



Paraneoplastic Neuromyelitis Optica Associated with Lung Adenocarcinoma in a Young Woman

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Dear Editor,

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory disorder of the central nervous system that preferentially affects the optic nerve, spinal cord, and area postrema.¹ The serum anti-aquaporin-4 antibody (anti-AQP-4 antibody) is specific for NMOSD. There are only a few reports of NMOSD presenting in the context of paraneoplastic neurological syndromes. Here we report a young woman who developed recurrent NMOSD in the setting of a lung adenocarcinoma.

A previously healthy 37-year-old woman presented with a palpable mass on the right side of the neck. The patient was diagnosed with metastatic adenocarcinoma after a biopsy of the mass, which was in a neck lymph node. Chest computed tomography and whole-body positron-emission tomography/computed tomography (PET-CT) revealed that the main mass was in her lung and that multiple metastases were present, classifying it as stage 4 (Fig. 1A). An *EGFR* mutation (deletion of exon 19) was also detected in the biopsied tissue.

During the diagnostic workup she developed progressive weakness of all extremities. When she visited our clinic, a neurological examination revealed weakness of Medical Research Council grade 3 to 4 in the upper extremities and grade 1 in the lower extremities, with hypoesthesia below the neck. She did not have an oral or genital ulcer, sicca syndrome, abnormal rash, or other manifestations implicating autoimmune disorders. Spine magnetic resonance imaging (MRI) showed a T2-weighted hyperintense lesion from level C2 to level T7 with gadolinium enhancement (Fig. 1B and C). Brain MRI revealed no abnormality. Cerebrospinal fluid analysis showed pleocytosis (60 cells/ μ L, 98% mononuclear cells) and an elevated protein level (138.2 mg/dL) without malignant cells or an oligoclonal band. Anti-AQP-4 antibody (indirect immunofluorescence test; Euroimmun, Lübeck, Germany) was detected in the serum. She was negative for antinuclear antibody. Based on these results she was diagnosed with NMOSD and was treated with a daily intravenous infusion of 1 g of methylprednisolone for 5 days, followed by a tapering course of oral prednisolone from an initial 45 mg daily [1 mg/kg body weight (47 kg)] to 10 mg daily at 3 months after the onset of myelitis. The lung adenocarcinoma was treated concurrently with gefitinib.

Three months after presenting with myelitis she experienced a painful visual disturbance in the left eye. An examination revealed bilateral papilledema and a visual field defect of the lower quadrant in the left eye. The visual acuity of her left eye was finger counting at 50 cm. Orbit MRI revealed an enlarged bilateral optic nerve with segmental enhancement of the left optic nerve (Fig. 1D and E). Optic neuritis was diagnosed. At this time her cancer was stable with gefitinib treatment. She was treated with another steroid pulse therapy (daily intravenous infusion of 1 g of methylprednisolone for 5 days), followed by a tapering course of oral prednisolone as for the previous myelitis. In addition, azathioprine was added at 150 mg daily [2.5 mg/kg body weight (60 kg)]. At 8 months after presenting with optic neuritis she was taking 5 mg of prednisolone and 150 mg of azathioprine daily. At 1 month after presenting with

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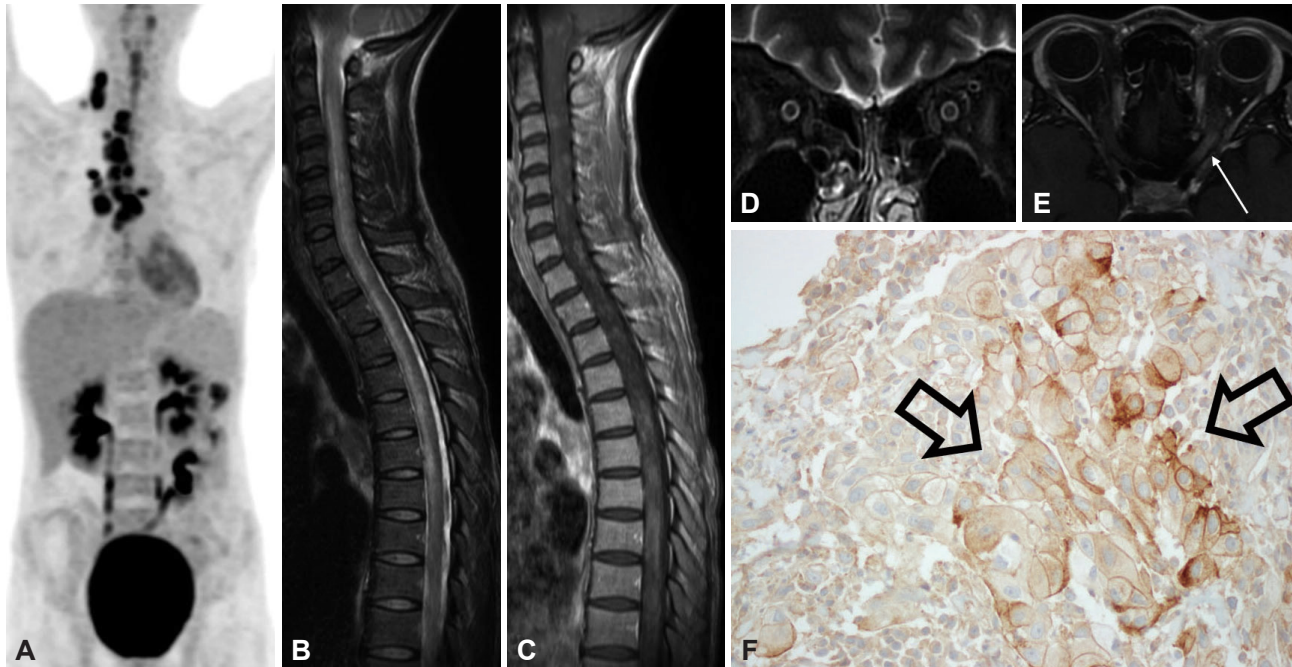


Fig. 1. Findings of imaging and immunohistochemistry studies. A: Positron-emission tomography/computed tomography showed increased FDG uptake in the lung and multiple lymph-node metastases. B: Sagittal T2-weighted image of the spine revealing a hyperintense lesion from level C2 to level T7. C: Sagittal T1-weighted image of the spine after infusing gadolinium showing multifocal enhancement. D: Coronal T2-weighted image of the orbit revealing bilateral optic nerve enlargement. E: Sagittal T1-weighted image of the spine after infusing gadolinium showing segmental enhancement of the left optic nerve (arrow). F: Immunohistochemistry of the patient's neck lymph nodes showed positive membranous anti-aquaporin-4 immunoreactivity (open arrows) ($\times 400$).

optic neuritis her visual acuity recovered to 0.7. At the latest follow up, which was performed 8 months after presenting with optic neuritis, she remained relapse-free with an EDSS score of 3.5.

Immunohistochemistry of formalin-fixed paraffin-embedded slides of the patient's neck lymph nodes showed positivity for membranous AQP-4 immunoreactivity in the cluster of the metastatic carcinoma [anti-AQP4 antibody (A5971, Sigma-Aldrich, St. Louis, MO, USA)] (Fig. 1F).

Paraneoplastic NMOSD has been reported recently,² with some studies showing AQP-4 expression in the actual tumor cells.^{3,4} AQP-4 may have role in tumor progression, invasion, and metastasis.⁵ However, the pathophysiology underlying paraneoplastic NMOSD remains to be elucidated.

Combined treatment of anticancer therapy and an immunosuppressive agent usually results in paraneoplastic NMOSD that is episodic.^{3,6} One recurrent case occurred under the circumstance of cancer relapse.⁷ However, in our patient the NMOSD recurred in spite of combined treatment and relatively stable cancer. Therefore, the clinician should keep the possibility of recurrence in mind, and might consider additive immunosuppressive treatment upon the recurrence of paraneoplastic NMOSD.

Conflicts of Interest

The authors have no financial conflicts of interest.

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