Chorea and antiphospholipid antibodies: Treatment with methotrexate

S. Paus, MD; B. Pützsch, MD; J.H. Risse, MD; T. Klockgether, MD; and U. Wüllner, MD

Chorea may occur in systemic lupus erythematosus (SLE) and primary antiphospholipid antibody syndrome (PAPS). Vascular lesions and immune-mediated excitatory mechanisms have been proposed as the underlying pathophysiology.1,2 Accordingly, immunosuppressive therapy has been employed in antiphospholipid antibody (aPL)-associated chorea.3-5 We report the correlation between clinical symptoms, laboratory activity of aPL, and striatal hypermetabolism in 18F-fluorodeoxyglucose (FDG) PET in a patient with aPL-associated hemichorea. This patient was successfully treated with low-dose methotrexate.

Case report. A 41-year-old right-handed woman developed involuntary movements of the left hand in June 1999. Within 2 weeks, the symptoms progressed to uncontrollable jerks of the left arm and leg, with clumsiness of finger movements, twitching of the left face with squeezing of the eye, and speech difficulties due to clumsiness of the tongue. She was unable to continue working. Her medical history included moderate hypertension treated with losartan 50 mg per day, hysterectomy, and cigarette smoking (12 pack-years). Family history of movement disorders was negative.

A cranial MRI revealed no ischemic lesion. CSF, EEG, intracranial and extracranial DCT, and ophthalmologic examination results were normal. Tests for lupus anticoagulant (LA) were positive, with increased activated partial thromboplastin time (aPTT) (38.7 s; normal, 18.4–36.0 s) and dilute Russell viper venom time ratio (dRVVT-ratio) (2.2; normal, <1.2); the anticardiolipin antibody titer (IgG) (aCL-IgG) was elevated (86.0 U/mL; normal, <18 U/mL). All other laboratory results including platelet count, complement factor 3 and 4, anti–ds-DNA antibodies, antinuclear antibodies, HIV antibodies, treponema pallidum hemagglutination assay (serum and CSF), acanthocytes, serum copper and ceruloplasmin, and thyroid function were normal. A preliminary diagnosis of aPL-associated chorea was made.

Six weeks after the first manifestation of chorea, treatment was initiated with low-dose methotrexate, 20 mg orally once per week, which led to a rapid improvement. After 4 weeks of continuous medication, choreatic movements were no longer detectable and the laboratory follow-up showed an improved result for aCL-IgG (55.7 U/mL) and a downward trend of LA (aPTT 34.5 s; dRVVT-ratio 1.7).

Methotrexate treatment was discontinued after 9 weeks. Eight days after the last intake, the patient again noticed involuntary movements of the left hand and foot. Neurologic examination 12 days after the last methotrexate intake confirmed a mild to moderate relapse of left-sided hemichorea. Laboratory results showed increased LA (aPTT 39.5 s; dRVVT-ratio 1.9) and aCL-IgG (75.2 U/mL). An FDG PET performed to study striatal hypermetabolism revealed an increase of FDG uptake in the right caudate nucleus as compared with the left side (6.36 ± 1.5%; p < 0.05) (figure). Medication was started again at 20 mg methotrexate per week. After 2 weeks, choreatic movements were no longer detectable. After 6 weeks of continuous medication, FDG PET revealed no difference between FDG uptake values of the left and right caudate nucleus. The laboratory follow-up showed a downward trend of dRVVT-ratio (1.7) and aCL-IgG (67.3 U/mL), whereas aPTT was nearly unchanged (42.0 s).

Discussion. This case of aPL-associated hemichorea documents an association between intensity of choreatic symptoms, laboratory activity of aPL, striatal hypermetabolism, and immunosuppressive therapy with methotrexate. Our results are consistent with earlier suggestions that aPL-associated chorea is caused by an immune-mediated excitatory effect of aPL resulting in striatal hypermetabolism measurable by PET, rather than a consequence of ischemic lesions in the basal ganglia.6,7 Chorea associated with aPL in adults has been reported in SLE, lupus-like syndrome, and PAPS.3,8 In patients who do not fulfill the criteria of the American College of Rheumatologists for these disorders, as in our case, chorea might be an early symptom of SLE or PAPS, antedating the disease for several years, or the only manifestation of aPL.

A search of the literature revealed high-dose corticosteroids, cyclophosphamide, and combinations of the two as the most frequently used medication in aPL-associated chorea. The dramatic response to oral application of low-dose methotrexate, however, demonstrates that treatment with methotrexate alone may provide a reasonable and effective alternative.

Figure. 18F-fluorodeoxyglucose (FDG) PET during a relapse after withdrawal of methotrexate. FDG uptake is enhanced in the right caput nuclei caudati (CNC) as compared with the contralateral side. Regions of interest in this plane revealed maximal standard uptake values of 6.3 (right CNC) and 5.8 (left CNC).

References
NeuroImages

Localization of the “sneeze center”
John N. Fink, MBChB, Brookline, MA

The existence of distinct sneeze-evoking centers in the brainstem has been demonstrated in cats, represented bilaterally along the ventromedial spinal trigeminal nuclei and in the adjacent pontomedullary lateral reticular formation. In humans, unilateral damage to the sneeze center in cases of lateral medullary syndrome has resulted in inability to sneeze. The case presented here demonstrates the localization of the sneeze center in humans with more precision.

A 23-year-old woman presented with 10 days of progressive numbness of the face and arms, diplopia, oscillopsia, and dysphagia. She reported an inability to sneeze or yawn and meals were followed by 5 minutes of hiccups. She had a history of venous thrombosis and a family history of systemic lupus erythematosus (SLE). General examination was remarkable for malar rash. On neurologic examination there was upbeat nystagmus but normal range of eye movement. Left facial sensation was reduced. Facial movement and hearing were normal. Palatal sensation was intact but movement was absent. Cough, swallowing, and tongue movements were impaired. Touch and pin sensation were reduced in the arms but there were no other long tract signs. MRI revealed evidence of extensive brainstem demyelination, but no other abnormalities (figure). The diagnosis of SLE was supported by positive ANA and anti-Ro antibodies. CSF was acellular; oligoclonal bands were not present. She was treated with IV methylprednisolone, followed by oral prednisone. Eight months later her only symptom was persistent inability to sneeze. Nasal irritation resulted in a strong desire to sneeze and she was able to mimic a sneeze voluntarily, but without relief of symptoms. The examination was otherwise normal. Repeat MRI (see the figure) demonstrated a small residual abnormality in the rostral dorsolateral medulla only, where the “sneeze center” has been predicted.