

# Exaggerated placental site/placental site trophoblastic tumor: an underestimated risk factor for emergency peripartum hysterectomy

J.R. De Miguel<sup>1</sup>, R. Quintana<sup>1</sup>, I. González-Rodilla<sup>2</sup>, J.M. Odriozola<sup>1</sup>, J. Schneider<sup>1</sup>

Departments of Obstetrics & Gynecology<sup>1</sup> and Pathology<sup>2</sup>, Hospital Universitario "Marqués de Valdecilla", Universidad de Cantabria, Santander (Spain)

## Summary

**Objective:** To assess the indications and possible underlying causes of emergency peripartum hysterectomy (EPH) at the present hospital during the 2001-2011 period. **Materials and Methods:** A revision of the charts and pathology reports corresponding to 42,728 parturients. **Results:** During the study period, 25 peripartum hysterectomies were performed (0.61/1.000), of which 23 were EPHs (0.54/1.000) and two were planned cesarean hysterectomies. The indication for EPH was acute postpartum hemorrhage in 22 of 23 instances (95.7%). Roughly two-thirds of the operated uteri (16/25, 64%) showed placental site anomalies, half corresponding to different degrees of placental accretism and half to anomalies derived from the implantation site intermediate trophoblast. In five cases (31%), the anomaly was an exaggerated placental site and three cases corresponded to placental site trophoblastic tumors. Of the 16 cases showing placental site anomalies, ten (62.5%) were associated with one or more previous cesarean sections. **Conclusions:** Roughly one-third of EPHs performed at the present center during the last ten years were associated with placental site anomalies originating in the implantation site intermediate trophoblast (exaggerated placental site and placental site trophoblastic tumor). This association has not been described before, and should be taken into consideration when facing acute peripartum hemorrhage predisposing to EPH.

**Key words:** Emergency peripartum hysterectomy; Placental site.

## Introduction

In modern obstetric practice of developed countries, unmanageable postpartum hemorrhage or other conditions requiring emergency peripartum hysterectomy (EPH) are rather exceptional. However, during the last two decades there has been an apparent rise in the frequency of EPH precisely in these countries [1]. Two factors preeminently associated with the incidence of EPH in modern series from the developed world are placental site anomalies, specifically different degrees of accretism, and previous cesarean section, which are themselves interrelated. Since cesarean section rates in developed countries are nowadays significantly higher than in the immediate past, the corollary is that the rising cesarean section rate has carried with it an upsurge of EPH as an unwanted side-effect [1, 2]. In comparison, classical risk factors such as uterine atony, uterine rupture, placenta previa, and sepsis are still the major risk factors for EPH in less developed countries, even in those with the most up-to-date technical facilities [3-5].

In our medium there is a prevalent feeling, especially among midwives, that the incidence of EPH is not only rising, but getting out of control, although the objective figures tell us that the real incidence has remained stable over the years, and well within the boundaries of international standards. However, it may well be that the pattern

of related causes has significantly shifted during later times, as has happened in other countries, giving the false impression that there is an unjustified explosion of EPHs, because formerly they were almost exclusively associated with uncontrollable uterine atony, something that has virtually disappeared from modern obstetric wards. Therefore, in the absence of the major classical cause of EPH, it appears inexplicable that there might be a relative increase thereof. The present authors have carried out the present study in order to analyze the exact situation regarding EPH and its indications in the present hospital, which is a tertiary-care, university-based teaching center.

## Materials and Methods

The authors revised the charts of mothers submitted to EPH at Hospital Universitario "Marques de Valdecilla", Cantabria University, Santander, Spain, between January 1<sup>st</sup>, 2001 and December 31<sup>st</sup>, 2011. During this period, there were 23 EPHs and two planned cesarean hysterectomies among 42,728 deliveries, for an overall incidence of 0.61 per 1.000 deliveries, and an adjusted incidence specifically for EPH of 0.54. The cesarean section rate remained stable around 20% (range: 18.1 – 24.9%) during this time span, with a slight decline during 2001 and 2002 and during the last two years of the study.

The clinical variables studied in relationship with EPH were age, parity, previous obstetric history, present obstetric history, kind of delivery, placental site anomalies, uterine anomalies, time interval between the onset of uterine hemorrhage and hysterectomy, medical interventions, indication for hysterectomy and pathological status of the surgical specimens. All excised

Revised manuscript accepted for publication December 3, 2013

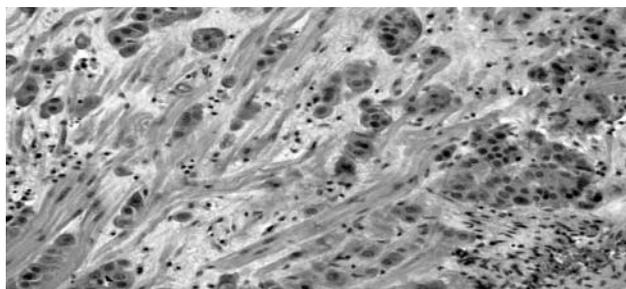


Figure 1. — Infiltration of the myometrium by intermediate trophoblast.

uteri and placentae were examined or revised by the same pathologist (IGR), who is the consultant for Obstetric and Gynecologic Pathology at the present hospital.

## Results

In all, 25 hysterectomies (14 total, 11 subtotal) were performed during the study period, of which 23 were EPHs and two planned cesarean hysterectomies. Of the corresponding 25 mothers, 18 (72%) delivered by cesarean section and seven vaginally. If compared to the general study population, this difference in the incidence of cesarean section is statistically significant (Chi-square test,  $p < 0.0001$ ). The indication for EPH was acute postpartum hemorrhage in 22/23 instances (95.7%). The only exception was a patient who developed a uterine necrosis secondary to an episode of acute appendicitis on the eighth day of puerperium. Out of the 22 patients with acute postpartum hemorrhage requiring EPH, 11 (50%) additionally developed disseminated intravascular coagulation. The onset of acute postpartum hemorrhage took place within the first hour postpartum in ten cases and between one and eight hours postpartum in 12 cases.

Two patients, finally, underwent planned cesarean hysterectomies, because of placental insertion anomalies (placenta increta and placenta percreta), correctly suspected by ultrasound and diagnosed by magnetic resonance imaging during their gestation.

Patient features associated with the indication of EPH were, in descending order: age above 35 years (17/25, 68%), one or more previous cesarean sections (11/25, 44%), and placenta previa (8/25, 32%).

The pathological examination of the operative specimens disclosed that roughly two-thirds of the uteri (16/25, 64%) showed placental site anomalies. Half of them corresponded to different degrees of accretism (five placenta accreta, two placenta increta, and one placenta percreta). In five cases (31%), the anomaly consisted of a seldom diagnosed entity in this context, exaggerated placental site (Figure 1). An additional case was a combination of exaggerated placental site and placenta accreta, and was as-

Table 1. — *Emergency peripartum hysterectomies 2001-2011. Pathological findings (n = 25).*

Pathological findings	n	%
Placental anomalies	16/25	64.0%
Placenta accreta	8/16	50.0%
Exaggerated placental site	5/16	31.3%
Placental site tumour	3/16	18.7%
Uterine necrosis	1	
Amniotic fluid embolism	1	
Abruptio placentae	1	
Normal puerperal uterus	6	24.0%

cribed to the just mentioned group of placenta accreta. The remaining three cases were placental site trophoblastic tumors, also a relatively rare condition. Of these 16 cases showing placental site anomalies, finally, ten (62.5%) were associated with one or more previous cesarean sections. All pathological diagnoses are summarised in Table 1.

## Discussion

The reported incidence of peripartum hysterectomy in some of the most advanced obstetric services of developed countries ranges between 0.4 and 0.85 per 1,000 deliveries [1, 2], which is approximately ten times lower than the figures reported for developing countries with comparable hospital facilities [3-5]. Our incidence of 0.54 per 1,000 lies well within the range for developed countries, of which our own forms part. Furthermore, the present authors registered also the same rate of main predisposing or associated causes reported in modern maternities, i.e., abnormal placentation causing postpartum hemorrhage, associated in turn to a history of previous uterine (cesarean) scar [1, 2]. In fact, roughly two-thirds of the present patients presented with anomalies of the placental site, and again roughly two-thirds of these arose on uteri having undergone one or more previous cesarean sections. One unexpected finding in the present series was that, of the placentation anomalies found, half of them, eight in all, typically corresponded to different degrees of macroscopically evident placental accretism, whereas, out of the other eight cases, five corresponded to exaggerated placentation, and three to placental site trophoblastic tumors. To the present authors' knowledge, the latter two entities have not been associated with an increased incidence of EPH before. It is interesting to note that, although both placental site trophoblastic tumor and exaggerated placental site derive from the same cell family, i.e., implantation site intermediate trophoblast [6], they are not genetically related [7], and therefore, one cannot be considered a precursor of the other. Nevertheless, it can be speculated that some kind

of alteration involving implantation site intermediate trophoblast, the implantation site itself or, more likely, the interaction between both, predisposes the uterus to acute peripartum hemorrhage, which in its turn leads to EPH.

In conclusion, roughly one-third of EPHs performed at the present center during the last ten years were associated with placental site anomalies originating in the implantation site intermediate trophoblast (exaggerated placental site and placental site trophoblastic tumor). This association has not been described before, and should be taken into consideration when facing acute peripartum hemorrhage predisposing to EPH.

## References

- [1] Awan N., Bennett M.J., Walters W.A.: "Emergency peripartum hysterectomy: a 10-year review at the Royal Hospital for Women, Sydney". *Aust. N. Z. J. Obstet. Gynecol.*, 2011, 51, 210.
- [2] Wong T.Y.: "Emergency peripartum hysterectomy: a 10-year review in a tertiary obstetric hospital". *N. Z. Med. J.*, 2011, 124, 34.
- [3] Chibber R., Al-Hijji J., Fouda M., Al-Saleh E., Al-Adwani A.R., Mohammed A.T.: "A 26-year review of emergency peripartum hysterectomy in a tertiary teaching hospital in Kuwait - years 1983-2011". *Med. Princ. Pract.*, 2012, 21, 217.
- [4] Rabi K.A., Akinlusi F.M., Adewunmi A.A., Akinola O.I.: "Emergency peripartum hysterectomy in a tertiary hospital in Lagos, Nigeria: a five-year review". *Trop. Doct.*, 2010, 40, 1.
- [5] Omole-Ohonsi A., Olayinka H.T.: "Emergency peripartum hysterectomy in a developing country". *J. Obstet. Gynecol. Can.*, 2012, 34, 954.
- [6] Shih I.M., Kurman R.J.: "The pathology of intermediate trophoblastic tumors and tumor-like lesions". *Int. J. Gynecol. Pathol.*, 2001, 20, 31.
- [7] Dotto J., Hui P.: "Lack of genetic association between exaggerated placental site reaction and placental site trophoblastic tumor". *Int. J. Gynecol. Pathol.*, 2008, 27, 562.

Address reprint requests to:

J. SCHNEIDER, M.D.

Hospital Universitario "Marqués de Valdecilla"

(Ginecología), Avenida Herrera Oria S/N,

39008 Santander (Spain)

e-mail: k049@humv.es