Cranial imaging spectrum in hypertensive disease of pregnancy

S. Topuz¹, I. Kalelioğlu¹, A.C. Iyibozkurt¹, S. Akhan¹, R. Has¹, M. Tunaci², L. İbrahimoğlu¹

¹Department of Obstetrics & Gynecology and ²Department of Radiology, Istanbul University, Istanbul School of Medicine (Turkey)

Summary

Objective: To determine cranial imaging findings in patients with severe preeclampsia, eclampsia and HELLP syndrome and the correlation between these findings and neurological symptoms. *Materials and Methods:* CT or MRI findings of 120 patients diagnosed with severe preeclampsia, eclampsia and/or HELLP syndrome between January 1998 and December 2005 are presented. *Results:* Pathological imaging findings were observed in 28.1% (n = 32) of the severe preeclampsia group, in 43.3% (n = 30) of the HELLP group, in 51.35% (n = 27) of the eclampsia group and in 61.9% (n = 21) of the eclampsia + HELLP group and in 45% of all patients. Thirty-five patients had specific pathology defined as ischemic lesions, edema, and perivascular microhemorrhage. Infarcts were found in seven, intracranial hemorrhage in seven, hydrocephaly in two, dural sinus thrombosis in two and a pineal cyst in one patient. Specific lesions were generally located in the posterior parietal and occipital lobes. Five patients died due to intracranial hemorrhage and one patient due to septic shock. *Conclusion:* A wide imaging spectrum from the ischemic lesion to severe intracranial hemorrhage can be detected in complicated cases of hypertensive diseases of pregnancy. It is essential to perform cranial imaging in patients with symptoms and neurological deficits.

Key words: Imaging spectrum; Pregnancy; Hypertensive disease.

Introduction

Severe preeclampsia, eclampsia and HELLP syndrome are complicated forms of pregnancy-induced hypertension with an incidence of 5-10% of pregnant wome [1, 2]. Intracranial complications are the leading causes of maternal mortality and morbidity. Early diagnosis improves prognosis in patients with neurological symptoms. Clinical studies have indicated that intracranial pathologies are not rare, particularly in preeclamptic patients (3, 4). However, there were no studies comparing the cranial pathologies in severe preeclampsia, eclampsia and HELLP syndrome and correlations between cranial pathologies and symptoms have not been investigated before.

In the present study, we aimed to investigate cranial imaging findings of hypertensive disease during pregnancy and whether there were differences in spectrum and incidence of lesions.

Materials and Methods

Between January 1998 and December 2005, 120 patients who underwent computed tomography (CT) and/or magnetic resonance imaging (MRI) with a diagnosis of severe preeclampsia, eclampsia or HELLP syndrome at the Department of Obstetrics and Gynecology, Istanbul School of Medicine were included in the study. Symptoms of the patients were recorded and all patients were examined by a neurologist. Patients were grouped as Group 1 (n = 32) severe preeclampsia, group 2 (n = 30) HELLP syndrome, group 3 (n=37) eclampsia and group 4 (n = 21) eclampsia with HELLP syndrome. All patients were examined carefully by a neurologist and cranial imaging was performed for clinically suspicious cases. MRI was performed in 48 patients and CT in 72 patients. Cranial imaging was performed within the first 24 hours in patients with eclampsia, and within the first 48 hours of diagnosis in other cases. Contrast medium was not used in any of the patients. The neuroradiologist who evaluated the radiograms was blinded to clinical details.

Results of the following laboratory tests were recorded at admittance: complete blood count, transaminase levels and coagulation parameters. Patients with intracranial hemorrhage were compared with the others regarding age, gestational age, symptoms, neurological findings, platelet count, transaminase levels and coagulation parameters.

The study was designed prospectively. Fisher's exact chisquare, Student's t and one-way ANOVA tests were used in statistical analyses. Level of statistical significance was defined as a p value of less than 0.05.

Results

Characteristics such as age, gestational age, parity, blood pressure values at admittance, clinical symptoms and pathological imaging findings for all groups are summarized in Table 1.

Imaging findings were evaluated as normal in 66 (55%) patients. Among the other 54 (45%) patients, the pathological findings were as follows: specific lesions which could be evaluated as edema, ischemic lesions or petechial hemorrhage in 35 (29.2%) cases; intracranial hemorrhage in seven (5.8%) cases; infarcts in seven (5.8%) cases; hydrocephaly in two (1.6%) cases; dural sinus thrombosis in two (1.6%) cases; and pineal cyst in one (0.8%) case. Distribution of findings according to the groups is shown in Table 2. The ratio of patients who had

Revised manuscript accepted for publication June 1, 2007

SPE	$\begin{array}{l} \text{HELLP} \\ (n = 30) \end{array}$	Eclampsia	H+E	p	All groups
(n = 32)		(n = 37)	(n = 21)	value	(n =120)
27.4 ± .13	28.3 ± 9.43	26.7 ± 4.19	27.3 ± 6.36	0.629	27.56 ± 5.78
(19-44)	(19-39)	(18-39)	(19-37)		(18-44)
32.52 ± 4.11	32.95 ± 5.73	32.80 ± 4.50	33.6 ± 5.34	0.945	32.9 ± 4.49
(24-40)	(25-40)	(19-39)	(24-40)		(19-40)
166.52 ± 23.08	163.18 ± 16.7	164.03 ± 28.70	161.33 ± 19.22	0.167	164.01 ± 22.6
(140-230)	(140-200)	(140-280)	(140-210)		(140-280)
104.34 ± 15.61	107.27 ± 2.41	103.46 ± 15.47	108 ± 18.20	0.732	105.46 ± 15.15
(60-130)	(90-130)	(80-160)	(90-160)		(60-160)
1.34 ± 1.64	1.22 ± 1.06	1.19 ± 1.29	1.13 ± 1.18	0.965	1.22 ± 1.16
(0-5)	(0-6)	(0-5)	(0-7)		(0-7)
9/32:28.1%	13/30:43.3%	19/37:51.35%	13/21:61.9%	0.033	54/120:45%
	$\begin{array}{c} \text{SPE} \\ (n = 32) \end{array}$ $\begin{array}{c} 27.4 \pm .13 \\ (19-44) \\ 32.52 \pm 4.11 \\ (24-40) \\ 166.52 \pm 23.08 \\ (140-230) \\ 104.34 \pm 15.61 \\ (60-130) \\ 1.34 \pm 1.64 \\ (0-5) \\ \end{array}$	$\begin{array}{c ccccc} & \text{SPE} & \text{HELLP} \\ (n = 32) & (n = 30) \\ \hline \\ 27.4 \pm .13 & 28.3 \pm 9.43 \\ (19-44) & (19-39) \\ 32.52 \pm 4.11 & 32.95 \pm 5.73 \\ (24-40) & (25-40) \\ 166.52 \pm 23.08 & 163.18 \pm 16.7 \\ (140-230) & (140-200) \\ 104.34 \pm 15.61 & 107.27 \pm 2.41 \\ (60-130) & (90-130) \\ 1.34 \pm 1.64 & 1.22 \pm 1.06 \\ (0-5) & (0-6) \\ \hline \\ 9/32:28.1\% & 13/30:43.3\% \\ \end{array}$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

Table 1. — Characteristics of severe preeclampsia (SPE), HELLP syndrome, eclampsia and eclampsia + HELLP syndrome (H+E) patients.

Table 2. — Distribution of imaging findings according to groups.

	Severe Preeclampsia (n = 32)	HELLP syndrome (n = 30)	Eclampsia (n = 37)	HELLP + eclampsia (n = 21)	All groups (n = 120)	Ratio (%)	
Normal	23	17	18	8	45	55	
Specific finding	gs 7	8	14	6	35	29.16	
Intracranial							
hemorrhage	-	2	2	3	7	5.8	
Infarct	2	2	1	2	7	5.8	
Hydrocephaly	-	-	1	1	2	1.6	
Dural sinus							
thrombosis	-	1	-	1	2	1.1	
Pineal cyst	-	-	1	-	1	1.6	
Number of patients							
with patholog	ical						
finding	9	13	19	13	54	45	
Ratio of patient	s						
with pathological							
findings (%)	28.1	43.3	51.35	61.9	45		

pathological imaging findings was 28% in the severe preeclampsia group, 43.3% in the HELLP group, 51.5% in the eclampsia group and 61.9% in the eclampsia with HELLP group and there was a statistically significant difference between groups (p = 0.033).

Specific lesions were mostly in the posterior parietal and occipital lobes, temporal and frontal lobes and basal ganglia, in the cortex, white-gray matter intersection, subcortical white matter or in deep white matter. These lesions were seen as hypodense areas in CT, hypo or isointense foci in T1-weighted MRI sequences, but hyperintense foci in T2-weighted sequences.

Intracranial hemorrhage was observed in seven patients and five of these died. The patients who survived were operated on and discharged from the hospital with right hemiplegia and total aphasia. In all patients with intracranial hemorrhage the main symptom was sudden loss of consciousness (Table 3). When these patients were compared with those without intracranial hemorrhage, blood pressure at admittance, age, transaminase levels, symptom and neurologic finding ratio and FDP values were higher, and gestational age, platelet count and fibrinogen levels were lower (Table 4). Patients with intracranial hemorrhage had elevated PT and APTT values, although no significant difference between the groups was found (p > 0.005).

Clinical prognoses of patients were followed, but no imaging examination was needed except in two patients. One hundred and twelve (93%) patients were discharged as healthy without neurological symptoms; two patients with intracranial hemorrhage who underwent surgery were discharged with sequels. Five patients died of intracranial hemorrhage, and one patient died due to septic shock despite normal imaging findings. The general mortality rate was 5%.

Discussion

Neurological complications of hypertensive disease in pregnancy might be fatal [6]. With the use of high resolution CT and MRI, both major life-threatening pathologies and minor pathologies which do not alter clinical prognosis can be determined in early stages [2, 4]. Results of recent studies on the subject have differed. Sibai and colleagues [5] reported that the incidence of pathological imaging findings in 20 patients with atypical eclampsia was 0%, while Richard *et al.* [2] reported the incidence in 192 patients with eclampsia as 75%; Digre and colleagues [6] in 16 patients with severe preeclampsia as 50%. Our study was important since these four groups of patients were compared.

In the present study, no significant differences were found among severe preeclampsia, eclampsia, HELLP syndrome and eclampsia with HELLP syndrome groups regarding age, gestational age, parity and blood pressure at admittance (p > 0.05). On the other hand, increases in pathological imaging findings were significant (p < 0.05). If the diseases described above were evaluated as the stages of the same disorder, it may be concluded that in parallel to the severity of the disease, symptoms and cranial pathologies tended to increase.

Within the spectrum of pathological imaging findings

Diagnosis	Age (yrs)	Gestational age (years)	Complaint	Blood pressure (mmHg)	Hemorrhage localization	Prognosis
Eclampsia with HELLP syndrome	37	24	LOC	210/160	In white matter at right parieto- occipital area $(8 \times 7 \times 4 \text{ cm})$ and in brainstem $(2 \times 3 \text{ cm})$	Died on 5^{th} day
Eclampsia with HELLP syndrome+ oligo-hydramnios	27	38	LOC	180/100	In left parietal lobe (7 x 3 cm)	Operated, right hemiplegic and totally aphasic
HELLP syndorme	34	28	LOC	190/120	In left parietal lobe (4 x 5 cm) and also in the liver	Died on 6 th day
Eclampsia with type II diabetes	39	28	LOC	280/160	In left putamen (5x5 cm) which flowed to the 3rd ventricle	Died on 5 th day
HELLP syndrome	30	26	LOC	180/100	Originated from the brainstem and flowed to the 3 th , 4 th and arterial ventricles	Died on 4 th day
Eclampsia with HELLP syndrome	32	24	LOC	220/130	Brain stem and in the left parieta-occipital area	Died on 4 th day
HELLP syndrome	34	28	LOC	200/110	Left parietal lobe	Operated, discharged with right hemiplegy

Table 3. — Characteristics of patients with intracranial hemorrhage.

Table 4. — Comparing of patients with and without intracranial hemorrhage regarding age, gestational age, blood pressure, symptoms, neurological findings and laboratory values.

	Patients with intracranial hemorrhage (n = 7)	Patients without intracranial hemorrhage (n = 113)	p value
Age	33.5 ± 4.85	27.28 ± 5.62	0.014
Gestational age	28.7 ± 4.80	33.41 ± 4.71	0.032
Systolic blood pressure	209.27 ± 43.18	160.41 ± 19.15	0.0001
Diastolic blood pressure	129.32 ± 28.45	105.12 ± 13.65	0.0003
Symptom (%)	100 (7/7)	56 (64/113)	0.0240
Neurological finding (%)	100 (7/7)	39 (45/113)	0.0170
Platelets	67.200 ± 34.800	180.540 ± 55.730	0.0002
SGOT (U/l)	145.63 ± 70.42	46.65 ± 17.42	0.0001
SGPT (U/I)	135.26 ± 45.62	46.43 ± 11.98	0.0001
PT	16.25 ± 4.86	12.9 ± 5.01	0.223
APTT	36.32 ± 6.15	30.12 ± 6.50	0.0723
Fibrinogen (mg/dl)	270.95	375.66 ± 70.31	0.0017
FDP (µ/ml)	45.57 ± 8.65	31.70 ± 8.30	0.0018

due to complications of hypertension during pregnancy, intracranial hemorrhage, diffuse cerebral edema, infarcts, hydrocephaly, dural sinus thrombosis and some other specific lesions have been observed [6, 9-11]. The disturbance patterns of lesions observed in the present study were in accordance with the literature, but no diffuse cerebral edema was seen in any of our cases. In addition, pathologes such as pineal cyst (in one patient) and hemorrhagic infart (in one patient) not related to pregnancy were observerd.

The specific lesions affecting mostly the middle and posterior cerebral artery perfusion areas were thought to represent hypoxic brain damage, perivascular hemorrhage, perivascular microinfarcts, and particularly edema [12]. Specific lesions are generally reversible and do not affect the patient's prognosis [9, 10]. Occipital and parietal lesions were mostly bilateral and symmetrical, whereas temporal lobe, frontal lobe and basal ganglia lesions were infrequently bilateral and generally asymmetrical. The reason for the predominant involvement of the posterior circulation areas is not clear, but it has been reported that the vessels which supply posterior circulation have less sympathetic innervations than those of anterior circulation and therefore the permeability of these vessels increases due to the loss of autoregulation during hypertensive attacks [13-16].

Intracranial hemorrhage is the most severe complication in hypertensive complications of pregnancy and it usually causes sequels in surviving patients [11, 17]. In the present study, seven (5.8%) patients had intracranial hemorrhage; five of these died and the other two patients lived with hemiplegy and total aphasia. In these patients, several common features were observed. The diagnosis of these seven patients was not only preeclampsia but it was also complicated by eclampsia or HELLP syndrome [HELLP syndrome (n = 2), HELLP + eclampsia (n = 3), eclampsia (n = 2)]. Hemorrhage localization of the patients who did not survive was in the brainstem or it flowed to the ventricles. In one patient hepatic intraparenchymal hematoma was determined. The loss of consciousness developed suddenly in all patients with intracranial hemorrhage, and death occurred between four and six days. When compared with the patients without intracranial hemorrhage, these patients were significantly older and had higher blood pressure at admittance, and lower gestational age. As a consequence, we thought that high blood pressure, older maternal age and younger gestational age increased the severity of preeclampsia and therefore, risk for intracranial hemorrhage.

It was reported in the literature that MRI was superior to CT to determine intracranial pathologies due better contrast and resolution in the images [6, 18, 19]. Although CT was the first method to diagnose acute hemorrhage, it was stated that MRI was more sensitive to demonstrate chronic and subacute small residual hemorrhage.

We believe that cranial imaging should be performed in selected patients with neurological findings and undetermined clinical status. No imaging examinations are needed in asymptomatic patients or patients without any neurological findings, since such cranial lesions are temporary and reversible, and there is no specific therapy for these lesions. Patient symptoms should be questioned and neurological examination is required for symptomatic patients. Patients with severe symptoms such as loss of consciousness, confusion, loss of motor power or focal neurological findings should be examined immediately with CT to mainly diagnose any hemorrhage. MRI should be reserved for patients with a stable clinical situation or for patients with persistent symptoms despite normal CT findings.

Acknowledgement

The first part of this study with 86 patients was presented at 7^{th} the Turkish-Hellenic Obstetrics; Maternal-fetal Medicine & Perinatology Congress in Istanbul in 17-20 April 2002 and published in the Turkish Journal of Gynecology and Obstetrics.

References

- Porapakkham S.: "An epidemiologic study of eclampsia: Observation from 67 recent cases". *Obstet. Gynecol.*, 1979, 58, 609.
- [2] Richards A.M., Moodley J., Graham D.I., Bulock M.R.R.: "Active management of the unconscious eclamptic patient". Br. J. Obstet. Gynaecol., 1986, 93, 554.
- [3] Lopez-Lera M., Liares M.R., Hernandez H.: "Maternal mortality rates in eclampsia". Am. J. Obstet. Gynecol., 1976, 124, 49.

- [4] Barton J.R., Sibai B.M.: "Cerebral pathology in eclampsia". P. 891. In: Sibai B.M. (ed.): Clinics in Perinatology. Philadelphia, WB Saunders, 1991.
- [5] Sibai B.M., Spinnato J.M., Watson D.L., Anderson G.D.: "Eclampsia. IV. Neurologic findings and future outcome". Am. J. Obstet. Gynecol., 1985, 152, 184.
- [6] Digre K.B., Varner M.W., Osborn A.G., Crawford S.: "Cranial magnetic resonance imaging of in severe preeclampsia versus eclampsia". Arch. Neurol., 1993, 50, 399.
- [7] Gutierrez-Garcia J.M., Carreres A.: "Brain stem involvement in eclampsia and HELLP syndrome". *Rev. Neurol.*, 1999, 28, 1162-6.
- [8] Beck D.W., Menezes A.H.: "Intracerebral hemorrhage in a patient with eclampsia". J. Am. J. Obstet. Gynecol. Med. Assoc., 1981, 246, 1442.
- [9] Brown C.E.L., Purdy P., Cunningham F.G.: "Head computed tomography scans in women with eclampsia". Am. J. Obstet. Gynecol., 1988, 159, 915.
- [10] Sanders T.G., Cayman T.A., Sanches-Ramos L. et al.: "Brain in eclampsia: MR imaging with clinical correlation". *Radiology*, 1991, 180, 475.
- [11] Richards A., Graham D., Bullock R.: "Clinopathological study of neurological complications due to hypertensive disorders of pregnancy". J. Neurol., Neurosurg. Psychiatry, 1988, 51, 416.
- [12] Sheehan H.L., Lynch J.B.: "Pathology of pregnancy". Baltimore, Williams & Wilkins, 1973.
- [13] Beausang-Linder M., Bill A.: "Cerebral circulation in acute arterial hypertension-protective effects of sympathetic nervous activity". Acta Physiol. Scand., 1981, 111, 193.
- [14] Schwartz R.B., Jones K.M., Kalina P., Bajakian R.L., Montello M.D., Grada B., Holman B.L.: "Hypertensive encephalopathy: findings on CT, MR imaging, and SPECT imaging in 14 cases". Am. J. R., 1992, 159, 379.
- [15] Lamy C., Oppenheim C., Meder J.F., Mas J.L.: "Neuroimaging in posterior reversible encephalopathy syndrome". J. Neuroimaging, 2004, 14, 89.
- [16] Covarrubias D.J., Luetmer P.H., Campeau N.G.: "Posterior reversible encephalopathy syndrome: prognostic utility of quantitative diffusion weighted MR images". A.J.N.R. Am. J. Neuroradiol., 2002, 23, 1038.
- [17] Drislane F.W., Wang A.: "Multifocal cerebral hemorrhage in eclampsia and severe pre-eclampsia". J. Neurol., 1997, 244, 194.
- [18] Dahmus M.A., Barton J.R., Sibai B.M.: "Cerebral imaging in eclampsia: magnetic resonance imaging versus computed tomography". Am. J. Obstet. Gynecol., 1992, 167, 935.
- [19] Friese S., Fetter M., Küker W.: "Extensive brainstem edema in eclampsia: diffusion weighted MRI may indicate favorable prognosis". J. Neurol., 2000, 247, 465.

Address reprint requests to: S. TOPUZ, M.D. Erzurum Sitesi, Palandöken Sk. Yazıcı Apt. No:14/1 Daire 4, Altunizade-Istanbul (Turkey) e-mail: samettopuz@yahoo.com