Peertechz

CLINICAL GROUP

GLOBAL JOURNAL OF Medical and Clinical Case Reports OPEN ACCESS JOURNAL

ISSN: 2455-5282 DOI: https://dx.doi.org/10.17352/gjmccr

Case Report

Posterior Reversible Encephalitis Syndrome (PRES) in a paediatric patient in the intensive care unit

Mata-Perera C[1], López-Álvarez JM[1,2]* and Lorenzo-Villegas DL[2]

[1]Unit of Pediatric Intensive Medicine, Mother and Child University Hospital of the Canary Islands, Las Palmas de Gran Canaria, 35016, Spain

[2]Faculty of Health Sciences, University Fernando Pessoa-Canarias, Santa Maria de Guia, 35450, Spain

Received: 23 January, 2024
Accepted: 01 February, 2024
Published: 02 February, 2024

***Corresponding authors:** López-Álvarez JM, Unit of Pediatric Intensive Medicine, Mother and Child University Hospital of the Canary Islands, Las Palmas de Gran Canaria, 35016, Spain,
Email: jmlopez@ufpcanarias.es, jmloal@hotmail.com

ORCiD: https://orcid.org/0000-0002-4523-9571

Keywords: Pediatric patient; Posterior Reversible Encephalopathy Syndrome (PRES); Intensive care unit

https://www.peertechzpublications.org

Check for updates

Abstract

Posterior Reversible Encephalopathy Syndrome (PRES) is an entity that has gained importance in recent years. The diagnosis is clinical-radiological. Clinically, the patient presents neurological alterations such as headache, decreased level of consciousness, seizures, and visual disturbances. Radiologically, it includes cerebral oedema, predominantly of the white matter of parietal-occipital regions on magnetic resonance imaging. Multiple situations can trigger this condition, including high blood pressure, immunosuppressants, steroids, and chemotherapy well-known risk factors. An early diagnosis and adequate treatment are essential to avoid the appearance of sequelae in these patients.

This case consists of a patient diagnosed at 11 years of age with a bifocal non-germline tumour in the brain who, after treatment with chemotherapy, presented a clinical deterioration with instability compatible with septic shock. Subsequently, he presented a sudden alteration in the level of consciousness accompanied by hypertension and renal failure, which was suspected of PRES after a brain CT imaging test.

Introduction

Posterior Reversible Encephalopathy Syndrome (PRES), classically known as posterior reversible leukoencephalopathy, is a clinical entity that has gained importance in recent years. Although initially described in adult patients with a mean age of 50 years, cases have also been seen in paediatric patients [1]. Its actual incidence is unknown due to a wide variety of presentations that complicate its differential diagnosis [2].

PRES consists of different symptoms of neurological characteristics associated with radiological alterations in the central nervous system that are usually reversible, but potentially severe [3-6]. As for the symptoms, vomiting, headache, blindness, altered level of consciousness or seizures can appear. These are usually preceded by arterial hypertension (HBP) or renal failure, although they are also associated with immunosuppressive treatment or with the presence of autoimmune diseases [7,8].

Radiological findings point to transient brain dysfunction with a component of cerebral oedema in specific locations of the CNS, predominantly the white matter of parietal and occipital regions, although without an exclusive involvement of the white matter [3-5,9].

It is very important to have a high index of suspicion since it is often misdiagnosed or belatedly diagnosed. To suspect it, the triad of concordant clinical symptoms, risk factors, and complementary tests is important [3-5].

Treatment consists of reducing or eliminating the triggers of the syndrome with the aim of decreasing the risk of irreversible damage [10].

Citation: Mata-Perera C, López-Álvarez JM, Lorenzo-Villegas DL (2024) Posterior Reversible Encephalitis Syndrome (PRES) in a paediatric patient in the intensive care unit. Glob J Medical Clin Case Rep 11(1): 001-004. DOI: https://dx.doi.org/10.17352/2455-5282.000178

Presentation of the case

A male patient diagnosed at the age of 11 with a bifocal cerebral pituitary germ cell tumour was treated with polychemotherapy, PEI (cisplatin, etoposide, and ifosfamide), and showed the following complications during treatment: poor digestive tolerance, bone marrow aplasia, and bacteraemia due to *S. epidermidis*. After administering up to 3 cycles of chemotherapy, the total disappearance of the two tumour foci was observed. He received a fourth cycle of chemotherapy that led to a subsequent hospitalization due to the side effects of cytostatic treatments. Finally, he was treated with radiotherapy and a good response was observed.

Since then, he has continued with analytical and MRI checks periodically. At 17 years of age, a brain MRI showed signs of tumour recurrence at the level of the pituitary stalk with extension to the hypothalamus with suggestive data of infiltration of the optic chiasm and proximal portion of the left optic tract.

Four months later, he was admitted to the hospital because of a right middle cerebral artery stroke with left facial paralysis and left hemiparesis with subsequent partial recovery due to intratumoral haemorrhage in the pituitary stalk with minimal tumour growth and secondary ischemia. Clinically, a progressive loss of visual acuity with complete loss in the left eye and greatly diminished in the right eye is striking.

After discharge, an endoscopic endonasal biopsy was performed and a mixed germ cell tumour was diagnosed (immature teratoma in 90% of the tumour, embryonal carcinoma in 5%, and yolk sac tumour in 5%).

Therefore, he was admitted again for a new cycle of chemotherapy due to local recurrence. Two days later, after the start of treatment with PEI, he was admitted for febrile neutropenia with severe clinical worsening until the diagnosis of septic shock secondary to *Klebsiella pneumoniae* was established. Due to a decreased level of consciousness, hemodynamic instability, and acute renal failure, he was admitted to the Paediatric Intensive Care Unit. At the same time, the patient presented an alteration of the third cranial nerve and an EEG was performed whose tracing showed a slowed basal rhythm without epileptiform activity. He was treated with antibiotic therapy with meropenem, multiple red blood cell and platelet transfusions, as well as colony-stimulating factors.

The next day after admission to the ICU, his condition worsened again with a sudden alteration in the level of consciousness, hypertension, and desaturation that required oxygen therapy at 10l pm. A CT scan of the brain was performed and was highly suggestive of reversible posterior encephalopathy (Figure 1).

After symptomatic treatment, the patient presented a progressive clinical improvement until the level of consciousness was restored and vision partially improved. At discharge, he was vigilant and connected, answering questions in a coherent way and understanding conversations with the persistence of the sequelae of his tumour (panhypopituitarism and decreased visual acuity) as well as his middle cerebral artery infarction (hemiparesis).

At approximately 2 months, a follow-up brain MRI was performed, which showed resolution of the parietal and frontal cortical-subcortical lesions described in the previous CT scan, attributable to recovered Posterior Reversible Encephalopathy Syndrome (PRES) (Figure 2).

The clinical case is summarized in Table 1.

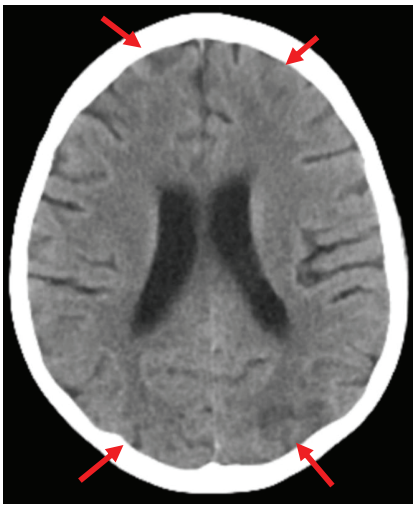

Figure 1: Brain CT scan with hypodense, bilateral, symmetrical cortical-subcortical posterior parietal and frontal lesions that could be in the context of Posterior Reversible Encephalopathy Syndrome (PRES). Red arrows show the affected areas.

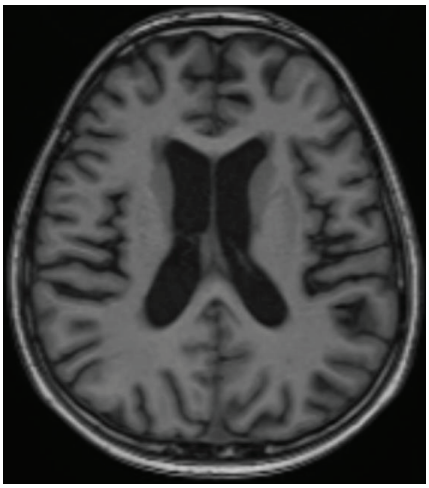

Figure 2: MRI with complete resolution of the parietal and frontal cortical-subcortical lesions described in the previous CT scan, attributable to recovered Posterior Reversible Encephalopathy Syndrome (PRES).

Table 1: Risk factors, symptomatology, and image tests of this clinical case.

Risk factors	Symptomatology	Image Tests
-Polychemotherapy: cisplatin -Granulocyte colony-stimulating factor -Septic shock -High blood pressure -Renal failure	-Decreased level of consciousness -Cranial nerve III alteration -Slowed EEG -Renal failure	-Brain CT scan with PRES involvement compatible with PRES -Brain MRI control with resolution

Citation: Mata-Perera C, López-Álvarez JM, Lorenzo-Villegas DL (2024) Posterior Reversible Encephalitis Syndrome (PRES) in a paediatric patient in the intensive care unit. Glob J Medical Clin Case Rep 11(1): 001-004. DOI: https://dx.doi.org/10.17352/2455-5282.000178

Discussion

PRES is either acute or subacute encephalopathy. Four theories that can explain the pathophysiology of PRES are established. The first one, the vasogenic theory of hyper flow, due to an increase in capillary leakage pressure by exceeding the capacity of the brain for self-regulation, especially in the posterior distribution areas, which seem to be more susceptible to these rapid changes in blood pressure, and which could be explained by the reduced sympathetic innervation in this area [11]. However, this theory would not explain the appearance of normotensive or hypotensive patients. The second theory is cytotoxic: the presence of toxins, chemokines, or chemotherapeutic agents and immunomodulatory therapy in the bloodstream can generate endothelial dysfunction. The third theory is immunogenic, which insists on the activation of T lymphocytes with the subsequent release of cytokines (nitric oxide, interleukin 1, tumour necrosis factor-alpha, etc.) and culminates in endothelial dysfunction. The fourth theory, neuropeptides, explains that the release of potent vasoconstrictors, such as prostacyclin, endothelin 1, and thromboxane A-2, generates vasospasm and ischemia with subsequent oedema [12]. These four hypotheses converge in the existence of vasogenic oedema secondary to increased capillary filtration pressure with endothelial dysfunction that generates leakage from the blood-brain barrier. Endothelial dysfunction may lead to a lowered threshold for loss of brain flow autoregulation [13].

PRES is an uncommon complication of chemotherapy use, the incidence of which is increasing due to the increased survival associated with chemotherapy [3,14]. In a series of cases from the *Children's Oncohematology Unit of the Hospital Complex of Navarra*, coincidences were observed in the treatment received by the 5 patients: vincristine was administered in 4 or methotrexate in 3. The drugs are thought to produce cytotoxicity on the vascular endothelium [3,14].

Arterial hypertension (HBP) is an important factor for the development of PRES, being a feature of all cases in the study of the *Children's Oncohematology Unit of the Hospital Complex of Navarra* [3]. There is a theory that supports that hypertension leads to arteriolar vasodilation with hyperperfusion with damage to the blood-brain barrier creating vasogenic edema.

In a case series of patients diagnosed with PRES in the *Paediatric Intensive Care Unit of the Reina Sofía Hospital*, it was found that 85.7% of the patients received chemotherapy or immunosuppressive drugs before presenting encephalopathy, frequently presenting acute renal failure and hypertension [2].

Our case shows an oncological patient who was treated with drugs that potentially cause PRES syndrome and who presented with hypertension for the first time, in addition to having sepsis. Possibly, in our case, the cytotoxic and vasogenic theories may both explain the pathophysiology.

Gewirtz, et al. have reported that inadequate control of arterial hypertension worsens the morbidity of cerebral oedema, so antihypertensive treatment should be performed, usually in the intensive care unit, with drugs in continuous intravenous infusion, with the aim of slowly and progressively reducing BP levels to avoid cerebral ischemia [15]. In paediatrics, the most commonly used drugs for hypertensive emergencies are labetalol or nicardipine, with sodium nitroprusside increasingly falling into disuse as it is considered a high-risk drug [16].

In a study from *Mexico*, the most common underlying disease was acute lymphoblastic leukaemia. In terms of clinical symptoms, 86.3% had convulsive seizures and 45.5% had altered levels of consciousness. 27.2% of patients were receiving cyclosporine at the time of PRES, 54.5% were receiving steroids, and 22.7% received chemotherapy before presenting PRES [10].

Although PRES is characterized by its reversibility and good prognosis in up to 75-90% of cases, it is a serious entity with a mortality rate between 3% and 6% with neurological sequelae in approximately 10% - 20% of patients [15]. Patients should be admitted to a *Paediatrics Intensive Care Unit* for proper observation and treatment [8].

To avoid irreversibility with sequelae, early symptomatic treatment is important, such as controlling blood pressure or treating seizures and excluding triggers such as some drugs [17]. If the patient has had seizures, it is advisable to keep the anticonvulsants for around 3-6 months and indicate their withdrawal if there are no abnormalities in the MRI or EEG. It is possible to restart chemotherapy once the acute phase has passed [3,5,18].

Our patient had a good subsequent recovery, possibly due to the high initial index of suspicion and the speed in the establishment of symptomatic treatment. The next cycle of chemotherapy was not given until one month after PRES syndrome.

Regarding the location of involvement, it has classically been described in the parietal-occipital lobes. The imaging test of choice is MRI, as it is able to differentiate between vasogenic oedema (without restriction on the diffusion of water molecules) and cytotoxic oedema (if there is a restriction, with a worse prognosis) [3,9,19]. Currently, it is more widely accepted that PRES manifests itself as vasogenic oedema rather than cytotoxic, although their concomitance is possible.

In a series of cases, MRI was performed in 85.7% of the patients, with findings suggestive of PRES in 75% of the cases and with a three-month follow-up with improvement or resolution of the lesions [2].

A relationship between neuroimaging findings and the severity of the syndrome has not been established [20]. In the work of Singh, et al. all of them presented early reversibility of neurological symptoms, but when reviewing the control MRI of the eleven patients, in three no reversibility of vasogenic edema was observed and two of them already had sequelae such as encephalomalacia and lamellar necrosis, so it is important to perform the control MRI to evaluate the parenchymal damage that could remain despite being considered a reversible syndrome in most cases [10].

Citation: Mata-Perera C, López-Álvarez JM, Lorenzo-Villegas DL (2024) Posterior Reversible Encephalitis Syndrome (PRES) in a paediatric patient in the intensive care unit. Glob J Medical Clin Case Rep 11(1): 001-004. DOI: https://dx.doi.org/10.17352/2455-5282.000178

Although the test of choice is MRI, an urgent CT scan was performed in our patients due to his instability.

Reviews have been carried out to assess the existence of clinical predictors, with hypertension, renal insufficiency, and chemotherapy being the most accurate [21].

Conclusion

PRES is a relatively uncommon complication of chemotherapy treatment in paediatric patients, but the increase in the prevalence of childhood cancer, as well as longer survival, is likely to increase the incidence of the condition in the upcoming years.

Our results suggest that an imaging test should be performed on every patient showing any neurological alteration and PRES risk factors, so this will help initiate timely treatment to reduce the risk of non-reversibility or complications.

With respect to the relevance of these conditions, larger paediatric studies are needed to know the true prevalence of this disease, as well as the clinical symptoms that may occur in patients with less severity and fewer comorbidities.

Ethical considerations

With respect to the undertaken for the case and its publications, a patient's familial relation's consent was obtained as required by the unit admission protocol.

References

1. Prasad N, Gulati S, Gupta RK, Sharma K, Gulati K, Sharma RK, Gupta A. Spectrum of radiological changes in hypertensive children with reversible posterior leucoencephalopathy. Br J Radiol. 2007 Jun;80(954):422-9. doi: 10.1259/bjr/81758556. Epub 2007 Mar 28. PMID: 17392398.

2. Montero Yéboles R, Manzanares-Santos S, Martínez-Mesones L, Díaz-Rueda L, Ruiz-Sáez B. PRES Posterior Reversible Encephalopathy Syndrome in pediatric population. Presentación de casos y revisión bibliográfica. Neurología Argentina. 2022 Jul;14(3):197–200.

3. San Martín García I, Urabayen Alberdi R, Díez Bayona V, Sagaseta de Ilúrdoz Uranga M, Esparza Estaun J, Molina Garicano J, et al. Posterior Reversible Encephalopathy Syndrome: 5 chemotherapy-related cases. An Pediatr (Barc). 2014 Feb 1; 80(2):117-21.

4. Castellano-Martinez A, Roldán-Cano V, Morales-Arandojo P, Rodriguez-González M. Posterior reversible encephalopathy syndrome as a debut of postinfectious glomerulonephritis. An Pediatr (Engl Ed). 2022 May;96(5):452-454. doi: 10.1016/j.anpede.2021.06.012. Epub 2022 May 7. PMID: 35537941.

5. Casali Rey JI, Dávalos EG, López Amalfara A, Julio Muñoz D, Pagano MA. Posterior Reversible Encephalopathy Syndrome: presentation of clinical cases. Rev neurol (Ed impr). 2003; 224-7.

6. Fugate JE, Rabinstein AA. Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. Lancet Neurol. 2015 Sep;14(9):914-925. doi: 10.1016/S1474-4422(15)00111-8. Epub 2015 Jul 13. Erratum in: Lancet Neurol. 2015 Sep;14(9):874. PMID: 26184985.

7. PRES in Children Undergoing Hematopoietic Stem Cell or Solid Organ Transplantation – PubMed. https://pubmed.ncbi.nlm.nih.gov/25917987/

8. Ishikura K, Hamasaki Y, Sakai T, Hataya H, Mak RH, Honda M. Posterior reversible encephalopathy syndrome in children with kidney diseases. Pediatr Nephrol. 2012 Mar;27(3):375-84. doi: 10.1007/s00467-011-1873-2. Epub 2011 May 11. PMID: 21556718.

9. Lamy C, Oppenheim C, Méder JF, Mas JL. Neuroimaging in posterior reversible encephalopathy syndrome. J Neuroimaging. 2004 Apr;14(2):89-96. PMID: 15095552.

10. Urias DS, Zaltzman S, Garza GG, Murata C. Encefalopatía posterior reversible. Experiencia en el Instituto Nacional de Pediatría. Ciencias Clínicas. 2014 Jan 1; 15(1):14–21.

11. Fischer M, Schmutzhard E. Posterior reversible encephalopathy syndrome. J Neurol. 2017 Aug;264(8):1608-1616. doi: 10.1007/s00415-016-8377-8. Epub 2017 Jan 4. PMID: 28054130; PMCID: PMC5533845.

12. Granata G, Greco A, Iannella G, Granata M, Manno A, Savastano E, Magliulo G. Posterior reversible encephalopathy syndrome--Insight into pathogenesis, clinical variants and treatment approaches. Autoimmun Rev. 2015 Sep;14(9):830-6. doi: 10.1016/j.autrev.2015.05.006. Epub 2015 May 18. PMID: 25999210.

13. Marra A, Vargas M, Striano P, Del Guercio L, Buonanno P, Servillo G. Posterior reversible encephalopathy syndrome: the endothelial hypotheses. Med Hypotheses. 2014 May;82(5):619-22. doi: 10.1016/j.mehy.2014.02.022. Epub 2014 Mar 1. PMID: 24613735.

14. Vagace JM, de la Maya MD, Caceres-Marzal C, Gonzalez de Murillo S, Gervasini G. Central nervous system chemotoxicity during treatment of pediatric acute lymphoblastic leukemia/lymphoma. Crit Rev Oncol Hematol. 2012 Nov;84(2):274-86. doi: 10.1016/j.critrevonc.2012.04.003. Epub 2012 May 11. PMID: 22578745.

15. Gewirtz AN, Gao V, Parauda SC, Robbins MS. Posterior Reversible Encephalopathy Syndrome. Curr Pain Headache Rep. 2021 Feb 25;25(3):19. doi: 10.1007/s11916-020-00932-1. PMID: 33630183; PMCID: PMC7905767.

16. Seeman T, Hamdani G, Mitsnefes M. Hypertensive crisis in children and adolescents. Pediatr Nephrol. 2019 Dec;34(12):2523-2537. doi: 10.1007/s00467-018-4092-2. Epub 2018 Oct 1. PMID: 30276533.

17. Anastasopoulou S, Eriksson MA, Heyman M, Wang C, Niinimäki R, Mikkel S, Vaitkevičienė GE, Johannsdottir IM, Myrberg IH, Jonsson OG, Als-Nielsen B, Schmiegelow K, Banerjee J, Harila-Saari A, Ranta S. Posterior reversible encephalopathy syndrome in children with acute lymphoblastic leukemia: Clinical characteristics, risk factors, course, and outcome of disease. Pediatr Blood Cancer. 2019 May;66(5):e27594. doi: 10.1002/pbc.27594. Epub 2018 Dec 27. PMID: 30592147.

18. Baytan B, Ozdemir O, Demirkaya M, Evim MS, Gunes AM. Reversible posterior leukoencephalopathy induced by cancer chemotherapy. Pediatr Neurol. 2010 Sep;43(3):197-201. doi: 10.1016/j.pediatrneurol.2010.05.005. PMID: 20691942.

19. Peter P, George A. Posterior reversible encephalopathy syndrome and the pediatric population. J Pediatr Neurosci. 2012 May;7(2):136-8. doi: 10.4103/1817-1745.102579. PMID: 23248696; PMCID: PMC3519074.

20. Yamamoto H, Natsume J, Kidokoro H, Ishihara N, Suzuki M, Tsuji T, Kubota T, Yamada A, Ozeki M, Kato Z, Kawamura Y, Yoshikawa T, Okumura A, Ando N, Saitoh S, Takahashi Y, Watanabe K, Kojima S. Clinical and neuroimaging findings in children with posterior reversible encephalopathy syndrome. Eur J Paediatr Neurol. 2015 Nov;19(6):672-8. doi: 10.1016/j.ejpn.2015.07.005. Epub 2015 Jul 22. PMID: 26232050.

21. Faille LD, Fieuws S, Van Paesschen W. Clinical predictors and differential diagnosis of posterior reversible encephalopathy syndrome. Acta Neurol Belg. 2017 Jun;117(2):469-475. doi: 10.1007/s13760-017-0750-6. Epub 2017 Jan 31. PMID: 28144796; PMCID: PMC5440491.

Citation: Mata-Perera C, López-Álvarez JM, Lorenzo-Villegas DL (2024) Posterior Reversible Encephalitis Syndrome (PRES) in a paediatric patient in the intensive care unit. Glob J Medical Clin Case Rep 11(1): 001-004. DOI: https://dx.doi.org/10.17352/2455-5282.000178