CASE REPORT

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Secondary postpartum hemorrhage caused by subinvolution of the placental site

Hemorragia posparto secundaria causada por subinvolución de lecho placentario

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ABSTRACT

Postpartum hemorrhage is a major cause of obstetric morbidity and mortality, being associated with hemorrhagic shock and risk of disseminated intravascular coagulopathy. Primary postpartum hemorrhage occurs within 24 hours of delivery and cases classified as secondary occur after 24 hours and up to 6 weeks postpartum. A rare cause of secondary postpartum hemorrhage is vascular subinvolution of the placental implantation site. The underlying pathophysiological mechanism is unknown. However, this condition is considered idiopathic and non-iatrogenic because of its process of occurrence and development. Without other secondary causes of postpartum hemorrhage, this condition is characterized by prolonged and/or excessive uterine bleeding, which can lead to fulminant hemodynamic collapse. The anatomopathological diagnosis is based on the finding of persistent, patent, large, dilated and partially thrombus-occluded myometrial arteries, which are adjacent to normally involuted vessels. Hysterectomy is the treatment for cases of severe hemorrhage. The aim of the study is to present a case of secondary postpartum hemorrhage caused by subinvolution of the placental site.
Key words: Postpartum hemorrhage, Placenta subinvolution, Placental extracts

RESUMEN

La hemorragia posparto es una de las principales causas de morbimortalidad obstétrica, al asociarse con choque hemorrágico y riesgo de coagulopatía intravascular diseminada. La hemorragia posparto primaria ocurre en las 24 horas posteriores al parto y los casos clasificados como secundarios ocurren después de las 24 horas y hasta las 6 semanas posteriores al parto. Una causa rara de hemorragia posparto secundaria es la subinvolución vascular del sitio de implantación placentaria. El mecanismo fisiopatológico subyacente es desconocido. Sin embargo, esta condición es considerada idiopática y no iatrogénica por su proceso de aparición y desarrollo. Sin otras causas de hemorragia posparto secundarias, esta condición está caracterizada por sangrado uterino prolongado y/o excesivo, que puede provocar colapso hemodinámico fulminante. El diagnóstico anatomopatológico está basado en el hallazgo de arterias miometriales persistentes, permeables, grandes, dilatadas y parcialmente ocluidas por trombos, que están adyacentes a vasos normalmente involucionados. La histerectomía es el tratamiento para los casos de hemorragias severas. El objetivo del estudio es presentar un caso de hemorragia posparto secundaria causada por subinvolución del lecho placentario.
Palabras clave. Hemorragia posparto, Placenta, subinvolución, Extractos placentarios

Introduction

Postpartum hemorrhage (PPH) is an obstetric emergency that can follow vaginal or cesarean delivery. It is one of the main causes of maternal mortality with an incidence of approximately 5-20% of deliveries. The current definition, based on the quantification of blood loss, has limitations, so there is great variability in the frequency of diagnosis[(1)]. It can be classified as primary or secondary. Cases considered as primary occur within 24 hours after delivery, while secondary postpartum hemorrhage occurs between the mid puerperium and 6 weeks after delivery. Its incidence is 1-2% in pregnant women and is generally associated with greater morbidity than maternal mortality[(2)].

Subinvolution of the placental site (SPS) is a cause of secondary PPH due to inadequate regression of the endovascular trophoblast after delivery. Uteroplacental arteries that underwent physiological changes to adapt to fetoplacental needs do not involute or return to their pregesta-

tional state. The characteristic clinical picture is hemorrhage of abrupt onset, which can produce fulminant hemodynamic collapse, accompanied by an enlarged uterus and whose maximum incidence is during the second week of puerperium[3]. The diagnosis is based on clinical findings and evidence of subinvoluted vessels in the placental bed in the absence of placental debris[4]. A case of secondary postpartum hemorrhage caused by subinvolution of the placental site is presented.

Case report

A 29-year-old female patient, gestation III, para II, cesarean section I, came to the obstetric emergency room for moderate intensity bleeding with clots, accompanied by dizziness, headache and nausea. She had a history of cesarean section for acute fetal distress 26 days before the onset of symptoms, with satisfactory postoperative evolution. She was discharged on the third postpartum day with hemoglobin of 9.1 g/dL, coagulation parameters within normal values and oral iron supplementation. She denied personal history of trauma, thrombophilias or malignant neoplasms.

On admission she was afebrile, sweating and with marked cutaneous-mucosal pallor. Hemodynamic parameters were blood pressure 90/50 mmHg, heart rate 125 beats per minute and respiratory rate 18 breaths per minute. The abdomen was soft, depressible and non-painful. There was a Pfannenstiel type abdominal incision with correct healing, without evidence of erythema or purulent discharge. The uterus was at the midpoint between the symphysis pubis and the umbilical scar. Gynecologic examination showed genital bleeding in moderate amount, accompanied by clots. Speculoscopy presented the cervix closed with no evidence of tears or lacerations. There was no evidence of lesions or tears in the vulvovaginal region.

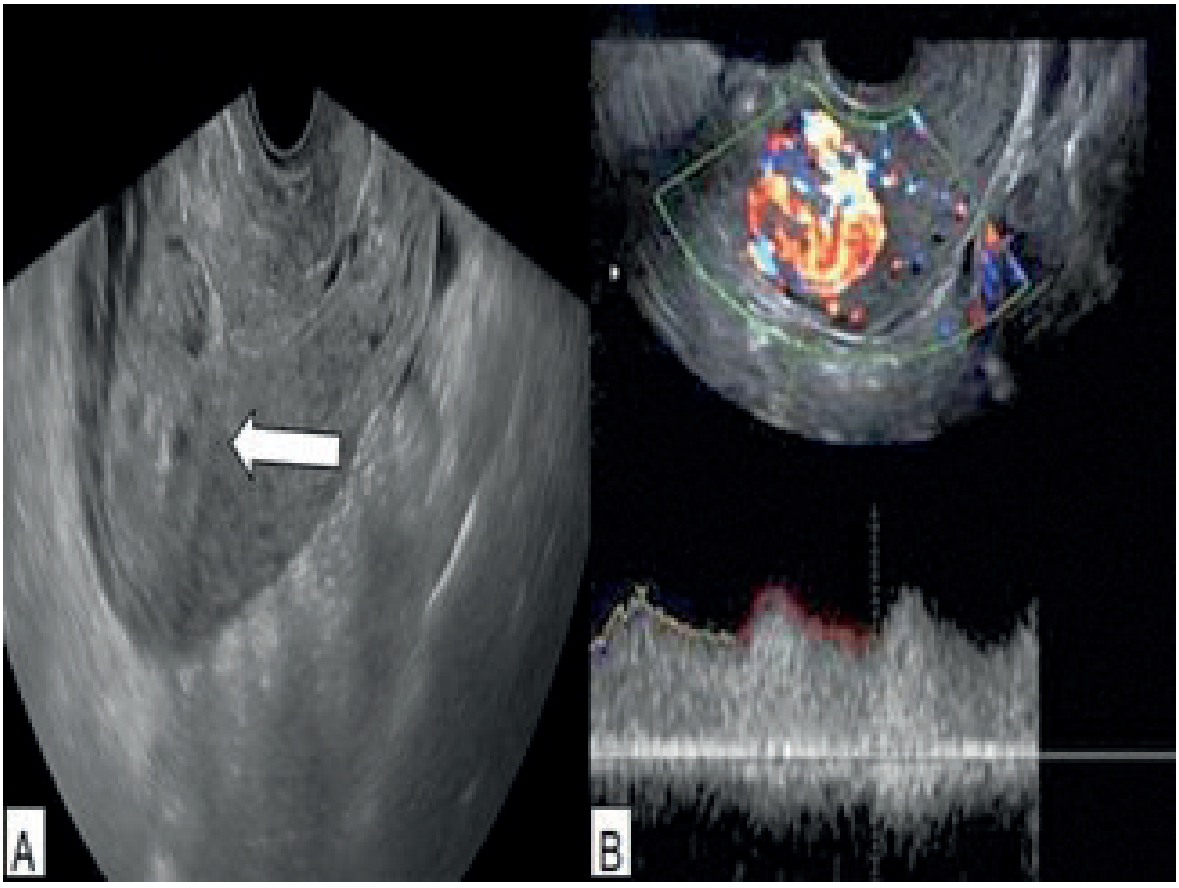
Laboratory test results were hemoglobin of 6.5 g/dL with hematocrit of 21%. Leukocyte count and formula, renal and hepatic functionalism, electrolytes, coagulation, thrombophilias, C-reactive protein, erythrocyte sedimentation rate, and urine examination were within normal limits. Human chorionic gonadotropin test was negative. Transvaginal ultrasonography showed an enlarged uterus, with concavity occupied in the middle third by a 4 x 2-centimeter heterogeneous echogenic image on the posterior aspect of the uterine isthmus, without signs of retained placental tissue or a visible uterine scar abnormality. Color Doppler evaluation showed increased peak systolic velocity with low resistance wave in the area of the concavity (Figure 1).

In view of the clinical and imaging findings, fractionated uterine curettage was performed under general anesthesia obtaining little material during the procedure, and it was decided to place an intrauterine catheter and use uterotonics (intravenous oxytocin, intramuscular methylergometrine and rectal misoprostol) and blood products (3 units of globular concentrate). As the patient's condition did not improve, it was determined to perform a gynecological laparotomy.

During surgery, the uterus was enlarged and pale in color. The lower segment showed no signs of hysterorrhaphy dehiscence or active bleeding. There was no evidence of blood collections or intra-abdominal secretions. In view of the above, the decision was to perform a subtotal hysterectomy with preservation of the left adnexa. Postoperative recovery was uneventful, and the patient was discharged after 5 days.

Anatomopathologic examination showed a large uterus with sutured surgical incision in the lower anterior wall of the uterus with adherent clot (Figure 2). Microscopic evaluation noted endometrial areas with multiple dilated and permeable thick-walled distorted vessels with deposition of fibrinoid material replacing the media. These vessels showed partial absence of endothelial lining with variable sized, partially occlusive, recanalized thrombi in the subendometrial and myometrial regions, but were absent in the thickness of the myometrium. Trophoblastic cells were also found in and around the spiral arteries, degenerative in appearance, large, pale and often vacuolated. Microscopic sections of the adherent clot contained inflamed necrotizing decidua. The surrounding myometrium had normally involuted vessels adjacent to the subinvoluted vessels, which had lax adventitia, bright eosinophilic mid-layer, thickened intima and identifiable endothelial lining, with small slit-like vascular lumina (Figure 3). There was no retained placental tissue, signs of placental

Figure 1. Transvaginal ultrasound images. A) Tumor along the inner third of the myometrium of the posterior aspect of the uterus. B) Doppler ultrasound showing hypoechoic tortuous vessels with increased peak systolic velocity and low resistance waves.



accreta or evidence of malignant lesions. These findings were compatible with the diagnosis of late PPH associated with SPS.

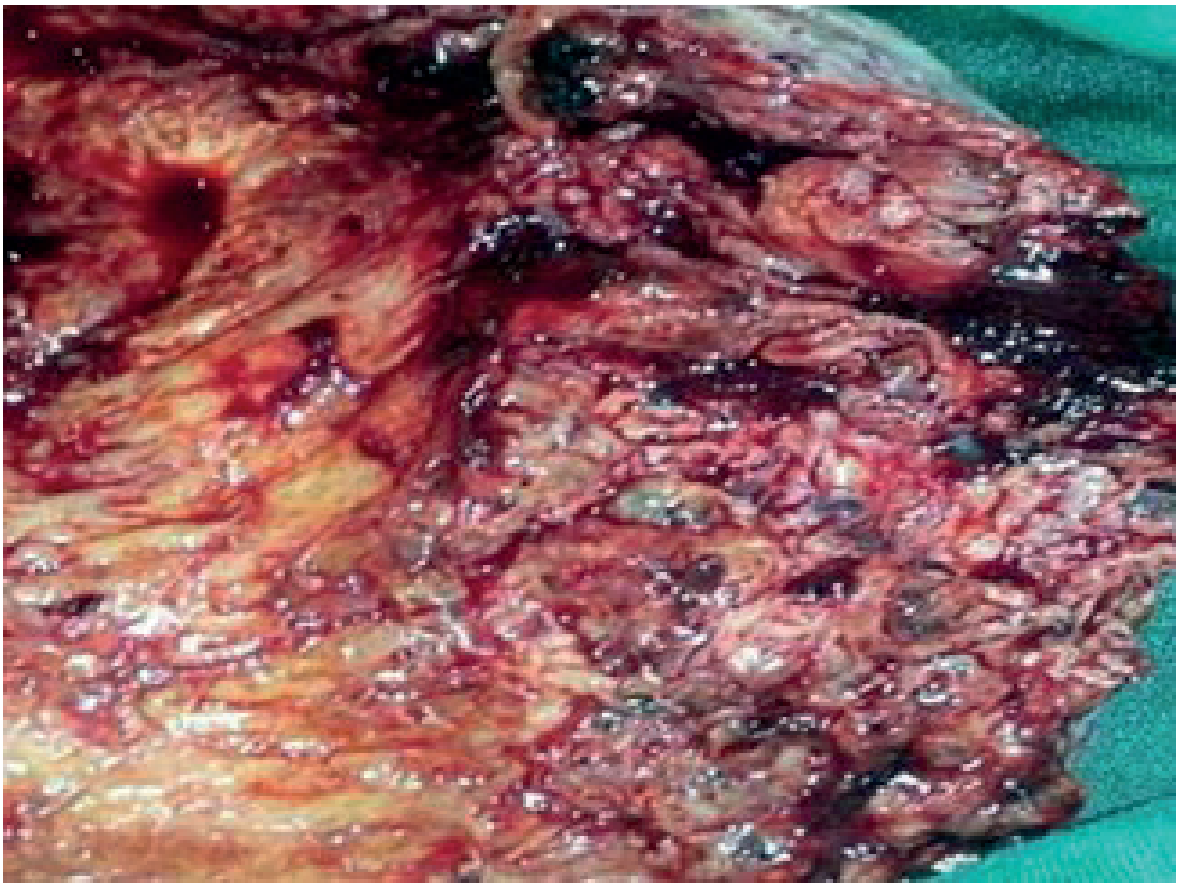
Discussion

PPH is an obstetric emergency that occurs regardless of the type of delivery. It can occur within 24 hours after delivery (primary) or within 24 hours after delivery up to 6 weeks postpartum (secondary)[5]. Primary and secondary PPH share common causes which may include uterine atony, retained placental debris, placental accreta, endometrial infections, hereditary thrombophilias, consuming coagulopathies, and perineal injuries. However, secondary PPH has attracted less attention, probably due to its low frequency and that it is associated more with maternal morbidity than maternal mortality[1].

The mechanism of placental site involution after delivery is still not clearly defined. The uteroplacental arteries undergo thrombosis and reorganization following contraction of the placental site and endometrial regeneration[6]. In SPS, the uterine arteries and the placental bed musculature fail to involute and return to their pregestational state. The vessels are dilated, tortuous and partially hyalinized, with loss of endothelial lining and internal elastic lamina. The endovascular trophoblast does not involute, resulting in persistent dilatation of the vessels, leading to the onset of postpartum bleeding. This process is idiopathic rather than iatrogenic in origin[1].

The exact pathophysiology of SPS is unknown. Some authors have proposed the involvement of immunological components leading to abnormal interaction between maternal tissues and the fetal trophoblast[7]. However, there is evidence showing that the deposits of complement components and immunoglobulins are similar between pregnant women with SPS and healthy pregnant women[8]. Other studies have proposed that abnormal activity of complement components or long-lasting expression of apoptotic genes (such as the Bcl-2 oncoprotein that inhibits apoptosis and increases cell survival)

Figure 2. Congestive uterus showing region of placental site with multiple blood clots.



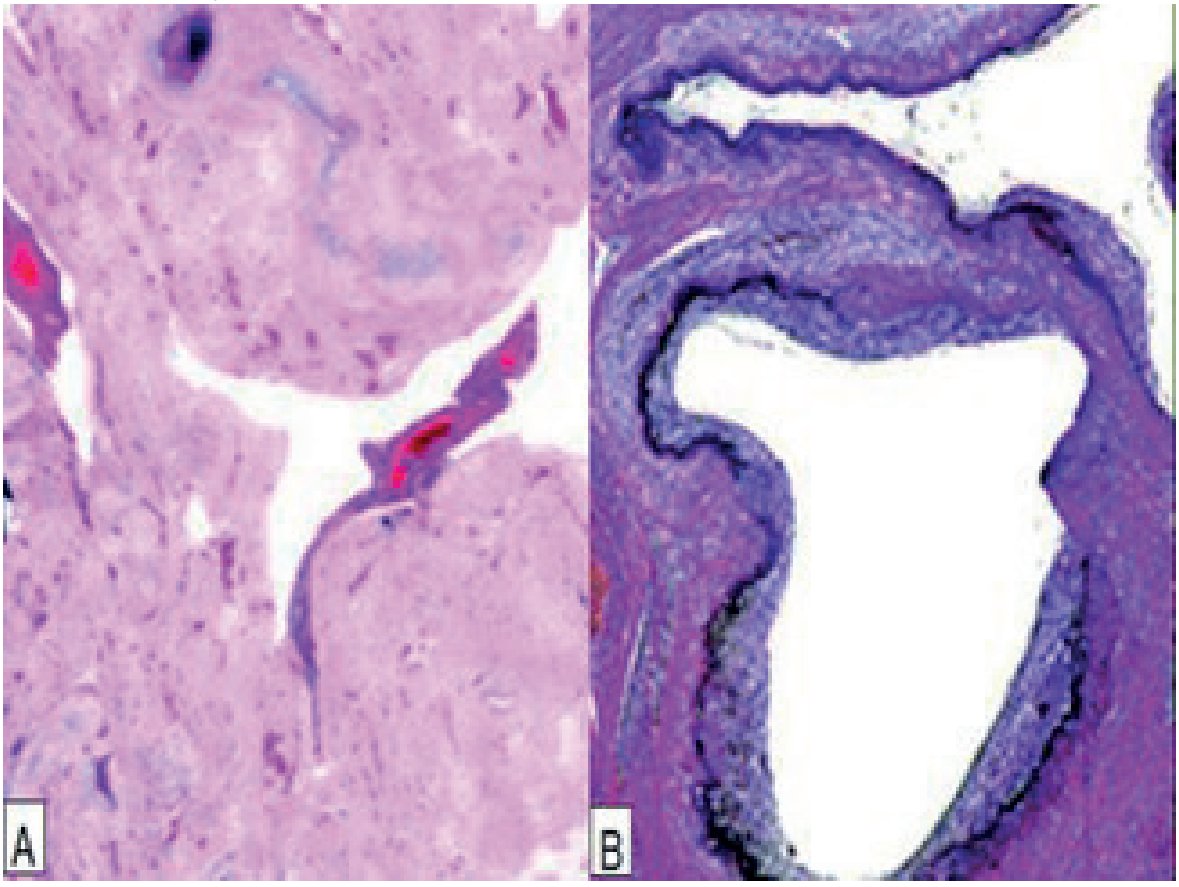
lead to partial and temporary luminal occlusion of uterine vessels in the superficial myometrium at the site of placental implantation[9].

Most cases of SPS are diagnosed within the second week after delivery, but there are reports of cases up to two months after delivery. Generally, the onset of genital bleeding is usually abrupt, prompting patients to seek immediate medical attention[1]. The main differential diagnoses include gestational trophoblastic disease, retained placental debris, placental accreta, and endometritis. Laboratory findings, such as elevated chorionic gonadotropin levels, inflammatory markers, and positive blood/vaginal cultures, along with examination of the birth canal, are essential to identify the cause of PPH[3].

The severity of PPH may be exacerbated by local tissue proinflammatory factors[10]. In addition, it may be increased by the presence of active infection, which may lead to the development of disseminated intravascular coagulation[11]. Some authors have proposed that this condition is more frequent in patients undergoing cesarean section, probably associated with mechanical changes (alteration of myometrial contraction and involution, fibrotic proliferation in the scar), immunological (autoimmune processes, reaction to suture material, local inflammation, lymphomonocytic and cytokine activity) or molecular (over- or underexpression of growth factor genes involved in uterine healing). These genes modify the replacement of decidua by endometrium, decreasing vascular collagen deposits, platelet aggregation and factor XIII activity at the maternal-fetal interface[12].

Ultrasound diagnosis of SPS can be made by pulsed wave Doppler ultrasound showing hypoechoic tortuous vessels with low-resistance vascular waves along the inner third of the myometrium. However, these alterations may be difficult to differentiate from congenital or acquired arteriovenous malformations. On the other hand, retained ovarian debris may present similar sonographic findings, so it is important to document the presence of echogenic placental tissue in the endometrial cavity[3].

Figure 3. Pathologic examination images. A) Dilated, tortuous and partially thrombosed arteries at the site of placental implantation together with involuted arteries (Hematoxylin-eosin stain, 20X). B) Patent myometrial artery with fibrinoid degeneration of its walls (hematoxylin-eosin stain, 100X).



Evaluation of the placental bed by examination of the entire uterus is the only way to make the diagnosis of SPS. In this condition hyalinized fragments of distended and patent uterine arteries with partial occlusion by thrombosis can be observed[2]. Unlike trophoblastic tumors, in the subinvoluted placental site the presence of endovascular trophoblast is an isolated finding and does not show a proliferation of trophoblastic cells. Fibrinoid changes of the vascular wall and the presence of inflammatory cells may suggest gynecologic or systemic vasculitis; but there are trophoblastic cells replacing the vascular endothelium[13].

The incidence of secondary PPH caused by SPS is very low, so its therapeutic management is similar to primary PPH[4]. The main objective is immediate hemodynamic stabilization and avoidance of coagulopathy. However, the use of measures other than hysterectomy remains controversial, especially in cases with severe bleeding[14]. Conservative treatment options include surgical evacuation of the uterine cavity, treatment with uterotonics and selective percutaneous arterial embolization of the uterine arteries, but the usefulness of these measures is not supported by sufficient data[15].

In conclusion, SPS is a rare form of secondary PPH. It is caused by the absence of changes in the uterine arteries in their pregestational state. Its pathophysiology is unknown and should be considered as a differential diagnosis to other causes of secondary PPH. It is essential to quickly identify the severity of bleeding to avoid hemodynamic shock and the development of coagulopathies. SPS is an important process to be aware of, as it implies an idiopathic, rather than iatrogenic, cause of PPH.

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