

# Cushing Syndrome Complicated by Multiple Pathological Spinal Fractures and Posterior Reversible Encephalopathy Syndrome in the Post-delivery Phase

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**Abstract** A 28-year-old female with central obesity, moon face and multiple sites of acne vulgaris began to experience generalized convulsions after complaining of severe back pain during hospitalization on post-first-delivery day 5. After an infusion of diazepam, she showed severe hypoxia and underwent tracheal intubation. She had a history of gestational diabetes mellitus (DM), acne vulgaris, osteoporosis and thoracolumbar fracture. She also felt severe back pain after falling down two weeks previously and underwent Caesarean section. Her blood pressure was remained 100–160 mmHg during the perinatal period. Whole body computed tomography revealed bilateral low density in the parieto-occipital white matter, bilateral aspirated lesions in her lungs, and enlargement of the right adrenal gland. The tentative diagnosis was posterior reversible encephalopathy syndrome (PRES) with convulsion, aspirated pneumonia and Cushing syndrome with DM and pathological fracture due to osteoporosis. She underwent an infusion of levetiracetam, sedatives, analgesics and a depressor were administered to control blood pressure strictly. She was extubated two days after her respiratory function showed improvement. After controlling her pain and treating osteoporosis, a blood test was compatible with Cushing syndrome. She finally underwent adenectomy in four months. Pathology was adenoma. This is a rare case of Cushing syndrome complicating pathological spinal fractures and PRES in the post-delivery phase. Aggressive control of pain and blood pressure in the perinatal period may be required to prevent the onset of PRES.

**Keywords:** Cushing syndrome, convulsion, spinal fracture, posterior reversible encephalopathy syndrome

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## 1. Introduction

Posterior reversible encephalopathy syndrome (PRES) is a neurological disorder of acute onset characterized by varied neurological symptoms, which may include headache, impaired visual acuity or visual field deficits, disorders of consciousness, confusion, seizures, and focal neurological deficits. [1,2,3] PRES frequently develops in the context of cytotoxic medication, eclampsia (convulsion during perinatal period), sepsis, renal disease or autoimmune disorders. In the majority of patients, the clinical presentation includes elevated arterial blood pressure, up to a level that represents a hypertensive emergency. [1,2,3] Although the pathophysiological changes underlying PRES are not fully understood, endothelial dysfunction is a key factor. [1,2,3] Magnetic resonance imaging (MRI) facilitates a prompt diagnosis and treatment and leads to good outcomes. MRI shows

hyperintensity on fluid-attenuated inversion recovery images and apparent diffusion coefficient mapping, and iso-intensity on diffusion weighted images involving the parieto-occipital or posterior frontal cortical-subcortical regions, reflecting vasogenic edema, which are recognized in >90% of patients. These lesions are principally reversible neuroimaging abnormalities. The treatment is symptomatic and is determined by the underlying condition. The overall prognosis is favorable, however, neurological sequelae, including long-term epilepsy, may persist in individual cases.

We herein report the first reported case of Cushing syndrome complicated by multiple spinal fractures and PRES in the post-delivery phase.

## 2. Case Presentation

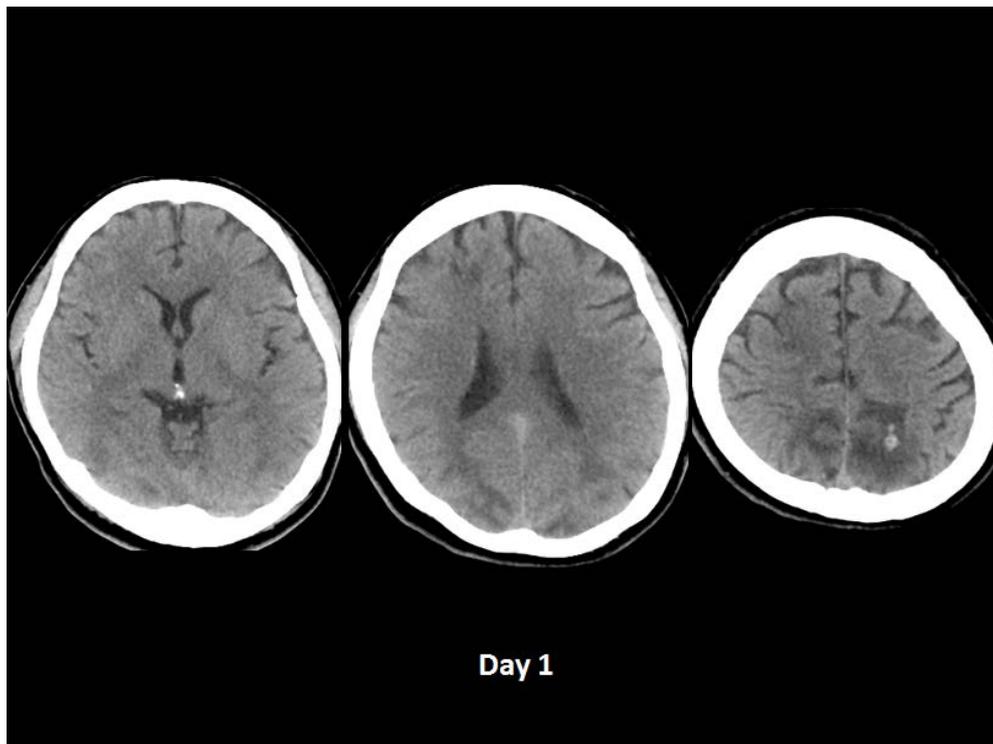
A 28-year-old female (gravidity 3, parity 1) began to experience generalized convulsions after complaining of

severe back pain during hospitalization on post-first-delivery day 5. After an infusion of diazepam, she showed severe hypoxia (percutaneous saturated oxygen, 30% under 15 L/min of oxygen), prompting a code blue response. She had a history of gestational diabetes mellitus (DM), acne vulgaris, osteoporosis and thoracolumbar fracture, which occurred in the 8th month of pregnancy, necessitating intermittent epidural anesthetic block and the prescription of tramadol hydrochloride, acetaminophen, loxoprofen, and rebamipide. She also felt severe back pain after falling down two weeks previously and underwent Caesarean section because it was impossible to place the patient in the lithotomy position for delivery. Her blood pressure was remained 100–160/60-90 (systolic/diastolic pressure) mmHg during the perinatal period. When an emergency physician checked her, she had a Glasgow Coma Scale of 8, a blood pressure of 150/80 mmHg, a heart rate of 150 beats per minute, a respiratory rate of 20 breaths per minute and an SpO<sub>2</sub> of 90% under 15 L/min of oxygen. A visual inspection revealed, central obesity, moon face, multiple sites of acne vulgaris on her face, and a lower abdominal midline incision wound. Auscultation revealed bilateral moist rales. She underwent tracheal intubation using sedative and muscle relaxant drugs. A venous gas analysis revealed the following findings: pH, 7.351; PaCO<sub>2</sub>, 41.5 mmHg; HCO<sub>3</sub><sup>-</sup>, 22.4 mmol/L; base excess, -2.5 mmol/L; and lactate, 3.7 mmol/L. The results of a biochemical analysis on the same day are shown in [Table 1](#).

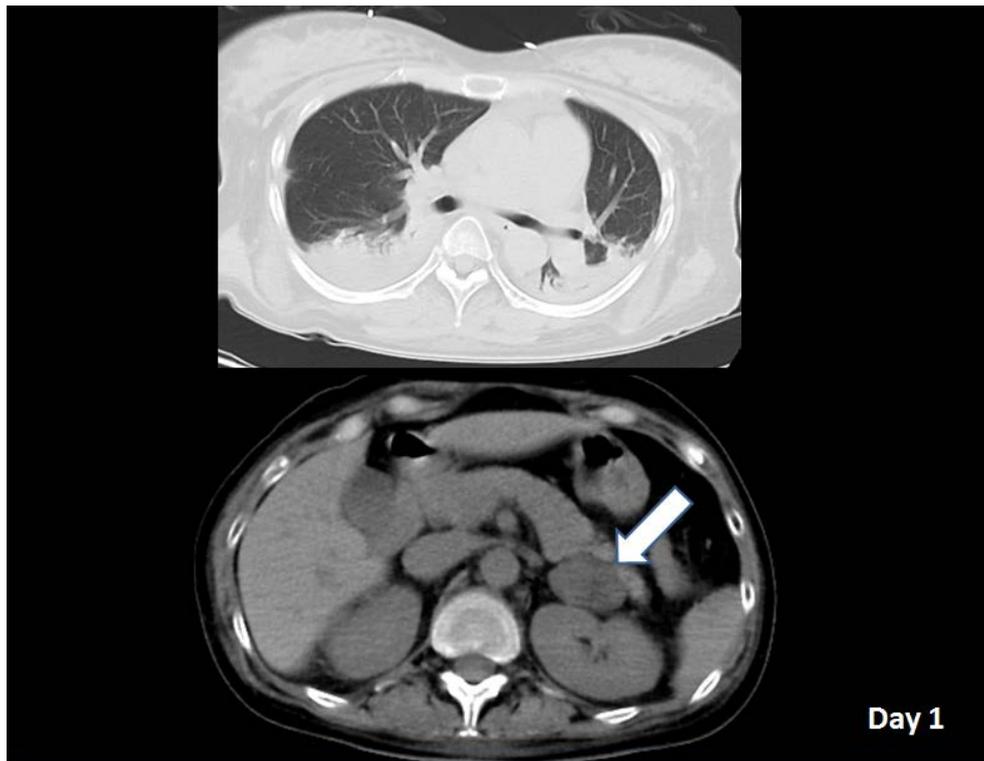
Whole body computed tomography (CT) before moving to an intensive care unit revealed bilateral low density in the parieto-occipital white matter with a minute high-density spot on her brain, bilateral aspirated lesions in her lungs, and enlargement of the right adrenal gland ([Figure 1](#) and [Figure 2](#)).

**Table 1. Laboratory data at the time of deterioration**

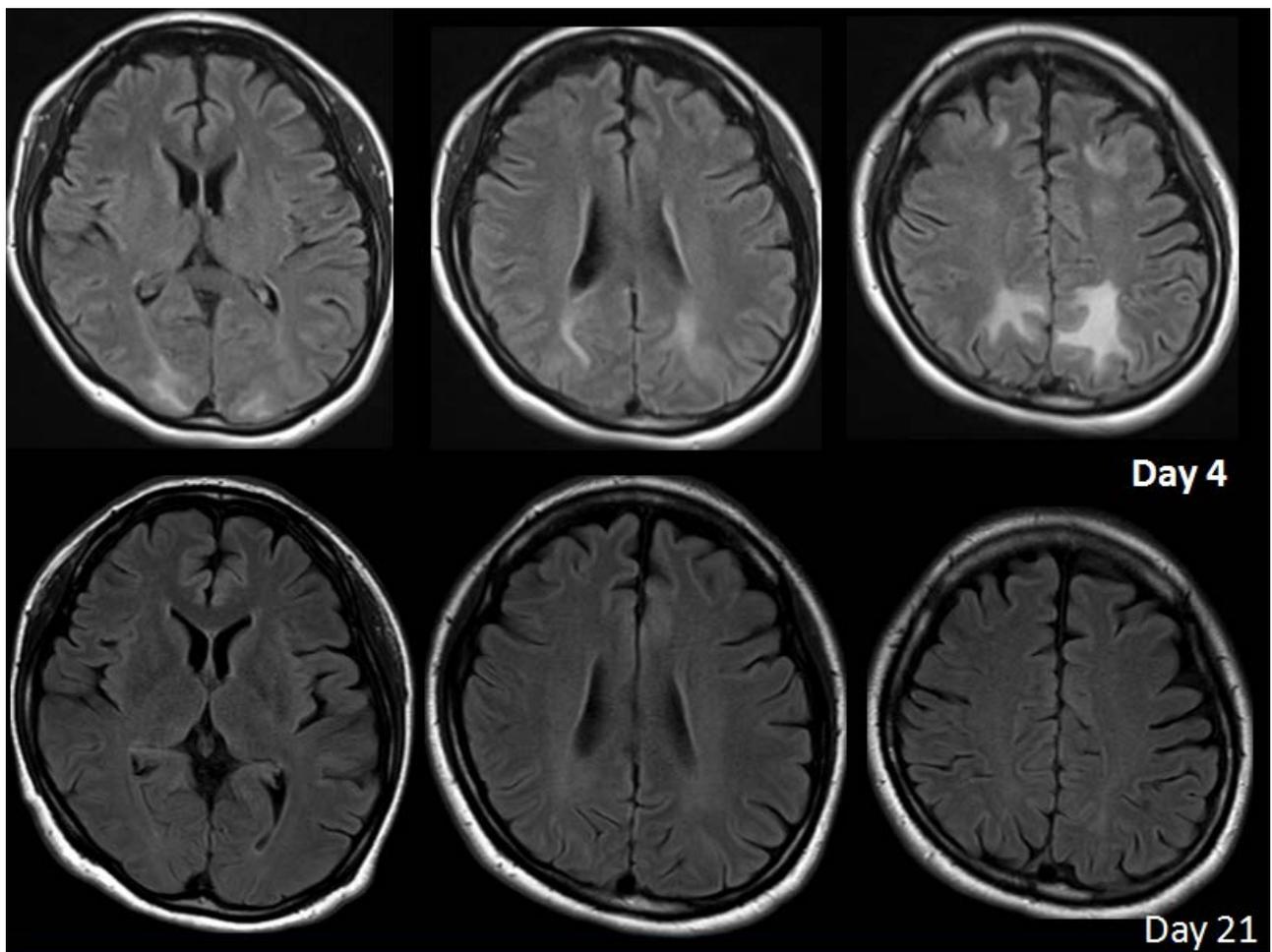
White blood cell	12,700 /μL
Hemoglobin	12.5 g/dL
Platelet	31.6×10 <sup>4</sup> /μL
Total protein	6.0 g/dL
Albumin	3.0 g/dL
Total bilirubin	0.1 mg/dL
Aspartate aminotransferase	38 IU/L
Alanine aminotransferase	28 IU/L
Alkaline phosphatase	402 IU/L
γ- glutamyltransferase	93 IU/L
Lactate dehydrogenase	536 IU/L
Amylase	99 IU/L
Blood urea nitrogen	7.6 mg/dL
Creatinine	0.32 mg/dL
Creatine kinase	96 IU/L
Glucose	148 mg/dL
Sodium	143 mEq/L
potassium	2.8 mEq/L
Chloride	102 mEq/L
Calcium	9.3 mg/dL
Phosphate	3.0 mg/dL
C-reactive protein	1.60 mg/dL
Brain natriuretic peptide	52.5 pg/mL
Prothrombin time	11.7 (11.7) seconds
Activated partial thromboplastin time	26.4 (27.3) seconds
Fibrinogen	185 mg/dL
Fibrinogen degradation products	23.5 μg/mL
Rheumatoid factor	3.3 (0-15 IU/L)
Anti nuclear antibody	negative
Anti-DNA antibody	negative
Proteinase 3 Antineutrophil cytoplasmic antibody	negative
Myeloperoxidase-anti-neutrophil cytoplasmic antibody.	negative
Urine protein	negative
Urine occult blood	negative



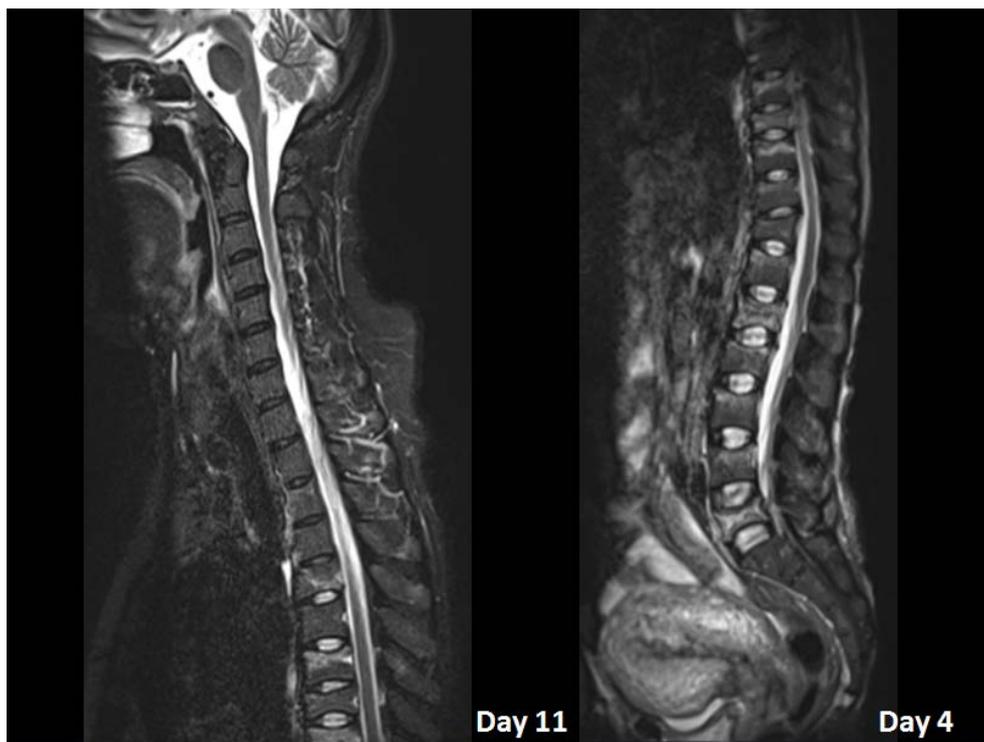
**Figure 1. Head computed tomography (CT) on code blue.** CT showed bilateral low density in the parieto-occipital white matter with a minute high-density spot in her brain



**Figure 2. Truncal computed tomography on code blue.** CT revealed bilateral aspirated lesions in the lungs (upper) and enlargement of the right adrenal gland (lower, arrow)



**Figure 3. Head magnetic resonance image (MRI) on day 4 after code blue.** MRI showed bilateral high-intensity signals in the fronto-parieto-occipital white matter (upper) on fluid attenuated inversion recovery imaging, which resolved later (lower). This was compatible with posterior reversible encephalopathy syndrome



**Figure 4.** Spinal magnetic resonance image (MRI) on days 4 and 11 after code blue. Spinal MRI shows a loss of vertebral height of the Th11, L1 and L5 vertebrae. The MRI also reveals multiple high intensity signals in the multiple vertebral bodies and discs on short-TI inversion recovery imaging. These suggest multiple compression fractures, bone and disc bruises deteriorated due to the patient’s convulsions

The tentative diagnosis was PRES with convulsion, aspirated pneumonia and Cushing syndrome with DM, skin lesions and pathological fracture due to osteoporosis. She underwent an infusion of levetiracetam (1000 mg) to control convulsions, sedatives and analgesics were administered, a depressor was administered to control blood pressure strictly, and antibiotics (sulbactam/ampicillin) were administered to treat aspiration pneumonia. She was extubated two days after her respiratory function showed improvement. Head MRI on the following day showed bilateral high intensity in the front-parieto-occipital white matter on fluid-attenuated inversion recovery imaging that resolved later, which was compatible with PRES (Figure 3).

Thoracolumbar MRI revealed multiple high intensity signals in multiple vertebral bodies and discs on short-TI inversion recovery imaging, suggesting bone and disc bruises, which deteriorated as a result of the patient’s convulsions (Figure 4).

After controlling her pain and treating osteoporosis with prescriptions of calcium, vitamin D and bisphosphonate, a blood test was performed to determine her hormone levels (Table 2 and Table 3). These results were compatible with Cushing syndrome. She is currently waiting to undergo adenectomy, which will be performed after the complete resolution of PRES and back pain. She was temporally moved to another medical facility for rehabilitation. She finally underwent adenectomy at four months. The pathological diagnosis was adenoma.

**Table 2. Basic hormone levels in the morning**

Adrenocorticotrophic hormone	2	(7.2-63.3 pg/mL)
Serum Cortisol	29.3	(4.5-21.1 µg/dL)
Urine free Cortisol	207	(11.2 ~ 80.3 µg/day)
Thyroid-stimulating hormone	1.31	(0.56-4.3 µIU/mL)
Free T3	1.4	(2.4-4.5 pg/mL)
Free T4	1	(1-1.7 ng/dL)
Growth hormone	0.33	(0.11-3.90 ng/mL)
Follicle stimulating hormone	0.2	(0 mIU/mL)
Estrogen	13.9	(0 pg/mL)
Luteinizing hormone	<0.2	(0 mIU/mL)
Progesterone	0.5	(0 ng/mL)
Prolactin	9.4	(6.1-30.5 ng/mL)
Antidiuretic hormone	1.3	(0-4.3 pg/mL)
Renin	0.5	(0 pg/mL)
Aldosterone	5	(3.6-24 pg/mL)
Metanephrine	0.02	(0.04-0.18 mg/day)
Normetanephrine	0.02	(0.1-0.28 mg/day)
Dehydroepiandrosterone sulfate	208	(0 µg/dL)
Adrenaline	0.01>	(0-0.1 ng/mL)
Noradrenalin	0.01>	(0.1-0.5 ng/mL)
Dopamine	0.01>	(0-0.03 ng/mL)

**Table 3. Results of diurnal variation & suppression test**

	6 O'clock	12 O'clock	18 O'clock	24 O'clock	DST
Adrenocorticotrophic hormone (pg/mL)	2	2	2	2	2
Cortisol (µg/dL)	28.7	28.4	27.7	29.8	25.9

DST, dexamethasone suppression test (8 mg).

### 3. Discussion

We herein report the first case of Cushing syndrome complicated by multiple pathological spinal fractures and PRES in the post-delivery phase. This was merely a case of eclampsia-related PRES; however, we focused on the relationship between Cushing syndrome and PRES. [4] Lodish et al. reported that a 6-year-old girl with adrenocorticotropin hormone (ACTH)-independent Cushing syndrome secondary to bilateral adrenal hyperplasia, presented with hypertension and seizures, and magnetic resonance imaging showed transient changes consistent with PRES. [5] In addition, Kasaliwal et al. reported that a 13-year-old girl presented multiple episodes of headache, decreased vision following generalized convulsions, and altered sensorium. [6] The findings of repeated head MRI was compatible with PRES. A nodule in the right lung was bronchial carcinoid which produced ectopic adrenocorticotropin hormone. In addition, Irvin et al. reported the case of a 48-year-old woman who was started on dexamethasone (4 mg, oral, every 6 hours) in preparation for potential external-beam radiation therapy for brain metastases. [7] The patient became progressively disoriented and agitated and developed hypertension. The repeated MRI findings were most consistent with PRES. The dexamethasone dose was quickly tapered, which resulted in the resolution of her delirium. Furthermore, Parikh et al. performed a retrospective review of radiology reports for cases of PRES and identified 99 cases. [8] The median age was 55 years and 74% of the patients were women. Surprisingly, steroid therapy at the time of the onset of PRES was identified in 44 of 99 cases; thus, they considered that steroids may contribute to the development of PRES. Taken together, all of the reports concluded that steroid-mediated hypertension might have played a causative role in the occurrence of PRES. Regarding the mechanism underlying the development of PRES in the present case, hypertension induced by the perinatal period, severe pain due to pathological spinal fractures, and/or excess steroid levels induced by Cushing syndrome may be causative of PRES. Accordingly, aggressive control of pain and blood pressure in the perinatal period may be required in order to prevent the onset of PRES.

Fractures in association with generalized convulsive status epilepticus and convulsive seizures in adult patients are well known incidents. Posterior fracture-dislocations of the shoulders, thoracic and lumbar vertebral compression, fractures of the skull and jaw, and bilateral femoral neck fractures have been most frequently reported. [9] Preventive measures, including bone densitometry, calcium/vitamin D supplementation, and bisphosphonate therapy should be reinforced in epilepsy patients at risk of

osteoporosis, similarly to the present case. [10] Physicians are urged to heighten their awareness regarding seizure-associated fractures, especially in patients with postictal pain.

### 4. Conclusion

We report a rare case of Cushing syndrome complicating multiple pathological spinal fractures and PRES in the post-delivery phase. Aggressive control of pain and blood pressure in the perinatal period may be required to prevent the onset of PRES. A further analysis with the accumulation of similar cases will be necessary.

### Acknowledgements

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### References

- [1] Fischer M, Schmutzhard E. Posterior reversible encephalopathy syndrome. *J Neurol*. 2017 Aug; 264(8): 1608-1616.
- [2] Tetsuka S, Ogawa T. Posterior reversible encephalopathy syndrome: A review with emphasis on neuroimaging characteristics. *J Neurol Sci*. 2019 Sep 15; 404: 72-79.
- [3] Fugate JE, Rabinstein AA. Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. *Lancet Neurol*. 2015 Sep; 14(9): 914-925.
- [4] Garg RK, Kumar N, Malhotra HS. Posterior reversible encephalopathy syndrome in eclampsia. *Neurol India*. 2018 Sep-Oct; 66(5): 1316-1323.
- [5] Lodish M, Patronas NJ, Stratakis CA. Reversible posterior encephalopathy syndrome associated with micronodular adrenocortical disease and Cushing syndrome. *Eur J Pediatr*. 2010. PMID: 19415327 Free PMC article.
- [6] Kasaliwal RR, Kakade H, Budyal S, Lila AR, Bandgar T, Shah N. Posterior reversible encephalopathy syndrome due to ectopic Cushing's syndrome: an uncommon presentation of a rare disease. *Indian J Pediatr*. 2015. PMID: 24986194.
- [7] Irvin W, MacDonald G, Smith JK, Kim WY. Dexamethasone-induced posterior reversible encephalopathy syndrome. *J Clin Oncol*. 2007 Jun 10; 25(17): 2484-6.
- [8] Parikh NS, Schweitzer AD, Young RJ, Giambrone AE, Lyo J, Karimi S, Knobel A, Gupta A, Navi BB. Corticosteroid therapy and severity of vasogenic edema in posterior reversible encephalopathy syndrome. *J Neurol Sci*. 2017 Sep 15; 380: 11-15.
- [9] Grzonka P, Rybitschka A, De Marchis GM, Marsch S, Sutter R. Bone fractures from generalized convulsive seizures and status epilepticus-A systematic review. *Epilepsia*. 2019 May; 60(5): 996-1004.
- [10] Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. *Lancet*. 2011. Apr 9; 377(9773): 1276-87.

