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Ovarian thrombosis and uterine synechiae after arterial embolization for a late postpartum haemorrhage

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ABSTRACT

Background: We report two unusual separate complications after uterine artery embolization for a late postpartum haemorrhage. This report appeared important to us in view of the apparent absence of any other publications on this topic.
Case presentation: We report the case of a 25-year-old woman, gravida 3, para 1, admitted for uterine bleeding 7 days after a spontaneous delivery at term, in our university hospital. A suction curettage and then, after persistent bleeding, uterine artery embolization were necessary. Immediately after the embolization, a bilateral ovarian thrombosis occurred, subsequently followed by amenorrhea, due to uterine synechiae, and depression. Hysteroscopic surgery was performed to remove the adhesions. A complete work-up for thrombophilia showed a heterozygous mutation of the factor V gene R506Q. The pathology examination found subinvolution of the placental bed. One month after treatment of the synechiae (and insertion of a copper IUD for contraception), the woman's menstrual cycle returned to normal. Her clinical examination 19 months later was normal.
Conclusions: This case teaches us that one rare complication can hide another! It is important to consider the diagnosis of subinvolution of the placental bed in cases of late PPH and to know the complications associated with vascular artery embolization in order to provide the most rapid and least invasive treatment.

1. Introduction

The extent of the problems associated with postpartum haemorrhage (PPH) is significantly underestimated, primarily because of the lack of consensus about its definition and diagnosis [1]. In France, PPH is defined as blood loss from the genital tract of 500 mL or more in the 24 h after the baby's delivery [2], and severe PPH as blood loss from the genital tract of 1000 mL or more in the first 24 h after delivery [3]. PPH is generally classified PPH as primary if it occurs within 24 h and secondary if it is more than 24 h but less than 12 weeks after delivery [1].

The overall estimated prevalence of PPH (blood loss ≥ 500 mL) reported by Carroli et al. [3] in a systematic review was 6.09% [95% CI: 6.06–6.11], and the prevalence of severe PPH (blood loss ≥ 1000 mL) 1.86%, while Zhang et al. [4] found an incidence of 4.6 per a thousand deliveries in a European survey. A British district hospital reported an incidence of secondary PPH of 0.8% [5].

PPH is the leading cause of maternal deaths in the European Union, accounting for 13.1% [6]. Obstetric haemorrhage is estimated to cause 25% of all maternal deaths, and nearly half of postpartum deaths are due to immediate PPH [7]. The incidence of women with blood transfusions for PPH is 2.1 per 1000 women in France, and the hysterectomy rate following delivery is 0.3 per 1000 [6]. Severe maternal morbidity due to PPH has been estimated at 4.5–6.7 per 1000 deliveries [8,9].

We report here the case of an unusual delayed PPH treated by uterine artery embolization and followed by two different medical complications: ovarian thrombosis and uterine synechiae.

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2. Case Description

This 25-year-old woman, gravida 3, para 1, was hospitalized at postpartum day 7 for heavy bleeding. Her medical history included only a simple allergy to mites and dust, an appendectomy; she had never smoked. Her obstetric history was more complex: a spontaneous first-trimester abortion, which had required two vacuum extractions 4 years earlier, and one caesarean delivery during labour at 41 weeks of gestation for lack of progress in dilatation at 7 cm and suspected macrosomia, two years earlier. That child weighed 4350 g at delivery. The mother had no notable family history.

She gave birth spontaneously at 39 weeks and 1 day to her second child in cephalic presentation. Labour lasted 6 h. Because she carried *Streptococcus* B, she received prophylactic amoxicillin. Active management of the third stage of labour began with 5 IU of oxytocin at delivery of the shoulders. Manual removal of the placenta and exploration of the uterus were both necessary, under antibiotic prophylaxis, because the placenta was not expelled. No haemorrhage occurred. At birth, the child weighed 3770 g and had an umbilical artery pH of 7.25 and Apgar scores of 9 at 3 min and 10 at both 5 and 10 min. Superficial tears of the labia minora were sutured. Total blood loss was estimated at less than 500 cm^3. Prenatal cares had included several ultrasound examinations; the last, at 32 weeks and 3 days, showed an unremarkable anterior placenta, normally inserted. Clinical and laboratory findings were satisfactory throughout pregnancy. Bacteriologic analysis of the placenta was requested after delivery because of meconium-stained amniotic fluid, but the results were negative. The postpartum period was uncomplicated, and the mother was discharged at postpartum day 5.

Two days later, she was hospitalized again on an emergency basis for vaginal bleeding, with a blood pressure of 80/40 mm Hg and numerous clots coming from the uterus. The emergency ultrasonography showed a picture compatible with partial placental retention within the uterus. The laboratory results reported haemoglobin at 11.1 g/dL, platelets at 281×10^9/L, normal coagulation, white cells at 10.72 g/L, and C-reactive protein at 131.7 mg/L. She was transferred to the operating room for suction curettage under general anaesthesia. The pathology examination of the curettage product showed delayed involution of the pregnant endometrium with zones retaining polymorphonuclear neutrophil infiltration. We noted patent uteroplacental artery residues, with no thrombotic occlusion. No placental villi or decidual remnants were present.

Despite the oxytocin treatment, uterine atony persisted. Intravenous prostaglandins, administered by an electric syringe, were the next treatment attempted. When they also failed, uterine artery embolization was performed, in a therapeutic angiography unit equipped with a high-speed large-matrix (10242) digital angiography system (Siemens Multistar Top, Germany) and using high-resolution digital fluoroscopy, an automatic injector, and low osmolality iodine contrast media. The embolization was performed after puncture of the femoral artery with a 4 Fr catheter that had a single distal aperture (hydrophilic Cobra 4 F catheter, Terumo, Japan). After aortography to determine arterial anatomy (which was modal) and locate the site of contrast agent extravasation, the left and right uterine arteries and the anterior trunk of the hypogastric artery were selectively catheterized. Embolization was performed under fluoroscopic guidance. A gelatin sponge (Spongel_Houde, Hoechst), usually considered to produce temporary occlusion, was used for the embolization. Fundal arterial blush was observed on selective injection of the right uterine artery. Packed red blood cells (3 units) were administered during the embolization.

After less than 24 h in the intensive care unit (ICU) for post embolization monitoring, she returned to the obstetrics/gynaecology department. From her return, she was in severe pain, required morphine, and had a temperature of 38 °C. An abdominopelvic CT scan 24 h after embolization showed retention of intrauterine clots as well as bilateral ovarian thrombophlebitis (Fig. 1). Gentle uterine aspiration was repeated, under general anaesthesia. Anticoagulant treatment by heparin was administered at a curative dose (20 IU/kg/h) with an electric push-syringe once the bleeding stopped, 2 days after embolization. She was discharged on day 11 of this second hospitalization, after an anti-vitamin K anticoagulant replaced low-molecular-weight heparin on day 10 (to be continued for 4 months).

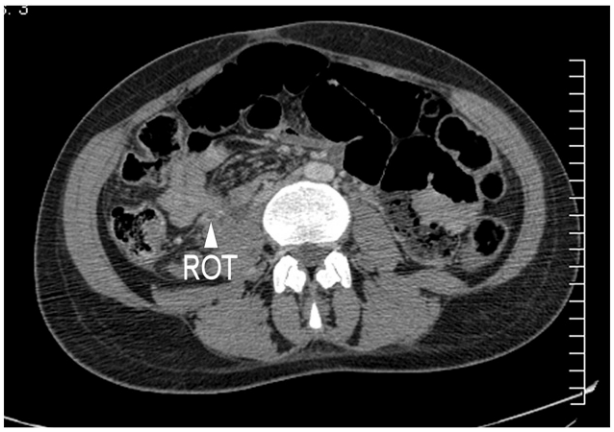

Fig. 1. Abdominopelvic CT scan showed ovarian thrombophlebitis. (ROT) Right ovarian thrombophlebitis. Portal phase of axial contrast-enhanced CT scan depicts a low attenuation thrombus expanding into the iliac portion of right ovarian vein (arrow). Neither the ovarian vein or the collateral vessels were enlarged, due to the limited extension of the thrombus. The left ovarian thrombosis is not clearly visible here.

A follow-up pelvic CT scan 5 weeks later was unremarkable. The mother later presented a reactive depression for which she refused psychological care, as well as amenorrhea, which suggested uterine synechiae. The later thrombophilia work-up showed activated protein C resistance with a factor V Leiden mutation. The rest of the work-up was normal (antithrombin, protein C, protein S, anticardiolipin and anti-B2GP1 antibodies, lupus anticoagulant, and the prothrombin G20210A mutation). A progesterone test was performed because of the amenorrhea, and the uterine synechiae were confirmed by transvaginal sonohysterography performed 6 months after the PPH (General Electric, Voluson E8, USA) (Fig. 2). The probe stopped at 5 cm from the external os. Intrauterine passage of the fluid in the uterine cavity was slight. Nine months after the PPH, hysteroscopic surgery was performed with a Gynecare Versapoint electrosurgical system (Ethicon Corp, USA) (Fig. 3). The adhesion was circumferential at the level of the isthmus, predominant on the right edge of the isthmus, and presented a millimetric channel. Moreover, once this channel was crossed, another right lateral synechiae masked the right tubal ostium. This synechiae

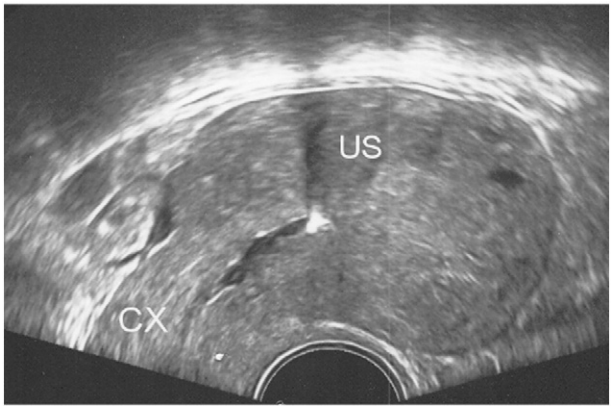

Fig. 2. Transvaginal sonohysterographic evaluation shows the uterine synechiae. (US) Uterine synechiae. (CX) cervix.

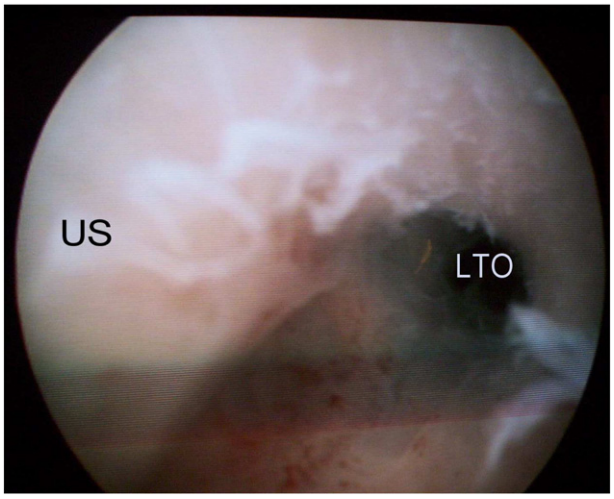

Fig. 3. Hysteroscopy shows the uterine synechiae along the right part of the uterine cavity. (US) The uterine synechiae are located to the right and block a large part of the uterine cavity. (LTO) Only the left tubal ostium can be observed.

was removed completely, and both tubal ostia and the uterine cavity, apparently normal, were visualized. A copper intrauterine device (IUD) was placed during the same procedure. Normal menstruation subsequently resumed. Nineteen months after the PPH, the patient's clinical examination was normal. Nonetheless, she had been seen on several occasions in the emergency department for abdominal–pelvic pain, although numerous ultrasound examinations found only pelvic varicose veins and multifollicular ovaries.

3. Discussion

Although the frequency of delayed PPH peaks during the second week after delivery [5,10,11], in our case the haemorrhage occurred one week after delivery. A study (n = 132) identified only two significant risk factors for late PPH: a history of primary PPH (OR 9.3; 95% CI 6.2–14.0) and manual removal of the placenta (OR 3.5; 95% CI 1.6–7.5) [5]. Associated morbidity was high: 84% required hospital admission, 63% surgical evacuation, and 17% blood transfusions. In women undergoing evacuation only, retention of placental tissue was confirmed after surgery for 37% [5]. The placenta had been manually removed in our case.

The initial ultrasound suggested placental retention, but the pathology examination of the placenta showed that the actual cause was subinvolution of the placental bed. Only a few published cases discuss this subinvolution [12–15]. It may be an underestimated cause of severe late PPH and can lead to hysterectomy [14]. It may have promoting factors, such as molar pregnancy [13]. Involution of the placental bed is shown in pathology examinations by hyalinised fragments of uteroplacental spiral arteries, either collapsed or completely thrombosed. On the other hand, subinvolution of the placental bed, as in our case, is characterized by widely distended and patent residues of uteroplacental arteries with only partial thrombotic occlusion [12]. Khong concluded that retained placental fragments, which reflect placenta accreta, and subinvolution of the placenta bed are both important causes of late postpartum haemorrhage [12].

In France, elective arterial embolization is considered a safe and effective method for controlling obstetric haemorrhage, and a conservative alternative to hysterectomy when other noninvasive measures fail. However, in our earlier survey (which did not include this case), 5.6% of the women had amenorrhea documented after embolization, and hysteroscopic investigation showed diffuse uterine synechiae [16]. Femoral vein thrombosis also occurred in 4% of women and pulmonary embolism in 1.7% [16]. This patient immediately developed an ovarian venous thrombosis. A large study found a rate of venous thromboembolisms (deep vein thrombosis, pulmonary embolus, or both) during pregnancy and the postpartum period of 1.72 per 1000 deliveries, with 1.1 deaths per 100,000 [17]. The risk of thromboembolism was higher for women aged 35 years or older and for black women. Other significant risk factors included thrombophilia, lupus, heart disease, sickle cell disease, obesity, fluid and electrolyte imbalance, postpartum infection, and transfusion. There is evidence that storage and preservation of red blood cells increase their aggregability, which may contribute to an increased risk of thrombosis [18]. Half of pregnancy-related venous thromboembolisms occur postpartum [17]. In a systematic review, Romero et al. found that the principal risk factors for venous thromboembolic disease during pregnancy and the puerperium are thrombophilia, bed rest for more than 3 days, previous deep vein thrombosis, varicose veins in the lower limbs and age greater than 35 [19]. Ovarian vein thrombosis is a rare event, and failing to diagnose it can have devastating consequences. As in our case, pelvic pain (which we treated by morphine) associated with fever requires radiologic exploration to look for a postpartum ovarian thrombosis [20,21].

Our patient had several different risk factors for venous thrombosis: postpartum period, bed rest, uterine artery embolization, blood transfusion, pelvic varicose veins, and an unknown inherited thrombophilia. Inherited thrombophilia is present in 30%–50% of women with pregnancy-associated venous thromboembolisms [22]. Factor V Leiden is the most frequently identified inherited thrombophilia in the white population [22]. Protein C deficiency, however, is associated with a high risk; the risk of venous thromboembolism during pregnancy is lower in women heterozygous for factor V Leiden [22].

Our patient had two etiologic factors for her synechiae: arterial embolization and two curettages [16,23]. A retrospective study of French women (n = 102) reported that complications from pregnancy-related curettage were the most common cause of uterine synechiae [23]. Transvaginal sonohysterography, which combines transvaginal sonography with intrauterine injection of isotonic saline solution, is the gold standard for identifying an abnormal uterine cavity, as in our case [24]. Operative hysteroscopy is the method of choice for treating patients with intrauterine adhesions, which are associated with reproductive problems (51%) and menstrual disorders (43%) [23]. The risk of synechiae observed after artery embolizations for PPH also exists after placement of compression sutures that transverse the uterine cavity (26.7%) [25].

Finally, severe postpartum haemorrhage may have a long-term psychological impact on women despite uterine preservation. A survey of French women with severe PPH found that 67.6% reported a very negative recollection of their delivery; for 35.3%, their principal memory was fear of dying [26]. Our patient was depressed, but did not want the psychological support that might have been helpful to her [27].

4. Conclusion

In conclusion, this case teaches us that one rare complication can hide another! It is important to consider the diagnosis of subinvolution of the placental bed in cases of late PPH and to know the complications associated with vascular artery embolization in order to provide the most rapid and least invasive treatment.

Conflict of Interest

The authors declare that they have not competing interests.

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