Foix-Chavany-Marie syndrome as the presenting sign of HIV-related PML

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We present a 28-year-old woman diagnosed with HIV and comorbid cerebral toxoplasmosis 10 years prior. Four years after discontinuation of HIV therapy, she was admitted to our neurology department with progressive speech and swallowing difficulties for 2 weeks. Neurologic examination showed intact eye blinking and eyebrow raising, but muscular weakness during all voluntary oromandibular and tongue movements with a paralytic dysarthria. The swallowing reflex and emotional expressions (yawning, crying, smiling) were maintained. Furthermore, there was a mild paresis of the right hand.

Blood investigation showed positive HIV serology (viral load 209,000 copies/mL), CD 4 count 30/mm³, and CD4% 4.69%. Screening was negative for syphilis, *Borrelia*, *Cytomegalovirus*, *Mycoplasma*, herpes simplex virus, varicella-zoster virus, toxoplasmosis (only positive immunoglobulin G), and *Cryptococcus*. Antiganglioside antibodies and anti-aquaporin-4 antibodies were negative. Cerebral MRI (figure 1) showed multiple pre-existent toxoplasmosis lesions, punctiform or linear, and a new focal hyperintense zone in the left (dominant) central operculum, with involvement of the immediate subcortical white matter, without enhancement or mass effect. CSF showed a borderline elevated protein (65 mg/dL), normal glucose (CSF 54 mg/dL, serum 93 mg/dL), 2 white blood cells/mm³ with oligoclonal bands (only present in CSF), and PCR positive for JC virus.

The patient was diagnosed with definite progressive multifocal leukoencephalopathy (PML), causing Foix-Chavany-Marie syndrome (FCMS). A nasogastric tube was placed and HIV therapy was restarted (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide). After several weeks, the patient developed a rapidly progressive right hemiplegia. Blood investigation showed a decrease in viral load (196 copies/mL) and increase in CD4 count (120/mm³) and CD4% (15.75%). A follow-up MRI (figure 1) showed important lesion expansion to the fronto-insular and parietal white matter with mass effect, suggestive for PML-immune reconstitution inflammatory syndrome (IRIS). No contrast was administered. Furthermore, a new contralateral opercular lesion appeared. We started IV methylprednisolone (120 mg/d) for 5 days, followed by continuation with oral therapy, 64 mg phased out over 3 months. There was an improvement of motor function and reduction of white matter lesions and edema on MRI. The FCMS persists to this day.

Discussion

FCMS is a rare neurologic disorder characterized by a pseudobulbar voluntary palsy of the facial-lip-pharyngeal-laryngeal musculature with preservation of reflexes and automatic movements.¹ It is caused by a lesion in the bilateral opercular region, which covers the insula and represents motor function of all lower cranial nerves (figure 2). Preservation of involuntary movement seems possible though indirect corticobulbar pathways.²

PRACTICAL IMPLICATIONS

In patients with oromandibular palsy, examine both voluntary and automatic movements and consider Foix-Chavany-Marie syndrome, even in the absence of bilateral opercular lesions on MRI.

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Cerebral MRI with typical progressive multifocal leukoencephalopathy (PML) lesions. A fluid-attenuated inversion recovery sequence shows (A) a focal hyperintense signal in the subcortical white matter and involvement of immediate subcortical U fibers in the left hemisphere (arrow) with an old subcortical toxoplasmosis lesion contralateral and (B) no abnormalities in the brainstem or cerebellum. A diffusion-weighted imaging (DWI) sequence (C) shows accompanying diffusion restriction (arrow). A follow-up DWI sequence after 2 months (D) shows important extension of the left lesion with mass effect, suggestive for PML-immune reconstitution inflammatory syndrome, and appearance of a new PML lesion in the right opercular region (arrow).

FCMS is usually caused by a bilateral stroke, with a minority of patients having other vascular, inflammatory, traumatic, tumoral, iatrogenic, developmental, or neurodegenerative disorders.²⁻⁴ PML-associated FCMS is rare. PML, caused by the polyomavirus JC, is an HIV-related opportunistic infection.⁵ MRI is a sensitive tool for detecting PML lesions at an early stage, which typically are located in subcortical and juxtacortical white matter.⁶ PML causes a broad spectrum of focal neurologic deficits that typically develop over weeks.⁵ Our patient showed subtle MRI findings (figure 1), but because of the dramatic clinical presentation of a lesion in this

specific region, we were able to diagnose PML in a relatively early stage.

The patient presented with a unilateral juxtacortical lesion on the left (dominant) opercular border. Most patients with FCMS have bilateral involvement of the operculum or its subcortical projections.² Rarely, patients show a unilateral lesion in the dominant hemisphere.^{3,4} Our patient, however, showed a contralateral opercular lesion on a follow-up MRI after 2 months. This may suggest that PML affects cerebral function prior to structural MRI lesions. Future studies are necessary to confirm

Cerebral MRI with the progressive multifocal leukoencephalopathy lesion (arrow) on a coronal fluid-attenuated inversion recovery sequence, with a homunculus superimposed that shows the motor representation of different regions within the primary motor cortex. The affected region represents the facial motor function.

this finding and investigate the value of JC virus screening in high-risk patients with neurologic deficits and a normal MRI.

If PML develops in a patient with HIV, the best therapeutic option is (re)initiation of anti-HIV treatment. A 1-year survival rate of 50% has been shown, as opposed to 10% in those without treatment.⁵ After restarting therapy, the patient developed PML-IRIS. The literature shows conflicting results on use of steroids in PML-IRIS, but expert opinions tend to recommend the use of steroids in case of a marked neurologic deterioration or radiologic signs of swelling.⁷ As our patient showed both, we started treatment with corticosteroids. Despite the fact that our patient had other opportunistic infections and developed muscular atrophy during treatment, there was an improvement of neurologic outcome.

FCMS should be suspected in patients with isolated pseudobulbar voluntary palsy of the oromandibular musculature, even in the absence of bilateral opercular lesions on MRI. Differential diagnosis is extensive but should include PML, especially in immunocompromised patients.

Author contributions

Femke Dijkstra: writing the first draft of the manuscript.
Kaat Guldolf: critical revision of the manuscript for

important intellectual content regarding clinical neurology. Katlijn Schotsmans: clinical supervision, critical revision of the manuscript for important intellectual content regarding clinical neurology. Emke Maréchal: clinical supervision, critical revision of the manuscript for important intellectual content regarding clinical neurology, homunculus drawing. Danielle Hernalsteen: interpretation of MRI results and critical revision of the manuscript for important intellectual content regarding neuroimaging. Roeland Crols: clinical supervision, critical revision of the manuscript for important intellectual content regarding clinical neurology.

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