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Evaluation of placental pathologies in cases of placenta previa
Plasenta previa olgularında plasenta patolojilerinin değerlendirilmesi

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ÖZ

Amaç: Çalışmamızın birincil amacı, plasenta previanın (PP) altında yatan plasental patolojileri değerlendirmektir.

Gereçler ve Yöntem: Üçüncü basamak bir merkezde PP tanısı alan hastaların iki yılı aşkın verileri retrospektif olarak edinildi. Rutin olarak, PP tanısı konulan hastaların plasentaları patolojik incelemeye gönderilir. Hastaların klinikodemografik verileri kaydedildi. Plasental patolojik bulgular maternal vasküler lezyonlar, fetal vasküler lezyonlar, inflamatuar durumlar, umbilikal kord bulguları ve normal olmak üzere 5 ana grupta sınıflandırılıp değerlendirildi. Ayrıca hastaların hastaneye yatış anındaki tam kan sayımı sonuçları ve yenidoğan sonuçları kaydedildi.

Bulgular: Çalışmaya PP tanısı alan 32 hasta dahil edildi. Medyan yaş 34 (22-42), medyan gravida 3 (1-6) idi. PP hastalarının yaklaşık yarısında patolojik bulgu olarak maternal vasküler lezyonlar izlendi (43.75 %). Sırasıyla 10 hastada (32.25 %) enflamasyon, 8 hastada (25.0 %) umbilikal kord bulguları ve 2 hastada (6.25 %) fetal vasküler lezyon gözlendi. 3 hastada normal plasenta olduğu bildirildi. Ayrıca hastaların medyan nötrofil, nötrofil lenfosit oranı ve beyaz küre sayımı hastaneye yatış anında yüksek bulundu.

Sonuç: Maternal vasküler lezyonlar ve inflamasyon, PP hastalarında en sık saptanan plasental patolojik raporlardı. Ancak komplike olmayan gebeliklerin plasentalarını da içeren çalışmalar patolojik durumu fizyolojik durumdan ayırt etmek için literatüre ışık tutacaktır.

Anahtar kelimeler: Plasenta previa, patoloji, maternal vasküler lezyonlar, inflamasyon

ABSTRACT

Objective: The primary aim of our study was to evaluate the underlying placental pathologies of placenta previa (PP).

Materials and Methods: Over two years data of patients diagnosed to be PP in a tertiary center were obtained retrospectively. Routinely, the placentas of patients diagnosed to be PP were sent for pathological examination. Clinicodemographic data of the patients were recorded. The placental pathological findings were classified and evaluated in 5 main groups: maternal vascular lesions, fetal vascular lesions, inflammatory situations, umbilical cord findings, and normal. Additionally, complete blood count results at admission time for hospitalization and the outcomes of the neonates were recorded.

Results: Thirty-two patients diagnosed to be PP were included in the study. The median age was 34 (22-42), and the median gravidity number was 3 (1-6). Maternal vascular lesions were observed in nearly half of the PP patients as a pathological finding (43.75 %). Inflammation was observed in 10 patients (31.25 %), umbilical cord findings in 8 patients (25.0 %), and fetal vascular lesions in 2 patients (6.25 %), respectively. 3 patients were reported to have normal placentas. In addition, the median neutrophile, neutrophile lymphocyte ratio, and white blood count were found to be high at admission time for hospitalization

Conclusion: Maternal vascular lesions and inflammation were the most common detected placental pathological reports in PP patients. However, studies including the placentas of uncomplicated pregnancies will shed light on the literature to distinguish the pathological condition from the physiological condition.

Keywords: Placenta previa, pathology, maternal vascular lesions, inflammation

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INTRODUCTION

Placenta previa (PP) is the situation in which the placenta extends over the cervix uteri partially or completely. It is usually detected while performing detailed ultrasonography around 20 weeks of gestation (1). The incidence of PP has increased with raising cesarean section (CS) rates worldwide, occurring in up to 0.5 % of pregnancies (2). It is associated with life-threatening complications such as bleeding and hysterectomy, as well as fetal complications such as intrauterine growth restriction (IUGR) (3). The most known and proven risk factors of PP are previous PP and CS (4).

Studies have examined placental disorders in patients with the placenta accreta spectrum (5). Patients with recurrent adverse pregnancy outcomes were also examined as to chronic inflammation in the placental specimens (6). Furthermore, placental pathologies were examined to determine the effect of PP on the growth of the fetus and also the pregnancy outcomes (7).

PP is thought to be due to previous surgeries resulting in insufficient vascularization of the decidual areas. Thus, that promotes trophoblast implantation, and additionally, the trophoblasts grow into the lower uterine cavity (8). Yet, the underlying pathogenesis is still not clear. On that account, the primary aim of our study was to evaluate the underlying placental pathologies of PP.

MATERIALS AND METHODS

Approval was obtained from the institutional review board (E2-22-2196). Patients diagnosed to be PP in a tertiary center were obtained retrospectively from the data of the hospital. Over a 2 years data were included.

The diagnosis of PP was made by transvaginal ultrasonography and was confirmed in the third trimester by perinatologists. While performing ultrasonography, the bladders were emptied. If the distance between the cervical os and the edge of the placenta was <20 mm but not over the internal os, the placenta was considered as low lying placenta and was excluded from the study. In addition, patients delivered <32nd gestational weeks, fetal structural anomalies, multiple pregnancies, smokers, patients using drugs else than multivitamins and antianemics, and patients with chronic illnesses were excluded from the study. Patients who have undergone hysterectomy were also excluded.

Age, gravidity, parity, gestational age at the time of delivery, body mass index (BMI) were recorded as to the study data. Moreover, complete blood counts (CBC) at admission time for hospitalization were recorded. The birth weights, APGAR scores, cord blood pH, head circumference, and the height of the neonates were recorded.

Routinely, the placentas of patients diagnosed to be PP, were sent for pathological examination. The pathologists were blinded as the study was held retrospectively. The pathological evaluation of the placentas were classified as to previous studies (7, 9). The placental pathological findings were classified and evaluated in 5 main groups as maternal vascular lesions (placental hemorrhage, acute atherosis, fibrin deposition increase, villous agglutination, villous hypoplasia and infarct), fetal vascular lesions (chorionic plate and stem villous vessels thrombosis, avascular villi), inflammatory situations such as chorioamnionitis, umbilical cord findings (hypo/hyper coiling, abnormal cord insertion), and normal.

Statistical Analysis

SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Kolmogorov- Smirnov analysis was used to evaluate the normal distribution of continuous variables. Whereas mean ± standard deviation was used to show the nominal data with normal distribution, median (min-max) was used to show the non-normal distributed nominal data. Numbers (n) and percentages (%) were used to show the categorical data.

RESULTS

Thirty-two patients diagnosed to be PP were included in the study. All the PP patients have undergone CS. In Table 1, the clinicodemographic and CBC parameters of PP patients at the time of admission to the hospital were shown. The median age was 34 (22-42), the median gravidity number was 3 (1-6), and the average BMI was 28.7 ± 2.79. The median Hemoglobin level was 10.5 (8.6-12.7) g/dL. As Hemoglobin < 11 g/dL is known and accepted to be anemia during 3rd trimester of pregnancy (10), our study group can be considered as anemic. Additionally, the median neutrophile level was 19.67 (8.73-21.14) $x10^9$/L, and the median neutrophile lymphocyte ratio (NLR) was 9.32 (3.87 -13.38) and high. Also, the median white blood count (WBC) of the patients was 18.34 $x10^9$/L at admission time for hospitalization (Table 1).

Table 1. Clinicodemographic characteristics and complete blood count parameters of placenta previa

Variables	Placenta previa (n:32)
Age (year)	34 (22-42)
Gravidity (n)	3 (1-6)
Parity (n)	1 (0-5)
BMI (kg/m^2)	28.7 ± 2.79
Basophil (x10^9/L)	0.01 (0.01-0.04)
Basophil (%)	0.1 (0.0-0.3)
Eosinophil (x10^9/L)	0.04 (0.03-0.20)
Eosinophil (%)	0.3 (0.2-1.6)
Hematocrit (%)	33 (25.8-37.1)
Hemoglobin (g/dL)	10.5 (8.6-12.7)
Luc (x10^9/L)	0.09 (0.06-0.16)
Luc (%)	0.4 (0.2-1.2)
Lymphocyte (x10^9/L)	1.47 (0.96-2.54)
Lymphocyte (%)	6.6 (5.4-18.3)
Mch (pg/cell)	25.1 (21.8-31.7)
Mchc (g/dL)	32.8 (31.2-34.1)
Mcv (fL)	78.9 (69.2-92.9)
Monocyte (x10^9/L)	0.86 (0.45-1.09)
Monocyte (%)	3.9 (2.8-7.9)
Mpv (fL)	10.0 (6.8-11.3)
Neutrophile (x10^9/L)	19.67 (8.73-21.14)
Neutrophile (%)	88.9 (71.0-92.4)
Pdw (%)	63.7 (52.4-71.6)
Platelet (x10^9/L)	284 (146-330)
Rbc (x10^{12}/L)	4.08 (3.66-4.18)
Rdw (%)	14.14 ± 0.19
WBC (x10^9/L)	18.34 (11.03-22.10)
NLR	9.32 (3.87 -13.38)

BMI: Body mass index, Luc: large unstained cells, Mch: mean corpuscular hemoglobin, Mchc: mean corpuscular hemoglobin concentration, Mcv:mean corpuscular volume, Mpv: mean platelet volume, Pdw: platelet distribution width, Rbc: red blood cell, Rdw: red cell distribution width, WBC: white blood cell, NLR: neutrophile lymphocyte ratio
Values were presented as mean±standard deviation and median (min-max).

Table 2. Placental pathology evaluation results

Variables	Placenta previa (n:32)
Maternal vascular lesions	14 (43.75)
Fetal vascular lesions	2 (6.25)
Inflammation	10 (31.25)
Umbilical cord findings	8 (25.00)
Normal	3 (9.37)

Values were presented as number (%).
n: number
*Some patients were included in more than one pathological classification group.

In Table 3, the data of the neonates were shown. The median gestational age at birth was 34 (32-37) weeks. The median APGAR scores at 1st and 5th minutes were 7 (4-7) and 8 (6-9), respectively.

Table 3. Perinatal outcomes

Variables	Placenta previa (n:32)
Gestational age at birth (week)	34 (32-37)
Birth weight (grams)	2372±358
APGAR 1	7 (4-7)
APGAR 5	8 (6-9)
Head Circumference (cm)	33.5±2.27
Height (cm)	44.7±3.6
Cord pH	7.29 (7.18-7.36)

Values were presented as mean±standard deviation and median (min-max).

Maternal vascular lesions were observed in nearly half of the PP patients as a pathological finding (43.75 %). Inflammation was observed in 10 patients (31.25 %), umbilical cord findings in 8 patients (25.0 %), and fetal vascular lesions in 2 patients (6.25 %), respectively. 3 patients were reported to have normal placentas (Table 2).

DISCUSSION

In this study we evaluated the underlying placental pathologies of PP. Maternal vascular lesions were observed in almost half of the PP patients. Inflammation was observed in more than 30 percent of the patients. Umbilical cord findings were observed in 25.0 % of the patients. The median neutrophile level, NLR, and WBC of the patients were found to be higher than the normal thresold.

Although studies have examined placental pathologies to de-

termine the effect of the placenta on the pregnancy outcomes in patients with recurrent adverse pregnancy outcomes and placenta accreata spectrum (5-7), to our knowledge, this is the first study to evaluate the placental pathologies in PP patients.

In the study conducted by Dutta et. al., 10 patients who have undergone peripartum hysterectomy due to abnormal placentation and hemorrhage were evaluated. Histopathologically, 4 patients were reported to have placenta accreta, 4 patients were reported to have placenta increta, and 2 patients were reported to have placenta percreta (5). Although excluded from the study, peripartum hysterectomy was performed in 16 patients in our hospital during the study period and the most common pathological finding was maternal vascular lesions including placental hemorrhage, congestion, fibrin deposition increase, and villous degeneration.

Fibrin depositions which were evaluated under maternal vascular lesions were reported to be found with an increasing rate as the gestational age increases and it was reported to be a physiological finding in term placentas (11, 12). It was thought to occur as a response to trophoplast injury (13). This may be the reason why maternal vascular lesions were detected most frequently in the pathology reports in our study.

In a systematic review, adverse pregnancy outcomes such as miscarriages, severe IUGR, fetal death were attributed to placental inflammatory pathological disorders (6, 14). In the review it was stated that, chronic inflammatory placental pathologies were also in association with a significant risk of recurrence. However, it was also reported that chronic villitis was detected in almost one of three patients' placentas and most of the patients had normal clinical outcomes (15). In our study, inflammation was observed in 31.25 % of the placentas concurrent with this study. We think that the inflammatory process may lead to adhesion disorders of the placenta. Additionally, the median WBC of our patients was 18.34 $x10^9$/L. During pregnancy, WBC values vary in trimesters. In pregnant women, the upper limit is generally accepted as 15.00 $x10^9$/L (16). However, WBC increases in the last trimester of pregnancy and although it is observed to be 10.00- 16.00 $x10^9$/L at the time of delivery, the studies also have shown that the WBC level increases up to 29.00 $x10^9$/L (17, 18). Therefore, it is difficult to determine whether the increase in WBC is associated with the relatively high rate of detected inflammation of pathological examination of placentas, or a physiological increase. The accompanying high neutrophil level and NLR was observed in the current study. And, a NLR level > 9 was shown to be in association with moderate inflammation and stress (19). Perhaps, the presence of inflammation in the placental site in the early period of pregnancy, defective trophoblast invasion in this site, and then placentation disorders may have developed one after the other.

As to the timing of delivery in PP patients, it is reported and recommended in the literature that the delivery should be planned between 36- 37 6/7 weeks for PPs who do not have obstetic or bleeding complications (20). In our hospital, delivery is planned for PP patients whose labor actively started, non-reassuring non-stress test combined with a low biophysical profile, and active vaginal bleeding. In our study, the median birth week was 34 (32-37) weeks in accordance with the literature mentioned above. We owe this result to working in a tertiary center, teamwork, and close follow-up.

To our knowledge, the placental pathological findings of PP patients have not been studied before. Therefore, we think our study can contribute to the literature. Our hospital is a referral center and PP cases are referred to the Perinatology Clinic of our hospital from all over the country. However, we have some limitations. Placentas were not sent for pathological evaluation in normal uncomplicated pregnancies. Therefore, it is difficult to compare the true prevalence and say how valid our findings are in clinical use and to distinguish the pathological condition from the physiological condition. In addition, we don't have a placental pathologist in our hospital, which can be considered another limitation of the study.

CONCLUSION

In conclusion, maternal vascular lesions and inflammation were the most common detected placental pathological reports in PP patients. However, studies including the placentas of uncomplicated pregnancies will shed light to the literature to distinguish the pathological condition from the physiological condition.

Conflict of interest

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