Scientific Research Publishing

Journal of Cancer Therapy, 2025, 16(9), 307-314
https://www.scirp.org/journal/jct
ISSN Online: 2151-1942
ISSN Print: 2151-1934

Acute Neurological Complication of Chemotherapy: A Case of Posterior Reversible Encephalopathy Syndrome Following Chemotherapy with Oxaliplatin and a Fluoropyrimidine

Najlae Demnati Sadki*, Mounir Belcadi, Hafsa El Hilali, Hind Majd, Kaoutar Maadin, Mohammed Tarik Saoudi, Ouiame El Meliani, Lamiae Amaadour, Karima Oualla, Zineb Benbrahim, Samia Arifi, Nawfel Mellas

Hassan II University Hospital of Fez, Fez, Morocco
Email: *naaajlaae@gmail.com

How to cite this paper: Demnati Sadki, N., Belcadi, M., El Hilali, H., Majd, H., Maadin, K., Saoudi, M.T., El Meliani, O., Amaadour, L., Oualla, K., Benbrahim, Z., Arifi, S. and Mellas, N. (2025) Acute Neurological Complication of Chemotherapy: A Case of Posterior Reversible Encephalopathy Syndrome Following Chemotherapy with Oxaliplatin and a Fluoropyrimidine. *Journal of Cancer Therapy*, **16**, 307-314.
https://doi.org/10.4236/jct.2025.169023

Received: August 7, 2025
Accepted: September 5, 2025
Published: September 8, 2025

Abstract

Posterior reversible encephalopathy syndrome (PRES) is a transient neuroradiological condition marked by seizures, altered consciousness, and visual disturbances. MRI typically reveals reversible hyperintense lesions in the posterior cerebral regions. While most cases are reversible, PRES remains a rare and potentially severe complication of chemotherapy. This article aims to describe the clinical and radiological features of this chemotherapy-induced complication, supported by a review of similar cases in the literature. We report a case from the oncology department of Hassan II University Hospital in FES, of a 44-year-old male patient with no comorbidities, who was admitted for sudden bilateral blindness several hours after the administration of his first course of chemotherapy based on 5-FU and oxaliplatin for gastric cancer, he was admitted to the oncology emergency unit. The patient's blood pressure was within normal limits. Brain MRI revealed bilateral hyperintensities on FLAIR sequences involving the parieto-occipital regions. The patient was treated with intravenous corticosteroids and clonazepam with strict monitoring of blood pressure. The neurological symptoms fully regressed over the course of a few days. These findings, in correlation with the clinical picture, led to the diagnosis of posterior reversible encephalopathy syndrome (PRES). This case highlights the importance of considering PRES in any cancer patient presenting with acute neurological symptoms, even in the absence of

hypertension.

Keywords

Posterior-Reversible Encephalopathy Syndrome, Chemotherapy, Visual Disturbances, Cerebral MRI

1. Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological entity first described in 1996 by Hinchey *et al.* [1]. It is characterized by a variable combination of seizures, altered level of consciousness, headaches, visual disturbances, nausea and vomiting, and focal neurological deficits [2] [3].

Although often reversible, PRES can present with severe manifestations that may be life-threatening, such as coma or status epilepticus [4] [5].

2. Case Presentation

A 44-year-old male patient, with no significant medical history, initially presented with epigastric pain and persistent vomiting, occurring in the context of unquantified weight loss and refractory to symptomatic treatments, evolving over the course of several weeks. Upper gastrointestinal endoscopy (EGD) revealed a non-stenosing ulcerative and exophytic lesion located at the antro-fundic junction.

Histological examination of the biopsies confirmed a poorly differentiated adenocarcinoma, partially composed of discohesive (signet-ring) cells.

A thoracoabdominopelvic (TAP) CT scan, performed as part of the staging workup, showed diffuse peritoneal carcinomatosis, retroperitoneal, precaval, and hepatic lymphadenopathy, along with mild ascites. HER2 immunohistochemistry score: 0.

In our patient, phenotyping revealed elevated plasma uracil of 20 ng/mL (reference < 16 ng/mL), consistent with partial DPD deficiency.

The patient was started on a FOLFOX chemotherapy regimen (combining 5-fluorouracil at 50% of the standard dose, leucovorin, and oxaliplatin).

36 hours following his first cycle of chemotherapy, the patient was admitted to the oncology emergency department with an acute neurological syndrome consisting of:

- Sudden-onset bilateral blindness,
- Dysarthria, and
- A reported episode of generalized tonic-clonic seizure.

These symptoms warranted urgent hospitalization.

On admission, the patient was classified as WHO performance status 3, and was somnolent, with normal heart rate and blood pressure ranging between 110 - 130 mmHg systolic and 60 - 70 mmHg diastolic.

On neurological examination, visual acuity was limited to bilateral light perception. The patient was unable to count fingers at a distance of one meter, and there was no blink response to threat. However, pupillary light reflexes were preserved, indicating intact cranial nerve function. These findings were consistent with acute-onset cortical blindness.

A bilateral coordination disturbance was also observed, characterized by dysmetria on finger-to-nose testing, suggestive of a kinetic cerebellar syndrome.

Taken together, the clinical picture was indicative of acute cortical visual impairment associated with cerebellar dysfunction, occurring in the context of a generalized tonic-clonic seizure episode.

Electrocardiogram (ECG) was normal.

The initial differential diagnoses included:

- Chemotherapy-induced posterior reversible encephalopathy syndrome (PRES)
- Cerebral venous thrombosis (CVT)
- Cerebral metastases

In the emergency setting, an initial non-contrast brain CT scan was performed, which showed no abnormalities (Figure 1).

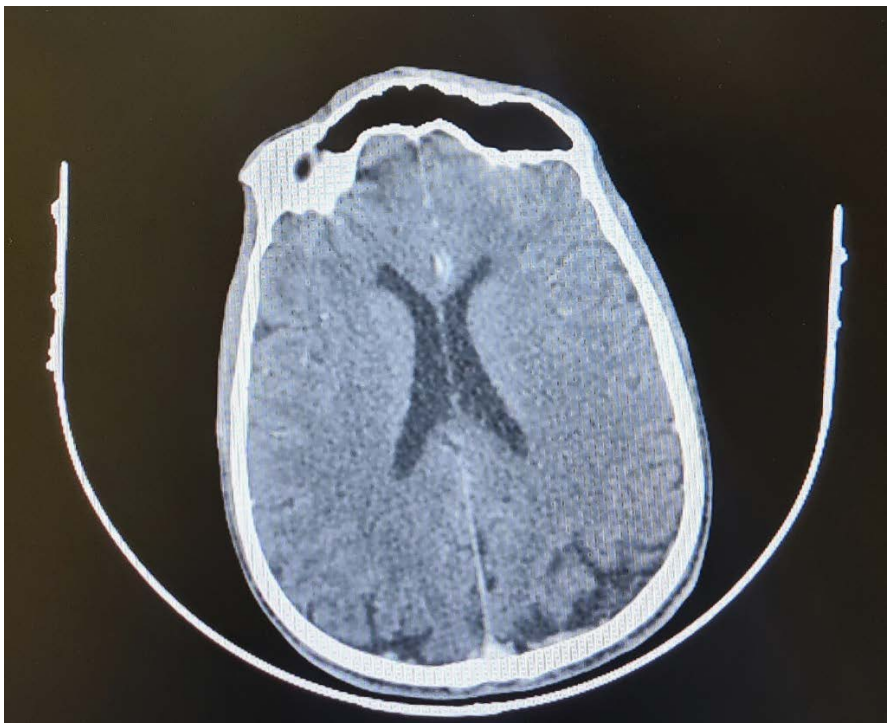

Figure 1. Axial section of a brain CT demonstrating no abnormalities.

Brain MRI revealed bilateral hyperintensities on FLAIR sequences involving the parieto-occipital regions (Figure 2), consistent with findings typically seen in posterior reversible encephalopathy syndrome (PRES). No abnormalities were noted on T1-weighted images, and there was no evidence of intracranial hemorrhage, excluding cerebral metastases and cerebral venous thrombosis.

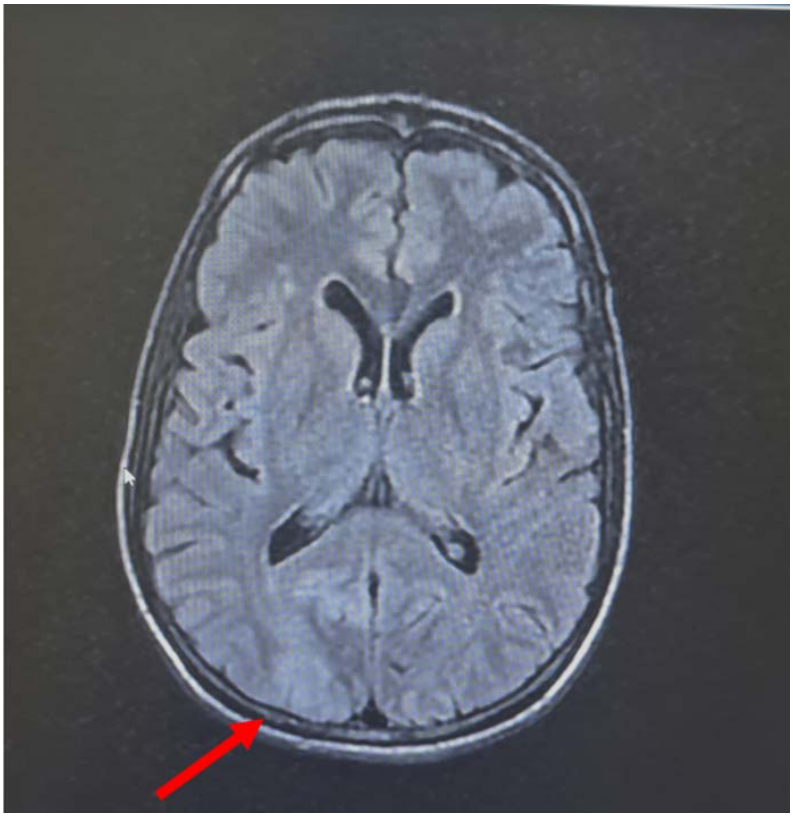

Figure 2. Axial section of brain MRI demonstrated bilateral hyperintensities on FLAIR sequences affecting the parieto-occipital regions.

Given the clinical and radiological findings, PRES was diagnosed.

The patient was managed with:

- Methylprednisolone 120 mg/day intravenously
- Clonazepam (Urbanyl®) 5 mg/day, administered as ½ tablet three times daily
- Strict monitoring of blood pressure, which remained within normal limits throughout hospitalization

The patient showed rapid clinical improvement, with complete resolution of neurological symptoms by day 3. A follow-up ophthalmological examination on day 5 was normal. No recurrence of symptoms was observed during follow-up.

Given the lack of alternative therapeutic options, FOLFOX chemotherapy was reintroduced.

To reduce the risk of recurrence, the following precautionary measures were implemented:

- Hospital admission prior to chemotherapy for enhanced premedication.
- Strict blood pressure monitoring during and after the infusion.
- Prolonged infusion duration of the chemotherapy protocol.
- Inpatient observation for 72 hours post-chemotherapy to ensure close neurological and hemodynamic surveillance.

The patient tolerated the subsequent cycles well, with no recurrence of neurological symptoms.

3. Discussion

The pathophysiology of posterior reversible encephalopathy syndrome (PRES) remains a subject of ongoing debate. An acute hypertensive surge may disrupt the blood–brain barrier, particularly in the posterior circulation, due to its limited capacity for autoregulation. This breakdown leads to vasogenic edema, predominantly in posterior regions, which are more vulnerable owing to their relatively sparse sympathetic innervation [5]. In addition, endothelial dysfunction—whether or not associated with elevated blood pressure—also plays a significant role in the pathogenesis of PRES.

Exposure to toxic agents is one of the most common etiologies associated with posterior reversible encephalopathy syndrome (PRES), reported in approximately 11% to 61% of cases. [5]

The pathophysiological link between fluoropyrimidines and encephalopathy remains poorly understood. However, three main mechanisms have been proposed. One of the most studied theories implicates a deficiency in dihydropyrimidine dehydrogenase (DPD)—the rate-limiting enzyme in fluoropyrimidine catabolism—as a contributing factor to severe and systemic 5-fluorouracil (5-FU) toxicity. DPD deficiency impairs the breakdown of 5-FU, leading to the accumulation of neurotoxic metabolites. Retrospective data suggest that DPD deficiency may account for up to 50% of 5-FU-related toxicities [6] [7].

While we emphasized the role of fluoropyrimidine, it is important to recognize that oxaliplatin alone has also been implicated in PRES, suggesting a possible direct endothelial toxic effect even in the absence of fluoropyrimidine. For example, an isolated case described a normotensive patient developing PRES with vasogenic edema confined to the pons during oxaliplatin-based treatment—without concurrent 5-FU—which resolved completely after withholding oxaliplatin [8].

A notable characteristic that aids in differentiating PRES from bilateral posterior cerebral artery infarction is the relative sparing of the calcarine and paramedian occipital lobes. While the posterior regions are most commonly involved, the cerebellum and brainstem may also be affected. In more extensive or severe cases, frontal and temporal lobe involvement has been reported [9].

The most common and characteristic clinical feature of posterior reversible encephalopathy syndrome (PRES) is non-specific encephalopathy, observed in up to 94% of patients, with a spectrum ranging from mild confusion to deep coma. Headache is reported in approximately 50% of cases, typically described as dull and diffuse, though it may present more acutely as a sudden thunderclap headache in some instances [10].

Seizures—either focal or generalized—occur in nearly three-quarters of patients during the course of the syndrome, though they are infrequently the initial presenting symptom. In severe cases, seizures may evolve into status epilepticus, reported in up to 18% of patients [11].

Visual disturbances, seen in 20% - 39% of cases, may include blurred vision, visual field deficits, visual neglect, hallucinations, or even complete cortical blind-

ness [1] [10].

Cerebral CT is often normal in cases of PRES. When abnormalities are present, they typically appear as hypodense areas with a distribution suggestive of the syndrome's characteristic topography [5].

Magnetic resonance imaging is essential for confirming the diagnosis of PRES. T2-weighted and FLAIR sequences are the most sensitive for detecting the characteristic abnormalities, which typically appear as hyperintensities in the affected regions [3] [4]. FLAIR sequences provide superior contrast between cortical and subcortical lesions, while T1-weighted sequences typically show hypointensity in the same areas. Gadolinium-enhanced MRI may reveal contrast enhancement in approximately 50% of patients, which likely reflects disruption of the blood-brain barrier [12] [13].

In follow-up studies, radiologic abnormalities resolve in 66% - 70% of cases within weeks to months. Severe presentations may include mass effect, herniation, hemorrhages, or restricted diffusion. Vascular imaging (angiography or angio-MRI/CT) may show segmental vasoconstriction or vasodilation, but such findings are not specific to PRES [14].

Management of PRES secondary to cytotoxic agents involves a multidisciplinary approach, including strict blood pressure control, seizure management, and immediate withdrawal of cytotoxic or causative agents [15]. The primary goal in hypertensive emergencies is to reduce diastolic blood pressure to approximately 100 mmHg, while avoiding an initial reduction of more than 25% of the presenting value, to prevent compromising cerebral autoregulation and inducing ischemia. Oral antihypertensives are often insufficient in such acute settings, and intravenous agents are typically preferred for rapid and controlled BP lowering.

Antiepileptic drugs should be initiated promptly in patients with seizures. These medications can usually be tapered off within 1 to 2 weeks as clinical and radiological recovery is achieved. However, persistent or delayed seizures have been reported in some patients, warranting prolonged antiepileptic therapy [16].

PRES is characterized by vasogenic edema from endothelial dysfunction, which in chemotherapy-associated cases may be driven by toxic injury to the blood-brain barrier. In selected reports, short courses of methylprednisolone have been associated with rapid clinical and radiologic improvement, presumably via anti-inflammatory effects and stabilization of capillary permeability [17].

Additionally, electrolyte imbalances should be promptly corrected to minimize neuronal excitability and associated complications [18].

Standard PRES management emphasizes withdrawal of the offending trigger (when identifiable), BP control, seizure treatment, and supportive care; most reviews therefore discourage routine re-exposure. Nevertheless, in oncology-related PRES, several series and reviews note that carefully selected, closely monitored rechallenge can be reasonable once patients have complete clinical and radiologic resolution and modifiable risks are controlled. In a cancer-focused review, repeat administration of potentially offending agents (including cytotoxics) was at-

tempted without recurrent PRES in multiple patients, leading the authors to suggest that judicious chemotherapy re-exposure may be safe with vigilant monitoring and tight blood-pressure control; individual reports even describe successful rechallenge of agents previously linked to PRES [19].

4. Conclusions

Posterior reversible encephalopathy syndrome (PRES) remains a rare and challenging diagnosis, largely due to the nonspecific nature of its clinical presentation.

The association between cytotoxic chemotherapeutic agents and PRES is now well-documented, although mostly through isolated case reports. This potential complication should be recognized by all healthcare professionals involved in cancer care, particularly in emergency and oncology settings.

Management is largely symptomatic, requiring immediate withdrawal of the offending agent, rigorous control of blood pressure, correction of metabolic imbalances, and antiseizure therapy when indicated. The prognosis is generally favorable, with resolution of clinical and radiological findings within days in most cases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Hinchey, J., Chaves, C., Appignani, B., Breen, J., Pao, L., Wang, A., *et al.* (1996) A Reversible Posterior Leukoencephalopathy Syndrome. *New England Journal of Medicine*, **334**, 494-500. https://doi.org/10.1056/nejm199602223340803

[2] Fischer, M. and Schmutzhard, E. (2017) Posterior Reversible Encephalopathy Syndrome. *Journal of Neurology*, **264**, 1608-1616. https://doi.org/10.1007/s00415-016-8377-8

[3] Bartynski, W.S. (2008) Posterior Reversible Encephalopathy Syndrome, Part 1: Fundamental Imaging and Clinical Features. *American Journal of Neuroradiology*, **29**, 1036-1042. https://doi.org/10.3174/ajnr.a0928

[4] McKinney, A.M., Short, J., Truwit, C.L., McKinney, Z.J., Kozak, O.S., SantaCruz, K.S., *et al.* (2007) Posterior Reversible Encephalopathy Syndrome: Incidence of Atypical Regions of Involvement and Imaging Findings. *American Journal of Roentgenology*, **189**, 904-912. https://doi.org/10.2214/ajr.07.2024

[5] Fugate, J.E. and Rabinstein, A.A. (2015) Posterior Reversible Encephalopathy Syndrome: Clinical and Radiological Manifestations, Pathophysiology, and Outstanding Questions. *The Lancet Neurology*, **14**, 914-925. https://doi.org/10.1016/s1474-4422(15)00111-8

[6] Van Kuilenburg, A., Meinsma, R., Zoetekouw, L. and Van Gennip, A. (2002) High Prevalence of the IVS14 + 1G>A Mutation in the Dihydropyrimidine Dehydrogenase Gene of Patients with Severe 5-Fluorouracil-Associated Toxicity. *Pharmacogenetics*, **12**, 555-558. https://doi.org/10.1097/00008571-200210000-00007

[7] Boisdron-Celle, M., Remaud, G., Traore, S., *et al.* (2007) 5-Fluorouracil-Related Severe Toxicities: A Comparison of DPD Deficiency Screening Methods in 1,117 Patients. *Clinical Cancer Research*, **13**, 6043-6049.

[8] Tang, K. (2015) Oxaliplatin-Induced Posterior Reversible Encephalopathy Syndrome with Isolated Involvement of Pons. *Journal of Cancer Research and Therapeutics*, **11**, 1022. https://doi.org/10.4103/0973-1482.146134

[9] Evin, C., Lassau, N., Balleyguier, C., Assi, T. and Ammari, S. (2022) Posterior Reversible Encephalopathy Syndrome Following Chemotherapy and Immune Checkpoint Inhibitor Combination in a Patient with Small-Cell Lung Cancer. *Diagnostics*, **12**, Article 1369. https://doi.org/10.3390/diagnostics12061369

[10] Legriel, S., Pico, F. and Azoulay, E. (2011) Understanding Posterior Reversible Encephalopathy Syndrome. *Acta Clinica Belgica*, **66**, 437-441.

[11] Fugate, J.E., Claassen, D.O., Cloft, H.J., Kallmes, D.F., Kozak, O.S. and Rabinstein, A.A. (2010) Posterior Reversible Encephalopathy Syndrome: Associated Clinical and Radiologic Findings. *Mayo Clinic Proceedings*, **85**, 427-432. https://doi.org/10.4065/mcp.2009.0590

[12] Covarrubias, D.J., Luetmer, P.H. and Campeau, N.G. (2002) Posterior Reversible Encephalopathy Syndrome: Prognostic Utility of Quantitative Diffusion-Weighted MR Images. *American Journal of Neuroradiology*, **23**, 1038-1048.

[13] Lee, V.H., Wijdicks, E.F.M., Manno, E.M. and Rabinstein, A.A. (2008) Clinical Spectrum of Reversible Posterior Leukoencephalopathy Syndrome. *Archives of Neurology*, **65**, 205-210. https://doi.org/10.1001/archneurol.2007.46

[14] Geocadin, R.G. (2023) Posterior Reversible Encephalopathy Syndrome. *New England Journal of Medicine*, **388**, 2171-2178. https://doi.org/10.1056/nejmra2114482

[15] Verma, R., Mukherjee, A., Mehta, A. and Bhandari, A. (2012) Posterior Reversible Encephalopathy Syndrome (PRES) Secondary to chemotherapy: A Rare Case Report. *Case Reports in Oncological Medicine*, **2012**, 1-3.

[16] Bahirwani, R., Rana, S., Liu, K.T. and Tzamaloukas, A.H. (2013) Posterior Reversible Encephalopathy Syndrome in a Patient on Oxaliplatin-Based Chemotherapy: A Case Report and Literature Review. *Case Reports in Oncological Medicine*, **2013**, Article ID: 306983.

[17] Meyer, M., Niemöller, U., Stein, T., Schmetsdorf, S., Arnold, A., El-Sheik, M., *et al.* (2019) Positive Effect of Steroids in Posterior Reversible Encephalopathy Syndrome. *Case Reports in Neurology*, **11**, 173-177. https://doi.org/10.1159/000500410

[18] Legriel, S., Schraub, O., Azoulay, E., Hantson, P., Magalhaes, E., Coquet, I., *et al.* (2012) Determinants of Recovery from Severe Posterior Reversible Encephalopathy Syndrome. *PLOS ONE*, **7**, e44534. https://doi.org/10.1371/journal.pone.0044534

[19] Singer, S., Grommes, C., Reiner, A.S., Rosenblum, M.K. and DeAngelis, L.M. (2015) Posterior Reversible Encephalopathy Syndrome in Patients with Cancer. *The Oncologist*, **20**, 806-811. https://doi.org/10.1634/theoncologist.2014-0149