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CLINICAL ARTICLE

Obstetrics

Pregnancy outcomes in patients with portal cavernoma: A case series study

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Abstract

Objective: Non-cirrhotic portal vein cavernoma (PVC) is a cause of portal hypertension (PH) frequently affecting women of childbearing age. Cavernous transformation of the portal vein is frequently associated with prothrombotic disorders and often entails multiple hemodynamic changes, porto-collateral shunt development and thrombopenia, all of which can affect the course of pregnancy. Our aim was to evaluate the risk of PH-related complications and pregnancy outcomes in patients with PVC.

Methods: Retrospective case series study of patients with PVC undergoing pregnancy in a tertiary care hospital.

Results: Eight pregnancies fulfilled the eligibility criteria. All patients had a predisposing factor for PVC. One episode of variceal bleeding was reported at week 28. Six cesarean sections were scheduled to avoid labor while two urgent surgeries were indicated due to fetal distress and intrauterine growth restriction (IUGR). In all but one case, anticoagulation was prescribed after delivery. No hemorrhagic or thrombotic complications were reported. There were four cases of IUGR with no case of miscarriage or stillbirth.

Conclusion: Pregnancy in patients with PVC has an overall favorable outcome albeit a higher risk of PH-derived complications, and IUGR may be expected. Hence, PVC must not be considered a contraindication for pregnancy although larger prospective studies are necessary.

KEYWORDS
portal cavernoma, portal hypertension, portal vein thrombosis, pregnancy

1 | INTRODUCTION

Non-cirrhotic portal vein thrombosis (NCPVT) is a rare disease with an estimated incidence of 3.8/100.000 people, 25% of whom are women of childbearing age.[1] NCPVT may develop acutely or it can have a chronic course frequently progressing to portal vein cavernoma (PVC). Cavernous transformation of the portal vein is frequently associated with prehepatic portal hypertension (PH) which promotes portal flow redistribution with the risk of developing large porto-collateral shunts. Although often asymptomatic, PVC may cause variceal bleeding, ascites, or, less frequently, hepatic encephalopathy. Interestingly, a significant proportion of patients

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with PVC have an underlying prothrombotic condition such as myeloproliferative neoplasms or inherited disorders of the coagulation cascade.[2] Secondly, the physiological hemodynamic changes and the prothrombotic state seen during pregnancy are relatively similar to what is found in patients with PH.[3] Hence, a higher risk of PH-derived complications could be expected in pregnant patients with PVC. The available information in this scenario is scarce. We herein describe the results of a short series of patients with non-cirrhotic portal cavernoma undergoing pregnancy.

2 | PATIENTS AND METHODS

A retrospective case study was designed to include all patients with PVC without cirrhosis who had undergone pregnancy. To identify patients who fulfilled the mentioned criteria, we reviewed the medical records of all female patients with a previous diagnosis of PVC followed in the monographic clinic for vascular liver diseases in our department. Likewise, high-risk pregnancy clinic records were screened to find patients who may had been referred directly to the obstetric department. In all patients, cirrhosis was discarded by the combination of transient elastography, laboratory results, and liver imaging. Confirmatory liver biopsy was performed when diagnosis was uncertain. Portal cavernoma was diagnosed by either abdominal computed tomography or vascular magnetic resonance. As recommended by clinical guidelines,[4] endoscopic assessment of esophageal varices was performed at diagnosis of PVC as well as before each pregnancy, except if prophylaxis for variceal bleeding with beta-blockers had been already initiated. Clinical and laboratory data were obtained from their medical histories. During pregnancy, all patients were followed up in the high-risk pregnancy clinic by obstetricians and hepatologists. After delivery, they continued their follow-up in the vascular liver diseases clinic with abdominal ultrasound, blood analysis, and clinical evaluation every 6 months. In the case of newborns, they were evaluated daily after birth until hospital discharge. Subsequently, they were followed in the hospital neonatology clinic for several months (mean follow-up time of 8 months) before referral to their general pediatrician. To evaluate newborn morbidities, clinical histories, physical explorations, and ancillary tests performed during their follow-up in the hospital clinic were reviewed. The study was classified as consent waived by the ethics committee of the University General Hospital Gregorio Marañón, given its retrospective and observational nature. The manuscript has been drafted in accordance with CARE guidelines for case reports. Results are expressed as mean (standard deviation) and as frequencies. All statistical analyses were carried out using the SPSS package (version 24.0; IBM, Armonk, NY, USA).

3 | RESULTS

Five patients with a total of eight pregnancies who fulfilled the previously mentioned criteria were identified. Clinical data and pregnancy outcomes are depicted in Table 1. The mean age was 34.7 (3.2) years old. The mean time between PVC diagnosis and the first pregnancy was 21.4 (9) years. All patients had an identified underlying condition associated with thrombotic events. The existence of PVC and its predisposing condition was identified before pregnancy in all cases. In two patients PVC was associated with congenital antithrombin III deficiency, and in two patients the cavernoma was attributed to infectious omphalitis. Finally, patient 4 had a prior diagnosis of porto-sinusoidal vascular disease, arrived at while studying radiological signs of PH (cirrhosis was excluded by liver biopsy, which showed nodular regenerative hyperplasia). Two patients had a previous history of PH-derived complications (variceal bleeding and ascites) and a third patient had large esophageal varices receiving propranolol as primary prophylaxis. One patient underwent in vitro fertilization on two occasions while the remaining six pregnancies were spontaneous. In all but one patient, anticoagulant therapy was prescribed during pregnancy. Only one patient had a PH-derived complication during pregnancy, consisting of variceal bleeding at week 28, which was successfully treated with somatostatin and endoscopic variceal band ligation. Mean platelet count at delivery was 69 000/μL (27 500). One patient with severe thrombocytopenia (below 50 000/μL) received platelet transfusion prior to both cesarean sections without any hemorrhagic complication during surgery. In six cases, programmed cesarean sections were scheduled to avoid labor. In two patients, the cesarean sections were unanticipated: in one patient because of cardiotocographic signs of fetal distress at week 33, and in the second patient, due to stage 3 intrauterine growth restriction (IUGR) diagnosis, indicating surgery at week 30. All patients underwent general anesthesia for cesarean sections owing to the low platelet count, which was considered a contraindication for regional anesthesia. Following delivery, six out of eight patients received low-molecular-weight heparin for 6 weeks. Anticoagulation was not administered in patient 1 after her first pregnancy, given the recent variceal bleeding, and in patient 3 anticoagulation was interrupted after 10 days due to her low platelet count. Mean gestational age at birth was 35.5 (2.9) weeks and mean weight was 2.280 (798) g. Mean arterial umbilical cord pH was 7.3 (0.3) and mean Apgar scores were 7.12 (1.8) and 8.7 (0.9) at 1 and 5 min, respectively. Maternal mean follow-up after their first delivery was 131 (90) months. During this time no relevant complications were reported. Overall, there were four cases of IUGR without any miscarriages, infant deaths, or malformations. No complications were reported in newborns after a mean follow-up of 8 (2.2) months.

4 | DISCUSSION

We herein report what is the largest series of patients with PVC undergoing pregnancy. Non-cirrhotic PVC is a rare condition consisting of a chronic thrombotic occlusion of the portal vein which is replaced by numerous small-caliber vessels. In our series, all patients had an identified underlying factor frequently associated with thrombotic events. Accordingly, in non-cirrhotic patients, only 15% of PVCs are considered idiopathic, being more frequently secondary to prothrombotic disorders or to local factors such as history of complicated abdominal surgery or sepsis.[2]

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TABLE 1 Patients characteristics and outcomes.

	Patient 1		Patient 2	Patient 3		Patient 4		Patient 5
Clinical findings								
Prior diagnosis of cavernoma	Yes		Yes	Yes		Yes		Yes
Cause of portal cavernoma	Neonatal omphalitis		Antithrombin III deficiency	Antithrombin III deficiency		Porto-sinusoidal vascular liver disease		Neonatal omphalitis
Esophageal varices	Yes		No	Yes		No		No
Prominent collateral circulation	No		Splenorenal shunt	Gastrohepatic, peripancreatic, and splenorenal shunt		Splenorenal shunt		Splenoperitoneal shunt
Prior complications of PH	None		None	Variceal Bleeding		None		Ascites
Baseline anticoagulation	No		Yes	Yes		No		No
Beta-blockers	Propranolol		No	Propranolol		No		Propranolol
TIPS	No		No	No		No		No
Pregnancy information								
Number of pregnancies	2		1	2		2		1
	Pregnancy 1	Pregnancy 2		Pregnancy 1	Pregnancy 2	Pregnancy 1	Pregnancy 2	
Spontaneous pregnancy	Yes	Yes	Yes	Yes	Yes	No (IVF)	No (IVF)	Yes
Age (y)	31	37	36	32	36	37	39	30
Anticoagulation during pregnancy	No	No	LMWH	LMWH	LMWH	LMWH	LMWH	LMWH
PH complication	Variceal bleeding (week 28)	None	None	None	None	None	None	None
Thrombotic complication	None	None	None	None	None	None	None	None
Antenatal corticosteroid therapy	Yes	No	No	Yes	No	No	No	Yes
Delivery	Scheduled cesarean	Scheduled cesarean	Scheduled cesarean	Urgent cesarean[a]	Scheduled cesarean	Scheduled cesarean	Scheduled cesarean	Urgent cesarean[b]
Platelet count at delivery	650700	60000	64000	37000[c]	35000[c]	76000	95000	117000
Anticoagulation during postpartum (duration)	No	LMWH (6 wk)	LMWH (6 wk)	LMWH (10 d)	LMWH (10 d)	LMWH (6 wk)	LMWH (6 wk)	LMWH (6 wk)
Pregnancy outcomes								
Gestational age at birth (wk)	36	37	38	33	34	38	38	30

(Continues)

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TABLE 1 (Continued)

	Patient 1		Patient 2	Patient 3		Patient 4		Patient 5
Umbilical cord arterial pH	7.36	7.27	7.32	7.21	7.35	7.31	7.37	7.23
Apgar score (at 1/5 min)	8 / 9	7 / 9	7 / 9	5 / 7	8 / 9	9 / 9	9 /10	4 / 8
Child weight (g)	2160 (IUGR)	2020 (IUGR)	2930	1270 (IUGR)	2700	2710	3360	1094 (IUGR)
Child morbidities	None	None	None	None	None	None	None	None

Note: LMWH was adjusted according to each patient's weight, renal function, and platelet count. It was suspended 24 h prior to surgery.

Abbreviations: IUGR, intrauterine growth restriction; IVF, in vitro fertilization; LMWH, low-molecular-weight heparin; PH, portal hypertension; TIPS, transjugular intrahepatic portosystemic shunt.

[a]Urgent cesarean was performed in week 33 due to cardiotocographic signs of fetal distress with diagnosis or IUGR.

[b]Urgent cesarean was performed in week 30 due to stage 3 IUGR diagnosis.

[c]Platelet transfusion was administered before cesarean section.

As seen in our series, the subsequent prehepatic PH caused by the cavernoma often results in the development of esophageal and ectopic varices as well as in portosystemic shunts, which can lead to hemorrhagic events, ascites, or encephalopathy. Patients with PH undergo several hemodynamic changes (hyperdynamic circulation, increased plasma volume, lower peripheral vascular resistance, and higher portal blood flow), many of which are similar to those physiological changes seen in pregnant women. Hence a higher risk of PH-derived complications could be expected.[3] This is the rationale behind the classical advice against pregnancy in patients with PH. Nevertheless, in recent years, multiple small-number case series studies[5–7] have been published showing a low complication rate during pregnancy in patients with PH.

In our study, all patients had a prior gastrointestinal endoscopy (GIE) to evaluate the presence of esophageal and ectopic varices. Likewise, all patients received beta-blockers, if indicated by clinical guidelines, and in every patient, thromboprophylaxis was initiated, with the exception of patient 1, in whom, given the prior diagnosis of large esophageal varices, no anticoagulation was prescribed. This decision was made based on previous reports in the literature[8–10] which point to variceal bleeding as the most frequent complication in this scenario, with a previously reported incidence as high as 20%.[11] In our series, there was only one case of variceal bleeding, which was successfully treated with splanchnic vasoconstrictors and variceal band ligation. Interestingly this event occurred in the only patient without anticoagulation, which emphasizes that a correct prophylactic management of varices, instead of avoiding anticoagulation, is of paramount importance, as has been previously reported.[2,12]

Current guidelines based on expert consensus recommend variceal screening prior to pregnancy and in the second trimester,[11] when the mentioned hemodynamic changes are more pronounced.[13] If high-risk varices are detected, bleeding prophylaxis with beta-blockers is recommended, as in cirrhotic patients. Although propranolol and carvedilol are labeled as category C by the Food and Drug Administration.

(FDA) due to the risks of fetal hypoglycemia and bradycardia, the benefits clearly outweigh the risks given the high mortality associated with variceal bleeding (4%–13%).[14] When variceal bleeding occurs, standard treatment with band ligation is recommended, as the performance of a GIE has been proven to be safe during pregnancy. Likewise, somatostatin should be used as splanchnic vasoconstrictor (FDA category B), while terlipressin must be avoided given that it has been associated with spontaneous abortion and child malformation.

In terms of delivery management, consistent with previous reports in the literature,[6–8,15] cesarean was the mode of delivery in all cases aiming to avoid labor and the consequent acute portal pressure increase during the Valsalva maneuver repeatedly performed by the mother.[16] No significant hemorrhagic complications were reported. Nevertheless, routine cesarean section is currently not recommended,[11] given the higher risks of thrombotic events during the postpartum period, but the available evidence is scarce. Thus, individualization according to bleeding risk is advised, although in the case of vaginal delivery, efforts to shorten the second stage of labor are clearly recommended.

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The overall outcome was favorable in all pregnancies without any associated child morbidities, yet four cases of IUGR were reported. This high rate of IUGR could be explained by the placental circulatory disturbances derived from PH. None of our patients had other complications that have also been associated with these patients, such as pre-eclampsia or HELLP syndrome.[6] These outcomes cannot be extrapolated to patients with other causes of PH, such as cirrhosis, in which the complication rate may be much higher due to the hepatocellular dysfunction not present in patients with NCPVT.

Finally, no thrombotic complications were reported during the postpartum period, which could be explained by the beneficial effect of anticoagulation. The major limitation of our study is the small number of patients included, owing to the low prevalence of this condition. In addition, its retrospective nature and the absence of a control group mean we cannot make any firm recommendations.

5 | CONCLUSION

Although pregnancy in patients with PVC is theoretically associated with a higher risk of PH-related complications, the overall outcome is favorable. Hence, our data do not support the assumption that PVC is a contraindication for pregnancy. However, a higher risk of IUGR can be expected, and thus preconception counseling, close monitoring during pregnancy, and a multidisciplinary approach in highly specialized units are advised. In our experience, the careful management of anticoagulation, an adequate prophylaxis of variceal bleeding, and the early indication of cesarean section are responsible for the excellent clinical results observed.

AUTHOR CONTRIBUTIONS

AC contributed to the conception and design of the work, the acquisition of data as well as designing and writing the manuscript. LI-S contributed to the conception and design of the work as well as designing and writing the manuscript. MFM and VO contributed to the design of the work and the acquisition of data. AFY, MR, FY, and MVC contributed to the acquisition of data and drafting the manuscript. SG-TL contributed to the design of the work as well as revising the manuscript critically for important intellectual content. RB oversaw the project, contributed to the conception and design of the work as well as writing the manuscript and revising it critically for important intellectual content. All authors approved the final published version and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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