Depression and Violent Automatism in Lissencephaly with Epilepsy: A Case Report

Lissencephaly, the absence or decreased cerebral convolutions, is a malformation of the cortex resulting from disorganized neuronal migration [1, 2]. This condition usually presents itself with various types of epilepsy and developmental retardation [1, 2]. Reports of rare psychiatric manifestations exist in published lissencephaly cases [3-5]. Here, we present the case of a patient with depressed moods, suicide attempts, visual hallucinations, and violent automatism. His magnetic resonance imaging (MRI) results are consistent with those of a patient with pachygyria.

Case Report

The 43-year-old male patient reported to have depressed moods and suicide attempts. He was classified by our hospital as an emergency admission. The patient was born full-term with normal labor, and delivery and no sign of asphyxia. His mother reported no delay of developmental milestones. He had no family history of epilepsy or psychiatric illness. Since adolescence, he was reported to be quarrelsome and to have stubborn behavior patterns. He attended a general class and graduated from a college. The patient had ten years of work experiences, and he had been unemployed for five years afterward. He expressed out-of-body experiences between ages 16 and 25 years. He suffered from a head injury at the age of 36 years. He showed no evidence of brain hemorrhage at the emergency department, and he was discharged home without hospitalization.

Afterward the patient developed psychomotor seizures with hyperkinetic behaviors such as grabbing, pedaling, and scratching. He had received follow-up treatments at the neurology outpatient clinic since he was 41 years old. He had poor drug compliance and allergic history to antiepileptic drugs, valproic acid and zonisamide. He was referred to a psychiatrist from a neurologist because of depressed moods, insomnia, and low self-esteem. He also displayed some queer behaviors, such as clutching his mother's neck and calling for help with elder voice during work, but he did not remember those events.

On admission, the findings of patient's mental state examination showed depressed mood, suicidal ideation, sleep disturbances, psychomotor retardation, social withdrawal, and visual hallucinations. He had a hostile and suspicious attitude. He was normal on neurological examination. Hematological and biochemistry blood test results (including thyroid function test, and cortisol levels) were within normal range without revealing any other related medical conditions. On day 7 after admission, after our staff interviewed and inquired him about his family history, he was found staring and unresponsive, and then he struck our staff with beating and kicking behaviors. Afterward, he recalled little of the violent episode. Electroencephalography (EEG) showed the findings of increased beta activity with amplitude attenuation but no epileptiform discharge or spike. Magnetic resonance imaging showed the finding of focal cortical thickening over the right frontoparietal lobe consistent with pachygyria (Figure 1).

After admission, the patient started to receive 25 mg agomelatine per day. The daily dosages of 3,000 mg levetiracetam and 600 mg trileptal were added to topiramate on day 7. His antipsychotic agent was switched from aripiprazole 5 mg/day to olanzapine 5 mg/day on day 8. He had no violent behaviors after day 8. He got improved in depressed moods, sleep disturbances, and visual hallucination under those medical treatments, and he was discharged after a 31-day hospitalization.

Comment

Lissencephaly is a spectrum of cortical malformations, ranging from agyria (absence of cerebral convolutions) to pachygyria (decreased cerebral convolutions). A total absence of cortical gyri and sulci is rarely seen. Lissencephaly had two major pathologic subtypes. Classical (type I) lissencephaly is characterized by a poorly organized four-layered cortex. Cobblestone (type II) lissencephaly is characterized by total absence of cortical layering and displays irregular grooves imparting a cobblestone pattern [1].

The diagnosis of lissencephaly is based on the findings of computed tomography or MRI displays of the brain. Neuroradiological findings demonstrate lack of gyri, smooth brain surface, thicken of the cortex, and smooth gray-white

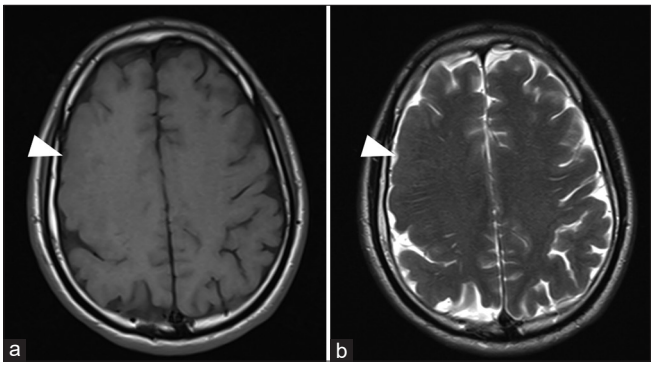

Figure 1. Magnetic resonance imaging demonstrated showed decreased cerebral convolutions and focal thickened cortex over the right frontoparietal lobe (arrow head) consistent with pachygyria. (a) T1-weighted sequences; (b) T2-weighted sequences.

matter junction. The clinical manifestations of this condition are diverse, ranging from asymptomatic patients to patients with intractable seizures or fatal disorders, comprising hypotonia, facial dysmorphism, and developmental retardation [1, 2]. The patient with lissencephaly early in life can have seizures including infantile spasms or akinetic-myoclonic, tonic, tonic-clonic, or atypical complex partial seizures [1, 2]. Some EEG records showed generalized paroxysmal fast activity and amplitude higher than 50μV [6].

The etiology of lissencephaly remains unclear, and it has possible links to genetic factors [1, 2]. Many genetic mutations have been reported in patients with lissencephaly, and the two most common causal genes are LIS1 and DCX (XLIS) [7]. Deletion of 17p13.3, which causes Miller-Dieker syndrome, is the first reported genetic cause of lissencephaly [2]. Mutations in the lissencephaly-related Reelin gene (RELN) also play a rôle in major depressive disorder, bipolar disorder, and schizophrenia [8]. Previous research discovered that decrease in hippocampal Reelin protein levels has been found in patients with major depressive disorder [8]. Teixeira et al. investigated the effect of Reelin overexpression in animal models, and found that decreases in *N*-methyl D-aspartate receptor subtype 2B (NMDA-NR2B) mediate neurotransmission [9]. Increased levels of Reelin in the brain have therapeutic effects on depression-like and anxiety-like behaviors in mice [9].

In our case, the patient had a history with seizure for about six years. At first on admission, he had symptoms with depressed mood, suicidal ideation, sleep disturbances, psychomotor retardation, social withdrawal, and visual hallucinations. The impressions were major depressive disorder with psychotic feature and mood disorder due to epilepsy. On day 7 after the admission, he had symptoms of temporal staring, unresponsive, and violence automatism. Seizure attack was diagnosed according to the past history. But, the patient's clinical features differed from typical complex partial seizure with automatism. Brain MRI was arranged to exclude other structure disease, and lissencephaly was seen from the imaging findings. Nataliya et al. have established a classification system to predict possible causative gene and clinical outcomes by MRI imaging patterns [7]. In our case, MRI imaging with partial pachygyria (anterior predominant, subtype 1-3) aligned with Nataliya et al.'s grade of "mild clinical severity," which typically manifests with borderline to moderate intellectual disability, seizures of variable severity, and expected survival into adulthood.

The association with lissencephaly and psychosis in our case is a critical question. Three reported cases of lissencephaly with psychosis feature have been found in the literature review [3-5]. Abnormal brain development has been implicated in the pathophysiology of psychosis. We considered that this patient's congenital brain lesion had a crucial influence on his vulnerability to psychiatric symptoms. Nevertheless, a conclusive statement that the psychosis in our case is owing to lissencephaly cannot be made. According to the history of seizure, psychosis due to epilepsy should be considered as a differential diagnosis. The implication of lissencephaly and psychiatric symptoms remains unclear. (This case report was approved by the institutional review board for publication at Kaohsiung Armed Forces General Hospital [protocol number = KAFGHIRB 110-031, and date of approval = November 4, 2021] without the need to obtain written signed consent from the patient.)

Financial Support and Sponsorship

Nil.

Conflicts of Interest

The authors declare no conflicts of interest.

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Received: Dec. 28, 2021 revised: Feb. 11, 2022 accepted: Feb. 13, 2022
date published: Jun. 29, 2022

Access this article online

Quick Response Code:

Website: www.e-tjp.org

DOI: 10.4103/TPSY.TPSY_19_22

How to cite this article: Lo YT, Hsu YF. Depression and violent automatism in lissencephaly with epilepsy: A case report. Taiwan J Psychiatry 2022;36:95-6.