Global Journal of Medical Research: a
Neurology and Nervous System
Volume 17 Issue 1 Version 1.0 Year 2017
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Case Report: Posterior Reversible Encephalopathy Syndrome in a Paediatric Patient as First Presentation of Thrombotic Thrombocytopenic Purpura

By Abdullah Alasaad, Roaa Amer & Eman Bakhsh
King Saud Bin Abdulaziz University

Abstract- Posterior reversible encephalopathy syndrome (PRES) usually presents with rapid onset of neurologic symptoms with characteristic vasogenic oedema in imaging studies. PRES is most importantly associated with hypertension and kidney disease. We describe a case of PRES in a 13-year-old female patient who presented with normal vital signs, neurological symptoms, oliguria, and laboratory test results consistent with thrombotic thrombocytopenic purpura (TTP). Head computed tomography (CT) scan revealed subtle hypodensity in the white matter of the right parietal lobe, strongly suggesting PRES, with multiple hemorrhagic foci in the right frontal lobe and right basal ganglia. Aggressive TTP treatment was initiated; however, she developed rapidly progressive glomerulonephritis and renal failure. Twelve days since presentation, she developed severe acute respiratory distress, which resulted in death. Therefore, PRES need not be a complication; it can be the presenting sign of an undiagnosed disease and a high index of suspicion is required in such cases.

Keywords: posterior reversible encephalopathy syndrome, thrombotic thrombocytopenic purpura, seizures, hypertension, renal failure, paediatrics, vasogenic oedema, renal failure, headache, oliguria.

GJMR-A Classification : NLMC Code: WL 141.5, WH 315

Case Report: Posterior Reversible Encephalopathy Syndrome in a Paediatric Patient as First Presentation of Thrombotic Thrombocytopenic Purpura

Abdullah Alasaad [α], Roaa Amer [σ] & Eman Bakhsh [ρ]

Abstract- Posterior reversible encephalopathy syndrome (PRES) usually presents with rapid onset of neurologic symptoms with characteristic vasogenic oedema in imaging studies. PRES is most importantly associated with hypertension and kidney disease. We describe a case of PRES in a 13-year-old female patient who presented with normal vital signs, neurological symptoms, oliguria, and laboratory test results consistent with thrombotic thrombocytopenic purpura (TTP). Head computed tomography (CT) scan revealed subtle hypodensity in the white matter of the right parietal lobe, strongly suggesting PRES, with multiple hemorrhagic foci in the right frontal lobe and right basal ganglia. Aggressive TTP treatment was initiated; however, she developed rapidly progressive glomerulonephritis and renal failure. Twelve days since presentation, she developed severe acute respiratory distress, which resulted in death. Therefore, PRES need not be a complication; it can be the presenting sign of an undiagnosed disease and a high index of suspicion is required in such cases.

Keywords: posterior reversible encephalopathy syndrome, thrombotic thrombocytopenic purpura, seizures, hypertension, renal failure, paediatrics, vasogenic oedema, renal failure, headache, oliguria.

I. Introduction

Posterior reversible encephalopathy syndrome (PRES) is a complication with various medical conditions which usually presents with rapid onset of neurological symptoms such as seizures, altered mental status, and visual disturbances (Hobson et al, 2012). It was initially believed to be associated with eclampsia, post-transplant use of cyclosporine, and acute hypertension (Bartynski, 2008). Further studies showed a relationship between PRES and hypertension, immunosuppressive drugs, and post-transplant status, and autoimmune and vascular diseases, which are mostly found in patients with renal diseases (Hobson et al, 2012). Furthermore, PRES is a clinicoradiological syndrome characterized by its unique symptoms and pathognomic radiological findings (Bartynski, 2008). Here, we present a case of PRES in a patient with clinical and laboratory evidence of thrombotic thrombocytopenic purpura who developed severe acute renal dysfunction in the absence of hypertension. Although the standard treatment was initiated, the patient died due to severe respiratory distress.

Author α σ: King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. e-mails: a.alasaad12@gmail.com, roaa1414@hotmail.com
Author ρ: King Fahad Medical City, Riaydh, Saudi Arabia. e-mail: emanbakhsh2000@hotmail.com

II. Case Report

A 13-year-old female patient presented to the emergency department with nausea, vomiting, headache, confusion, seizures, and oliguria. She had no significant past medical history and no previous similar episodes were reported. Family history was unremarkable, with no evidence of any blood disorder in the family. On initial examination, the patient looked dehydrated and somnolent with a Glasgow coma scale score of 10. Vital signs, including blood pressure, were within normal limits on different occasions.

The patient underwent a head computed tomography (CT) scan to assess the extent of the neurological pathology, which demonstrated multiple subcortical hypodensities in the right frontal and parietal lobes, highly suggestive of PRES, as well as multiple well-defined hyperintensities in the right frontal lobe and right basal ganglia, suggesting multiple haemorrhagic foci (Figure-1A, and 1B).

Initial blood workup showed anaemia (haemoglobin 7 mg/dL), thrombocytopaenia (40,000 mg/dL), high erythrocyte sedimentation rate (160 mm/hour), and high C-reactive protein (20 mg/L) levels. Additionally, signs of haemolysis such as high lactate dehydrogenase (900 IU/L) and bilirubin (5 mg/dL) levels were also present. Further laboratory tests assessing renal functions showed normal serum creatinine (80 umol/L) and glomerular filtration rate (GFR) (98 ml/min/1.73m^2). Serology tests revealed a positive perinuclear antineutrophilic cytoplasmic (p-ANCA), anti-glomerular basement membrane (anti-GBM), and anti-myeloperoxidase antibodies. A lumbar puncture was performed to exclude infectious causes and it showed normal coloured cerebrospinal fluid with normal cell and protein counts. Polymerase chain reaction assays for

herpes-simplex virus, cytomegalovirus, and Epstein-Barr virus were negative.

Targeted treatment for the underlying cause was delayed due to the haemodynamic instability. After the patient was stabilized, a diagnosis of thrombotic thrombocytopenic purpura (TTP) was suspected based on laboratory results. Subsequently, the patient was started on 500 mg/day intravenous methylprednisolone and 30 mg/day oral prednisolone, and she underwent multiple plasma exchange procedures along with infusions of fresh frozen plasma. Due to the suspicion of TTP, genetic testing was done. However, the results were not available at the time as it required 5 days. After 10 days, a follow-up brain MRI showed bilateral parietal high signals on FLAIR sequence and diffusion ADC map (figure-2A and 2B). MR angiography showed patent posterior cranial circulation.

Despite the active treatment for TTP, the patient developed rapidly progressive glomerulonephritis; the GFR drastically decreased to 6 ml/min/1.73m^2 and serum creatinine was extremely high at 657 umol/L. Histopathological examination of the renal biopsy revealed glomerular crescent formation with linear IgG, IgA, IgM, and C3 deposits on the glomerular capillary walls. The patient was started on dialysis immediately.

Dialysis was continued for the patient, with no significant improvements in the first 5 days. Unfortunately, the patient's family refused any further investigations or interventions because they had not seen any improvement since her first presentation. Twelve days after her initial presentation, the patient developed severe acute respiratory distress, which resulted in death. Postmortem, the results of genetic testing revealed a 70% deficiency in ADAMTS 13 levels.

III. Discussion

PRES is a rare neurotoxic state that is coupled with a rapid onset set of symptoms, most commonly seizures, visual disturbances, headache, and altered mental state (Hobson et al, 2012) and characteristic vasogenic oedema seen in imaging studies (Bartynski, 2008). PRES is also associated with multiple clinical diseases, most importantly hypertension and kidney diseases (Bartynski, 2008; Hobson et al, 2012). In this case, we report the course of a paediatric patient who came to the emergency room with PRES as the first presentation of TTP. PRES has been reported as a complication of TTP before; however, it usually occurs in adults and is considered rare in children with a poor prognosis if early treatment is not initiated (Bhat et al, 2015).

The relationship between the two diseases lies in the pathophysiology of PRES: the first mechanism being theorized as disturbances in the brain's autoregulation of blood flow caused by hypertension (Hobson et al, 2012), and the other being endothelial dysfunction caused by inflammatory processes (Hobson et al, 2012). These mechanisms explain the association of PRES with many autoimmune diseases such as Henoch-Schonlein purpura (Sivrioglu et al, 2013), scleroderma (Chen et al, 2016), and juvenile idiopathic arthritis (Zhang et al, 2014). Both the processes can be found in TTP due to the formation of microthrombi (Yu et al, 2015).

However, in this case, the diagnosis of PRES was difficult due to multiple reasons. First, TTP can also manifest with neurological symptoms; therefore, the differentiation between PRES and TTP in this case was only possible through imaging studies (Bhat et al, 2015), which could not be obtained emergently due to the patient's hemodynamic instability. However, brain MRI was performed 10 days later, which showed bilateral parietal high signals on FLAIR sequence and diffusion ADC map. Secondly, although the patient's laboratory findings are consistent with TTP, she was totally asymptomatic until she developed a seizure. Furthermore, the variable presentations of PRES and the difficulty in diagnosing it (Burrus et al, 2010) led to a delay in the diagnosis and treatment, which should have been commenced immediately to prevent permanent neurological damage, similar to what happened in this case (3).

Additionally, the presence of PRES in paediatric patients with TTP is uncommon. However, when discussing the risk factors and their correlation to PRES in general, hypertension plays a pivotal role. Recent studies on the correlation of TTP and PRES among paediatric population have shown the presence of hypertension in 100% of the patients with PRES (Bhat et al, 2015). Nevertheless, significant correlation between the degree of hypertension and PRES could not be established (Bhat et al, 2015; Burrus et al, 2010). The only significant risk factors common to, both, acute TTP and PRES were GFR and worsening renal failure (Burrus et al, 2010) as were seen in this case.

The diagnosis of PRES is based on clinical presentation and radiological findings on CT scan or MRI. In acute settings, CT scan is usually used due to its rapid availability (Hobson et al, 2012); however, CT scan lacks sensitivity and, therefore, normal findings could be seen. MRI, on the other hand, is considered the superior imaging study, but many diverse findings of PRES were not detected on MRI (Hobson et al, 2012). The typical findings on MRI include symmetrical bilateral cortical and subcortical vasogenic oedema in the vascular watershed areas, most commonly in the occipital and parietal regions (Bartynski, 2008; Hobson et al, 2012) followed by the frontal lobes, the inferior temporal-occipital junction, and the cerebellum (Bartynski, 2008). Furthermore, PRES can also show atypical findings on imaging studies such as asymmetrical involvement, haemorrhage, cortical lesions, and the involvement of only the frontal lobe (Hobson et al, 2012). Such atypical

findings were found in this patient in the form of multiple cortical and subcortical hypodensities in the right frontal and parietal lobes, with multiple haemorrhagic foci in the right frontal lobe and right basal ganglia.

Although neuroimaging is not usually done in patients with TTP, it is used in the patients with neurological manifestations to exclude microangiopathic thrombosis or haemorrhage. Recent imaging studies on the findings in patients with acute TTP have revealed that imaging could show signs of PRES, haemorrhage, or acute infarcts. More importantly, they demonstrated that the most common neurological finding among those patients was PRES (Burrus et al, 2009; Yu et al, 2015). Furthermore, the studies also demonstrated that the abnormalities found on imaging studies did not affect the clinical outcomes, irrespective of how extensive they were (Burrus et al, 2009; Yu et al, 2015).

Our recommendations include the following. First, PRES should not be considered as a complication of a disease or a state by itself, as it may reveal itself as the first presentation of an undiagnosed disease. Secondly, in cases of acute TTP with neurological manifestations, PRES should be highly considered since it is the most common imaging finding in such patients. Finally, in those patients, prompt treatment must be initiated as soon as possible, especially in paediatric patients, as it alters the prognosis.

IV. Conclusion

PRES is a rare neurotoxic state that is coupled with a rapid onset of symptoms. PRES has been reported as a complication of TTP before; however, it usually occurs in adults and it is considered rare in children with a poor prognosis if not treated early. Nevertheless, maintaining a high index of suspicion is warranted, as PRES should not be considered only as a complication of a disease because it may reveal itself as the first presentation of an undiagnosed disease.

References Références Referencias

1. Bartynski, W. (2008). Posterior Reversible Encephalopathy Syndrome, Part 1: Fundamental Imaging and Clinical Features. *American Journal of Neuroradiology*, 29(6), 1036-1042. http://doi.org/10.3174/ajnr.a0928
2. Bhat, R. A, Wani, Z., Baasit, S. & Khan, I. (2015). Clinical course, laboratory parameters and outcome of TTP pediatric patients presenting with posterior reversible encephalopathy syndrome. *Renal Failure*, 37(6), 974-979.
3. Burrus, T., Mandrekar, J., Wijdicks, E. & Rabinstein, A. (2010). Renal Failure and Posterior Reversible Encephalopathy Syndrome in Patients With Thrombotic Thrombocytopenic Purpura. *Archives of Neurology*, 67(7), 831-834. https://doi.org/10.1001/archneurol.2010.119
4. Burrus, T., Wijdicks, E. & Rabinstein, A. (2009). Brain lesions are most often reversible in acute thrombotic thrombocytopenic purpura. *Neurology*, 73(1), 66-70. doi: 10.1212/WNL.0b013e3181aaea1 b.
5. Chen, C., Hung, S., Lee, Y., Lin, Y. & Pai, C. (2016). Delayed onset of posterior reversible encephalopathy syndrome in a case of scleroderma renal crisis with maintenance hemodialysis. *Medicine*, 95(52), e5725.
6. Hobson, E. V., Craven, I. & Blank, S. C. (2012). Posterior Reversible Encephalopathy Syndrome: A Truly Treatable Neurologic Illness. *Peritoneal Dialysis International*, 32(6), 590-594. http://doi.org/10.3747/pdi.2012.00152
7. Sivrioglu, A. K., Incedayi, M., Mutlu, H. & Meral, C. (2013). Posterior reversible encephalopathy syndrome in a child with Henoch-Schonlein purpura. *Case Reports*, 2013(aug14 1). http://doi.org/10.1136/bcr-2013-008900
8. Yu, W., Leung, T., Soo, Y., Lee, J. & Wong, K. (2015). Thrombotic thrombocytopenic purpura with concomitant small- and large-vessel thrombosis, atypical posterior reversible encephalopathy syndrome and cerebral microbleeds. *Oxford Medical Case Reports*, 2015(2), 179-182. https://dx.doi.org/10.1093/omcr/omv001
9. Zhang, P., Li, X., Li, Y., Wang, J., Zeng, H. & Zeng, X. (2014). Reversible posterior leukoencephalopathy syndrome secondary to systemic-onset juvenile idiopathic arthritis: A case report and review of the literature. *Biomedical Reports*. https://doi.org/10.3892/br.2014.380.

Appendix

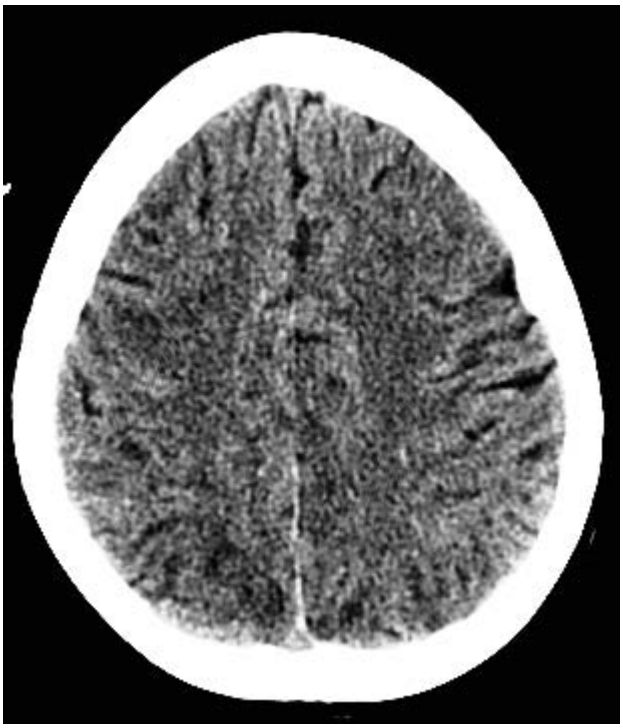

Figure 1A: Axial brain non-enhanced CT image showing multiple right frontal and right parietal subcortical hypodensities

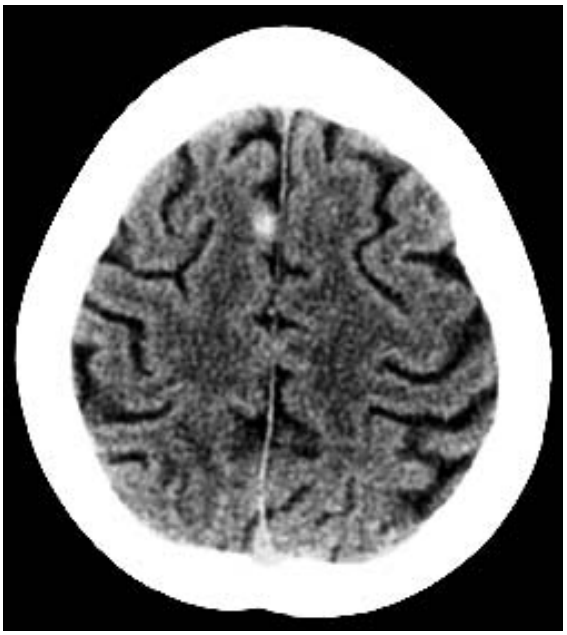

Figure 1B: Axial non-enhanced brain CT image showing focal rounded hyperdensities in the medial aspect of the right frontal cortex consistent with cortical bleeding

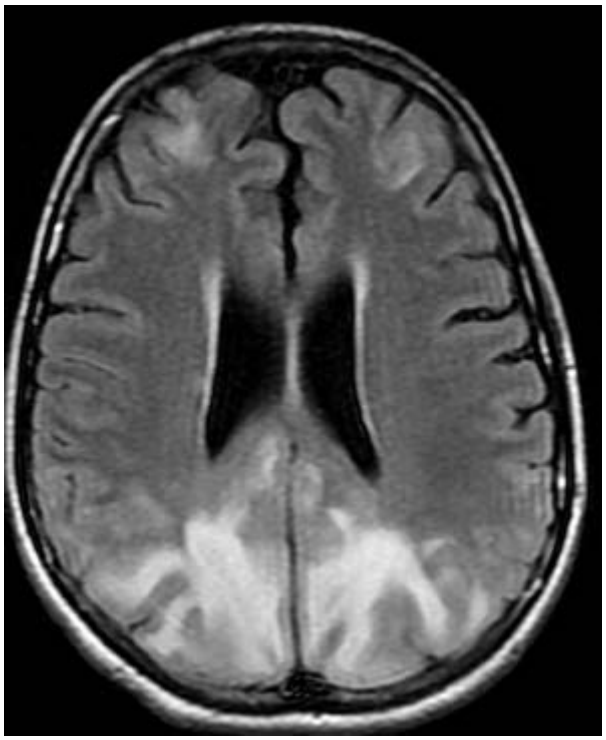

Figure 2A: Brain MRI axial FLAIR sequence demonstrating bilateral symmetrical cortical and subcortical high T2 signal in the frontal and parietal lobes

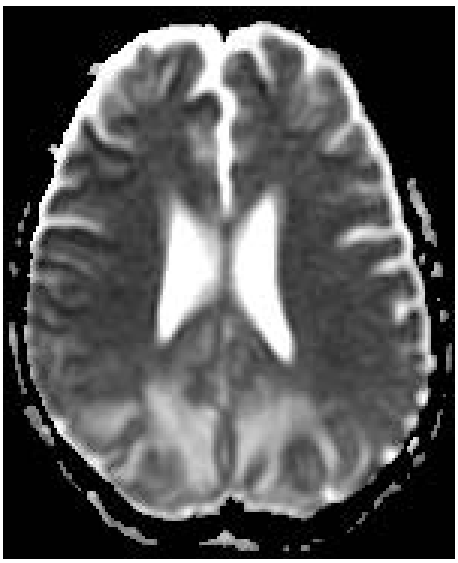

Figure 2B: Axial ADC map showing high ADC signal in the parietal lobes indicating vasogenic oedema