PREECLAMPSIA, TRISOMY 13, AND
THE PLACENTAL BED

Ronald F. Feinberg, MD, PhD,
Harvey J. Kliman, MD, PhD, and
Arnold W. Cohen, MD

Genetic predisposition and abnormal trophoblastic function are thought to contribute to the development of preeclampsia. A multipara developed severe preeclampsia and subsequently delivered a live growth-retarded infant with trisomy 13. Biopsy of the placental bed taken immediately after delivery demonstrated inadequate trophoblastic remodeling of the maternal uterine vasculature, with an absence of normal physiologic changes in the spiral arteries. This case suggests that fetal trisomy 13 can be associated with preeclampsia in multiparous women and that abnormal trophoblastic invasion may contribute to the pathophysiology. (Obstet Gynecol 78:505, 1991)

Preeclampsia is a common clinical syndrome with an unknown etiology and a complex pathophysiology. Although the significance of trophoblast function in this disease is not well understood, trophoblasts of normal pregnancy enhance blood flow to the placenta by invading and remodeling the uterine arteries into low-resistance channels. Pijnenborg et al.11 and Robertson et al.12 have proposed that inadequate trophoblastic invasion of the myometrial spiral arteries leads to preeclampsia through diminished uteroplacental blood flow, vasoospasm, and endothelial cell insult. The precise underlying biochemical defects that promote abnormal trophoblastic behavior and subsequent endothelial cell dysfunction are unknown. Recently, Boyd et al.13 proposed an association between fetal trisomy 13 and preeclampsia in nulliparous women, thus raising the possibility that the aberrant expression of genes on chromosome 13 could be relevant to the disease. We report a pregnant multipara who presented with severe preeclampsia, fetal trisomy 13, and the histopathologic findings of abnormal trophoblastic invasion into the uterine spiral arteries.

Case Report

A 30-year-old white woman, gravida 3, para 1, was transferred to the obstetric service of the Hospital of the University of Pennsylvania with severe preeclampsia at 31 weeks' gestation. Her previous pregnancy history included an elective termination 10 years earlier and cesarean delivery of a 3640-g female following a failed post-dates induction 3 years before this pregnancy. The patient's past medical history was remarkable for childhood petit mal epilepsy treated with dihydropyridine, and discoid lupus presenting with skin lesions 9 years before admission. She had no history of renal, pleural, pericardial, or central nervous system manifestations of systemic lupus erythematosus, and had never required steroids or nonsteroidal anti-inflammatory medications. In her previous, uncomplicated pregnancy, the patient had a positive antinuclear antibody and rheumatoid factor, but a negative lupus anticoagulant, anticardiolipin profile, and rapid plasmin reagent. There was no history of preeclampsia in her previous pregnancy, and the father was the same in the last two pregnancies.

From the Department of Obstetrics and Gynecology, and Pathology and Laboratory Medicine, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania.

Supported in part by Basil O'Connor Award no. 5-672 of the March of Dimes (RFF) and the University of Pennsylvania Research Foundation (RFF, HJC).

VOL. 78, NO. 3, PART 2, SEPTEMBER 1991

0029-7844/91/53.50 505
In this pregnancy, the woman initially presented at 14 weeks with a screening blood pressure of 120/70 mmHg and no proteinuria. Three weeks before admission, ultrasound had revealed an estimated fetal size that lagged 3 weeks behind the menstrual dates. On the day of admission, the patient complained of severe frontal headaches and was noted to have marked edema, 2+ proteinuria, and a blood pressure of 165/106 mmHg. At the time of transfer to our institution, her blood pressure was 190/110 mmHg. Sonography on admission indicated severe oligohydramnios and an estimated fetal weight of 850 g, based on measurements of the fetal femur and abdominal circumference. The abdominal diameter and femur length were over 2 standard deviations below the mean for 31 weeks. The estimated fetal weight was also below the tenth percentile for 31 weeks' gestation in our obstetric and neonatal population. Soon after admission, the patient was delivered by repeat cesarean of a live-born, 910-g female infant who was grossly malformed, with multiple craniofacial abnormalities, polydactyly, omphaloleole, and cardiac anomalies. After delivery, the patient's blood pressure normalized, and her postpartum course was complicated only by endomyometritis. Fetal karyotype subsequently revealed a 13q13q translocation (46,XX−13+t(13q; 13q)), resulting in a trisomic state for the long arm of chromosome 13.

Because this patient presented with severe and early preeclampsia, biopsy specimens of the placental bed were taken at cesarean, with previous patient written consent and Institutional Review Board approval at our institution. Histologic examination of three different biopsy sites revealed an absence of trophoblastic invasion into the myometrial segments of the maternal arteries. As shown in Figure 1, trophoblasts penetrated close to a spiral artery, but failed to invade and alter the thick muscular wall of the vessel. This is in marked contrast to a typical placental bed from a healthy pregnancy (Figure 2), where normal trophoblastic invasion has resulted in the appropriate physiologic conversion of thick muscular artery walls to dilated fibrinoid-walled vessels with lower resistance and higher capacitance.

Discussion

The clinical features of this case support the association proposed by Boyd et al., who first provided evidence for trisomy 13 as a factor in preeclampsia. Their study examined cases of fetal trisomy 13 over a 15-year period, focusing primarily on a series of five nulliparous women who developed preeclampsia. In their study, all five delivered females, as in our case. It is interesting that Boyd et al actually reported a paucity of preeclampsia in multiparas who delivered trisomy 13 infants. However, closer examination of their data indicates that in one of their nine nonprimigravid cases, there was a maximum blood pressure of 150/100 mmHg at 33 weeks, which may have signified the early development of preeclampsia. Subsequent to the study by Boyd et al, a published letter briefly described two cases of preeclampsia and coexistent fetal trisomy 13 in multiparous women (Thornton JG, O'Donovan P, Stigter R, Williams J. Pre-eclampsia and trisomy 13. Lancet 1987;i:794). Although it is difficult to carry out a thorough statistical analysis given the rarity of patients with trisomy 13 live births, our case also suggests that fetal trisomy 13 may contribute to the development of severe preeclampsia, even in multiparous patients. Furthermore, our case allowed us to examine the histology of the placental bed, which had not been previously described in trisomy 13-preeclamptic pregnancies.
Figure 2. Placental bed biopsy from normal pregnancy. Erythrocyte-filled myometrial segment of a uteroplacental artery shows fully developed physiologic changes as described previously by Pijnenborg et al.1 and Robertson et al.2 The muscular wall of the artery has been converted to a convoluted fibrinoid (F) layer by the penetrating trophoblasts (arrowheads). Some of the trophoblasts have replaced the endothelial layer (arrows). This vessel would have been even more dilated in situ, but after fixation it is artifically collapsed, resulting in a folded appearance. Bar (lower right) represents 20 μm (H&E, × 350).

Studies by Pijnenborg et al.1 and Robertson et al.2 have demonstrated that a pathognomonic feature of the placental bed in both preeclamptic and intrauterine growth retardation pregnancies is an absence of physiologic trophoblastic invasion of the deep maternal spiral arteries. This important trophoblast-maternal interaction, termed the second wave of trophoblastic invasion, occurs at 15–16 weeks' gestation and allows the development of low-resistance, high-capacitance channels within the myometrial segments of the spiral arteries. As hypothesized by these investigators, inadequate trophoblastic invasion leads to vascular spasm of the spiral arteries and restricted blood flow to the placental-fetal unit. In order to link vascular changes within the placental bed to hypertension, coagulopathy, and other systemic manifestations of preeclampsia, Roberts et al.8 proposed that diminished uteroplacental perfusion stimulates trophoblasts to release circulating compounds injurious to systemic vascular endothelium.

Although the precise etiology of preeclampsia is unknown, several complex factors—genetic, immunologic, and hematologic—are likely to contribute. Each may have a role in controlling trophoblastic invasion, placentation, and subsequent establishment of the uteroplacental circulation. In this case, the presence of a collagen vascular disease could have been a factor in the presentation, although the lack of systemic manifestations makes this less likely. To date, limited information exists to explain why the presence of genetically abnormal trophoblasts places certain patients at risk for preeclampsia. In gestational trophoblastic disease and triploidy, the association of genetically abnormal trophoblasts with early and severe preeclampsia appears to be significant.5–11 Recently, in a detailed examination of trisomic placentas, Rochelson et al.12 found unusual histologic alterations in both arterial muscle content and villous structure, although no correlation was made with the development of preeclampsia.

What does this case teach us about the contribution of genetically abnormal trophoblasts to the etiology of preeclampsia? Could a trophoblast gene product coded from chromosome 13 contribute directly or indirectly to preeclampsia? In this report, the placental bed histology raises the possibility that trophoblasts with an extra chromosome 13q were unable to properly invade and remodel the myometrial segments of uterine spiral arteries. More specifically, it is possible that aberrant expression of certain chromosome 13q genes could have contributed to abnormal trophoblast vascular remodeling. Genes mapped to chromosome 13q that might be relevant to the trophoblast-vascular interaction include the alpha 1 and 2 chains of type IV collagen, found in basement membranes, and clotting factors VII and X.13

The clinical presentation of this case, as well as the histologic findings in the placental bed, suggest that trisomy 13 may have been a factor overriding parity in the pathogenesis of this patient's preeclampsia. In chromosomally normal pregnancies, however, it is not known whether inadequate trophoblastic invasion represents a primary trophoblast defect or a consequence
of underlying maternal processes. Histologic and molecular analyses of preeclamptic placental bed tissue from chromosomally normal and abnormal pregnancies may eventually unravel those genetic factors controlling trophoblastic invasion and maternal vascular dysfunction. Moreover, unusual clinical situations that predispose to preeclampsia may provide some understanding of this perplexing, yet common, pregnancy complication.

References

Address reprint requests to:
Ronald F. Feinberg, MD, PhD
Department of Obstetrics and Gynecology
Hospital of the University of Pennsylvania
3400 Spruce Street
Philadelphia, PA 19104

Received April 3, 1990.
Received in revised form August 10, 1990.
Accepted September 28, 1990.

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PLACENTA PREVIA PERCERETA
INvolving the Urinary Bladder:
A Report of Two Cases and
Review of the Literature

Fredric V. Price, MD, Edward Resnik, MD, Kimberly A. Heller, MD, and Wayne A. Christopherson, MD

The incidences of both placenta previa and placenta accreta are increased in patients with scarred uteri, and patients with uterine scars and placenta previa are at increased risk

for also having placenta accreta. Two cases are presented of placenta previa percreta with involvement of the urinary bladder necessitating cesarean hysterectomy, partial cystectomy, and, in one case, bilateral ureteral reimplantation. Both patients had two previous cesarean deliveries. Serious hemorrhage is common in patients with placenta percreta. The primary goal of surgical management must be to control bleeding, which usually requires resection of all tissue involved by the infiltrating placenta. After hemorrhage is controlled, the surgeon must reestablish the integrity of the urinary system and reconstruct the pelvis as necessary. (Obstet Gynecol 78:508, 1991)

Placenta percreta involving the urinary bladder is fortunately a rare condition. When the placenta infiltrates anteriorly through the myometrium and pubocervical fascia, the normal cleavage planes between the placenta and uterus and between the lower uterine segment and the bladder are obliterated. Profuse hemorrhage is common and is responsible for the high