Pathological Laughter as an Unusual Manifestation of Acute Stroke

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Dear Sir,

Poststroke pathological laughter can develop during the acute or chronic stage following cerebral infarcts. The latter delayed-onset type, commonly known as emotionalism, is usually associated with the bilateral involvement of the descending corticobulbar pathways as a component of pseudobulbar palsy [1, 2]. The former, called 'fou rire prodromique' by Fere in 1903 [3], has been reported in just a few cases and is often confused with the delayed-onset form. This acute-onset type has been considered to be a unique situation rather than a symptom of acute ischemia because the spells of laughter are generally transient, often herald stroke as a single episode [4] or immediately follow the onset of focal deficits [5]. However, the clinical significance of the acute-onset type remains controversial. A recent case report suggested that the acute-onset type of pathological laughter might be a symptom of acute stroke [6]. We report a patient who experienced fluctuating pathological laughter simultaneously with neurological deficits following recurrent bilateral pontine infarcts, which supports the hypothesis that 'the acute-onset type of pathological laughter is one of the symptoms of acute stroke'.

Case Report

An 80-year-old woman was brought to the hospital complaining of dizziness, dysarthria and a mild right-sided weakness. She had a history of hypertension and stable angina pectoris, which were controlled with antihypertensive and antiplatelet agents. Diffusion-weighted images re-

Fig. 1. Diffusion-weighted images. **A** Diffusion-weighted MRI after the first stroke shows a left ventromedial pontine infarct. **B** Follow-up diffusion-weighted MRI after the second attack reveals a smaller contralateral pontine infarct.

vealed an acute infarction in the left side of the rostral basis pontis (fig. 1A). CT angiography showed a severe stenosis in the midbasilar artery. Nearly all of her neurological deficits had disappeared by the time she was discharged. However, she complained of general weakness, anorexia and a depressed mood. We prescribed a selective serotonin reuptake inhibitor (SSRI; citalopram 20 mg/day) in addition to the anticoagulation therapy.

Two months later, she experienced sudden dizziness, dysarthria and mild difficulty swallowing. She also noted transient alternating right and left facial paresthesia. She was alert and cooperative. The re-

sults of a neurological examination were grossly normal except for a right extensor plantar reflex and a slight gait ataxia. A second diffusion-weighted image revealed an acute right ventromedial pontine infarction, which was smaller than the previous contralateral pontine lesion (fig. 1B). She exhibited unmotivated forced laughter at the onset of the second attack, which occurred most frequently when she spoke. The laughter was also easily triggered by trivial stimuli such as eye contact. These episodes usually persisted from 30 s to 2 min. She was embarrassed in the presence of explosive laughter despite her feelings of anxiety and depression due to her

recurrent stroke attacks. We increased her citalopram dose to 40 mg/day, but the pathological laughter continued. After 2 weeks when her neurological symptoms (i.e. dysarthria and dysphagia) completely improved, the frequency and duration of her pathological laughter began to decrease gradually.

Approximately 1 month after her second attack, she experienced recurrent episodes of sudden neurological symptoms, involving dizziness, dysarthria and gait ataxia sustained for several hours during each attack, which typically occurred several times a day. She could not walk during the transient ischemic attacks due to ataxia and she also experienced several severe spells of pathological laughter. The pathological laughter markedly decreased to baseline when her neurological symptoms and signs disappeared and vice versa. A follow-up diffusion-weighted image did not show any new ischemic lesions. Her fluctuating focal symptoms and the severe cluster of laughter disappeared within 5 days. However, the occasional mild episodes of pathological laughter had completely subsided by the 7-month follow-up.

Discussion

Acute-onset pathological laughter after pontine infarction has rarely been described, and it is most frequently reported in cases of unilateral lesion [4–8]. In our case, pathological laughter began after bilateral pontine infarctions and fluctuated concurrently with transient ischemic attacks of the territory around the vertebro-basilar artery. The observed pathological laughter exactly matched the clinical course of the other neurological symptoms and the general status of the patient. These findings suggest that pathological laughter may be an unusual ischemic manifestation of bilateral pontine infarction. Gondim et al. [6] had also previously suggested fluctuating pathological laughter as an ischemic symptom to be considered as a heralding sign of extensive brainstem infarction.

Many speculative pathogenic mechanisms of pathological laughter have been suggested. It has been hypothesized that delayed-onset emotionalism is caused by a 'release phenomenon' or 'disinhibition' lesion of the voluntary pathway [1], and by an asynchronous recovery between the voluntary and involuntary laughing systems occurring during the reorganization process [9]. Recently, the role of the pontine serotonergic raphe nuclei [8], cere-

bropontocerebellar pathways [10] and the ischemic ephaptic stimulation of the descending corticopontine/bulbar pathways [6] in pathological laughter was reported. However, no specific mechanism has been suggested for acute-onset pathological laughter. Furthermore, a number of different pathomechanisms for pathological laughter have been suggested in various other neurological diseases [11–14].

SSRIs have been reported as rapid and efficient drugs for the treatment of delayed-onset pathological laughter (emotionalism) induced by stroke [15]. However, the responsiveness to SSRIs in cases of acute-onset poststroke pathological laughter remains unclear, especially in the acute phase [16]. To our knowledge, there was only 1 case of acute-onset pathological laughter after cerebellar lesion that showed good response to citalopram during the chronic stage [10]. Our patient's pathological laughter developed after the onset of her second pontine infarction while she was taking an SSRI for depression. Moreover, her pathological laughter continued despite an increase in the SSRI dose, and it fluctuated concurrently with the clinical course of the other neurological deficits. Based on the experience of our case and those previously reported in the literature, several hypotheses could be suggested to explain the occurrence of acute-onset pathological laughter: (a) acute-onset pathological laughter may have a different mechanism than the delayed-onset form; (b) a peculiar serotonin pathway may be induced in patients with previous SSRI use or depression, and (c) bilateral serotonin pathway damage due to recurrent pontine infarctions within short intervals may make it difficult to compensate for the dysfunction of the unilateral serotonin pathway, which is essential for emotion control.

In conclusion, pathological laughter may be the acute ischemic symptom in the patients with bilateral pontine infarcts. The clinical differences between the early-onset form and the delayed-onset form of poststroke pathological laughter, the differences between pathological laughter after unilateral stroke and after bilateral stroke, and the differences between pathological laughter after supratentorial stroke and after infratentorial stroke must be investigated in future studies in order to elucidate the mechanisms underlying the pathological laughter and to effectively manage the laughter.

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