

Effective Use of Sertraline for Pathological Laughing after Severe Vasospasm Due to Aneurysmal Subarachnoid Hemorrhage: Case Report

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Abstract

Pathological laughing, one subgroup of psuedobulbar affect, is known as laughter inappropriate to the patient's external circumstances and unrelated to the patient's internal emotional state. The authors present the case of a 76-year-old woman with no significant medical history who experienced pathological laughing after subarachnoid hemorrhage (SAH) due to rupture of an aneurysm, which was successfully treated with craniotomy for aneurysm clipping. In the acute stage after the operation she suffered from severe vasospasm and resulting middle cerebral artery territory infarction and conscious disturbance. As she regained consciousness she was afflicted by pathological laughing 6 months after the onset of SAH. Her involuntary laughter was inappropriate to the situation and was incongruent with the emotional state, and she could not control by herself. Finally the diagnosis of pathological laughing was made and treatment with sertraline, a selective serotonin reuptake inhibitor (SSRI), effectively cured the symptoms. Her pathological laughing was estimated to be consequence of infarction in the right prefrontal cortex and/or corona radiata, resulting from vasospasm. To the authors' knowledge, this is the first report of pathological laughing after aneurysmal SAH. The authors offer insight into the pathophysiology of this rare phenomenon. Effectiveness of sertraline would widen the treatment modality against pathological laughing.

Key words: pathological laughing, subarachnoid hemorrhage, psuedobulbar affect, sertraline

Introduction

Psuedobulbar affect is a disease entity of emotional expression disorder for which treatment medicine was approved recently in the United States.¹⁾ Symptoms of pathological laughing is characterized by uncontrollable burst of laughter disproportionate or incongruous with the underlying emotion and situation.^{2–4)} Pathological laughing occurs primarily in patients with neurologic disorders such as stroke, trauma, and multiple sclerosis. Pathological laughing is also often misunderstood by patients and their families, and is under-recognized by the clinicians caring for patients with this disorder, and the prevalence of it is much higher than expected.^{1,5)} However, so far as we know, there is no English language literature about pathological laughing after aneurysmal subarachnoid hemorrhage (SAH). Although the precise mechanisms that underlie pathological laughing are not fully known, accumulating data suggest involvement

of cortico-pontine-cerebellar circuits. Here, we present a case of pathological laughing secondary to cerebral infarction due to severe vasospasm after aneurysmal SAH. The symptom was treated by sertraline, an oral selective serotonin reuptake inhibitors (SSRIs).

Case Report

This 76-year-old, right-handed woman with no significant medical history presented to Yamashiro Public Hospital with the acute onset of headache and nausea while karaoke singing. Upon arrival to the hospital, she was alert and no neurological deficit was recognized. A noncontrast head computed tomography (CT) demonstrated SAH mainly in the right sylvian fissure (Fig. 1A), and subsequent intraarterial digital subtraction angiography (DSA) confirmed the presence of a 6.5-mm-diameter, saccular aneurysm at the posterior communicating segment of the right internal carotid artery (Fig. 1B). The patient underwent a frontotemporal craniotomy on day 2 and clip ligation of the aneurysm was performed. Postoperative

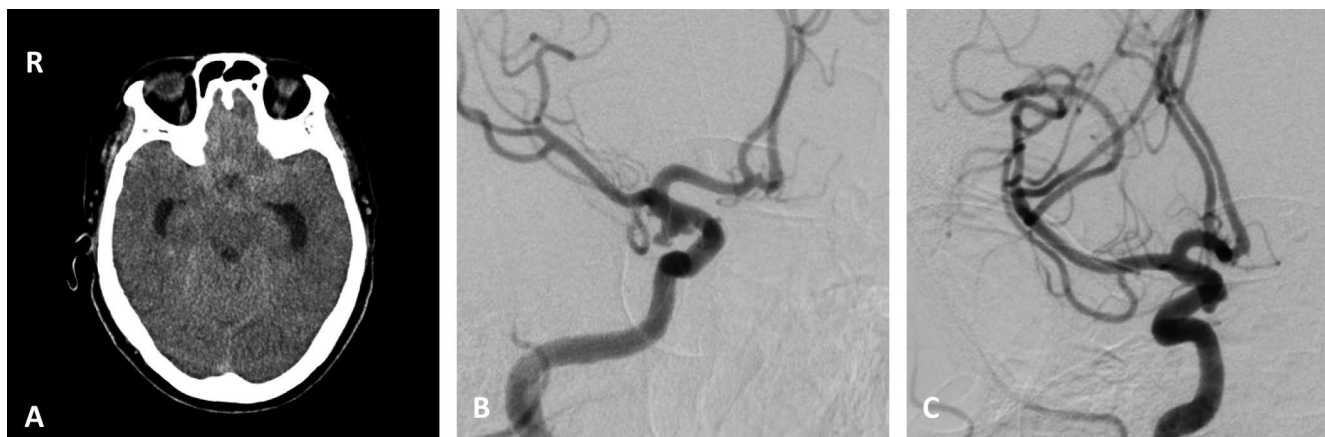


Fig. 1 Neuroimaging at the onset of subarachnoid hemorrhage. **A:** Axial computed tomography scan demonstrating diffuse subarachnoid hemorrhage in the basal cistern and bilateral sylvian fissure. **B, C:** Preoperative right carotid angiogram of **(B)** right oblique view showing a 6.5-mm saccular aneurysm attached to the posterior communicating segment of the right internal carotid artery, and **(C)** left oblique view showing major arteries without significant vasospasm.

course was uneventful as her Glasgow Coma Scale (GCS) score immediately after the operation was 15 and had no neurological complications, and had full oral intake until day 6 when she developed loss of consciousness and left hemiparesis (GCS score of 11). Intraarterial DSA revealed severe diffuse vasospasm in the right middle cerebral artery and right anterior cerebral artery (Fig. 2A). Despite several treatments, cerebral infarction in the right and prefrontal cortex and corona radiata resulted (Fig. 2B), and she was afflicted by persistent disturbance of consciousness. About 6 months after the onset of SAH, she gradually recovered from conscious disturbance and became alert and fully independent, with her GCS 15, but at the same time she recognized involuntary bouts of laughter that was not related to her emotion, was inappropriate to the situation, and was unable to be controlled by herself. She reported that during the laughter she was fully conscious and felt embarrassed about the laughter and that no inappropriate crying was coincide. To evaluate the pathogenesis of her pathological laughing, repeat magnetic resonance (MR) images were performed but no additional lesion other than scar of cerebral infarction could be found. She hesitated to have social life as before because she feared the outburst of laughing during inappropriate situation. The pathological laughing and crying scale (PLACS) score at that time was 18 that is above the recommended cutoff score of 13 to identify patients with pathological laughing.⁶⁾ The symptoms lasted for 4 years until treatment with sertraline at a daily dose of 50 mg commenced. She responded well with respect to her presenting symptoms, including her involuntary laughing, which resolved over 6 weeks as the PLACS scale decreased to 7.

Discussion

Pathological laughing may be defined as “involuntary laughter unaccompanied by mirth that is either unmotivated or disproportionately by a trivial stimulus.”⁷⁾ The episodes occur without an apparent triggering stimulus or following a stimulus that would not have led the subject to laugh or cry prior to the onset of the condition.⁸⁾ To describe the same or similar disorders, multiple names have been used so far, such as pathological laughing and crying, involuntary emotional expression disorder, emotional lability, affective lability, pathological emotionality, emotional dyscontrol, emotionalism and emotional incontinence,^{4,9)} that was one of the reasons this disorder of emotion has often been under- and misdiagnosed despite the condition’s impact on patient’s quality of life.¹⁰⁾ Since the approval of drug from Food and Drug Administration (FDA) of the United States to treat these genres of diseases in 2010, the term “pseudobulbar affect” is the preferred name in clinical use to refer to syndromes of exaggerated affective display including from emotional incontinence to pathological laughing and crying. However, for the precise description of the symptoms of the patient, we use here the term “pathological laughing” instead of “pseudobulbar affect.” Pathological laughing is distinguished with emotional incontinence in that the latter means objective expression of emotion out of proportion to, but appropriate to, normal fluctuation of subjective emotion. In association with stroke, there are some reports regarding “fou rire prodromique,” in which pathological laughing preceding the onset of apoplectic attack, but they are different in our case in that it is an uncontrollable laughter with sudden onset immediately preceding hemiplegia.^{7,11–13)}

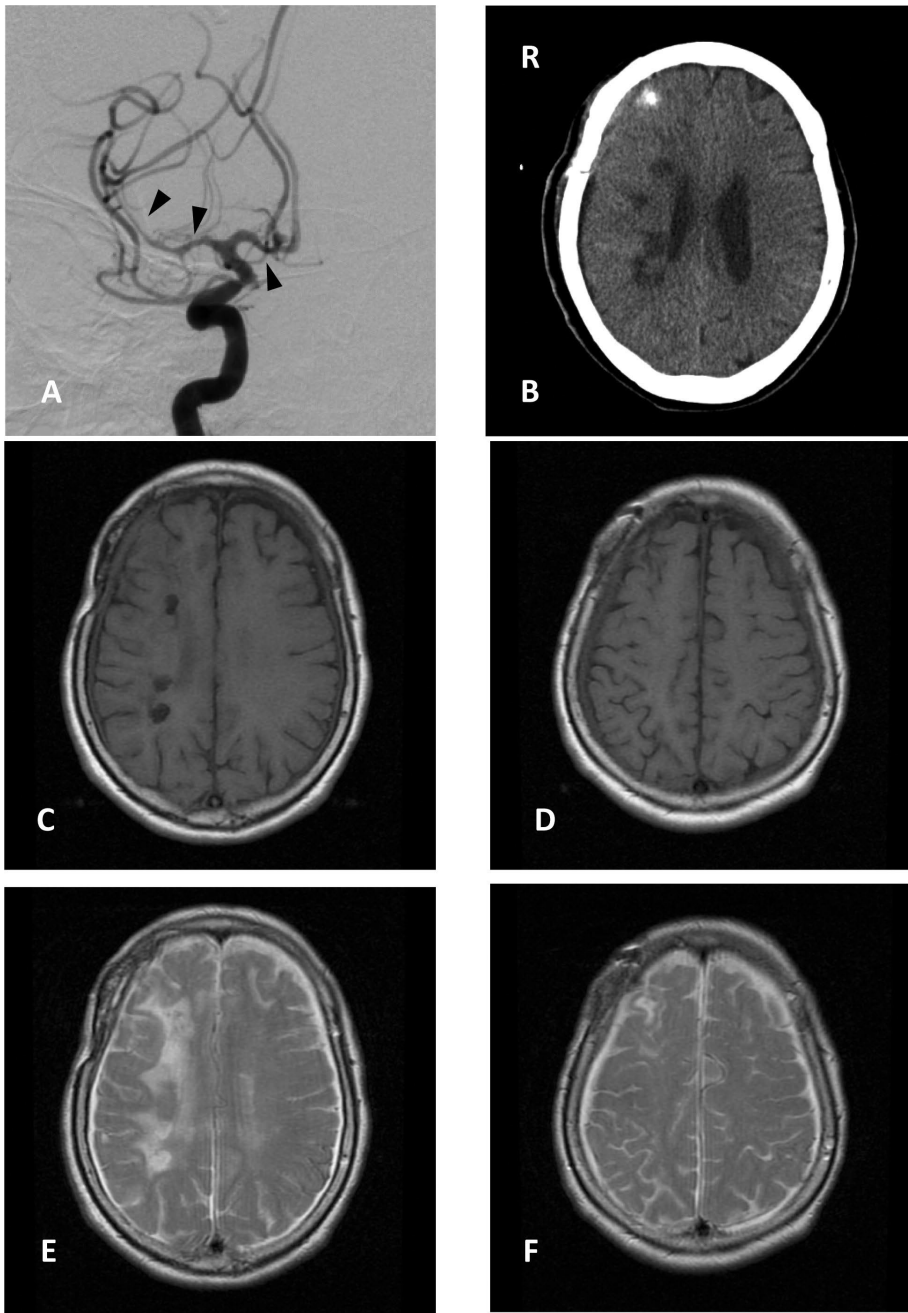


Fig. 2 A: Postoperative right carotid arteriogram obtained at day 9 showing severe vasospasm in the right middle cerebral artery and anterior cerebral artery (*arrow heads*). B: Axial computed tomography scan obtained at day 15 showing cerebral infarction in the right corona radiata. C–F: Axial magnetic resonance images of (C, D) T₁-weighted image and (E, F) T₂-weighted image 8 months after onset from subarachnoid hemorrhage indicating resultant cerebral infarction in the right prefrontal cortex (middle frontal gyrus) and corona radiata with surrounding edema.

Pathological laughing may be consequence of various neurological disorders such as stroke, trauma, amyotrophic lateral sclerosis (ALS), multiple sclerosis, Alzheimer's disease, and cerebral tumors. In our case, because pathological laughing was not seen immediately after SAH or the surgery but when she recovered consciousness after vasospasm-caused infarction, it is natural to conjecture the focus of her pathological laughing lies in the area affected by the infarction due to vasospasm. The right prefrontal cortex and corona radiata were the only affected brain region, therefore, we guess that either or both of

those was the causative lesion for pathological laughing. Also in our case, the affected lesion was non-dominant side of the brain and her left, dominant side was intact. Although some reports show relationship of the left cerebral hemisphere to the production of laughter,^{14,15} this case illustrates non-dominant hemisphere also have at least some influence. Although precise mechanism of pathological laughing is still unclear, extensive research to locate a precise area responsible for pathogenesis of pathological laughing has been done, but the following brain regions, namely basis pontis,^{12,13,16,17} cerebellar white

matter and gray matter,¹⁸⁾ basal ganglia, frontoparietal area, middle cerebral artery territory,^{11,14,19,20)} and frontal lobe²¹⁾ are advocated. In addition, by the study with ALS patients, McCullagh and Feinstein insisted the importance of the prefrontal cortex.²²⁾ According to recent hypothesis, laughter is caused by a lowered threshold for emotional response or a response incongruent to the circumstances that are induced by disruption of the cortico-pontine-cerebellar circuits.^{8,10,18)} There is also another hypothesis called “gate control theory,” in which reduction of inhibitory transmission from sensory cortices to motor and limbic cortices results in disinhibition of gate-control mechanism in the cerebellum, and therefore a lowered emotional expression threshold.²³⁾ Both of the hypotheses above support the notion that disruption not of one specific portion but of a neural circuit is causing pathological laughing, and both of them involve neural connection between prefrontal cortex and cerebellum. Standing on that point of view, it is understandable that so many different lesions induce same symptom—pathological laughing. Therefore, we speculate that in our case disruption of that circuit by infarction in the prefrontal cortex resulting from severe vasospasm lowered the emotional threshold, which led to the initiation of pathological laughing.

In most reported cases of pathological laughing after stroke, patients experience progressive amelioration over time.^{9,15,24)} But in our case, the symptoms continued long enough until sertraline treatment began. Other than FDA-approved medication dextromethorphan/quinidine (which is not available in Japan), tricyclic antidepressants, serotonin/norepinephrine reuptake inhibitors, and SSRIs including sertraline are also reported to be effective,^{1,6,25,26)} and indeed SSRI was effective in this case. Serotonergic receptors are widespread in many regions, especially in the paralimbic regions that Parvizi et al. have designated as emotion-induction and emotion-effector sites in the cortico-pontine-cerebellar circuits. Therefore, serotonin is supposed to be associated in the pathophysiology of pathological laughing through the diffuse cortico-limbic networks, or via serotonergic neurotransmission in the cerebellum. For that reason SSRIs and tricyclic antidepressants increase the synaptic availability of serotonin and are believed to improve pathological laughing symptoms through their serotonergic actions.¹⁰⁾

To our best knowledge, this is the first reported case of pathological laughing after SAH, suggesting indifference among neurosurgeons for this disease entity. However, recent reports reveal much higher prevalence of pathological laughing after stroke, and even the lowest estimation shows 4.4% of the stroke patients suffer pathological laughing. According to that report, among them less than half were given diagnosis.¹⁾ In other reports, prevalence of pathological laughing after stroke is estimated for 11–34%.^{15,24,27)} So that pathological laughing is speculated to occur in high incidence, much more patients than the neurosurgeons

notice may be suffering from this disease in such cases as situation after SAH-related infarction. In our case, pathological laughing began about 6 months after the onset of SAH, but theoretically this symptom may occur in the acute stage, in which neurosurgeons must spearhead the treatment. In fact, in our case the patient was left untreated for several months before we recognized her symptoms consistent with pathological laughing. Proper knowledge and precise diagnosis is needed for neurosurgeons for better quality of life for the patients because this disease entity is a heavy burden to the patients^{5,15)} and also high portion of the disease is responsible to drug treatment.

Conclusion

We report the first case of pathological laughing following sequela from vasospasm after aneurysmal SAH that was successfully treated with sertraline. Thanks to recent advancement of understanding the pathophysiology of pathological laughing, diagnosis and treatment of this disease entity will, especially in neurosurgical area, make much progress than before. Although this disease is seldom reported partly because previous confusion about the terminology, it can affect a patient's quality of life. Because this disease might have been underestimated, more attention should be devoted to symptoms suggesting pathological laughing.

Conflicts of Interest Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or findings specified in this paper. Among the authors, all of who are members of the Japan Neurological Society (JNS) have registered online self-reported COI Disclosure Statement Forms through the website for JNS members.

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