

## Case Report

# Posterior reversible encephalopathy syndrome in cancer patients: experience from a tertiary cancer center, South India

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### ABSTRACT

Posterior Reversible Encephalopathy Syndrome (PRES) is characterized by seizures, headaches, altered mental status, cortical blindness and typical transient lesions on MRI. PRES may be associated with chemotherapy, molecular targeted drugs and immunosuppressive agents used in patients with cancer. PRES is a very rare condition in cancer patients. PRES is usually reversible with appropriate supportive care and most patients can be restarted with treatment.

**Keywords:** Cancer, Chemotherapy, Immunosuppressive agents, Posterior reversible encephalopathy syndrome

## INTRODUCTION

Posterior Reversible Encephalopathy Syndrome (PRES) is a well described clinico-radiological syndrome characterized by symptoms of headache, seizures, altered sensorium and visual disturbances with characteristic neuroimaging lesions.<sup>1</sup> PRES is typically associated with hypertension, the puerperium and usage of immunosuppressive agents in solid organ and hematopoietic stem cell transplantation.<sup>2,3</sup>

The main theories concerning pathophysiology include an overwhelmed cerebral autoregulation and direct cytotoxic effect on endothelial cells leading to breakdown of blood brain barrier.<sup>4,5</sup>

The newer molecular targeted therapies have increasingly become important contributors to this condition. The present study is aimed at describing the demographics, clinical course and outcomes of PRES in patients with cancer.

## CASE REPORT

Author retrospectively identified the patients diagnosed with PRES at Vydehi Cancer Centre, Vydehi Institute of Medical Sciences and Research Centre (VIMS and RC), Bengaluru, India. All the chemotherapeutic and biologic targeted agents administered one month prior to PRES diagnosis were recorded. Here author present a series of cases that have been diagnosed as PRES syndrome in hospital over the last one year (January 2018- January 2019).

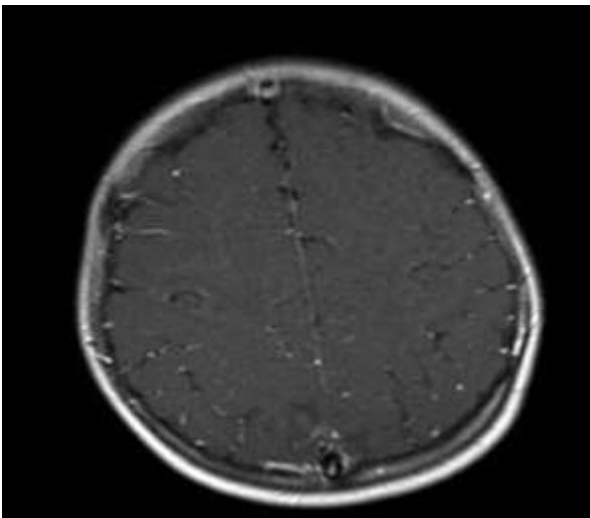
### Case 1

A 15-year-old girl presented with acute onset of pain abdomen and an ultrasound abdomen showed intra-abdominal collection along with perforation of colon. During this episode patient had severe hypotension and had seizures. Patient was administered antiepileptic agents and seizure was controlled. Magnetic Resonance Imaging (MRI) brain done showed features suggestive of

PRES. The patient was continued with antiepileptic drugs and surgery was done for colonic perforation. The histopathology was suggestive of DLBCL colon. She had another episode of seizure since patient had stopped taking the antiepileptics for 4 months. Reimaging showed scarring in the occipital region. On restarting the antiepileptic drugs, patient did not have any further seizure. Patient received 6 cycles of chemotherapy (RCHOP) and is on follow up. Patient is in remission as of last follow up.

### Case 2

A 10-year-old boy presented with mass per abdomen. Patient was evaluated for the presenting complaint and diagnosed as Wilm's tumor. Patient was treated according to SIOP protocol with Vincristine and Actinomycin-D. The patient's blood pressure was checked before each chemotherapy cycle and it was normal. After the completion of second chemotherapy cycle, patient presented with seizures. MRI brain was suggestive of PRES and patient had elevated blood pressure. Patient was disoriented for 2 days. The child was taken up for surgery as the lesion was operable after the 2 cycles of chemotherapy. The final histopathology report was suggestive of Renal cell carcinoma. The patient is asymptomatic and in remission on follow up.

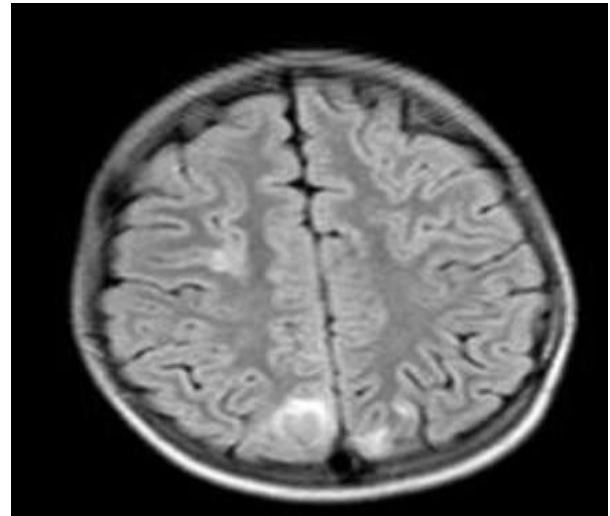


**Figure 1: T1 weighted images of brain of third patient.**

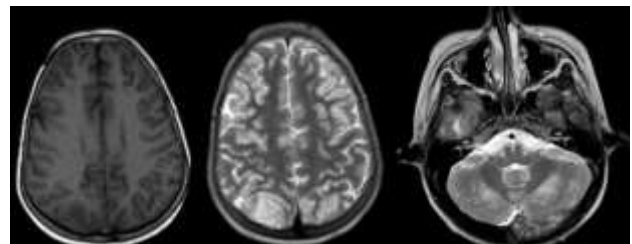
### Case 3

A 12-year-old boy was diagnosed with B Cell acute lymphoblastic leukemia (ALL) (Intermediate risk). Patient was started on treatment according BFM (Berlin Frankfurt Munster) 2002 protocol. Patient was in Re-induction phase and was treated with Dexamethasone, Vincristine, Adriamycin and L-Asparaginase. Patient had sudden onset of seizures, hypertension, disorientation and visual hallucination. MRI brain done was suggestive of PRES (Figure1-3). Patient was treated with anti-

hypertensives and antiepileptics. Patient was continued with the BFM protocol after recovering from seizure. Presently patient is on regular follow-up and is in clinical remission.



**Figure 2: T2 flair images showing hyper intensities in the occipital lobe.**



**Figure 3: T2 hyper intensities in the cerebellum.**

### DISCUSSION

PRES has been reported in cancer patients. Chemotherapeutic agents that have previously been described to be associated with PRES include Taxanes, Platinum derivatives, Vinca alkaloids, Antimetabolites, Anthracyclines, Angiogenic inhibitors, Folate antagonists and Immunosuppressants.<sup>6-8</sup> The main theory of the pathophysiological changes in PRES states that the rapidly developing hypertension exceeds the upper limit of cerebral autoregulation and hyper perfusion, breaking the blood brain barrier and allowing interstitial extravasation of plasma and macromolecules.<sup>9</sup> The patients with cancer are exposed to several chemotherapeutic agents. It is difficult to identify a direct association between PRES and chemotherapeutic drugs.

Patients presented with common symptoms of PRES, including high blood pressure, hypotension, altered mental status and seizures. Their neuro imaging findings involving both the hemispheres at perito-occipital regions were documented. The chemotherapeutic agents were

discontinued. All the patients showed complete clinical and radiological resolution of PRES.

PRES in first case was associated with underlying DLBCL of colon. Patient had presented with acute onset of abdominal pain secondary to intestinal perforation. Patient was having hypotension during the event and acute renal failure. The hypotension might cause or facilitate endothelial damage. This patient had elevation in LDH levels, an enzyme frequently used as a marker for tissue damage. MRI done showed the features of PRES. Patient was treated with antiepileptic drugs and supportive care. Patient improved following surgery.

Case 2 was a 10-year-old boy who was diagnosed as a wilm's tumor based on image findings. Received 2 cycles of chemotherapy according to SIOP protocol. Chemotherapy drugs mainly included were vincristine and actinomycin-D. Vinca alkaloids (vincristine, vinorelbine) have been reported to have caused PRES in few case reports. Bernardo Cacho-Diaz et al, reported PRES in a 60-year-old breast cancer patient who was treated with vinorelbine.<sup>10</sup> The cause for PRES in this case was unclear. One of the drugs in the regimen may have had a toxic effect on cerebral vasculature. Vincristine has been associated with neurological side effects, most commonly peripheral neuropathy and encephalopathy.<sup>11</sup> Third patient was a case of B-cell ALL on treatment as per the BFM-2002 protocol. Patient had received Re-induction-1 regimen. The drugs given were dexamethasone, vincristine, adriamycin and L-asparaginase. Small case series and case reports of PRES in ALL patients on treatment have been reported. Samuel singer et al, reported a case series of 31 patients with PRES, in which 2 patients treated with vincristine had PRES syndrome.<sup>12</sup> Investigators from Soochow University, China reported 11 cases of PRES in ALL patients on chemotherapy. During the ALL induction treatment, 4 patients were noted to have high blood pressure.<sup>13</sup>

Hypertension is a well-known adverse effect of corticosteroid therapy primarily mediated by its effects on mineralocorticoid receptor, and we hypothesize that this may be the etiology of PRES in this patient but implication of the other cytotoxic drugs cannot be excluded.<sup>14</sup> Blood pressure should be routinely monitored when patients are on steroids. The other causes of similar clinical presentation like cortical venous thrombosis, encephalitis, intracranial hemorrhage and leukemic infiltration should be ruled out.

PRES is a reversible neurological disorder that can be induced by many cytotoxic chemotherapy agents and immunosuppressants. There is no specific treatment for PRES other than eliminating the precipitating cause and use of anti-epileptic agents. The prognosis is usually favorable with most patients recovering from the event in 7-14 days. Most patients can be restarted with the treatment after the complete recovery from the PRES.

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