Reversible Splenial Lesion Syndrome Developing in the Setting of Sleep Deprivation

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Abstract

In this report, we present a rare case of reversible splenial lesion syndrome which was etiologically associated with sleep deprivation. Up to our knowledge, there is no previous research reporting sleep deprivation as an inducer agent of RESLES. To elucidate our observation, future reports of larger case series are surely warranted. The clarification of the possible association between sleep deprivation and the reversible splenial lesion may also provide substantial perspectives regarding the mechanisms and health impact of sleep deprivation; the functional and pathophysiological role of the splenial corpus callosum in sleep physiology. Besides, we think that the awareness of this entity should increase among clinicians to avoid unnecessary investigations as the case in our patient.

Key words: Neuroimaging; Pathogenesis; Reversible Splenial Lesion Syndrome; Sleep deprivation.

Introductio

Reversible splenial lesion syndrome (RESLES) is a disorder characterized by the presence of a focal splenial lesion that is shown to be completely reversible on follow-up magnetic resonance imaging. Various etiological conditions might lead to RESLES. However, we present an interesting case of RESLES in which we discuss sleep deprivation as a causal agent. Via the presentation of this case, we discuss possible pathophysiological mechanisms related to sleep deprivation leading to RESLES.

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Case Report

A 23-year old female patient was admitted due to acute onset symptoms of dizziness, double vision, and imbalance which had started abruptly two hours before admission. Her medical history was unremarkable. Of note, it was learned that the patient had given birth four months ago and had received a single dose of amoxicillin/clavulanate potassium (625 mg TB) due to mild cough and nasal draining. However, she had not continued medication and her complaints had resolved spontaneously. On the other hand, she stated that she was taking care of her 4-month-old baby and she had to wake up often during the nights and, therefore, suffered from severe acute insomnia over the last one week (she could sleep only 2-3 hours a day). Such that when the patient was asked to complete the insomnia severity index [1] retrospectively based on the last week, she got 23 points revealing severe acute clinical insomnia. At admission, the patient was fully orientated and cooperative. The other neurological examinations including cranial nerve functions and motor, sensory, cerebellar examinations were within normal limits. Vital signs were normal. Laboratory investigations including hemogram, biochemistry, folic acid, TSH were within normal ranges. However, the cranial MRI showed diffusion restriction in the splenial corpus callosum (Figure 1).

With a provisional diagnosis of acute ischemic stroke, antiplatelet (aspirin) and anticoagulant (enoxaparin) therapy were initiated and the patient was hospitalized for conducting follow-up and further etiological investigations. On the second day of hospitalization, her complaints were completely resolved and etiological investigations including ultrasound of the carotid and vertebral arteries,

echocardiography, and electrocardiography were evaluated as normal. However, the patient was discharged with antiplatelet therapy and referred to another center for conducting blood tests for early-onset stroke. When the initial cranial MRI and the clinical presentation retrospectively were re-evaluated, reversible splenial lesion syndrome (RESLES) was suspected. Supporting the diagnosis, the MRI was repeated one week later, which showed total resolution of the callosal lesion (Figure 2).

Ergo, the final diagnosis of RESLES was established. Based on the clinical presentation, severe symptoms of insomnia, and nonexistence of other potential inducer agents; sleep deprivation was considered as the etiological agent. The patient was informed about this entity and was discharged without any treatment.

Discussion

RESLES is a rare and complex clinico-radiological occurrence that may develop in association with several conditions and diseases. The clinical manifestations and detailed radiological features of RESLES have been reported in several recent reports.[2,3] However, there are many unknown aspects regarding the pathogenesis of RESLES. Edema with diffusion restriction in RESLES

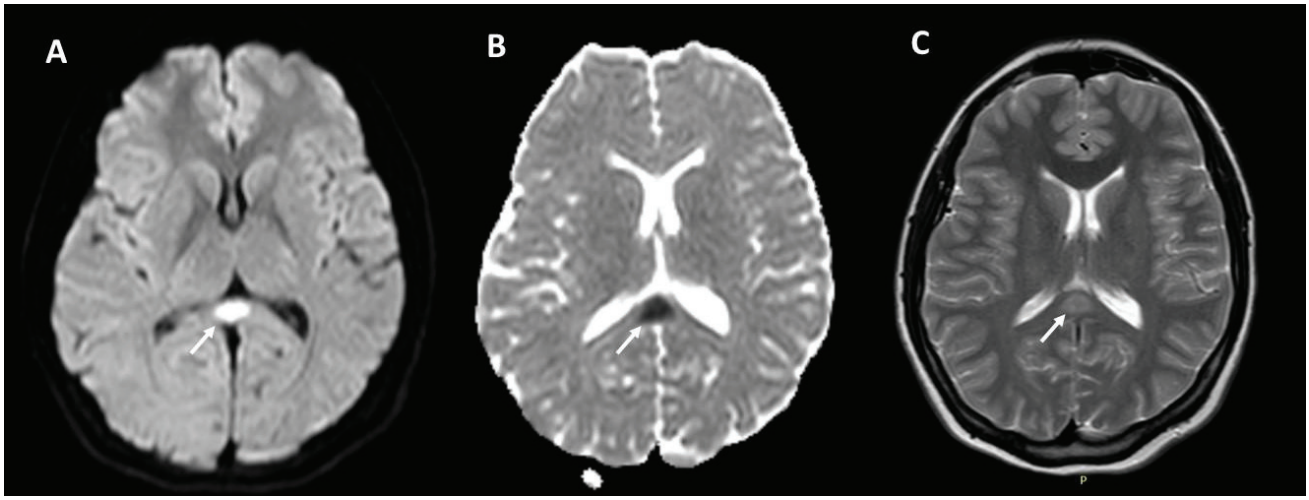

Figure 1. The Cranial MRI, performed at admission, showing the diffusion restricted lesion (A; DWI sequence, B; ADC sequence, C; T2-weighted sequence).

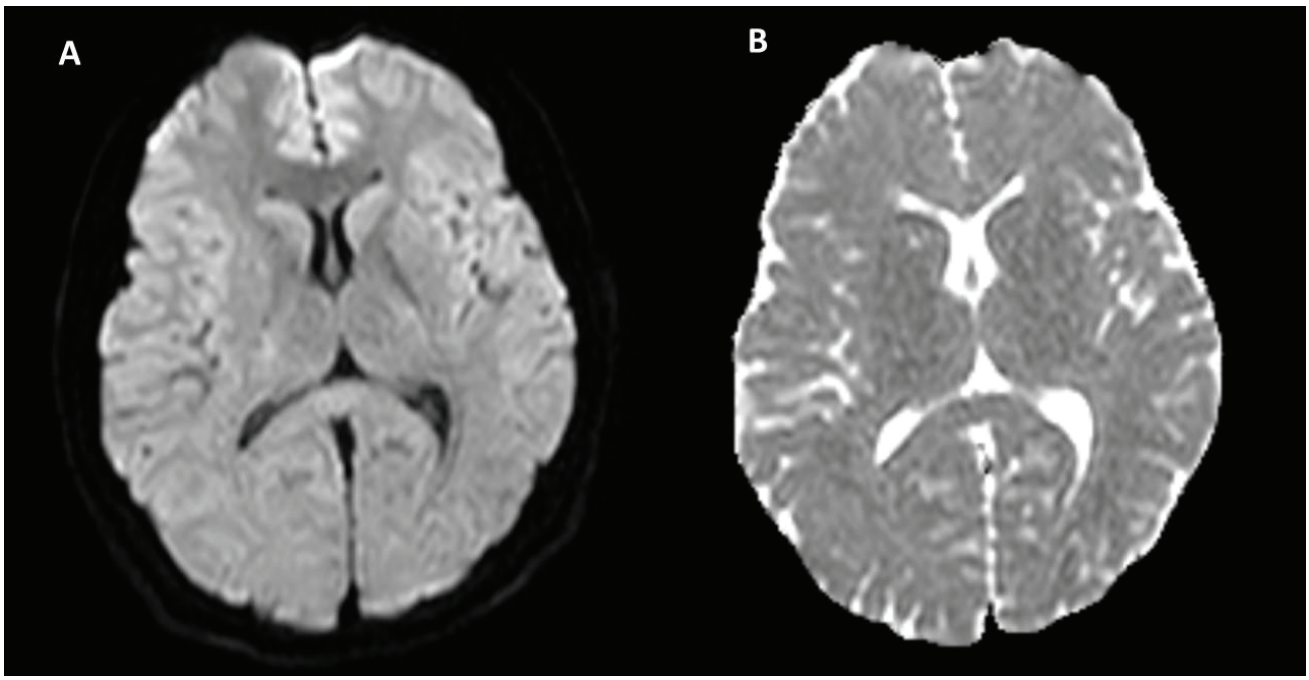

Figure 2. The Cranial MRI, performed one week after admission, showing the total resolution of the lesion (A; DWI sequence, B; ADC sequence).

has been attributed to excitotoxic mechanisms without brain ischemia.[4] Excitotoxic edema which is a form of cytotoxic edema develops due to increased glutamate concentration in the extracellular space. The increased glutamate concentration results in Na + and Ca ++ entrance to glial cells and myelin sheaths along with water diffusion.[4] Edema induced by glutamate in the excitotoxic mechanisms occurs predominantly in glial cells and myelinic sheaths.[4] It has been suggested that this kind of edema occurring in intramyelinic clefts results in the separation of myelin layers.[4] This mechanism is discussed to be responsible for avoiding irreversible damage of axon and neuron.[4] In accordance with this, the follow-up MRI, performed one week after admission, showed the total resolution of the lesion.The complete disappearance or a clear reduction in the lesion size and signal intensity was reported to occur at 17.5 ± 2.88 days after onset in a large groups of patients with RESLES. [5]

In this case, there was no history of medication, a concurrently occurring infectious disease, or a metabolic abnormality that might lead to this entity. However, the patient remarkably stated a period of sleep deprivation that had persisted over the last few days before emerging of her complaints. Sleep deprivation is shown to lead to elevated levels of excitatory neurotransmitters and abnormalities. Specifically, glutamate, a neurotransmitter to be associated with excitotoxic edema in RESLES, is found to increase in various brain regions including the hypothalamus and brain stem.[6] On the other hand, recent studies on rodents have consistently demonstrated the upregulation of myelin-related genes during sleep, suggesting that sleep represents a window of opportunity during which myelination occurs.[7] Considering RESLES is generally discussed in the context of intramyelinic edema, it can be hypothesized that sleep deprivation in our patient might have influenced through a mechanism of altered myelin plasticity in this output. Besides, supporting the involvement of the corpus callosum in sleep-wake dynamics, Rocklage et al found that the individuals those vulnerable to sleep deprivation had lower fractional anisotropy values (reflections microstructural integrity) in the corpus callosum.[8] Taken together, we suggest that sleep disturbance may be a potential factor that may lead to this syndrome. Cases of RESLES manifesting with consciousness alterations and sleep disturbances including hypersomnia have been several times reported previously.[2,3] However, up to our knowledge, there is no previous report remarking sleep deprivation as an inducer agent of RESLES. To elucidate our observation, future reports of larger case series are surely warranted.

The clarification of the possible association between sleep deprivation and the reversible splenial lesion may also provide substantial perspectives regarding the mechanisms and health impact of sleep deprivation; the functional and pathophysiological role of the splenial corpus callosum in sleep physiology. Finally, we think that the awareness of this entity should be increased among clinicians to avoid unnecessary investigations.

Conclusion

Sleep deprivation may be an inducer agent of RESLES in some rare clinical scenarios. The functional and pathophysiological role of the splenial corpus callosum in sleep physiology may constitute an interesting topic for further investigations.

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