Heliyon 10 (2024) e40915

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Case report

Rare association of posterior reversible encephalopathy syndrome (PRES) with hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome – A case report and review of the literature

Mirjana Ždraljević [a], Aleksa Pejović [a,b], Biljana Jocić- Pivač [c], Maja Budimkić [a,b], Dejana R. Jovanović [a,b], Milija Mijajlović [a,b,*]

[a] Neurology Clinic, University Clinical Center of Serbia, Belgrade, Serbia
[b] University of Belgrade, Faculty of Medicine, Belgrade, Serbia
[c] The Obstetrics and Gynaecology Clinic "Narodni Front", Belgrade, Serbia

ARTICLE INFO

Keywords:
PRES
HELLP
Pregnancy
Outcome
Case report

ABSTRACT

Introduction: The hemolysis-elevated liver enzymes-low platelet counts (HELLP) syndrome and posterior reversible encephalopathy syndrome (PRES) are rare conditions that can complicate pregnancy and the early postpartum period. Although both are closely related to hypertensive pregnancy disorders, their association is rarely described, so the outcome of these patients remains unknown. We present a case report of PRES associated with HELLP syndrome and a review of all previously published cases, including demographic characteristics, clinical presentation, treatment, and outcome.

Case presentation: A previously healthy 31-year-old woman in the 38th week of pregnancy was admitted to the obstetric department due to elevated blood pressure. The first laboratory findings were consistent with HELLP, which is why she was delivered by emergency caesarean section. Forty-four hours after the cesarean section, she presented with a severe headache, blurred vision, and instability, followed by two seizures. Magnetic resonance imaging (MRI) of the brain showed T2-weighted/FLAIR left-sided hyperintensity consistent with PRES. She was treated with antihypertensive, antiedematous, and other symptomatic therapy. The control brain MRI showed complete regression of the previously described changes, and she was discharged without a neurological deficit. So far, 33 cases of HELLP associated with PRES have been reported in the literature, including our case. Our review of 30 cases showed that although most patients have good outcomes, if not treated in time, patients may develop serious somatic complications and permanent neurological deficits, or even fatal outcomes.

Conclusion: PRES associated with HELLP syndrome is a rare combination of third trimester/postpartum complications which usually present with seizures, altered sensorium, headache, hypertension, and laboratory disorders. These disorders require mutual neurological, internal and gynaecological treatment, and if timely treated resolve completely in most of the cases. However, caution is required as these patients may develop serious somatic complications and permanent neurological deficits or even fatal outcomes.

* Corresponding author. Neurology Clinic, University Clinical Center of Serbia University of Belgrade, Faculty of Medicine 6, Dr. Subotica Street, 11000 Belgrade, Serbia.
E-mail address: milijamijajlovic@yahoo.com (M. Mijajlović).

https://doi.org/10.1016/j.heliyon.2024.e40915
Received 3 May 2024; Received in revised form 28 November 2024; Accepted 3 December 2024
Available online 4 December 2024

1. Introduction

The hemolysis-elevated liver enzymes-low platelet counts (HELLP) syndrome is a serious condition in pregnancy first described in 1982, characterized by hemolysis, elevated liver enzymes and low platelet count. It is a variant or complication of severe preeclampsia that occurs in 0.5–0.9 % of all pregnancies and up to 20 % of pregnancies complicated by severe preeclampsia [1]. As many as 70–80 % of HELLP syndrome cases are associated with preeclampsia [2]. In more than two-thirds of patients, HELLP syndrome occurs during pregnancy, mostly in the last trimester [1,2]. It is thought to arise due to abnormal placentation in the first trimester in response to abnormal products released from a stressed placenta. Inadequate immune tolerance towards the invading fetal trophoblast is mentioned as the basic initial step in the pathogenesis of both HELLP and preeclampsia. The results of some studies indicate that there is also a genetic predisposition for the development of HELP syndrome with the influence of multiple gene variants in combination with environmental factors [2]. Recognition of this syndrome is made difficult by the non-specific clinical picture, which mostly consists of malaise, epigastric pain, nausea, vomiting and headache. At the same time, visual disturbances may also occur in some cases [1]. The occurrence of HELLP syndrome can lead to severe complications for the mother and fetus, and even to death in a significant number of cases, which is mainly due to complications in mothers, and gestational age in the fetus [1–5].

Another condition closely related to hypertensive disorders of pregnancy such as preeclampsia and eclampsia is posterior reversible encephalopathy syndrome (PRES) [6,7]. This condition was first described in 1996, and is characterized by a typical neuroradiological presentation of parieto-occipital white matter changes due to bilateral reversible vasogenic edema and nonspecific clinical symptoms. The pathophysiology of PRES has not been fully investigated and currently, two theories explain the occurrence of vasogenic edema. According to the first theory, this edema occurs as a result of inadequate autoregulatory abilities of the cerebral vasculature to increase blood pressure, which is partly explained by the difference in the innervation of the posterior circulation (lack of sympathetic innervation). However, this theory can only be applied to patients with preeclampsia or eclampsia. According to the second theory, the basis of PRES is endothelial dysfunction caused by endogenous or exogenous agents [6]. The spectrum of clinical manifestations is wide-ranging from headache and visual disturbances to altered sensorium and seizures that occur in the most severe cases [6,8]. It occurs in about 20 % of pregnancies complicated by severe preeclampsia and in over half of pregnancies complicated by eclampsia [7, 8]. Apart from pregnancy, PRES is also common in early postpartum eclampsia, whose symptoms develop within 48 hours of delivery [7]. Although in most cases this condition is completely reversible, the reported maternal mortality rate is high at 5.3 %, while in almost 10 % of patients, it can leave permanent neurological consequences [6–9].

Although both of the previously mentioned syndromes are closely related to hypertensive disorders of pregnancy, their association is rarely described. The reasons for the rarely reported combined occurrence of these two conditions are unknown. It is possible that the association of these two conditions is underrecognized because the clinical picture of milder forms is insufficiently specific and a high level of suspicion and caution is needed to recognize them in time. There are also indications that the pathogenesis of these disorders is different, and that their development is determined by a person's genetic predisposition. Here we report a case of PRES associated with HELLP syndrome and eclampsia. Written consent was obtained from the patient for the use of anonymous data in scientific publications. Furthermore, an overview of all previously described cases with both conditions is provided, including demographic characteristics, clinical manifestations, findings of diagnostic procedures, treatment, and outcomes.

2. Case presentation

A previously healthy 31-year-old woman in the 38th week of her first pregnancy was admitted to the obstetrics department because of elevated arterial blood pressure. Graph 1 shows the most important segments of the patient's course of illness. The patient's past medical, surgical and family history was unremarkable. Pregnancy was conceived by in vitro fertilization (IVF), with good prenatal care and normal prenatal analyses. During a routine examination in the 30th week of pregnancy, the patient was found to have elevated arterial blood pressure. This is why methyl dopa was introduced into the therapy and regular monitoring of blood pressure values was indicated. On the day of admission, the patient measured elevated blood pressure values at home, which is why she went to the gynecologist. At the time of admission to the obstetrics department, her blood pressure was 200/110 mmHg, while laboratory findings were indicative of HELLP syndrome (RBC 3.24, Hb 93, Plt 72, SGOT 227, SGPT 213). An emergency caesarean section was performed without complications and the patient delivered a healthy female newborn weighing 3250 g with an Apgar score of 8 at the first minute and 9 at the fifth minute. In the initial postpartum period, her health condition was stable, with no subjective complaints except for postoperative pain in the wound area. Forty-four hours after cesarean section, the patient reported a severe occipital headache, blurred vision, and unsteadiness, followed by two generalized tonic-clonic seizures. She was transferred to the neurointensive care unit of the Emergency Department and then to the Department for Cerebrovascular Diseases and Headaches. Her somatic findings on admission were normal except for elevated arterial blood pressure of 150/90 mmHg. In the neurological finding, only midline ataxia was observed while the rest of the neurological examination was completely normal.

2.1. Laboratory analysis

Initial laboratory values showed the persistence of thrombocytopenia (Plt 170), anemia (RBC 3.23, Hb 99), elevated liver enzymes (SGOT 227, SGPT 213) and creatine kinase (CK 237). Other analysis including blood lipid and homocysteine levels, thyroid status, tumor markers (CEA, CEA 19-9, CEA 72- 4, CEA 15-3, CA 125, NSE, Cyfra 21-1) immunological analyses (ANA, ANCA, AMA, LKM, VDRL, AClA IgM and IgG), and extended coagulation profile (PT, INR, aPTT, fibrinogen, D-dimer, LA1, LA2, antithrombin, ProtC.ch,

ProtC.Global.NR, APCR.Ratio, plasminogen, FXIII, FIX, FVII, FFII, aPTT.PSL, aPTT.AFSL, wVF) were within normal ranges. A peripheral blood smear was normal. Screening for hereditary thrombophilias showed the patient to be normal homozygous for prothrombin G20210A and factor V Leiden mutations, heterozygous for MTHFR C677T mutation and homozygous for PAI-1 mutation, genotype 4G/5G. According to hematologists, this finding does not require persistent anticoagulant therapy.

2.2. Neuroimaging

A computerized tomography (CT) scan of the brain without contrast showed normal findings. Magnetic resonance imaging (MRI) of the brain showed hyperintensity on the T2-weighted and fluid attenuated inversion recovery (FLAIR) images in the left occipital lobe, without diffusion restriction and postcontrast enhancement, consistent with PRES (Fig. 1 a-c). Additional analyses CT angiography was normal, as well as MRI cerebral venography. According to these neuroradiological findings the diagnosis of PRES was established. Electroencephalogram (EEG) showed normal finding. Transcranial doppler (TCD) showed the global flow acceleration in all blood vessels with normal hemodynamic flow parameters. Fundoscopy showed the presence of hypertonic fundus level I. The presence of a hematometra was determined by a control gynecological examination and ultrasound, due to which a revision of the uterus was performed.

2.3. Treatment and outcome

During hospitalization, the patient was treated with antihypertensive (three drugs orally - amlodipine 5 mg daily, methyldopa 250 mg four times a day and nifedipine 20 mg daily), antiedematous (intravenous solution of 20 % mannitol 250ml four times a day), hormone (oxytocin) and analgesic therapy, as well as prophylactic doses of low molecular weight heparin (nadroparin calcium 3800 I. U. twice daily). She was also treated with antibiotic therapy due to the positive culture of the uterine swab (intravenous ceftriaxone 2000 mg daily for 14 days and intravaginal chloramphenicol suppositories twice daily for 14 days). The therapy was administered in the hospital by the medical staff. The patient well tolerated it and no adverse or unexpected side effects were reported. Control MRI of the brain two weeks later showed complete regression of the previously described changes (Fig. 1 d-f). Anaemia (RBC 3.47, Hb 111)

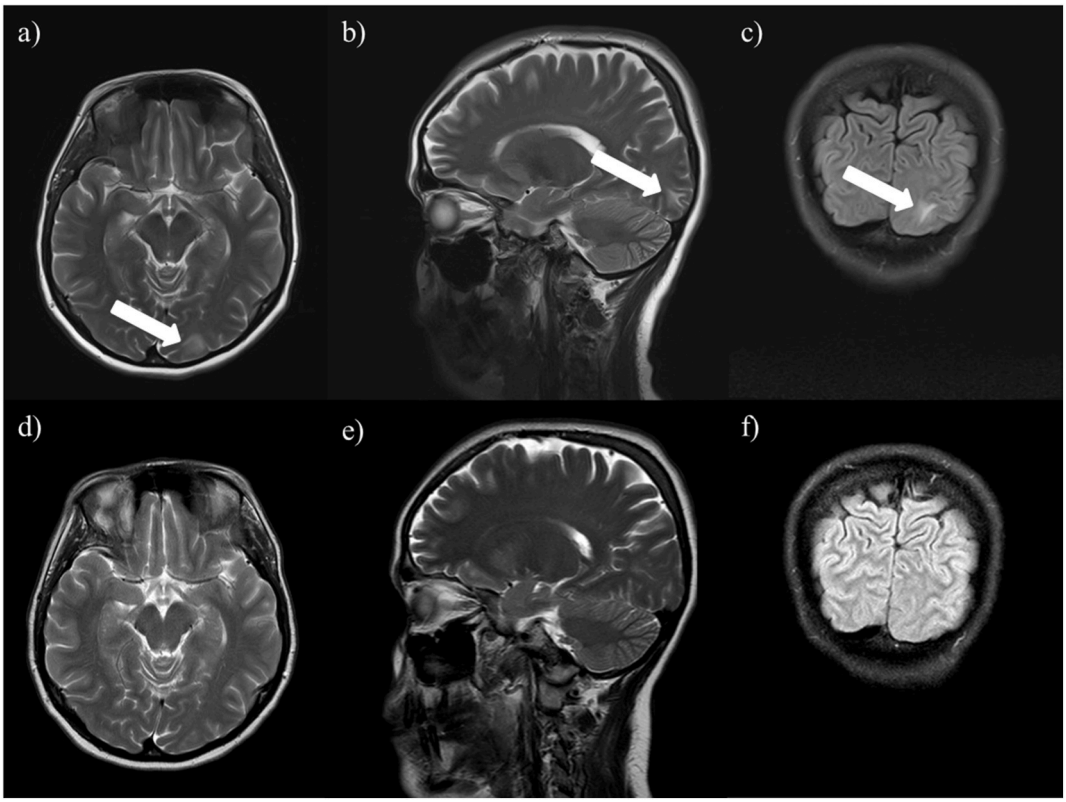
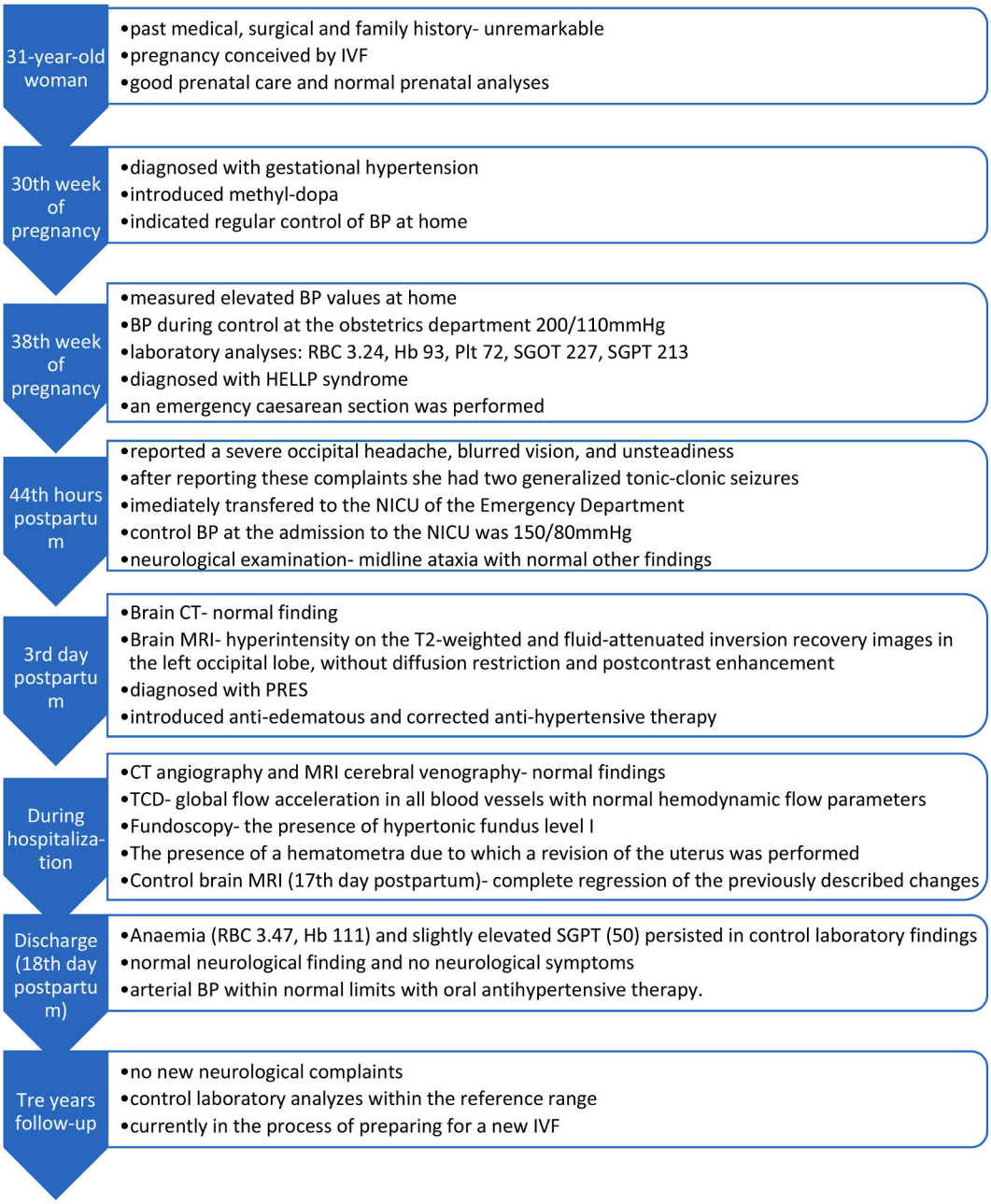


Fig. 1. a) Initial brain MRI/T2-weighted transversal plane section (3rd day postpartum)-hyperintensity in the left occipital lobe; b) Initial brain MRI/T2-weighted sagittal plane section (3rd day postpartum)- hyperintensity in the left occipital lobe; c) Initial brain MRI/FLAIR axial plane section (3rd day postpartum)- hyperintensity in the left occipital lobe; d) Control brain MRI/T2-weighted transversal plane section (17th day postpartum)- normal finding; e) Control brain MRI/T2-weighted sagittal plane section (17th day postpartum)- normal finding; f) Control brain MRI/FLAIR axial plane section (17th day postpartum)- normal finding. MRI- magnetic resonance imaging; FLAIR – fluid attenuated inversion recovery.



Graph 1. Time course of the patient's illness, including clinical picture, diagnostic results, prescribed therapy and outcome.
IVF = in vitro fertilization; BP = blood pressure; HELLP= Hemolysis, Elevated Liver enzymes and Low Platelets; NICU = neurology intensive care unit; CT= Computed Tomography; MRI = Magnetic Resonance Imaging; PRES= Posterior Reversible Encephalopathy Syndrome; TCD = Transcranial doppler.

and slightly elevated SGPT (50) persisted in control laboratory findings at discharge, while spontaneous correction of thrombocytopenia occurred. The patient was discharged eighteen days after delivery with normal neurological findings and no neurological symptoms, while her arterial blood pressure was within normal limits with oral antihypertensive therapy. During the three-year follow-up, the patient had no new neurological complaints, control laboratory analyses were within the reference range, and she is

currently in the process of preparing for a new IVF.

3. Review of the literature

A systematic literature search was performed in English on PubMed (MEDLINE), Google Scholar, Embase, and Cochrane up to March 15, 2024, independently by 2 researchers (M.Ž., A.P.). Using the search terms "HELLP syndrome", "PRES", "hemolysis-elevated liver enzymes-low platelet syndrome", "posterior reversible encephalopathy syndrome" and "pregnancy", 26 publications reporting 33 cases were identified, including ours [10–34]. After careful reading, one article in which 3 cases were published was excluded from the analysis due to insufficient data [34], while an overview of the remaining 30 cases is presented below [10–33].

3.1. Demographic features

The largest number of reported cases is from India (a total of 8 cases), followed by the USA, Turkey and Japan with 4 cases each, then Italy where 3 cases were reported and Brazil with 2 cases. One case was described each from Australia, Morocco, Belgium, the UK and Serbia. As both PRES and HELLP syndrome are associated with pregnancy, they are expected to occur in young women of childbearing age. The median age of patients diagnosed with PRES associated with HELLP syndrome was 27 (min 18- max 43) years. Most patients were previously healthy, while only five (16.7 %) had comorbidities [10–33]. Among comorbidities, sickle cell disease was reported in two patients (6.7 %) [17,21], one of whom previously had uraemia (3.3 %) [17]. Other reported comorbidities were primary ovarian failure (3.3 %) [13], Gilbert's syndrome (3.3 %) [32], and in our patient thrombophilia (3.3 %). None of the patients had previous hypertension, autoimmune diseases, neoplasms, or immunosuppressive states-conditions known to be associated with the PRES [10–33]. Except for sickle cell anaemia, in which the occurrence of HELLP syndrome and PRES was reported earlier, the other listed comorbidities were not previously recognized as a risk factor for the occurrence of the mentioned two syndromes [35–37]. However, the fact that only 2 of 30 patients had sickle cell anaemia and that most patients had no prior comorbidities suggests that there are no clear predisposing factors for PRES associated with HELLP syndrome. The number of pregnancies in general, as well as multiple pregnancies, do not seem to affect the risk of these complications. Nineteen (63.3 %) patients were primigravidae, seven (23.3 %) were multigravidae [10–33], and multiple pregnancies (triplets) were reported once (3.3 %) [11]. Pregnancies were a result of IVF in three cases (10 %), including ours [11,13]. One of these was a patient diagnosed with primary ovarian syndrome [13], ours was diagnosed with thrombophilia, while the third patient was without comorbidities [11]. These observations suggest that there are no clear premorbid risk factors for the combined occurrence of the two syndromes and that gestational factors play a dominant role. Delivery was performed by caesarean section in most patients with a known method of delivery (Table 1.) [10–33]. Medical termination of pregnancy was carried out in 2 cases, one due to intrauterine death of the fetus, and the other due to severe developmental anomalies [17,26]. Intrauterine growth restriction was detected in five (15.6 %) babies, which accounted for almost a third of infants with known status [17,19,21,24,27]. Severe fetal growth restriction was reported in two cases with onset of clinical presentation before 27th week of pregnancy [17,27]. Early-onset preeclampsia and HELP have previously been reported to be associated with fetal growth restriction [2].

3.2. Clinical presentation

The first symptoms usually appear in the third trimester of pregnancy, with a median reported length of pregnancy of 33 (min 16-max 39) weeks [10–33]. In the largest number of patients, the onset of symptoms was between the 27th and 37th week of pregnancy, which correlates with the reported results for the onset of HELLP syndrome [38]. The appearance of symptoms before the 27th week of pregnancy was reported in 2 patients who both had a medical termination of pregnancy, one due to intrauterine death of the fetus, and the other due to severe developmental anomalies of the fetus (Table 1.) [17,26]. The most commonly reported findings of HELLP syndrome were elevated liver enzymes (100 %), low platelet count (100 %), hypertension (93.3 %), hemolysis (73.3 %), and proteinuria (53.3 %) (Table 2.) [10–33]. Neurological symptoms of PRES occurred after delivery in slightly less than half of the patients (46.7 %) (Table 1.) [10–33], which is in line with previously published data [39]. Common neurological symptoms were seizures (66.7 %), altered sensorium (60.0 %), visual impairment (46.7 %), headache (43.3 %) and drowsiness (40 %), while instability was rarely reported (6.7 %) (Table 2.). Focal neurological deficit during the neurological examination was verified in eight patients (26.7 %), including our (Table 2.) [10–33]. These findings suggest that the majority of reported patients had severe clinical presentation of PRES, which could imply that most subtle clinical presentations are underrecognized. The most frequent non-neurological symptom reported by patients with PRES associated with HELLP syndrome was epigastric pain (26.7 %) (Table 2.) [10–33], which is a common manifestation of HELLP syndrome [38]. Our findings suggest that majority of patients with PRES had severe clinical presentation which could implicate that most subtile clinical presentation of PRES was underrecognized.

3.3. Neuroradiological findings

Hyperintense lesions on T2-weighted and FLAIR images without diffusion restriction were characteristic findings on MRI, while on CT these lesions were presented as hypodensities [10–33]. Findings were concordant only four out of 10 times when CT and MRI were done consecutively [10,14,17–19,25,26,29,30], which indicates that the sensitivity of MR in detecting these changes is much higher. The changes were bilateral in most cases (96.7 %), except ours [10–33]. This is in line with the results of one previously published study that included 76 patients with PRES, two of whom (2.6 %) had unilateral involvement [39]. As expected, the most common

Table 1
Sociodemographic, clinical, neuroradiological features and outcomes of patients with PRES associated with HELLP syndrome.

No	Publication	Age	Week of pregnancy	Delivery	Newborn condition	Neurological manifestations (befor/after delivery)	Initial CT of the bran	Initial MRI of the bran	Control MRI of the bran	Outcome
1.	Feske et al. (1997) [10]	36	39	CS	unknown	after	hypodensities in the thalami, midbrain, pons, and cerebellum	PRES involving the occipital lobes, thalami, midbrain, pons, and cerebellum	normal	mild residual loss of sensation on the left side of the face (discharged after 4 days)
2.	Marano et al. (2003) [11]	30	32	CS	helthy	before	x	asymmetric PRES in the subcortical parieto-occipital white matter bilaterally	normal	full recovery
3.	Negro et al. (2004) [12]	37	39	vaginal delivery	helthy	after	x	PRES involving both hemispheres, the thalamus, cerebellum, and mesencephalon	normal	full recovery
4.	Morton et al. (2005) [13]	26	28	CS	helthy/ preterm	before	low attenuation areas in the right frontal and both occipital lobes consistent with PRES	x	normal	full recovery
5.	Murphy et al. (2005) [14]	34	33	vaginal delivery	helthy	before	large left occipital hematoma with mass effect and a midline shift	interstitial edema in the right parietal and occipital lobes, findings suggestive of the PRES	evolving hematoma with encephalomalacia in the left occipital lobe and resolution of the vasogenic edema in the right parietal and occipital lobes consistent with PRES	visual impairment (one year postpartum)
6.	Peng et al. (2008) [15]	36	38	vaginal delivery	helthy	after	x	PRES in the anterior cortex and subcortical white matter of the right lobe and bilateral basal ganglia	normal	full recovery
7.	Grzesiuk et al. (2009) [16]	34	32	CS	helthy/ preterm	before	x	PRES cortical and subcortical, more intense in the occipital, parietal and frontal lobes	small areas of edema in the occipital and frontal lobes	full recovery
8.	Vijayalakshmi et al. (2009) [17]	28	16	medical termination of pregnancy	IGR, severe developme-ntal anomalies	before	areas of low density involving the region of the basal ganglia and internal capsule bilaterally, more on the right side	bilateral, almost symmetrical PRES in the head of the caudate, as well as the external capsules and adjacent basal ganglia bilaterally	normal	full recovery
9.	Hegde et al. (2009) [18]	21	unknown	vaginal delivery	helthy/ preterm	before	hypodense lesions in posterior temporal, parieto-occipital, high frontal and parietal region	bilateral PRES in posterior temporal, parieto-occipital, high frontal and parietal region; bilateral watershed territory	x	partial but resolving memory loss (discharged after 10 days)
10.	Aygün et al. (2010) [19]	23	36	CS	IGR	after	bilateral low-density areas involving the white matter of the posterior parietal lobe,	hyperintense areas in the bilateral parieto-occipital lobes indicating brain edema	normal	intermittent amnesia (four weeks postpartum)

(*continued on next page*)

Table 1 (*continued*)

No	Publication	Age	Week of pregnancy	Delivery	Newborn condition	Neurological manifestations (befor/after delivery)	Initial CT of the bran	Initial MRI of the bran	Control MRI of the bran	Outcome
							being more prominent on the right			
11.	Paul et al. (2013) [20]	27	unknown	unknown	unknown	after	x	changes suggestive of PRES in parietooccipital regions and brainstem; intracranial hemorrhage in right parietooccipital region	x	death
12.	Paul et al. (2013) [20]	27	36	CS	unknown	before	x	PRES with basal ganglion bleed	x	discharge
13.	Paul et al. (2013) [20]	27	unknown	unknown	unknown	after	x	bilateral parietooccipital PRES	x	discharge
14.	Paul et al. (2013) [20]	24	30	unknown	unknown	before	x	bilateral parietooccipital PRES	x	discharge
15.	Paul et al. (2013) [20]	23	unknown	unknown	unknown	after	x	bilateral parietal, frontal occipital cortical and subcortical changes suggestive of PRES	x	discharge
16.	Paul et al. (2013) [20]	23	36	CS	unknown	before	x	hemorrhage in the brainstem with PRES	x	death
17.	Sarmento et al. (2014) [21]	18	31	CS	IGR	before	bilateral occipital PRES that also reached the parietal region	x	x	full recovery
18.	Maramattom et al. (2014) [22]	23	33	CS	unknown	before	x	brainstem PRES	x	visual impairment (six months postpartum)
19.	Babahabib et al. (2015) [23]	31	38	CS	unknown	after	x	PRES interesting the cerebral cortex, parietal and occipital sub-cortical and the white matter	normal	full recovery
20.	Ates et al. (2015) [24]	29	36	CS	IGR	before	x	hyperintense signal changes in the right occipital, left cerebellar subcortical regions and right thalamus	normal	full recovery
21.	Takagi et al. (2016) [25]	37	39	vaginal delivery	helthy	after	discreet hypodensity on the right and left frontal lobes	high-intensity lesions in the superior frontal gyrus, the precentral gyrus and the cingulate gyrus	normal	full recovery
22.	Beker-Acay et al. (2016) [26]	18	24	medical termination of pregnancy	stilbirth	before	subarachnoid hemorrhage in the right temporal lobe and intraparenchymal hematoma in the right occipital lobe	increased signal intensities in both of the cerebral pedincules, posterior limb of the bilateral internal capsule, left putamen, left globus pallidus extending partially to the thalamus, bilateral occipital lobes, left frontal and	the hematoma in the right hemisphere, density and signal abnormalities expanded to the right part of the pons, and became more evident, whereas the subarachnoid hemorrhage disappeared	full recovery

(*continued on next page*)

Table 1 (*continued*)

No	Publication	Age	Week of pregnancy	Delivery	Newborn condition	Neurological manifestations (befor/after delivery)	Initial CT of the bran	Initial MRI of the bran	Control MRI of the bran	Outcome
								right parietal lobes, predominantly in gray-white matter junction areas		
23.	Takahashi et al. (2017) [27]	36	28	CS	IGR	after	x	bilateral occipital lobes symmetrically indicative of PRES	x	full recovery
24.	Tetsuka et al. (2017) [28]	38	29	CS	helthy/ preterm	after	x	PRES in the cortical and subcortical white matter in the occipital lobes, basal ganglia and callosal splenium	normal	full recovery
25.	Zemple et al. (2017) [29]	21	33	CS	helthy	before	diffuse anoxic brain injury	PRES in the parieto-occiptal region as well as indistinct areas of the basal ganglia, putamen and thalamus	x	full recovery
26.	Sarbu et al. (2019) [30]	24	35	unknown	unknown	before	bilateral symmetric hypodensity of the basal ganglia, without contrast enhancement	PRES involving symmetrically the lenticular and caudate nuclei, and with extension to the internal and external capsule	normal	full recovery
27.	Yilmaz et al. (2018) [31]	24	unknown	vaginal delivery	unknown	after	x	PRES in the cortex and white matter bilaterally in the occipital area; in the white matter, in the left temporal and right parietal areas; and, in the head of the right caudate nucleus and right thalamus	normal	full recovery
28.	Marcoccia et al. (2019) [32]	43	37	unknown	unknown	before	x	cortical and subcortical hyperintense lesions in both cerebellar lobes with elevated difusion	normal	full recovery
29.	Kini et al. (2021) [33]	26	unknown	unknown	unknown	after	x	hyperintensities in the posterior cortex bilateral	x	full recovery
30.	Ždraljević et al. (2024)	31	37	CS	helthy	after	normal	PRES in left occipital, left parietal and left temporooccipital regions	normal	full recovery

PRES = posterior reversible encephalopathy syndrome; HELLP = hemolysis-elevated liver enzymes-low platelet counts; CT = computerized tomography; MRI = magnetic resonance imaging; CS = caesarean section; IGR = intrauterine growth restriction.

Table 2
Laboratory and clinical features of patients with PRES associated with HELLP syndrome.

No	Publication	HTA	Hemolysis	Low Pt	Elevated liver enzyms	Proteinuria	Seizures	Altered sensorium	Visual impairment	Headache	Drowsiness	Instability	Focal neurological deficit	Other symptoms	Somatic complications	Gynecological complications
1.	Feske et al. (1997)[4]	yes	yes	yes	yes	yes	no	yes	no	no	yes	no	yes	no	no	no
2.	Marano et al. (2003)[5]	no	yes	yes	yes	no	yes	no	yes	no	no	no	no	no	no	no
3.	Negro et al. (2004)[6]	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	no	yes	no	no	no
4.	Morton et al. (2005)[7]	yes	no	yes	yes	yes	yes	yes	yes	no	yes	no	no	epigastric pain	ventilatory support	no
5.	Murphy et al. (2005)[8]	yes	yes	yes	yes	no	yes	no	yes	no	yes	no	yes	severe epigastric pain, nausea, vomiting, gross haematuria	disseminated intravascular coagulation, pulmonary edema, severe cardiomyopathy	no
6.	Peng et al. (2008)[9]	yes	no	yes	yes	yes	yes	no	no	no	no	no	no	no	no	no
7.	Grzesiuk et al. (2009)[10]	yes	yes	yes	yes	no	yes	Yes	yes	no	yes	no	no	no	no	no
8.	Vijayalakshmi et al. (2009)[11]	yes	yes	yes	yes	yes	no	no	yes	yes	no	no	yes	morning sickness, haematuria, epigastric discomfort, epistaxis	haematuria	profuse uterine bleeding
9.	Hegde et al. (2009)[12]	yes	yes	yes	yes	yes	status epilepticus	yes	no	no	no	no	yes	naso-oral bleeding and reduced urine output	acute kidney failure, ventilatory support	no
10.	Aygün et al. (2010)[13]	yes	no	yes	yes	yes	no	yes	no	no	no	no	yes	no	no	no
11.	Paul et al. (2013)[14]	yes	yes	yes	yes	yes	yes	yes	no	no	no	no	no	no	acute kidney failure, shock, ventilatory support	no
12.	Paul et al. (2013)[14]	yes	yes	yes	yes	yes	yes	yes	no	yes	no	no	yes	no	acute kidney failure, shock, ventilatory support	no
13.	Paul et al. (2013)[14]	yes	yes	yes	yes	yes	yes	yes	no	no	no	no	no	no	Shock, haematuria	hemoperitonium
14.	Paul et al. (2013)[14]	yes	no	yes	yes	no	yes	yes	no	yes	no	no	no	no	no	no
15.	Paul et al. (2013)[14]	no	yes	yes	yes	no	yes	yes	yes	no	no	no	no	no	acute kidney failure shock retinal detachment	hemoperitonium

(*continued on next page*)

Table 2 (*continued*)

No	Publication	HTA	Hemolysis	Low Pt	Elevated liver enzyms	Proteinuria	Seizures	Altered sensorium	Visual impairment	Headache	Drowsiness	Instability	Focal neurological deficit	Other symptoms	Somatic complications	Gynecological complications
16.	Paul et al. (2013)[14]	yes	yes	yes	yes	yes	yes	yes	no	yes	no	no	no	no	ventilatory support	no
17.	Sarmento et al. (2014)[15]	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	no	no	epigastric pain	hepatic infarction	no
18.	Maramattom et al. (2014)[16]	yes	yes	yes	yes	yes	no	no	yes	no	yes	no	yes	no	no	no
19.	Babahabib et al. (2015)[17]	yes	yes	yes	yes	yes	yes	yes	no	yes	no	no	no	no	no	no
20.	Ates et al. (2015)[18]	yes	yes	yes	yes	yes	no	no	yes	yes	no	no	no	no	no	no
21.	Takagi et al. (2016)[19]	yes	yes	yes	yes	no	yes	no	no	no	no	no	no	epigastralgia, vomiting and giddiness	no	no
22.	Beker-Acay et al. (2016)[20]	yes	no	yes	yes	no	no	yes	yes	yes	yes	no	no		no	no
23.	Takahashi et al. (2017)[21]	yes	no	yes	yes	no	no	no	yes	yes	no	no	no	epigastralgia	no	no
24.	Tetsuka et al. (2017)[22]	yes	no	yes	yes	no	no	yes	no	yes	yes	no	no	upper abdominal pain	acute kidney failure	no
25.	Zemple et al. (2017)[23]	yes	yes	yes	yes	no	yes	yes	no	no	no	no	no	no	ventilatory support	no
26.	Sarbu et al. (2019)[24]	yes	yes	yes	yes	no	no	no	no	no	yes	yes	no	no	no	no
27.	Yilmaz et al. (2018)[25]	yes	yes	yes	yes	yes	yes	yes	no	no	yes	no	no	no	no	no
28.	Marcoccia et al. (2019)[26]	yes	no	yes	yes	no	yes	no	yes	yes	yes	no	no	severe epigastric pain	no	no
29.	Kini et al. (2021)[27]	yes	yes	yes	yes	no	no	no	yes	yes	yes	no	no	no	no	no
30.	Ždraljević et al. (2022)	yes	yes	yes	yes	no	yes	no	yes	yes	no	yes	yes	no	no	haematometra

PRES = posterior reversible encephalopathy syndrome; HELLP = hemolysis-elevated liver enzymes-low platelet counts; HTA = hypertension; Pt = platelets.

localizations were occipital (73.3 %) and parietal (56.7 %) lobes. Less frequent changes were detected in basal ganglia (30.0 %), frontal lobe (26.7 %), thalamus (16.7 %), cerebellum (16.7 %), brainstem (13.3 %), and temporal lobe (10.0 %) [10–33]. Three patients (10 %) had a central variant of PRES with isolated involvement of the basal ganglia and brainstem without the involvement of subcortical white matter [17,24,30], which is slightly more than reported in the study by McKinney et al. (4 %) [40], but similar to the results published by Wen et al. (8.3 %) [39]. Five patients (16.7 %) had intracranial hemorrhage [14,20,26], which is in line with previously published studies where the incidence of intracranial hemorrhage in patients with PRES ranged between 9 and 19 % [39–42]. After various periods, control MRI was performed in 60 % of patients and most of them (83.3 %) showed complete resolution of previous findings (Table 1.) [10–33].

3.4. Additional diagnostic procedures

Additional diagnostic procedures were performed occasionally [10–33]. Fundoscopy was performed in 30 % of cases and pathological findings were detected in two-thirds. The most common findings were papilledema with flame-shaped retinal haemorrhages and exudates, followed by macular edema [14,17,18,21,22,24,27,33]. Vision disorders are described in up to 50 % of patients with the most severe hypertensive disorder of pregnancy (eclampsia) and in 25 % with milder disorders. Disorders described in patients with PRES associated with HELLP syndrome correspond to disorders described as part of hypertensive retinopathy occurring in preeclampsia and eclampsia, which do not require specific treatment and resolve spontaneously after delivery [43]. CT or MR angiography was performed in eight cases (26.7 %), and in all cases the findings were normal [10,12,20,21,30–32]. EEG was performed in only five patients (16.7 %), including ours [11,12,23,32]. In two patients the initial EEG showed regional slow waves that disappeared on follow-up [11,12], in one patient epileptic discharges were observed [32], while in an additional two patients, EEG findings were normal [23].

3.5. Treatment

Antihypertensive therapy is the mainstay of treatment because both PRES and HELLP syndrome are associated with hypertensive disorders of pregnancy. The most commonly used antihypertensive drugs were calcium channel blockers (40.0 %), followed by vasodilators (20 %) and alpha-2 adrenergic agonists (10 %), while other antihypertensive drugs were used in 16.7 % of patients [10–33]. Antiedematous therapy was administered to only four patients (13.3 %), including ours [14,15,19]. To treat HELLP syndrome, transfusion of blood products was administered to 11 (36.7 %) patients [10,14,16–18,20,23,24], nine (30 %) patients were treated with corticosteroids [12,14,18,19,21,22,28,29,32], while two (6.7 %) patients underwent plasma exchange [12,22]. No patient previously suffered from epilepsy. However, for the treatment and prevention of seizures, magnesium sulfate was administered in 14 (46.7 %), benzodiazepines in six (20.0 %), phenytoin in four (13.3 %), and phenobarbital in two (6.7 %) patients, while for one patient data on the anticonvulsive therapy are missing [10–33].

3.6. Complications and outcome

Even 40 % of patients had at least one somatic complication (Table 2.). The most frequent somatic complications were respiratory failure (20.0 %) and acute kidney failure (16.7 %), followed by shock (13.3 %) and haematuria (6.7 %). In one patient the presence of pulmonary edema and disseminated intravascular coagulation was noted, while in the other the presence of hepatic infarction was recorded [10–33]. All the listed complications, except for respiratory insufficiency, were previously described in patients with HELLP syndrome with the highest frequency of acute renal failure [4,5]. The occurrence of respiratory failure is described as a complication of PRES due to an altered state of consciousness [4]. Gynecological complications in the form of bleeding were reported in four cases (13.3 %), including ours (Table 2.). The case-fatality rate was 6.7 % (Table 1.) [10–33]. Both reported fatal cases are from India. According to the available data, both patients had respiratory failure that required ventilatory support, while one patient additionally had shock and acute renal failure [20]. Most patients (63.3 %) made a full recovery, two (6.7 %) had permanent visual impairment, and three (10.0 %) were discharged with resolving mild neurological deficit (memory problems in two and loss of sensation on the left side of the face in one), while for four (13.3 %) patients data on potential residual deficits are incomplete (Table 1.) [10–33].

The main limitations of our study are the nature of the case report and the small sample size created by searching the previous reports in the literature, which is why some data that would be valuable for more detailed analysis are missing. Also, there may be reporting bias given that in a series of 6 cases from India, 2 died, while all other individual reports had a positive outcome or some mild neurological deficit. To perform a more detailed analysis, a multicenter registry should be formed in which patients would be prospectively enrolled and monitored. Bearing in mind that both mentioned disorders carry a high risk of complications that can end in death, it is necessary to consider the possibility of their occurrence in all patients with hypertensive disorders during pregnancy to increase the chance of a favourable outcome with timely treatment.

4. Conclusion

PRES associated with HELLP syndrome is a rare third trimester/postpartum complication that usually presents with seizures, altered sensorium, headache, hypertension, and laboratory disorders. PRES should be considered in all patients with HELLP, especially with preeclampsia, and inevitably in patients with eclampsia, neurological symptoms and signs. PRES associated with HELLP syndrome request multidisciplinary neurological, internal and gynecological treatment. If they are recognized and treated in time, in most

cases the recovery is complete. However, caution is required as these patients may develop serious somatic complications and permanent neurological deficits or even fatal outcomes.

CRediT authorship contribution statement

Mirjana Ždraljević: Writing – review & editing, Writing – original draft, Visualization, Resources, Investigation, Conceptualization. **Aleksa Pejović:** Writing – original draft, Resources, Investigation, Conceptualization. **Biljana Jocić- Pivač:** Writing – original draft, Resources, Investigation. **Maja Budimkić:** Writing – original draft, Resources, Investigation. **Dejana R. Jovanović:** Writing – review & editing, Supervision, Conceptualization. **Milija Mijajlović:** Writing – review & editing, Supervision, Resources, Investigation, Conceptualization.

Informed consent statement

Written informed consent was obtained from the patient to use anonymous data in scientific publications.

Ethics statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Ethics Committee of the Neurology Clinic, University Clinical Centre of Serbia (NE 27-23).

Data availability statement

Data regarding the case report are available on request from the corresponding author. However, these data are not publicly available due to privacy or ethical restrictions. Other data included in article/supplementary material is referenced in the article.

Funding

This study was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia (Funding No. 451-03-66/2024-03/200110).

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Milija Mijajlovic and Dejana Jovanovic reports financial support was provided by Ministry of Education, Science and Technological Development of the Republic of Serbia (Funding No. 451-03-66/2024-03/200110). Milija Mijajlovic is an associate editor of the Heliyon journal. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] K. Haram, E. Svendsen, U. Abildgaard, The HELLP syndrome: clinical issues and management. A Review, BMC Pregnancy Childbirth 9 (2009) 8.
[2] U. Abildgaard, K. Heimdal, Pathogenesis of the syndrome of hemolysis, elevated liver enzymes, and low platelet count (HELLP): a review, Eur. J. Obstet. Gynecol. Reprod. Biol. 166 (2) (2013) 117–123.
[3] A. Turgut, O. Demirci, E. Demirci, M. Uludoğan, Comparison of maternal and neonatal outcomes in women with HELLP syndrome and women with severe preeclampsia without HELLP syndrome, J Prenat Med. 4 (3) (2010) 51–58.
[4] L.M. Dusse, P.N. Alpoim, J.T. Silva, D.R. Rios, A.H. Brandão, A.C. Cabral, Revisiting HELLP syndrome, Clin. Chim. Acta 451 (Pt B) (2015) 117–120.
[5] Q. Liu, G.J. Ling, S.Q. Zhang, W.Q. Zhai, Y.J. Chen, Effect of HELLP syndrome on acute kidney injury in pregnancy and pregnancy outcomes: a systematic review and meta-analysis, BMC Pregnancy Childbirth 20 (1) (2020) 657.
[6] R.C. Anderson, V. Patel, N. Sheikh-Bahaei, C.S.J. Liu, A.G. Rajamohan, M.S. Shiroishi, et al., Posterior reversible encephalopathy syndrome (PRES): pathophysiology and NeuroImaging, Front. Neurol. 11 (2020) 463.
[7] R.K. Garg, N. Kumar, H.S. Malhotra, Posterior reversible encephalopathy syndrome in eclampsia, Neurol. India 66 (5) (2018) 1316–1323.
[8] Y. Ando, Y. Ono, A. Sano, N. Fujita, S. Ono, Posterior reversible encephalopathy syndrome: a review of the literature, Intern Med 61 (2) (2022) 135–141.
[9] D.A. Tawati, W.S. Chan, A systematic review of posterior reversible encephalopathy syndrome in pregnant women with severe preeclampsia and eclampsia, Obstet. Med. 16 (4) (2023) 236–241.
[10] S.K. Feske, R.A. Sperling, R.B. Schwartz, Extensive reversible brain magnetic resonance lesions in a patient with HELLP syndrome, J. Neuroimaging 7 (4) (1997) 247–250.
[11] E. Marano, N. Scuteri, G. Vacca, G. Orefice, HELLP syndrome with reversible posterior leukoencephalopathy, Neurol. Sci. 24 (2) (2003) 82–84.
[12] A. Negro, G. Zuccoli, G. Regolisti, S. Mastrangeli, E. Rossi, Reversible posterior leukoencephalopathy associated with postpartum HELLP syndrome, Eur. J. Intern. Med. 16 (4) (2005) 291–293.
[13] A. Morton, S. Higgins, B. Mullins, HELLP, eclampsia and posterior reversible encephalopathy in a young woman with streak ovary syndrome, Aust. N. Z. J. Obstet. Gynaecol. 45 (2) (2005) 173–174.
[14] M.A. Murphy, M. Ayazifar, Permanent visual deficits secondary to the HELLP syndrome, J. Neuro Ophthalmol. 25 (2) (2005) 122–127.
[15] W.X. Peng, M. Nakaii, T. Matsushima, H. Asakura, Atypical case of reversible posterior leucoencephalopathy syndrome associated with puerperal HELLP syndrome, Arch. Gynecol. Obstet. 278 (3) (2008) 269–271.
[16] A.K. Grzesiuk, R. Melo, A.R. Carvalho, Hellp syndrome, reversible posterior leukoencephalopathy syndrome and eclampsia, Arq Neuropsiquiatr 67 (4) (2009) 1103–1105.

[17] B. Vijayalakshmi, F. Sethna, M. Manford, C.C. Lees, Posterior reversible encephalopathy syndrome in a patient with HELLP syndrome complicating a triploid pregnancy, J. Matern. Fetal Neonatal Med. 23 (8) (2010) 938–943.
[18] H.V. Hegde, R.P. Rao, Posterior reversible encephalopathy syndrome (PRES) in a patient of eclampsia with 'partial' HELLP syndrome presenting with status-epilepticus, Curr. Anaesth. Crit. Care 20 (5–6) (2009) 251–253.
[19] B.K. Aygün, Y. Baykuş, S. Berilgen, B. Kavak, H. Celik, B. Güratеş, Posterior Reversible Encephalopathy Syndrome in severe preeclampsia: case report and literature review, J. Turk. Ger. Gynecol. Assoc. 11 (4) (2010) 216–219.
[20] B.S. Paul, S.K. Juneja, G. Paul, S. Gupta, Spectrum of neurological complications in HELLP syndrome, Neurol. India 61 (5) (2013) 467–471.
[21] S.G. Sarmento, E.F. Santana, F.F. Campanharo, E. Araujo Júnior, F.R. Machado, N. Sass, et al., Microcirculation approach in HELLP syndrome complicated by posterior reversible encephalopathy syndrome and massive hepatic infarction, Case Rep Emerg Med 2014 (2014) 389680.
[22] B.V. Maramattom, Anterior ischemic optic neuropathy as a manifestation of HELLP syndrome, Case Rep Crit Care 2014 (2014) 671976.
[23] M.A. Babahabib, I. Abdillahi, F. Kassidi, J. Kouach, D. Moussaoui, M. Dehayni, Posterior reversible encephalopathy syndrome in patient of severe preeclampsia with Hellp syndrome immediate postpartum, Pan Afr Med J. 21 (2015) 60.
[24] S. Ates, R. Kemerdere, O. Sevket, T. Molla, B. Dane, Posterior reversible encephalopathy associated with HELLP syndrome: a case report and review of the literature, Neurol. India 20 (1) (2015) 91–94.
[25] H. Takagi, K. Matsunami, S. Ichigo, T. Katano, A. Imai, A typical case of posterior reversible encephalopathy syndrome associated with postpartum eclampsia-HELLP syndrome, Open J. Obstet. Gynecol. 6 (2016) 355–359.
[26] M. Beker-Acay, S. Unlu, N. Okur, E. Unlu, A. Yucel, Brain MRI findings of a 24-week pregnant woman with HELLP syndrome, Polish Annals of Medicine 23 (1) (2016) 34–38.
[27] H. Takahashi, T. Matsubara, S. Makino, K. Horie, S. Matsubara, Color vision abnormality as the sole manifestation of posterior reversible encephalopathy due to post-partum HELLP syndrome, J. Obstet. Gynaecol. Res. 43 (3) (2017) 592–594.
[28] S. Tetsuka, H. Nonaka, Importance of correctly interpreting magnetic resonance imaging to diagnose posterior reversible encephalopathy syndrome associated with HELLP syndrome: a case report, BMC Med Imaging 17 (1) (2017) 35.
[29] R.P. Zemple, T. Pelleg, M.R. Cossio, An unusual case of posterior reversible encephalopathy syndrome, Clin Pract Cases Emerg Med 1 (3) (2017) 208–211.
[30] M.I. Sarbu, N. Sarbu, Central PRES (posterior reversible encephalopathy syndrome) in HELLP syndrome, Intern Emerg Med 14 (4) (2019) 617–618.
[31] Z. Yılmaz, N. Voyvoda, P.B. Şirinocak, H. Terzi, Association of hemolysis, elevated liver enzymes, low platelets syndrome with posterior reversible encephalopathy and intracranial hypotension, Neurol. India 66 (1) (2018) 226–227.
[32] E. Marcoccia, M.G. Piccioni, M.C. Schiavi, V. Colagiovanni, I. Zannini, A. Musella, et al., Postpartum posterior reversible encephalopathy syndrome (PRES): three case reports and literature review, Case Rep Obstet Gynecol 2019 (2019) 9527632.
[33] A.T. Kini, S. Tabba, T. Mitchell, Othman B. Al, A.G. Lee, Simultaneous bilateral serous retinal detachments and cortical visual loss in the PRES HELLP syndrome, J. Neuro Ophthalmol. 41 (1) (2021) e60–e63.
[34] A.S. Chao, Y.L. Chen, Y.L. Chang, A. Chao, S.Y. Su, T.H. Wang, Severe pre-eclamptic women with headache: is posterior reversible encephalopathy syndrome an associated concurrent finding? BMC Pregnancy Childbirth 20 (1) (2020) 336.
[35] T. Shegekar, S. Pajai, A comprehensive review of pregnancy in sickle cell disease, Cureus 15 (6) (2023) e41165.
[36] D. Jain, P. Atmapoojya, R. Colah, P. Lodha, Sickle cell disease and pregnancy, Mediterr J Hematol Infect Dis. 11 (1) (2019) e2019040.
[37] A. Vargas, F.D. Testai, Posterior Reversible Encephalopathy Syndrome in adult sickle-cell patients: case series and literature review, J. Clin. Neurosci. 70 (2019) 249–250.
[38] K. Haram, E. Svendsen, U. Abildgaard, The HELLP syndrome: clinical issues and management. A Review, BMC Pregnancy Childbirth 9 (2009) 8.
[39] Y. Wen, B. Yang, Q. Huang, Y. Liu, Posterior reversible encephalopathy syndrome in pregnancy: a retrospective series of 36 patients from mainland China, Ir. J. Med. Sci. 186 (3) (2017) 699–705.
[40] A.M. McKinney, J. Short, C.L. Truwit, Z.J. McKinney, O.S. Kozak, K.S. SantaCruz, et al., Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings, AJR Am. J. Roentgenol. 189 (4) (2007) 904–912.
[41] R. Raman, R. Devaramane, G.M. Jagadish, S. Chowdaiah, Various imaging manifestations of posterior reversible encephalopathy syndrome (PRES) on magnetic resonance imaging (MRI), Pol. J. Radiol. 82 (2017) 64–70.
[42] H.M. Hefzy, W.S. Bartynski, J.F. Boardman, D. Lacomis, Hemorrhage in posterior reversible encephalopathy syndrome: imaging and clinical features, AJNR Am J Neuroradiol 30 (7) (2009) 1371–1379.
[43] Samra K. Abu, The eye and visual system in the preeclampsia/eclampsia syndrome: what to expect? Saudi J Ophthalmol 27 (1) (2013) 51–53.