



Posterior Reversible Encephalopathy Syndrome Associated with Sunitinib Presenting to the Emergency Department: A Case Report

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Abstract: The occurrence of posterior reversible encephalopathy syndrome (PRES) during sunitinib therapy highlights the complex interaction between iatrogenic effects related to vascular endothelial growth factor (VEGF) inhibition and underlying cerebral vascular vulnerability. Prompt diagnosis, discontinuation of the offending agent, blood pressure control, and management of complications remain the cornerstones of treatment. A multidisciplinary approach involving oncology and neurology specialists, along with systematic monitoring of cardiovascular and renal parameters, is *recommended to reduce risk and optimize patient outcomes*.

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a clinical and radiological entity characterized by the acute onset of headache, visual disturbances, seizures, and altered mental status, associated with brain imaging abnormalities typically involving the parieto-occipital regions on magnetic resonance imaging (MRI), reflecting reversible vasogenic edema [1]. Initially described in 1996 by Hinchey et al., PRES is now recognized as a neurological emergency with a favorable prognosis when diagnosis and management are initiated early [2]. The exact pathophysiological mechanisms of PRES remain controversial, with two main hypotheses proposed: failure of cerebral autoregulation leading to hyperperfusion and vasogenic edema, and severe endothelial dysfunction resulting in increased vascular permeability. Numerous triggering factors have been identified, including acute or malignant hypertension, immunosuppressive therapies, preeclampsia/eclampsia, acute or chronic renal failure, severe infections, and sepsis [3,4].

Sunitinib is a multi-targeted tyrosine kinase inhibitor (TKI) that primarily inhibits vascular endothelial growth factor receptors (VEGFRs). It is widely used as first-line therapy for metastatic renal cell carcinoma, significantly improving patient prognosis [5].

PRES represents a critical diagnosis in emergency medicine, as its clinical presentation—often polymorphic and potentially mimicking acute ischemic stroke, encephalitis, or prolonged seizure activity—requires early referral for brain imaging, particularly MRI. Rapid recognition allows targeted management, including blood pressure control, seizure treatment, and correction of underlying precipitating factors, which are essential for lesion reversibility [6].

In this context, we report a case of PRES managed in the emergency department, illustrating the heterogeneity of clinical presentations and emphasizing the importance of early diagnosis to optimize neurological outcomes.

CASE PRESENTATION

We report the case of a 70-year-old male patient, an active chronic smoker, followed in the oncology department for eight months for stage IV metastatic clear cell renal carcinoma (with adrenal, bone, and spinal metastases), classified as Heng score 3. The patient was receiving sunitinib at a dose of 50 mg daily.

After six months of treatment, he developed sudden-onset, severe headaches associated with decreased visual acuity. The clinical course rapidly progressed to altered mental status, with confusion followed by somnolence, prompting presentation to the emergency department.

On admission, the patient was in mild coma with a Glasgow Coma Scale score of 11. He was afebrile, with a capillary blood glucose level of 1.05 g/L. Vital signs revealed elevated blood pressure (150/85 mmHg), heart rate of 75 beats per minute, respiratory rate of 20 breaths per minute, and oxygen saturation of 96% on room air. Neurological examination showed no focal deficits, and the remainder of the physical examination was unremarkable. Electrocardiography demonstrated a regular sinus rhythm with a normal cardiac axis.

Laboratory investigations revealed renal impairment with a serum creatinine level of 186 $\mu\text{mol/L}$, without associated electrolyte disturbances.

In the absence of a clear initial diagnosis, a non-contrast brain computed tomography (CT) scan was performed emergently and showed no abnormalities. Brain MRI was subsequently obtained and demonstrated bilateral, symmetrical hyperintense lesions on T2-weighted and FLAIR sequences involving the parieto-occipital regions and thalami, associated with cerebellar involvement. Additional nodular signal abnormalities in the bilateral frontal subcortical white matter, hyperintense on T2 and FLAIR sequences, were also observed without evidence of hemorrhage. These findings were consistent with a diagnosis of PRES.

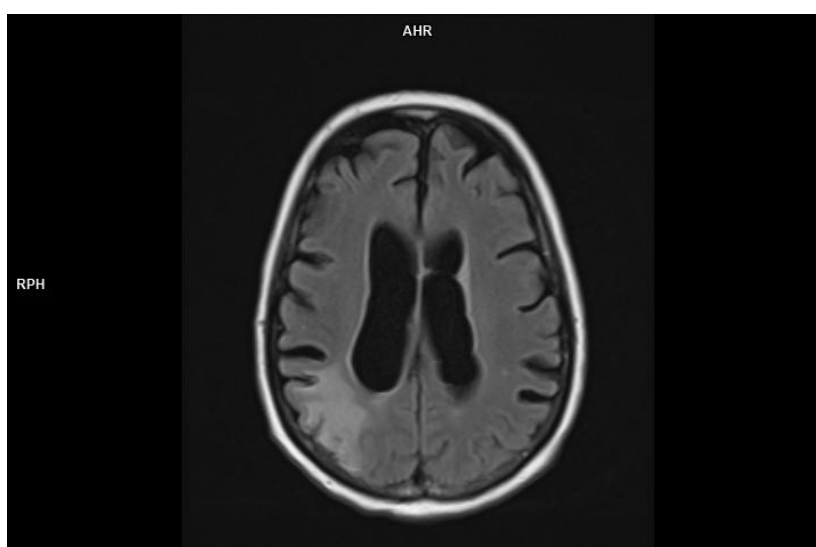


Figure: Axial FLAIR sequence showing a right parieto-occipital cortico-subcortical hyperintensity.

The patient was admitted to the intensive care unit for close clinical and biological monitoring. Sunitinib therapy was discontinued. Supportive measures included head-of-bed elevation to 30 degrees and optimization of ventilation. Blood pressure control was achieved using intravenous nicardipine administered as needed. The patient was subsequently transferred to the neurology department for further management.

DISCUSSION

This case illustrates the occurrence of posterior reversible encephalopathy syndrome in a patient treated with sunitinib for metastatic renal cell carcinoma. This observation falls within the spectrum of neurotoxicities, which are rare but potentially severe complications of targeted anti-angiogenic therapies. It supports existing literature identifying tyrosine kinase inhibitors (TKIs), particularly VEGFR inhibitors, as iatrogenic causes of PRES. By inhibiting VEGFR, platelet-derived growth factor receptor (PDGFR), and other kinases, sunitinib disrupts angiogenic signaling and endothelial function [7]. Although its antitumor efficacy is well established, its toxicity profile includes hypertension and, more rarely, neurological adverse events such as PRES.

Recent reviews of neurological complications associated with targeted therapies report that PRES typically occurs within the first months of treatment, often in the context of drug-induced or exacerbated hypertension, as observed in our patient. Other TKIs (sorafenib, pazopanib, axitinib) and the anti-VEGF monoclonal antibody bevacizumab have also been implicated, suggesting a class effect related to VEGF pathway inhibition.

The pathophysiology of PRES is multifactorial. In the context of anti-angiogenic agents, the prevailing hypothesis is direct toxic endothelial injury. VEGF plays a crucial role in maintaining blood-brain barrier integrity and regulating vascular permeability. Its inhibition by sunitinib leads to endothelial dysfunction, increased capillary permeability, and vasogenic edema, particularly in posterior cerebral regions, which have less dense sympathetic innervation and are therefore more susceptible to blood pressure fluctuations [8,9]. In our patient, moderate hypertension (150/85 mmHg) was present but not malignant, highlighting that PRES associated with anti-angiogenic therapy may occur even in the absence of severe hypertensive crises, with drug-induced endothelial injury acting as the primary trigger. Underlying renal impairment, common in renal cell carcinoma, represents an additional predisposing factor by impairing cerebral autoregulation [10].

The patient's clinical presentation—headache, visual disturbances, and altered consciousness—is typical of PRES [11]. The absence of seizures at admission does not exclude the diagnosis, as seizures are an inconstant feature. The main diagnostic challenge, illustrated in this case, lies in the normal initial brain CT scan. CT lacks sensitivity for detecting early vasogenic edema, and a normal result should not rule out PRES when clinical suspicion is high [12]. Brain MRI remains the gold standard diagnostic modality. The imaging findings in our patient—bilateral symmetrical parieto-occipital T2/FLAIR hyperintensities with thalamic and cerebellar involvement—are characteristic. The additional frontal white matter involvement, although less typical, underscores that “atypical” lesion distributions (frontal, temporal, brainstem) may be observed in up to 30% of cases without invalidating the diagnosis [13]. The absence of diffusion restriction supports the vasogenic (rather than cytotoxic) nature of the edema and is associated with a favorable prognosis.

Management is both symptomatic and etiological. The critical step, appropriately applied in this case, is immediate discontinuation of the suspected causative agent—sunitinib. This measure is essential to allow lesion reversibility. Careful blood pressure control, avoiding excessive or rapid reductions that could precipitate cerebral hypoperfusion, is a cornerstone of treatment. Intravenous nicardipine is appropriate due to its rapid onset and titratable effects [12]. Monitoring in a neurocritical care setting allows early detection and treatment of complications such as seizures or significant cerebral edema. Prognosis is generally favorable, with complete or near-complete resolution of neurological symptoms and radiological abnormalities within days to weeks following removal of the triggering factor, as reported in most TKI-associated cases. However, delayed diagnosis may result in permanent neurological sequelae or hemorrhagic or ischemic transformation.

CONCLUSION

Any new neurological symptom occurring in a patient receiving anti-angiogenic therapy—such as sunitinib, other TKIs, or bevacizumab—should raise suspicion for PRES, even in the absence of severe hypertension. In suspected cases, brain MRI is the key diagnostic tool and should be performed urgently, even when CT findings are normal. Definitive discontinuation of the offending agent is essential. Rechallenge with the same drug or another anti-VEGF therapy is generally contraindicated due to a high risk of recurrence. Multidisciplinary discussion is required to guide the selection of alternative therapeutic strategies.