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Absence of Decussation in Optic Pathway Inflammation in Neuromyelitis Optica and Its Implications for Astrocyte Localization

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Abstract: A 39-year-old woman presented with acute visual loss in her right eye. Brain and orbit MRI demonstrated T2 hyperintensity along a long section of her right optic nerve, chiasm, and tract with no evidence of decussation of the inflammation. Subsequent seropositivity for the aquaporin 4 antibody confirmed a diagnosis of neuromyelitis optica. Posterior pathway involvement is typical in neuromyelitis optica and supports the hypothesis that the condition is an astrocytopathy. Furthermore, the absence of decussation in the condition may be a function of astrocyte localization within the chiasm.

Journal of Neuro-Ophthalmology 2020;00:1–3
doi: 10.1097/WNO.0000000000000985
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FIG. 1. Axial image from a contrast T2 head MRI demonstrating long unilateral tract inflammation.
dsDNA, and serum protein electrophoresis were all normal. Additional serological testing for *Toxocara*, *Mycoplasma*, *Brucella*, *Bartonella*, *Toxoplasma*, CMV, HIV, Lyme, Mumps, EBV, *Treponema*, Measles, and acid-fast bacilli were all normal. Lumbar puncture demonstrated a normal opening pressure of 12 cm H₂O with normal white cells, glucose, and protein. An MRI of the brain and orbits showed a T2 high signal change in the intraorbital and prechiasmatic right optic nerve, the right optic chiasm, and right optic tract. The left optic nerve, chiasm, and tract were otherwise normal.

The patient was initially treated with IV methylprednisolone 500 mg daily for 3 days, commencing on day 2 of admission, followed by 60-mg oral prednisolone. Aquaporin 4, AQP4 antibodies were subsequently found to be positive. After steroid treatment, vision improved to hand movements in the right eye and the retro-orbital pain resolved. Repeat MRI brain and orbits on day 20 of admission demonstrated a reduction in T2 hyperintensity. The patient was subsequently started on long-term azathioprine.

This patient’s initial MRI (Figs. 1–3) demonstrated involvement of the right optic nerve, chiasm, and tract without any involvement of the contralateral tract. A radiographic 12-patient case series, which mapped optic pathway involvement in NMOSD, supports the notion that the absence of decussation of optic pathway inflammation is typical in neuromyelitis optica spectrum disease, NMOSD (1). Of these cases, 2 cases replicated our patient with ipsilateral nerve, chiasm, and tract involvement. Seven cases showed only nerve and chiasm involvement and the remaining 3 cases demonstrated bilateral nerve, tract, or chiasm involvement. No cases demonstrated involvement of the optic nerve with unilateral contralateral tract involvement. Furthermore, we could not identify any reported cases of apparent decussation of inflammation. We hypothesize that this pattern of anterior optic pathway inflammation, typical in NMOSD, is due to astrocyte localization within the chiasm.

In 75% of NMOSD patients, there is seropositivity for IgG binding AQP4 (2). AQP4 is a transmembrane protein that regulates transmembrane water flux. AQP4 is highly expressed in astrocytes found in the brain, spinal cord, and optic nerves. Astrocyte localization within the optic tract is therefore likely to influence the localization and pattern of inflammation (2). This hypothesis is supported by the observation that the anatomical localization of AQP4 within the brain and spinal cord correlates with patterns of disease involvement (3). We believe that the localization of astrocytes within the anterior optic pathway explains both the pattern of nerve involvement and the absence of decussating neuroinflammation seen in our case report.

Inflammation in NMOSD seems to have a greater predilection for optic tract involvement in comparison with multiple sclerosis/optic neuritis (1). This clinical observation may be explained by astrocyte localization; studies in the mouse optic tract have shown that astrocytes exist in higher concentrations in the posterior visual pathway (towards the latrogeniculate nucleus). Furthermore, within the optic nerves, tracts, and lateral chiasm, astrocytes are arranged longitudinally, parallel to the nerve fascicles in the interfascicular space (Fig. 4) (5). However, within the medial chiasm, glial cells take on a radial morphology where they form a palisade at the ventral midline. These glia may provide a physical barrier to the spread of inflammation, or they may be resistant to AQP4-mediated disease due to different protein

FIG. 2. Axial image from a contrast T2 head MRI demonstrating long unilateral tract inflammation.

FIG. 3. Axial image from a contrast T2 head MRI demonstrating long unilateral tract inflammation.
expression (5). This patient demonstrated a pattern of long-tract involvement without decussation, which is typical in NMOSD. We hypothesize that the localization of astrocytes within the optic tract explains the absence of decussation seen in NMOSD.

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