Placental massive perivillous fibrin deposition after a previous uncomplicated term pregnancy: report of two cases

Silvia Soddu, MD[1]
Giuseppina Parodo, MD[1]
Gavino Faa, MD[1]
Anna Maria Paoletti, MD[2]
Gian Benedetto Melis, MD[2]
Sara Deiana, MD[2]
Daniela Porru, MD[2]
Alessandra Meloni, MD[2]

[1] Department of Surgical Sciences, Division of Pathology, University of Cagliari, Italy
[2] Department of Surgical Sciences, Division of Obstetrics and Gynaecology, University of Cagliari, Italy

Correspondence to:
Silvia Soddu
Via Ospedale 46, 09100, Cagliari, Italy
E-mail: silvia_soddu@yahoo.it

Summary
Massive perivillous fibrin deposition (MPFD) and maternal floor infarction (MFI) are rare and poorly understood placental lesions often leading to preterm delivery, intrauterine fetal growth restriction (IUGR), and fetal death. An association between MPFD and thrombophilia has been reported. Here, we report two cases in which MPFD followed a previous uncomplicated term pregnancy. MPFD was diagnosed on the basis of standard criteria (transmural fibrinoid deposition).
Case 1 was a 33-year-old woman who presented with IUGR at 21 weeks; intrauterine fetal death occurred at 25 weeks. Case 2, a 32-year-old woman, noted reduced fetal movements and was diagnosed with IUGR at 29 weeks. Despite immediate cesarean section, the newborn survived for just a few days. Autopsy showed no abnormalities in either fetus. Placental histology showed villi (>60% of placental mass in both cases) entrapped by large amounts of deposited fibrinoid material. Neither woman had a medical history of autoimmune disease or any blood coagulation disorder. Complete thrombophilia screening was not performed.
Our data show that MPFD may occur in women after a previous normal term pregnancy. Given the high reported recurrence rate (~50%) of this placental pathology, further pregnancies should be considered at risk of MPFD. Women should be tested for thrombophilia in order to improve the management and fetal outcome of subsequent pregnancies.

Keywords: fetal death, growth retardation, placenta, placental circulation, premature birth.

Introduction

Massive perivillous fibrin deposition (MPFD) and maternal floor infarction (MFI) are unusual placental disorders with distinctive gross and histopathological features defined by enmeshment of chorionic villi in fibrinoid material, leading to varying degrees of placental insufficiency.
The terms MPFD and MFI are often used interchangeably in the literature even though "infarction" is formally incorrect, given that ischemic necrosis is absent and the lesion is not a true infarct.
Estimated incidence rates have been reported to be in the range of 0.028-0.5% (1,2). The etiology is uncertain. MPFD has been associated with recurrent pregnancy loss, preterm delivery, fetal growth restriction, stillbirth, neurodevelopmental impairment (3,4), and a high risk of recurrence in subsequent pregnancies.
Here we present two cases of MPFD occurring in women who had each previously had an uncomplicated term pregnancy. In both cases, intrauterine fetal growth restriction (IUGR) was diagnosed.

Case Reports

Case 1. A 33-year-old woman, with a clinical history of a previous extrauterine pregnancy followed by an uncomplicated term pregnancy five years earlier, presented in good health for a routine ultrasound check at 21 weeks of gestation.
The ultrasound scan revealed severe fetal growth restriction with head circumference and abdominal circumference below the 5th percentile and oligohydramnios. Doppler velocimetry showed central redistribution of blood flow. Subsequent examinations confirmed these findings. Maternal routine blood clotting tests (prothrombin time, partial thromboplastin time, antithrombin III, fibrinogen) were performed and all values were in the reference range. Fetal heart rate was monitored over the following days until, at 25 weeks of gestation, intrauterine fetal death was diagnosed.
The woman was admitted to our hospital where delivery was induced, resulting in a male fetus weighing 365 g. Autopsy showed morphometric measurements consistent with 22 to 23 weeks of gestation and no malformations or pathological lesions were found.
The formalin-fixed trimmed placenta weighed 180 g (fetoplacental weight ratio: 2.02, below the 10th percentile), measured 10.5 x 9 x 2 cm, and had a segment (length 7.5 cm) of umbilical cord paracentrally inserted.

Case 2. A 33-year-old woman reporting a previous live birth at term without complications three years before the present pregnancy presented at 29 weeks of gestation after noting reduced fetal movements. Except for a di-

agnosis of celiac disease at the age of 26, the medical history of the patient was unremarkable.
Ultrasound scan revealed IUGR with head and abdominal circumferences below the second negative standard deviation, femur length at the first negative standard deviation, and anhydramnios.
The patient was admitted to our hospital. Doppler velocimetry of the umbilical artery showed absent end-diastolic flow associated with a reduction of impedance to flow in the middle cerebral artery (pulsatility index, 1.31). Maternal routine blood clotting tests (prothrombin time, partial thromboplastin time, antithrombin III, fibrinogen, protein C, protein S) were in the reference range. Autoimmune disease screening, including anti-smooth muscle antibodies (ASMA), anti-mitochondrial antibodies (AMA), anti-parietal cell antibodies (APCA), extractable nuclear antigen antibodies (ENA), perinuclear anti-neutrophil cytoplasmic antibodies (pANCA), cytoplasmic anti-neutrophil cytoplasmic antibodies (cANCA) and antireticulin antibodies (ARA), was negative.
The patient underwent a cesarean section and delivered a live male infant weighing 850 g (10th percentile) with an Apgar score of 3 at the first minute. The baby was admitted to the Neonatal Intensive Care Unit with severe neurological impairment. He died 12 days later.
At autopsy, the baby had morphometric measurements consistent with 28 weeks of gestation. No malformation was detected on external examination. All thoracoabdominal organs were regularly positioned and formed, showing the proper volume and shape. The only pathological finding was a left intraventricular cerebral hemorrhage.
The formalin-fixed trimmed placenta weighed 279 g (feto-placental weight ratio: 2.94, below the 10th percentile), measured 13 x 10 x 2.8 cm, and had a segment (length 11.5 cm) of umbilical cord paracentrally inserted.

Pathology reports

Both placentas showed similar characteristics and MPFD was diagnosed on the basis of standard criteria (5).
On gross examination, both placentas shared several distinctive features. The basal plate was pale gray, firm and stiffened. On serial sectioning, the cut surfaces had a diffuse gray-brown appearance (Fig. 1).

Figure 1 - Gross examination: diffuse stiff gray-brown appearance of cut surfaces.

Histological examination showed immature villi entrapped by fibrinoid eosinophilic material; 70-80% and 50-60% of the placental mass was involved in case 1 and case 2 respectively (Fig. 2 a,b). The syncytiotrophoblast and capillary endothelium of the villi involved showed variable degrees of eosinophilia and karyorrhexis, but the intervillous space was not collapsed as it would have been in a true maternal infarct. The intervening areas showed hypercapillarization of villi with increased syncytial knots (Tenney-Parker change)

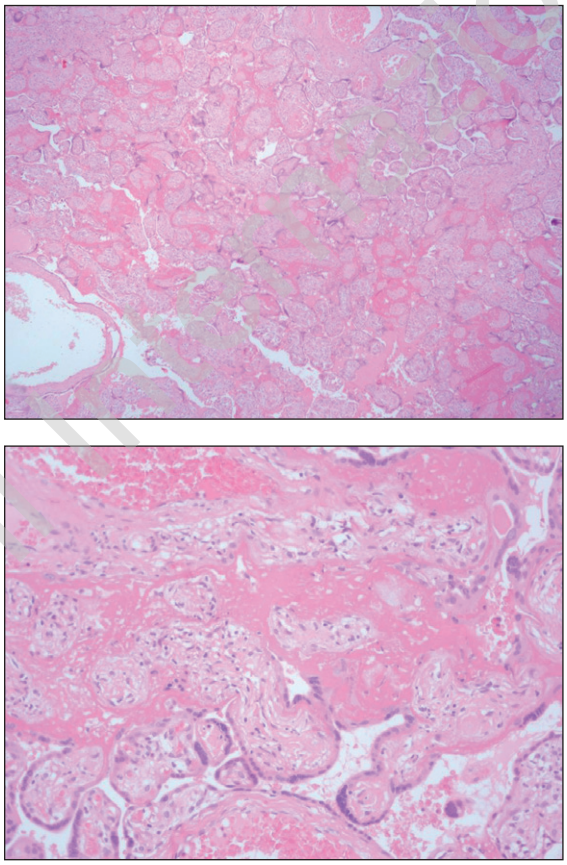

Figure 2 a,b - a) Hematoxylin and Eosin (HE) 4x; b) Hematoxylin and Eosin (HE) 10x.
More than 60% of villi in both cases were entrapped by fibrinoid material. The intervillous space was not collapsed.

Discussion

Massive perivillous fibrin deposition is an idiopathic placental disorder defined by the accumulation of eosinophilic fibrinoid material around large portions of the distal villous tree (6,7). This lesion must be distinguished from small amounts of fibrin or fibrinoid material, which are common histological findings in normal placentas at term and are not considered pathological lesions.
The obstruction of the intervillous space precludes gas exchange between the maternal and fetal blood. Fibrin deposition involving 40 to 50 percent of the placental mass is usually fatal for the fetus. Milder lesions, however, inter-

fere with maternal-fetal perfusion and cause IUGR in 24-100% of cases (8).

The etiology and pathogenesis of the disorder are not fully understood. Genetic factors have been considered possible causes. Gogia and Machin studied the frequency of acquired and genetic thrombophilias in cases with MFI and/or MPFD. They reported an identifiable thrombophilic factor in 40% of their series. Genetic factors accounted for more than 70% of all thrombophilias, the most common being protein S deficiency (9).

Since the rate of recurrence of MPFD approaches 50%, an autosomal dominant pattern of inheritance has been hypothesized, assuming that maternal heterozygosity would not be sufficient for development of the disorder. According to this hypothesis, MPFD would be fully expressed only when the mother and fetus both carry the mutation. It is thus necessary to consider the possibility not only of maternal but also of paternal inheritance, which might take the number of possible "thrombophilic hits on the placenta" to at least four (9).

Several cases of MPFD have been reported in association with autoimmune diseases, such as polymyositis, antiphospholipid antibody syndrome, scleroderma and SLE (10,11).

A primitive trophoblastic injury (immunological, ischemic or infectious) could downregulate expression of endogenous anticoagulants leading to a localized hypercoagulable state in the placenta, which might eventually trigger fibrin deposition (10,12).

Low incidence rates of MPFD contribute to poor knowledge and low awareness of this problem. However, the high risk of recurrence and the adverse consequences of MPFD make it a condition that warrants more attention. Fetal growth restriction, oligohydramnios, a hyperechoic appearance of the placenta on ultrasound, and elevated serum levels of -fetoprotein have been suggested by Mandsager (13) as signs alerting to the condition, especially in cases of recurrence.

Both the cases here reported were associated with IUGR, at 21 and 28 weeks of gestation respectively, and occurred in pregnancies that, until then, had been uneventful. This finding suggests that MPFD may develop rapidly, having a dramatic and specific negative effect on fetal growth.

Furthermore, both women had had one previous uncomplicated term pregnancy, which suggests that this lesion is not the inevitable result of maternal disease in any given pregnancy, as reported by others.

Our report highlights the possibility of the occurrence of MPFD after a previous normal pregnancy, and emphasizes the severe adverse fetal outcome of this albeit rare lesion. In view of the high reported recurrence rate (~50%) of this placental pathology, further pregnancies should be considered at risk of MPFD and women should be tested for thrombophilia in order to improve the management and fetal outcome of subsequent pregnancies.

References

1. Bane AL, Gillan JE. Massive perivillous fibrinoid causing recurrent placental failure. BJOG 2003;110:292–295
2. Naeye RL. Maternal floor infarction. Hum Pathol 1985; 16:823-828
3. Andres RL, Kuyper W, Resnik R, Piacquadio KM, Benirschke K. The association of maternal floor infarction of the placenta with adverse perinatal outcome. Am J Obstet Gynecol 1990;163:935–938
4. Adams-Chapman I, Vaucher YE, Bejar RF, Benirschke K, Baergen RN, Moore TR. Maternal floor infarction of the placenta: association with central nervous system injury and adverse neurodevelopmental outcome. J Perinatol 2002;22:236-241
5. Katzman PJ, Genest DR. Maternal floor infarction and massive perivillous fibrin deposition: histological definitions, association with intrauterine fetal growth restriction, and risk of recurrence. Pediatr Dev Pathol 2002;5:159-164

6). Frank HG, Kaufmann P. Nonvillous parts and trophoblast invasion. In: Benirschke K, Kaufmann P, Baergen R eds Pathology of the Human Placenta. New York; Springer 2006. Fifth edition: 281-284

7. Kraus FT, Redline RW, Gersell DJ, Nelson DM, Dicke JM. Placental Pathology. Atlas of Nontumor Pathology. Washington, DC; American Registry of Pathology 2004
8. Redline RW, Jiang JG, Shah D. Discordancy for maternal floor infarction in dizygotic twin placentas. Hum Pathol 2003;34:822-824
9. Gogia N, Machin GA. Maternal thrombophilias are associated with specific placental lesions. Pediatr Dev Pathol 2008;11:424-429
10. Al-Adnani M, Kiho L, Scheimberg I. Recurrent placental massive perivillous fibrin deposition associated with polymyositis: a case report and review of the literature. Pediatr Dev Pathol 2008;11:226-229
11. Sebire NJ, Backos M, Goldin RD, Regan L. Placental massive perivillous fibrin deposition associated with antiphospholipid antibody syndrome. BJOG 2002;109:570-573
12. Sebire NJ, Backos M, El Gaddal S, Goldin RD, Regan L. Placental pathology, antiphospholipid antibodies, and pregnancy outcome in recurrent miscarriage patients. Obstet Gynecol 2003;101:258-263
13. Mandsager NT, Bendon R, Mostello D, Rosenn B, Miodovnik M, Siddiqi TA. Maternal floor infarction of the placenta: prenatal diagnosis and clinical significance. Obstet Gynecol 1994;83:750-754