLAIR Images from Patient 1 Showing Classical MS Lesions and Mild Bilateral Caudate Atrophy

MRI Images from Patient 2 Showing Periventricular and Juxtacortical Demylinating Lesions Consistent with RIS + Bilateralcaudate Atrophy



Discussion

This is the first report of coexisting MS and HD. In 2012, Haghikia et al described a case of coexisting HD and multifocal autoimmune myelitis. Although this association between MS and HD could be coincidental, it is interesting that several recent studies have described abnormal immunity in HD mouse models and in presymptomatic patients. Immune dysfunction is thought to be an inciting factor for neurodegeneration in HD. This immune dysfunction is genetically determined and may anticipate higher risk for developing immune-mediated disorders like MS. Interestingly, both patients were continued on disease modifying therapy for MS without apparent benefit on the course or severity of HD, which supports the "trigger" concept of the immune dysfunction in HD as opposed to the ongoing process of immune-mediated injury seen in MS.

Conclusion

MS and HD may coexist and this should be sought for when symptoms cannot be explained by either disease alone. Immune-modulating therapy in presymptomatic HD patients may be an option for future Clinical trials.

References

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