Anti-*N*-Methyl-D-Aspartate Receptor Encephalitis in a Young Woman with a Mature Mediastinal Teratoma

Daniel G. Stover, MD, Rosana Eisenberg, MD,† and David H. Johnson, MD*‡*

Anti-*N*-methyl-D-aspartate (NMDA) receptor encephalitis is a recently described paraneoplastic disorder associated with germ cell tumors. Patients, typically young women, present with psychiatric disturbances and develop decreased consciousness, hypoventilation, seizures, dyskinesias, and autonomic instability.[1] Mediastinal teratomas in women are exceedingly rare. Extragonadal germ cell tumors represent only 1 to 3% of all germ cell tumors; more than 90% of these affect males.[2]

CASE REPORT

The patient was a 19-year-old woman who developed amnesia and personality changes 3 months before presentation. She demonstrated increasingly bizarre behavior including religious preoccupation, auditory hallucinations, and exhibited several distinct personalities. Shortly after presentation, she developed declining mental status, dystonic movements, and decreased respiratory drive requiring intubation and mechanical ventilation. She also developed resistant seizures requiring pentobarbital-induced coma to abrogate status epilepticus. Lumbar puncture yielded a mildly increased opening pressure of 42 cm; the results of extensive further studies and comprehensive cultures were otherwise negative. Brain magnetic resonance imaging was unrevealing.

Mediastinal widening was noted on chest x-ray, and computed tomography scan of the chest demonstrated a right anterior mediastinal mass with no adenopathy (Figure 1*A*). Positron emission tomography scan demonstrated intense fludeoxyglucose avidity in aspects of the mass with no evidence of metastasis (Figure 1*B*). Paraneoplastic antibody studies of the cerebrospinal fluid demonstrated the presence of anti-NMDA receptor antibody. She was started on plasma exchange and high-dose corticosteroids with little improvement in her ongoing seizure activity. The patient underwent resection of the mediastinal mass, 7.0 × 6.0 × 4.0 cm and 68.5 g. Serial sections demonstrated different types of tissue derived from all three germ layers (Figure 2): ectodermal: neural tissue and skin; mesodermal: cartilage, adipose tissue, and smooth muscle; endodermal: respiratory epithelium, gastrointestinal epithelium, and pancreatic tissue. The margins were negative.

Given ongoing symptoms postoperatively, she received 375 mg/m^2 rituximab three times and 800 mg cyclophosphamide once in addition to high-dose steroids and plasma exchange, resulting in improved seizure control. However, the patient developed malignant catatonia that ultimately responded to 13 electroconvulsive treatments. At follow-up, 2 months after discharge, she reported ongoing amnesia related to her hospitalization but had near-complete recovery of her ability to form new memories. She is planning to return to college.

DISCUSSION

Anti-NMDA receptor encephalitis is a rare paraneoplastic syndrome typically associated with germ cell tumors in young women. This disorder is characterized by antibodies against the heteromeric NR1–NR2 receptor complex.[3] In the largest series to date, the majority of identifiable tumors were ovarian teratomas (84%; 49 of 58).[1] In this report, we present the second case of this syndrome in a woman with a mediastinal teratoma.

Benign teratomas do not require systemic chemotherapy or radiation if the tumor is completely surgically resected, and there is no evidence of malignant transformation.[2,4] Early removal of the underlying tumor is associated with significantly improved outcomes and fewer relapses for anti-NMDA receptor encephalitis.[1] Even with early tumor resection, prolonged hospital stays (98 days in this case) are not atypical, possibly due to significantly slower decrease of antibody titers within the cerebrospinal fluid relative to the serum.[5] Rituximab and cyclophosphamide, shown effective in immune-mediated central nervous system disorders, may allow improved control of central nervous system immune response relative to corticosteroids, plasma exchange, or intravenous immunoglobulin.[1]

In conclusion, teratoma should be considered in patients with psychiatric disturbances, dystonia, and seizure, including evaluation of the mediastinum. Primary therapy should include resection of the primary tumor along with immunotherapy, with treatment considerations including rituximab and cyclophosphamide.

Departments of *Medicine and †Pathology and ‡Division of Hematology and Oncology, Vanderbilt University Medical Center, Nashville, Tennessee.

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Address for correspondence: David H. Johnson, MD, 777 Preston Research Building, 2220 Pierce Avenue, Nashville, TN 37232. E-mail: david.johnson@vanderbilt.edu

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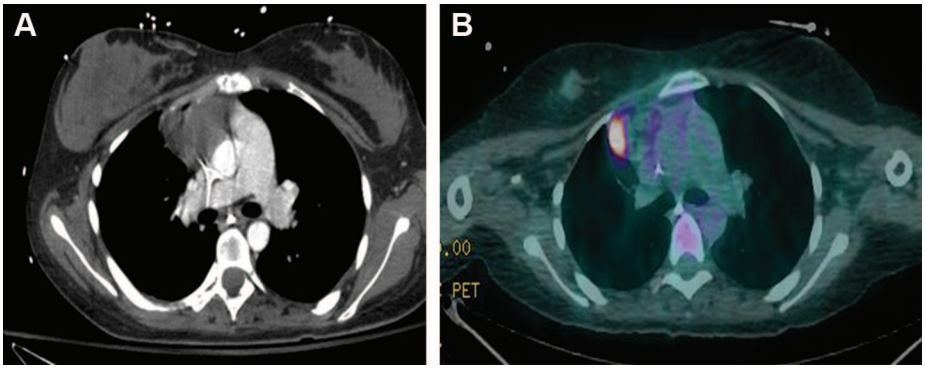

FIGURE 1. Imaging of mediastinal tumor. *A*, Computed tomography scan of the chest with intravenous contrast demonstrated a 3.5 cm × 6.2 cm right anterior mediastinal mass with scattered adipose signal; no adenopathy was present. *B*, Positron emission tomography scan demonstrated intense fludeoxyglucose uptake within the lateral aspect concerning for malignancy. There was no evidence of fludeoxyglucose avid metastasis.

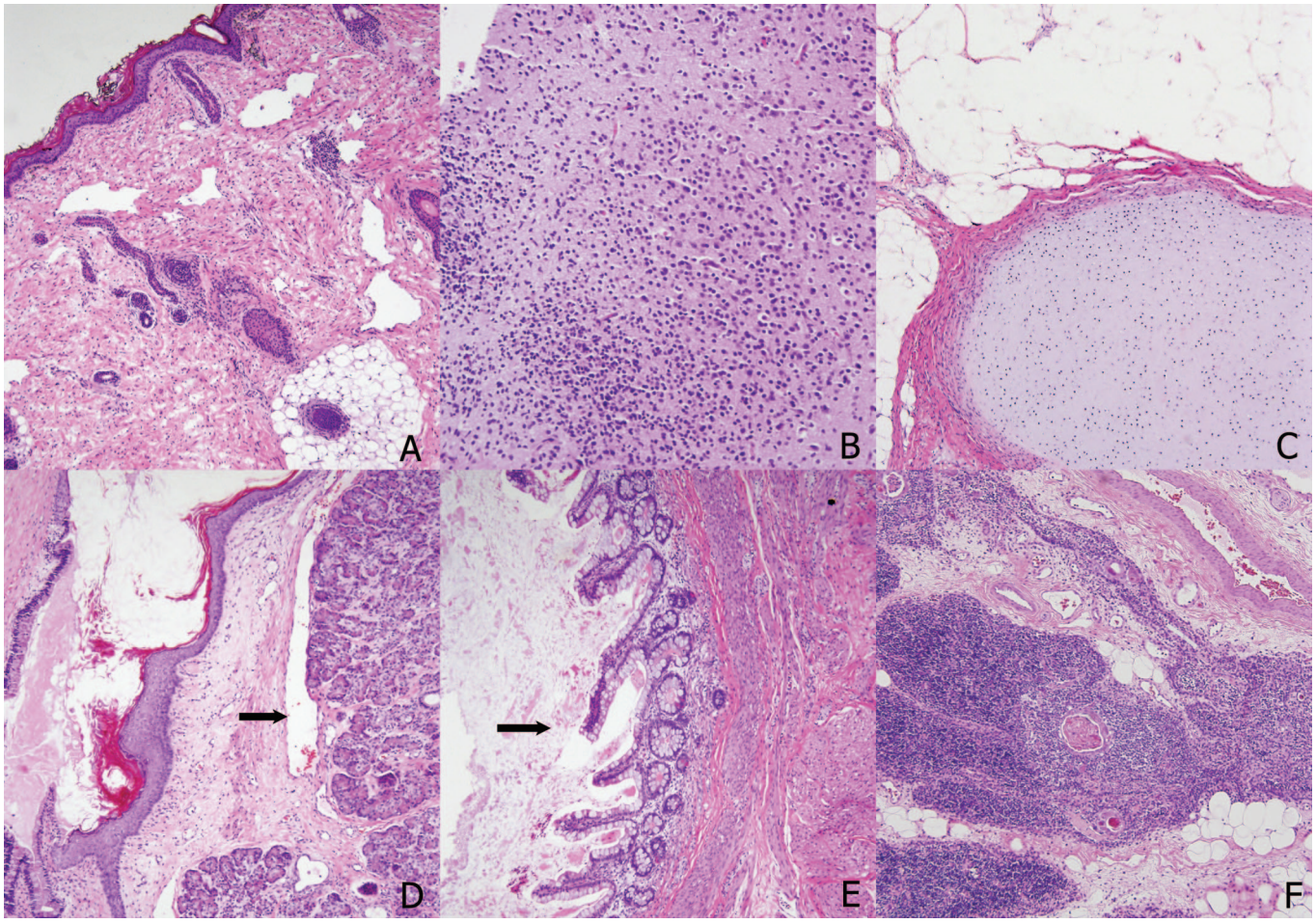

FIGURE 2. Histologic sections of the resected mature teratoma, located in the right inferior pole of the thymus, depicting different types of tissue. *A*, Skin including epidermis and dermis with adnexal structures. *B*, Mature neural tissue resembling cerebral cortex. *C*, Cartilage and adipose tissue. *D*, Pancreatic tissue (*arrow*) and cyst lined by keratinized squamous epithelium and mucinous glandular epithelium (*left*). *E*, Cyst lined by small intestinal type mucosa (arrow) and surrounded by smooth muscle. *F*, Residual thymic tissue.

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