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CASE REPORT

A Patient Presenting with Isolated Psychotic Depression Due to the Ischemic Stroke of Centrum Semiovale

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Post-stroke depression (PSD) is the most common neuropsychiatric complication of stroke, such that it can occur in one-third of stroke survivors. It has been tried to be explained by the disruption in the neural circuits involved in the mood regulation in the setting of some additional clinical risk factors. However, there is no consensus in this regard. Herein, we present a 58-year-old male patient presenting with isolated psychotic depression which was finally found to be associated with acute ischemic stroke of bilateral centrum semiovale. This report constitutes an extremely rare illustration of acute onset organic psychotic depression which was clearly demonstrated to be associated with ischemic stroke. Through the presentation of this patient and limited literature, we propose some discussions regarding the pathophysiology of PSD. We also remark the need for future reports of neuroimaging methods to clarify the unknown neural correlates in these manifestations.

Key words: Psychotic depression, stroke, centrum semiovale, pathophysiology

INTRODUCTION

Psychiatric manifestations such as depression, anxiety, and apathy are acknowledged to develop at high frequency in post-stroke patients.[1] Particularly, post-stroke depression (PSD) is the most common neuropsychiatric complication of stroke, such that a varying prevalence from 25% to 79%, either in the early or late stage following stroke has been reported.[2] However, the illustration of isolated depression in association with a newly occurring stroke is extremely rare in literature. In this report, through the presentation of this remarkable patient, we point out acute cerebrovascular disease as a rare cause of acute onset psychiatric symptoms. Based on this report and limited literature, we discuss some hypotheses regarding the underlying mechanisms.

CASE REPORT

A 58-year-old male patient, with an unremarkable medical history, was attended to the psychiatry policlinic by his relatives, due to depressive symptoms and psychotic symptoms which had started over the past 2 weeks. On history taking, it was learned that he had been suffering from mild depressive symptoms such as unhappiness, reluctance, decrement in the level of communication with other people that was compatible with dysthymia. However, over the past 2 weeks, the patient's depressive complaints had abruptly aggravated such that he had been continuously suffering from sadness, hopeless, inability to make a decision, and apathetic state. Besides, psychotic symptoms such as fear of being attacked, uncontrolled fear of death, visual hallucinations in the form of shadows, and auditory hallucinations had started within this interval. In addition, he had newly onset memory and concentration problems. He was unable to perform many of the daily living activities such as eating, taking a shower, shopping, and going to work. Due to this abruptly emerging clinic, the patient was brought to emergency service (another center's es) by his relatives 4 days ago. As far as, it can be learned from hospital discharge files, cranial computed tomography (CT) was performed which had shown normal findings. Laboratory examinations were in normal ranges (hemogram, biochemistry, and sedimentation). Taken together, organic etiology was not considered at that time, and the patient was discharged from the emergency service with a suggestion of psychiatry outpatient

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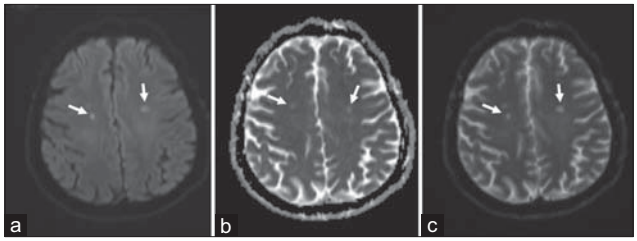

Figure 1: (a) Diffusion-weighted imaging showing high signal in bilateral centrum semiovale (compatible with T2 shine through which is seen in the subacute infarct). (b) Apparent diffusion coefficient images. (c) The initial T2 images showing high signal in the corresponding localizations

assessment. On psychiatric evaluation, the patient was evaluated as fully oriented and cooperated. The diminishment of self-care was apparent, and a decrease of speech rate as well as poverty of speech content was recognized. Depressive affect and mood state were present. Besides, persecutory and reference delusions in the thought content were apparent. Neurological examinations revealed normal motor, sensory, and cerebellar skills. However, a slight decrement in gait speed was recognized. Taken together, with a diagnosis of acute onset psychotic depression, the patient was hospitalized for adjustment and maintenance of medical treatments as well as further investigations of possible organic etiology. Hamilton depression scale (HAM-D) was evaluated as 32 at admission (very severe depression). Sertraline/mirtazapine combination (50 mg/15 mg) and quetiapine XL 150 mg were started. Cranial MRI (magnetic resonance imaging) showed bilateral millimetric subacute diffusion restriction in the bilateral centrum semiovale (CS) on the series of diffusion-weighted imaging (DWI) [Figure 1]. Hence, with a diagnosis of ischemic stroke, the patient was referred to the neurology clinic. Etiological investigations for ischemic stroke including CT brain/neck angiography, electrocardiography, echocardiography, and rhythm Holter were in normal limits. Tests including vasculitis-related biomarkers (performed for work-up in young stroke), tumor markers (CEA, CA 15-3, CA 19-9, CA125) and coagulation markers (D-dimer, prothrombin time, activated partial thromboplastin time, and fibrinogen) were also within normal limits. Besides, no a family history of juvenile stroke was taken. Ergo, a diagnosis of cryptogenic ischemic stroke was made, and aspirin 300 mg was added to the therapy. During the follow-up, he could not tolerate sertraline due to severe nausea; hence, it was switched to venlafaxine and titrated up to 225 mg over the next 2 weeks. During the following 4 weeks of hospitalization, the patient's depressive symptoms gradually improved such that weekly HAM-D scores were evaluated as 30, 18, and 11, respectively. His mood state improved, significantly and he started to give emotional reactions as his premorbid state. At 2nd month of follow-up on polyclinic visit, the patient was on treatments of venlafaxine 225 mg, quetiapine 50 mg XL (due to constipation quetiapine dosage was reduced) and olanzapine 10 mg, and his anxiety symptoms were almost totally recovered. Concurrently performed HAM-D score was 8. Daily living activities had significantly improved; however, he could not execute his work as efficient as his premorbid state. Of note, mini-mental state examination revealed a score of 26/30.

DISCUSSION

PSD is the most common neuropsychiatric complication of stroke, such that it can occur in one-third of stroke survivors.[3] Considering its destructive effect on cognitive functions, social activity, and stroke rehabilitation, it can be understood that the recognition and early treatment of PSD are critical for better clinical outcomes.[4] In the 1970s, it has been emphasized that depression after stroke could be an organic consequence of the brain damage rather than a predictable psychological reaction to neurological deficit.[5] On the other hand, currently, there is still no an accepted explanation regarding the responsible mechanisms as well as responsible disturbed neural networks. However, it has been tried to be explained by the disruption in the neural circuits involved in the mood regulation in the setting of some additional clinical risk factors such as a history of prior depression and social isolations.[6] The relationship between PSD and lesion localization has also constituted an interesting topic which has been multiple times addressed by many researchers. Although some localizations such as deep white matter, basal ganglia, thalamus, and left hemisphere have been suggested to be as risk factors for PSD;[7,8] there is also no consensus at this point. Such that many other researchers have not found any association between the lesion site and PSD.[9,10] Of note, in these reports, large numbers of patients were enrolled. However, the patients were diagnosed with chronic vascular lesions, which methodologically unable to provide a clear temporal association with neuropsychiatric symptoms and responsible lesion localization. In addition, in the following period from stroke to the psychiatric manifestations, many other confounding variables of stroke such as motor disability, social isolation, financial disturbances might interfere with the development of PSD avoiding a clear association between the psychiatric manifestations and ischemic brain damage. Ergo, in our opinion, the illustration of cases with acute onset depression in association with newly occurring ischemic lesions may add crucial perspectives about the unknown aspects of the pathophysiology of PSD. In a unique report by Badrin *et al*., a patient diagnosed with depression with psychotic symptoms was illustrated.[4] In this report, cranial CT had revealed the presence of a recent cerebral infarct in the right frontal lobe which they had associated with

the clinical manifestations. However, DWI was absent in this report which constitutes the main limitation and prevents a clear interpretation of the temporal association.

Therefore, we think that the presentation of our unique case may give substantial perspectives about the underlying mechanisms of this psychiatric manifestation. The role of cerebral white matter in the cognitive functions is rather a well-documented issue in the literature. Such that lesions of CS have been associated with worse performance in nonverbal reasoning and visuospatial cognitive ability.[11] Executive dysfunction and working memory problems were specifically emphasized to occur in patients with ischemic lesions in the CS.[12] On the other hand, in a recent, unique study by Liang *et al*., enlarged perivascular spaces which have been emerged as a marker of cerebral small vessel disease, were also found to be present significantly much more in the CS in patients with PSD.[13] On the other hand, psychotic symptoms were also distinguished among the psychiatric manifestations in our patient. Interestingly, volumetric neuroimaging studies have shown lower gray matter volume in prefrontal cortex and insula in patients with delusions and major depression.[14,15] We think that the lesions in the CS might have resulted in this clinic by disrupting the thalamocortical connections to the prefrontal cortex (suggested to be involved in psychiatric manifestations previously)[14,15] which were basically located in the CS. However, this can only be hypothesized as diffusion tensor imaging (DTI) was unavailable in our patient. We also think that based on a unique case, making certain conclusions might not be rational.

Remarkably, it has been reported that concurrently occurring depression in the acute period of stroke correlates with the mortality rate of the patients. Hence, the recognition of depression and early treatment of the patients have been emphasized for a better evaluation of the patients and clinical outcomes.[9] In our patient, an intensive medication therapy was needed to resolve the psychiatric symptoms. However, on evaluation at the 2nd month of stroke, the HAM-D score had improved from 32 to 8 and anxiety symptoms were ameliorated almost totally. Through the presentation of this report, we also remark that the identification of these symptoms is critical as early and appropriate initiation of the treatment provides substantial improvements in the patients' quality of life. Besides, accordantly, the use of antidepressant therapy is supported by numerous clinical studies demonstrating an overall benefit of pharmacotherapy for PSD.[16]

Of note, although detailed investigations for stroke etiology were conducted before making the diagnosis of cryptogenic stroke; genetic investigations for CADASIL, which is the most common monogenic disorder causing lacunar stroke and cerebral small vessel disease,[17] was not performed. However, there was no family history of juvenile stroke, no clinical findings such as headache or dementia, resembling CADASIL. In addition, MRI did not show ischemic lesions of the anterior temporal lobe and external capsules which are the predilection sites for white matter lesions in CADASIL.[17] Ergo, we did not plan further genetic investigations for CADASIL.

CONCLUSION

Herein, we illustrate an interesting case presenting with isolated psychotic depression clinic in a clear association with acute stroke which is extremely rare in literature. However, considering that this is extremely rare in stroke syndromes affecting CS, other individual features (genetic factor and dysthymic premorbid state) might also have influenced in this clinic. On the other hand, in a majority of PSD (particularly developing in the subacute-late phase following stroke), other indirect factors associated with stroke (social isolation, economic problems, and neurological deficit) may contribute to the pathophysiology of these psychiatric manifestations through mechanisms distinct from the direct role of brain damage. Ergo, we also propose the discussion of that if there may be a rationale in distinguishing PSD according to onset time following stroke? Future studies of larges cases may add more comprehensive contributions to our understanding of the pathophysiology of these psychiatric presentations after organic insult of CS. In addition, this report, illustrating a smart vivid sample of an organic cause of psychotic depression, may remark the need for future reports of neuroimaging methods (such as functional DTI) to clarify the unknown, ambiguous neural correlates in these atypical manifestations.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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