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LETTER TO THE EDITOR

Posterior reversible encephalopathy syndrome associated with chemotherapeutic agent and granulocyte colony-stimulating factor

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Posterior reversible encephalopathy syndrome (PRES) is a condition typically characterized by vasogenic edema in the posterior parietal and occipital regions. It typically presents with encephalopathy, seizure, visual disturbance, and headache. Etiological factors include preeclampsia, hypertensive episodes, organ transplantations, immunosuppressive and cytotoxic drugs, sepsis, and hyperammonemia.[1] As the treatment for PRES is directed toward the underlying cause, determining the etiology is crucial. Herein, we aim to draw attention to the usage of cytotoxic agents and recombinant granulocyte colony-stimulating factors (rhG-CSF), such as filgrastim and vinflunine, as an etiological factor for PRES.

A 71-year-old female patient with known metastatic renal cell carcinoma presented to the emergency service with altered consciousness and had an episode lasting 1 min with loss of consciousness, downward eye deviation in both eyes, and tonic-clonic contractions in bilateral upper and lower extremities. Neuroimaging did not reveal any diffusion restriction in diffusion-weighted magnetic resonance imaging (MRI). In the FLAIR (fluid-attenuated inversion recovery) sequence, hyperintensities extending into the bilateral parietooccipital subcortical and parasagittal frontal areas were observed (Figure 1). In the neurological examination, a tendency to sleep, intermittent cooperation with single commands, prolonged reaction time, and decreased attention were observed. The pupils were isocoric, and bilateral light reflexes were present. No lateralizing motor deficit was observed, and no pathological reflex was detected.

After evaluating the MRI findings and the clinical state, the patient was admitted to the neurology intensive care unit with the preliminary diagnosis of PRES. Upon a detailed history regarding PRES etiology, it was revealed that the patient received filgrastim and vinflunin. The patient was administered 250 mg of vinflunin a week ago for three days, followed by 300 mcg (30 million units) of filgrastim 24 h later after the last dosage of vinflunin. Electroencephalography showed slow-wave activity on both hemispheres. The spontaneous brain activity consisted of 5 to 6 Hz theta waves and was found to be insufficient. The patient's blood parameters showed leukopenia (white blood cell count: 1,960 cells/μL) and thrombocytopenia (platelet count: 81,000/μL). A lumbar puncture was performed due to the patient's existing immunosuppressive condition, and no cells were observed. Cerebrospinal fluid protein was mildly elevated at 540 mg/L (normal range: 150 to 450 mg/L). Microscopic examination of the cerebrospinal fluid did not reveal any microorganisms, and meningitis polymerase chain reaction screening and cerebrospinal fluid culture yielded negative results. Two weeks later, clinical

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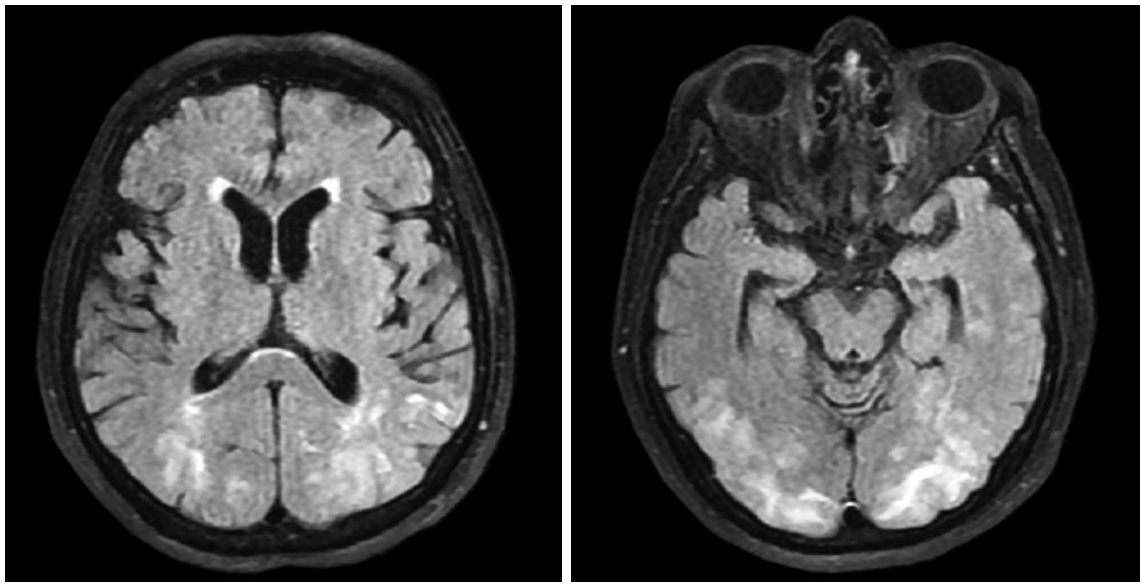

Figure 1. Fluid-attenuated inversion recovery hyperintensities in bilateral parietooccipital regions.

improvement in the mental status examination was observed, and follow-up MRI showed disappearance of the hyperintensities previously observed in the initial MRI. Due to the recurrence risk of PRES, filgrastim and vinflunin were discontinued.

The patient was diagnosed with PRES associated with the usage of vinflunin and filgrastim, given the absence of malignant hypertension at the emergency department presentation. Similar cases are also reported in the literature. Vinflunin is a cytotoxic vinca alkaloid that blocks microtubule polymerization and exhibits antitumor activity. It has shown benefit in patients with progression after platinum-based chemotherapy. Filgrastim is a granulocyte-macrophage colony-stimulating factor used to decrease bone marrow suppression associated with chemotherapy. A reported case of filgrastim-associated PRES in the literature was noted approximately five to six days after the initiation of filgrastim treatment.[2]

The pathophysiology of PRES involves theories such as the development of vasogenic edema with the disruption of cerebrovascular autoregulation due to severe hypertension, systemic inflammation causing endothelial dysfunction, or endothelial dysfunction induced by chemokine-like endotoxins or chemotherapeutic/immunosuppressive exotoxins.[3] A study reporting 70 cases of chemotherapy-associated PRES identified platinum-based agents (cisplatin, carboplatin, and oxaliplatin; 30 cases), doxorubicin (24 cases), vinca alkaloids (vincristine, vinorelbine, vinflunin, vinblastine, and vindesine; 21 cases), 5-fluorouracil (12 cases), and irinotecan (one case) as the most common agents leading to PRES.[4] In this study, 84% of cases showed neurological symptom improvement around the seventh day after symptom onset. Follow-up imaging, done approximately 20 days after the initial neuroimaging, revealed complete resolution of PRES lesions in 84% of cases. Continued treatment with the same chemotherapeutic agent in 17 patients from the same study did not result in recurrence of PRES in seven cases, while recurrence was observed in two cases. In cases of PRES development, symptomatic seizure treatment and antihypertensive therapy are recommended, along with the discontinuation of the suspected agent. If cerebral infarction does not occur, clinical and radiographic changes are reversible.[5]

In conclusion, with the increasing number of cancer patients worldwide, early recognition of the drug-induced PRES syndrome is critical, given its reversibility with drug cessation. We highlighted a rare cause in PRES etiology, the pathophysiology, and the management of PRES associated with vinflunin and filgrastim.

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Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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