Periodic Myoclonus Due to Cytomegalovirus Encephalitis in a Patient With Good Syndrome

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Background: Good syndrome (GS) refers to a constellation of thymoma and adult-onset immunodeficiency characterized by low or absent B cells, hypogammaglobulinemia, and variable defects in cell-mediated immunity with an inverted CD4/CD8 T-cell ratio. Patients may develop severe or chronic infections as a result of this immunodeficiency.

Objective: To describe a patient with GS who developed cytomegalovirus (CMV) encephalitis and showed a periodic electroencephalographic pattern and myoclonus.

Design: Case report.

Setting: Outpatient neurology clinic at a university medical center.

Patient: A 64-year-old man who developed periodic myoclonus involving the right half of his body and the left arm.

Results: Five years previously, the patient had undergone resection of a pathologically confirmed epithelial thymoma. Quantitative CMV polymerase chain reaction of the serum and cerebrospinal fluid showed strongly positive results (1:10,000), allowing the diagnosis of CMV encephalitis.

Conclusions: To the best of our knowledge, myoclonus and periodic electroencephalographic pattern have not previously been reported in CMV encephalitis. Opportunistic CMV infection should be considered early in the evaluation of patients with GS or a history of thymoma who develop unusual neurological symptoms.

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GOOD SYNDROME (GS) refers to a constellation of thymoma and adult-onset immunodeficiency characterized by low or absent B cells in the peripheral blood, hypogammaglobulinemia, and variable defects in cell-mediated immunity with an inverted CD4+ T-cell lymphopenia and an inverted CD4/CD8+ T-cell ratio.1-3 Patients often develop severe or chronic infections as a result of this immunodeficiency.2-3 We describe a patient with GS who developed cytomegalovirus (CMV) encephalitis and showed a periodic electroencephalographic pattern and myoclonus.

REPORT OF A CASE

In September 2001, a 64-year-old man developed involuntary jerks of the face and arms lasting from a few minutes to several hours. Five years previously, he had undergone resection of a pathologically confirmed epithelial thymoma. The attacks were not painful, were not aggravated by fatigue, and did not interfere with his level of consciousness. During the next 2 months, the episodes increased progressively in frequency and also began to involve the legs. Results of computed tomography of the brain were normal, but magnetic resonance imaging revealed a small T1-hypointense and proton density/T2-hyperintense lesion of the right putamen and globus pallidum. Carbamazepine, clonazepam, and gabapentin were given with no improvement. The involuntary movements became almost continuous, and the patient was referred to the neurology clinic at Federico II University in January 2002. He displayed periodic myoclonus involving mostly the right half of his body and the left arm. These movements persisted during sleep. Cognition was intact, but expressive ability was impaired owing to the jerks. Neurological examination revealed moderate rigidity, increased deep tendon reflexes, left-
followed by rhythmic, low-amplitude, alphalike activity with the jerks. Occasionally, the delta waves were fairly regularly every 4 seconds with a 1:1 relationship with the jerks. Generalized, high-voltage biphasic delta waves, occurring every 4 seconds, were synchronous with myoclonus.

Electromyographic coregistration demonstrated periodic stereotyped jerks followed by short, sustained muscular activity. Electromyography revealed muscle discharges lasting about 500 milliseconds (slow myoclonus), asymmetric and slightly asynchronous (EMG1: right orbicular oris; EMG2: left forearm muscles). The waveform of delta complexes on the C4 electrode and the relationship with EMG discharge is shown. No lag between the cortical discharge and EMG activity is present. The delta wave is occasionally followed by low-amplitude, rhythmic, alphalike activity. AVG indicates average; MKR, marker.

Hypogammaglobulinemia develops in 3% to 6% of patients with thymoma, and this association is referred to as GS. The pathogenesis of the immunodeficiency in GS remains unclear and appears to affect both humoral and cellular immunity. A bone marrow defect is suggested by the B- and T-cell lymphopenia, possibly of autoimmune origin.

As a result of the immunodeficiency, patients may develop severe opportunistic infections similar to human immunodeficiency virus–infected individuals, including gastrointestinal and retinal CMV infection. Central nervous system involvement in CMV infection has previously been reported in 2 patients with GS, both of whom died. Diagnosis is difficult, and the most specific diagnostic tool is the detection by PCR of CMV DNA in the CSF. In our case, the morbidity associated with the presence of retinitis, as well as the high positive predictive value of the detection by PCR of CMV DNA in the CSF of an immunocompromised host, strongly suggests that the patient’s illness was caused by cerebral CMV infection.

Generalized complexes with long periodicity associated with myoclonus are a rare neurological finding, typically seen in subacute sclerosing panencephalitis and, rarely, in other slow viral diseases such as rubella encephalitis. To the best of our knowledge, this pattern has not previously been reported in CMV encephalitis.
In our case, the origin of periodic complexes and slow myoclonus remains speculative. As suggested for subacute sclerosing panencephalitis, widespread damage of gray and white matter may be the pathologic substrate of this phenomenon, leading to abnormal neuronal excitability and modifying the responses to inputs from distant cerebral areas. Alternatively, periodicity may be mediated via potential neurotoxins (eg, glutamate, cytokines, nitric oxide, or quinolinic acid) produced by monocytes, as suggested in human immunodeficiency virus, or through fusion of neuronal processes leading to electrotonic coupling between cells and hence to increased excitatory interactions. Opportunistic central nervous system infection, including CMV infection, should be considered early in the evaluation of patients with GS or a history of thymoma who develop unusual neurological symptoms. Comprehensive immunologic and microbiologic investigation, including measurement of immunoglobulin levels, is mandatory in these cases.

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REFERENCES


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**Correction**

Error in Text. In the Observation by Striano et al titled “Periodic Myoclonus Due to Cytomegalovirus Encephalitis in a Patient With Good Syndrome,” published in the February issue of the *ARCHIVES* (2007;64:277-279), there was an error on page 278. The sentence should have read as follows: “Jerk-locked averaging analysis did not show a cortical correlate for electromyographic discharges, and there was no spreading of jerks from the proximal to distal muscles; conduction velocity did not correspond to pyramidal conduction, suggesting a subcortical rather than cortical origin for the myoclonus.” We regret the error.

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