CASE REPORT

Profound Sinus Node Dysfunction in Anti-N-Methyl-D-Aspartate Receptor Limbic Encephalitis

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A form of limbic encephalitis associated with antibodies against the N-methyl-D-aspartate receptor (NMDAR) was discovered in 2007. It is often a multistage illness that progresses from psychosis, memory deficits, seizures into a state of unresponsiveness with catatonic features, abnormal movements, autonomic, and respiratory instability. We present two cases of anti-NMDAR encephalitis to highlight the cardiac complications and their management. (PACE 2011;1–3)

sinus node dysfunction, encephalitis; N-methyl-D-aspartate receptor, arrhythmia, autonomic dysfunction

Case A

A 20-year-old Chinese woman with no significant medical history presented with three episodes of generalized tonic clonic seizures. She had a 3-day history of headaches and rhinorrhea. She had dyskinesias involving her right hand, shoulder, and hip and expressive dysphasia. She required endotracheal intubation for respiratory distress.

Serum autoimmune markers, ceruloplasmin levels, bacterial blood cultures were negative. Analysis of the cerebrospinal fluid (CSF) revealed lymphocytic pleocytosis and negative bacterial and viral workup. Magnetic resonance imaging of the brain was normal. Electroencephalography showed no epileptiform activity. Computed tomographic scan of her abdomen and pelvis revealed a large left ovarian dermoid cyst (see Fig. 1). Serum anti-N-methyl-D-aspartate receptor (NMDAR) antibody level was positive.

The diagnosis was anti-NMDAR limbic encephalitis associated with a left ovarian dermoid cyst. A successful resection of the dermoid cyst was performed and was histologically benign. The patient was also treated with intravenous immunoglobulins and her neurological status improved.

The patient developed severe hypotensive episodes due to autonomic dysfunction. This precipitated a type 2 acute myocardial infarction (AMI).[1] The electrocardiogram showed widespread downsloping ST-segment depression (see Fig. 2) and peak serum Troponin I level of 51 μg/L. Transthoracic echocardiography showed a normal left ventricular ejection fraction and no significant regional wall motion abnormality. Treatment was supportive with intravenous dopamine.

The patient also developed profound sinus node dysfunction, with marked sinus arrhythmia and frequent episodes of sinus arrest, longest duration being 9.2 seconds (see Fig. 2). These were refractory to intravenous atropine. A temporary transvenous pacing wire was inserted via the right internal jugular vein with a base rate of 60 beats perminute. The pacing wire was changed at weekly intervals to avoid line-associated sepsis. The patient required cardiac pacing support for

Figure 1. *Computed tomography scan of the abdomen and pelvis with the white arrow indicating a large left ovarian dermoid cyst.*

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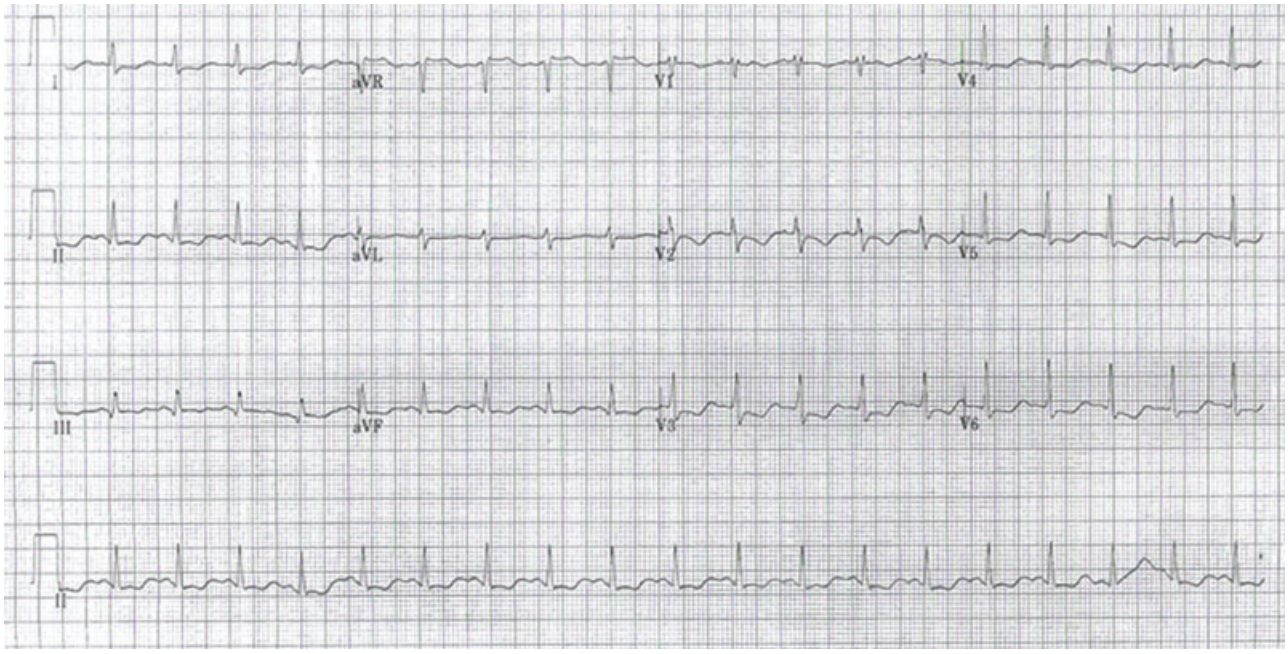

Figure 2. *Electrocardiography showing widespread horizontal and downsloping ST-segment depression in leads V2–V6, II, and aVF.*

16 days after which the pacing wire was removed with no further episode of sinus arrest.

Case B

A 33-year-old Japanese woman with no significant medical history presented with 3-day history of intermittent fever and occipital headaches, followed by short-term memory loss and paranoid delusions. She then became unresponsive, with orofacial dyskinesias and myoclonic jerks. She required endotracheal intubation for respiratory distress.

Serum autoimmune markers and tumor markers were negative. CSF analysis showed lymphocytic pleocytosis with no evidence of bacterial or viral infection. Serum anti-NMDAR antibody level was positive. Magnetic resonance imaging of her brain was normal. Serial electroencephalography did not reveal any epileptiform activity. Computed tomographic scan of her abdomen and pelvis revealed a 2-cm uterine fibroid and no other adnexal mass.

A diagnosis of anti-NMDAR limbic encephalitis was made. The patient was treated with intravenous immunoglobulins, intravenous methylprednisolone, and rituximab.

Due to autonomic dysfunction, the patient had episodes of hypotension, marked sinus arrhythmia, and frequent sinus pauses, longest being 5 seconds in duration (see Fig. 3). Treatment was supportive with intravenous dopamine. The autonomic instability and bradyarrhythmias resolved without need for cardiac pacing.

Discussion

The exact incidence of anti-NMDAR limbic encephalitis remains unknown. The disorder predominantly affects children and young adults, mostly women, and may be associated with ovarian tumors, especially ovarian teratomas.[2–4] Approximately 70% of patients have prodomal symptoms consisting of headache, fever, vomiting, diarrhea, or upper respiratory tract symptoms. Within several days, patients develop psychiatric symptoms such as anxiety, mania, and paranoia. Short-term memory loss is common. This initial phase is usually followed by decreased responsiveness that can alternate between periods of agitation and catatonia. At this stage, abnormal movements and autonomic instability are usual manifestations.[2–4]

The diagnosis is made based on the clinical features and the detection of anti-NMDAR antibodies in the blood or CSF. Screening tests should be done to look for associated tumors especially ovarian teratomas.

Patients are usually treated with tumor resection and immunotherapy. More than 75% of patients have substantial recovery that occurs in inverse order of symptom development and is associated with a decline of anti-NMDAR antibody titers.[4]

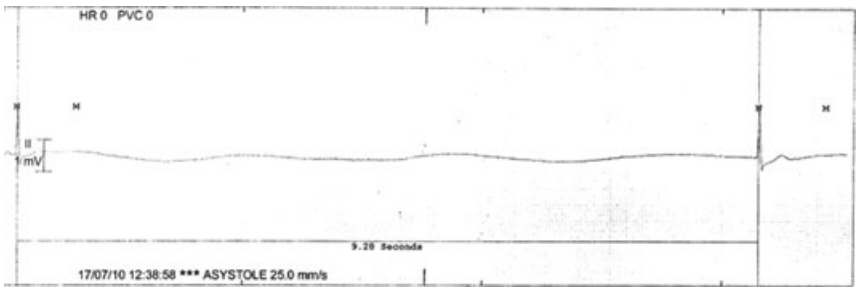

Figure 3. *Heart rate telemetry monitoring strip showing a long period of sinus arrest of 9.28 seconds.*

Cardiac complications include arrhythmias and labile blood pressure precipitated by autonomic storms. Treatment is supportive, with judicious use of intravenous inotropic agents in cases of severe hypotension and maintenance of optimum serum electrolyte levels. Patients should be on continuous telemetry heart rate monitoring. In cases of sinus arrest of more than 3 seconds, temporary cardiac pacing via transvenous or transcutaneous routes may be required, especially in the setting of associated hemodynamic instability. Permanent cardiac pacemakers should be avoided, as affected patients are generally young and the autonomic dysfunction will stabilize and resolve completely with treatment of the underlying encephalitis.

AMI in these patients is generally type 2 in nature, as the majority of patients are women of child-bearing age without significant risk factor for coronary artery disease. Imbalance of myocardial oxygen demand and supply may result from autonomic crisis or septic shock from nosocomial infections. Stress cardiomyopathy has been described in patients with anti-NMDAR encephalitis and attributed to episodes of extreme hypertension.[4] Treatment of type 2 AMI and stress cardiomyopathy is supportive. β-blockers and nondihydropyridine calcium channel blockers should be avoided in view of their propensity to aggravate bradyarrhythmias. The use of antiplatelet agents and statins in the treatment of type 2 AMI has not been well documented.

Cardiologists therefore play a largely supportive role in anti-NMDAR encephalitis, with immunotherapy being the mainstay of treatment and tumor resection where appropriate.

References

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