

Atypical presentation of anti-Ma2-associated encephalitis with choreiform movement

Nathalie Lamby, MD, Frank Leypoldt, MD, Jörg B. Schulz, MD, and Simone C. Tauber, MD

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Correspondence

Prof. Tauber

stauber@ukaachen.de

Ma2 antibody-associated encephalitis is an inflammatory brain disease that associates with a systemic tumor in more than 90% of patients, most commonly a testicular germ-cell tumor, lung cancer, or breast cancer. The Ma2 antibody-mediated autoimmune encephalitis presents mostly as limbic, mesodiencephalic, or brain stem encephalitis. Cranial MRI often detects T2-hyperintense lesions that may progress to atrophy. However, other areas of the CNS, such as the brainstem, the thalamus, the hypothalamus, the cerebellum, or the basal ganglia may also be affected. Approximately one-third of patients with Ma2 antibody-associated encephalitis initially show no abnormalities in MRI. Roughly two-thirds of cases present abnormalities in the CSF, such as pleocytosis, protein increase, and positive oligoclonal bands.¹ In cases of paraneoplastic encephalitis, tumor therapy is crucial for improvement and prognosis. Immunotherapy using high-dose IV steroids, IV immunoglobulins, plasma exchange, rituximab, and cyclophosphamide is recommended.^{2,3} Here, we present an unusual clinical presentation of a Ma2-associated autoimmune encephalitis.

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Case report

A 72-year-old Caucasian woman, a retired librarian, presented with a 2-year history of memory deficits and mood instability, as well as uncontrollable right arm movements in the past year. She had increasing difficulty remembering the content of conversations and often misplaced items. She was becoming progressively nervous and anxious. Symptoms suggestive of temporal lobe epilepsy were denied. Because of the depressive mood, the patient was prescribed a medication with mirtazapine, and she reported no other medication. The patient had a medical history of osteoporosis and scoliosis.

On examination, there was a permanent chorea of the right arm (video) and mild sensory polyneuropathy. Neuropsychological testing demonstrated a mild multimodal cognitive impairment with deficits in memory, attention, executive function, and semantic fluency and mild depressive symptoms. Cranial MRI showed moderate microangiopathy and atrophy of the left hippocampus without contrast enhancement, and the EEG revealed epileptic potentials over the left temporal lobe. Diabetes and thyroid dysfunction were excluded, and ceruloplasmin level and antinuclear antibodies were within the normal range. CSF analysis showed a normal cell count and normal total protein, and isolated oligoclonal bands were present. A β 40 and A β 42, their ratio as well as tau and phospho-tau protein in the CSF were normal. Genetic testing failed to detect a mutation consistent with Huntington disease or other genetic disorders associated with choreatic disease (Huntingtin, PRNP, NKX2-1, ADCY5, FRRS1L, GNAO1, PDE10A, ATM). Paraneoplastic Ma2 antibodies were detected in serum using commercially available primate tissue-based assays and antigen-specific line blots (Euroimmun, Lübeck). PET—CT did not show evidence of a tumor. The patient was treated with 1 g methylprednisolone iv over 3 days followed by 1 mg/kg bodyweight prednisolone, slowly tapered over 3 months. Anticonvulsive therapy with lacosamide 100 mg b.i.d. was initiated. No immediate response was noted.

From the Department of Neurology (N.L., J.B.S., S.C.T.), RWTH University Hospital, Aachen; Institute of Clinical Chemistry and Department of Neurology (F.L.), University Hospital Schleswig-Holstein, Kiel; and JARA-Institute Molecular Neuroscience and Neuroimaging (J.B.S.), Forschungszentrum Jülich GmbH and RWTH Aachen University, Aachen, Germany.

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Nine months later, chorea and cognitive dysfunction were unchanged and the patient was no longer taking lacosamide. Repeat neuropsychological testing showed a similar profile compared with earlier testing. Cranial MRI remained unchanged and Ma2 antibodies were still detectable in serum. The EEG continued to demonstrate epileptic activity in the left hippocampal region. Repeat whole body PET-CT did not show any malignancy. The patient did not want a symptomatic therapy for the movement disorder.

Discussion

Ma2 antibody-associated encephalitis typically presents as limbic, mesodiencephalic, or brain stem encephalitis. Single cases of cerebellar ataxia, myelopathy, or radiculoplexopathy have been described.¹ Symptoms of limbic encephalitis include memory impairment, behavioral or mood disorders, as well as new-onset epileptic seizures. Our patient with a to date non-paraneoplastic Ma2-associated syndrome developed chorea in the right arm in addition to classic symptoms of limbic encephalitis. Choreiform movement disorders have been described frequently in association with other autoimmune encephalitis, in particular, NMDA and CV2/CRMP5 antibody-associated encephalitis.^{4,5} Choreiform movement disorders can also be associated with other diseases such as systemic lupus erythematosus, anti-phospholipid syndrome, Wilson disease, thyroid dysfunction, or diabetes.⁶ In the context of Ma2 antibody-associated encephalitis, there is, to our knowledge, only one comparable case of a movement disorder associated with Ma2-Ab in an Iranian male patient.⁷ In our patient, we interpreted the failure of improvement by steroids because of the already long duration of the disease symptoms. By this time, the active inflammation of the limbic encephalitis had probably already subsided. For this reason, we decided against further immunosuppressive therapy. We conclude that the atrophy of the hippocampus is the result of limbic encephalitis, leading to symptomatic epilepsy and persistent neuropsychological deficits. In conclusion, autoimmune etiology should be considered in patients with chorea, especially in the presence of cognitive dysfunction and antineuronal antibody screening initiated.

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Appendix Author contributions

Name	Location	Role	Contribution
Nathalie Lamby, MD	Department of Neurology, RWTH University Hospital, Aachen, Germany	Author	Patient care, drafting the manuscript, editing, review of the literature
Frank Leypoldt, MD	Institute of Clinical Chemistry and Department of Neurology, University Hospital Schleswig-Holstein, Kiel, Germany	Author	Critical review of the manuscript, intellectual contribution
Jörg B. Schulz, MD	Department of Neurology, RWTH University Hospital, Aachen, Germany	Author	Patient care, contribution to manuscript editing
Simone C. Tauber, MD	Department of Neurology, RWTH University Hospital, Aachen, Germany	Author	Manuscript concept and design, critical review of the manuscript, editing of the final text

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