Clinical Reasoning: A 71-year-old man presenting with acute onset dysarthria and dysphagia

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Section 1

A 71-year-old man presented to the emergency department with sudden onset dysarthria and dysphagia. The patient suffered from arterial hypertension and unspecified tachyarrhythmia. Recently, he was evaluated for difficulties in fine motor skills and rest tremor of the left hand and he was diagnosed with vascular Parkinsonism. The medical history was otherwise unremarkable. He denied recent fever or infections. The neurological examination revealed a severe dysarthria, a positive finger-to-nose test on the left side, a slight hypomimia, and postural and rest tremor at the left arm. The patient was able to walk independently and Romberg sign was negative. Deep tendon reflexes were normally elicitable and symmetrical and plantar responses were flexor. Light touch, pinprick, position and vibration sense were intact. Blood pressure was mildly elevated (160/90 mmHg), heart rate was rhythmic, and the patient was afebrile. Given the abrupt symptom onset, a cerebrovascular etiology was first suspected. The patient underwent urgent brain CT scan, which was unremarkable, and CT-angiography (CTA) (figure 1). After the CT scan, the symptoms progressively improved and then completely subsided in about one hour.

Questions for consideration:

How would you describe the brain CTA findings (see figure 1)?

How would you manage this patient?

Section 2

The brain CTA showed a severe stenosis of the middle segment of the basilar artery (BA) (figure 1). Given the complete resolution of the symptomatology, the patient was considered not eligible for reperfusion therapy. Since the neurological deficits were consistent with a posterior circulation stroke, the BA stenosis was considered "symptomatic" and medical treatment with dual antiplatelet therapy (clopidogrel + aspirin) plus high-dose statin was started. He was admitted to the Stroke Unit. The following day, during the late afternoon, the symptoms relapsed. Urgent brain CT scan was again unremarkable. The symptoms progressively improved to resolve completely on the following day morning. On day three, another episode
of dysarthria lasting around five hours occurred. Standard brain MRI scan revealed no acute/subacute ischemic lesions only showing a mild leukoararyosis due to chronic ischemic insult. Stenting of BA was not taken into account because current evidences do not support stenting of symptomatic intracranial stenosis1.

Questions for consideration:

What differential diagnosis should be considered?

Which diagnostic tests would you perform?

Section 3

Even though brain MRI showed no ischemic lesions, a cerebrovascular etiology could not be ruled out. Indeed, it is well known that in ischemic stroke DWI-imaging yields a false negative rate of around 17%, particularly in brainstem and mild strokes (NIHSS < 4)2,3. In our patient, it could be hypothesized that a hemodynamic hypoperfusion in the brainstem territories downstream the stenosis could have resulted in transient ischemic attack (TIA). Actually, the most common mechanism underlying ischemic stroke in the BA territory is by far hemodynamic, associated with large artery occlusive disease, and TIA, isolated or followed by stroke, is a frequent presentation of BA atherosclerosis4. Alternatively, the atheromatous plaque of BA could have led to a temporary occlusion of the penetrating vessels (branch atheromatous disease) and, in turn, to the patient symptomatology5.

In amyloid angiopathy, the irritative effect of the blood products deposition in the cortex and in the subarachnoid space can result in transient, recurrent and stereotyped focal neurological deficits (the so-called amyloid spells)6. However, this diagnosis was considered unlikely, since susceptibility weighted imaging did not show findings suggestive of amyloid angiopathy.

Beyond a cerebrovascular etiology, several differential diagnoses have to be considered. In a case of a focal neurological deficit with spontaneous remission and a relapsing course, one should always consider an epileptic genesis of the disorder. However, seizures usually last for seconds to a few minutes, while the attack duration of our patient lasted several hours. Furthermore, the patient never experienced an alteration of consciousness and could perfectly remember about the episodes. Both standard EEG and 24-hour EEG
registration showed no specific epileptic discharges, making this hypothesis extremely unlikely. A paroxysmal speech disorder might also be due to migraine aura without headache, a rare form of migraine characterized by symptoms suggestive of typical migrainous aura, but not accompanied or followed by headache. Visual symptoms are the most common, followed by sensory alterations and speech/language disturbances. Symptoms typically last 5 to 60 minutes. The longer duration of our patient dysarthric spells basically ruled out this diagnostic option.

An involvement of the IX, X and XII cranial nerves (CNs) can result in dysphagia and dysarthria, and can be due to, among others, to neoplastic, traumatic and inflammatory causes. Neuroimaging ruled out a possible tumoral cause, and the patient had no history of head trauma. It is well known that an immune-mediated cranial neuropathy or brainstem encephalitis might present with dysarthria and dysphagia. However, autoimmune processes generally have a subacute onset, are characterized by others clinical signs, such as oculomotor deficits, ataxia and areflexia, and usually do not cause intermittent symptoms.

Considering the patient age, neurodegenerative diseases are a differential diagnosis. Amyotrophic lateral sclerosis (ALS) with bulbar-onset typically presents with dysarthria and dysphagia. However, the symptoms course is usually relentlessly progressive. An acute symptom onset followed by complete resolution and subsequent relapses, as seen in our patient, would be rather atypical for ALS. Conversely, given the fluctuating nature of the symptoms, a neuromuscular transmission (NMT) disorder ought to be considered among the possible differential diagnosis. Myasthenia Gravis (MG) is the most common acquired disorder of NMT, and is caused by antibodies (Abs) targeting proteins expressed at the post-synaptic side of the neuromuscular junction, which results in fluctuating muscle weakness. Abs to the nicotinic acetyl-choline receptor (AChR) are detected in around 85% of the cases and to muscle-specific tyrosin-kinase (MuSK) in around 5%. Most patients present ocular symptoms, such as ptosis and diplopia, fatigability of the upper and lower limb muscles and bulbar symptoms, such as dysarthria and dysphagia. Our patient had no history of ptosis or diplopia neither of exaggerated muscle fatigability.

Questions for consideration:

*What is the most likely diagnosis and what diagnostic exams would you perform?*

*How would you manage this patient?*
Section 4

The patient underwent 3 Hz repetitive nerve stimulation protocol on the nasalis muscle with facial nerve stimulation and on the trapezius muscle with accessory nerve stimulation. A compound muscle action potential decrement of $\geq 10\%$ was considered abnormal. The test demonstrated a decremental response with a U-shaped pattern. This finding is indicative of a post-synaptic disturbance of NMT, with a sensitivity of up to 80\% in generalized MG$^{10}$. The patient was clinically re-assessed with an MG focused neurological examination, which confirmed the presence of signs of exaggerated muscle fatigability. In more detail, the exam documented diplopia occurring after 10 seconds of sustained upward gaze, dysarthria when continuously speaking for more than 30 seconds, and a mild fatigable weakness of the deltoids and neck flexors (quantitative MG scale, QMG= 6). The positive finger-to-nose test on the left side was still present and it was interpreted as tremor due to parkinsonism. Patient serum was tested for anti-AChR and anti-MuSK Abs, and the former resulted positive (titer 16.1 nmol/L). This definitively confirmed the diagnosis of MG. Thorax CT-Scan was negative for thymoma. Treatment with pyridostigmine at dose of 30 mg t.i.d. and prednisone 5 mg daily was started, with a clear benefit. Given that the BA stenosis was no longer considered responsible for patient symptoms, clopidogrel was stopped; in consideration of the severe grade of the stenosis and the MRI finding of leukoarayosis, the patient was left on atorvastatin and low-dose aspirin. At the last follow-up visit, the patient reported no more episodes of dysarthria nor other symptoms suggestive of MG and the neurological examination documented a marked clinical improvement (QMG =1).

Discussion

Stroke is the leading cause of neurological disability worldwide and one of the most common neurological diseases, with an approximate incidence of 670-970 cases per 100,000 person-year among those aged 65 to 74$^{11}$. MG is a rare disorder with an annual incidence of 8-10 cases per million and an estimated prevalence of 150-250 per million$^{10}$. Cerebrovascular diseases are considered first in case of an abrupt onset of a focal neurological deficit, especially in the elderly population. In the described case, the clinical picture was further complicated by the \textit{a posteriori}-incidental finding of a BA stenosis, a plausible cause of a posterior circulation ischemic stroke consistent with the patient symptoms. On the other hand, a first presentation of
MG with an abrupt onset of isolated dysarthria and dysphagia is an extremely rare event. In these cases, the differential diagnosis with cerebrovascular diseases is extraordinary difficult, as previously reported.\textsuperscript{9,12} Nevertheless, after the acute phase, other symptoms such as fluctuating ptosis and diplopia or progressive respiratory difficulties usually help guiding the suspect toward a NMT disorder. In our case, “negative” MRI findings led us to consider other diagnosis beyond cerebrovascular diseases and symptoms fluctuation arose the suspicion of MG. However, when clinical presentation is not clear, a comprehensive neurological examination is essential to lead the diagnostic process. In the last decades, several reports documented a sharp increase in the incidence of late-onset MG (LOMG, i.e. MG with onset after the age of 50), especially among men\textsuperscript{10}. LOMG is nowadays the largest MG subgroup\textsuperscript{13} nonetheless the disease is probably still underrecognized and the diagnosis is particularly challenging in the elderly. On the other hand, a prompt identification of MG is of paramount importance since specific treatment may prevent further symptom deterioration, unnecessary or even dangerous drugs can be stopped, assuring the patient a better quality of life.
Appendix 1: Authors

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<tr>
<th>Name</th>
<th>Location</th>
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References


Figure legend

**Figure 1. Head and neck computed tomography angiography.**

Coronal (A) and sagittal (B) section showing a severe stenosis of the basilar artery; axial view (C) showing the middle cerebral arteries and the posterior cerebral arteries.
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