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RECURRENT ABRUPTIO PLACENTAE IN A CYNOMOLGUS MONKEY (*Macaca Fascicularis*)

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Abstract

Introduction—Abruptio placentae, defined as premature separation of a normally implanted placenta, is the life threatening pregnancy complication with unknown pathophysiology. A history of abruptio placentae is the major risk factor for this pregnancy complication in humans. We describe the first case of recurrent abruptio placentae in a *M. fascicularis*.

Material and methods—A pregnant *M. fascicularis* at term gestation was presented with weakness and hypothermia. Cesarean section revealed retroplacental hemorrhage with partial placental separation from the uterus.

Results—The weight of the female fetus was within the lower birth weight range for these species. The maternal side of placenta contained necrotic tissue, occupying approximately 60% of the maternal surface. The placental implantation bed demonstrated neutrophil infiltration. Perivascular collections of lymphocytes were noticed in the uterine smooth muscle.

Conclusion—This case report underlines the importance of neutrophil infiltration and uterine venous drainage in the cascade of events leading to abruptio placentae.

Keywords

Placenta; Abruptio; non-human primates; macaques

INTRODUCTION

Abruptio placentae, defined as premature separation of a normally implanted placenta, is a black box of pregnancy complications in humans and is one of the leading causes of maternal and fetal mortality, accounting for 10-20% of perinatal deaths. The greatest

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determinant of abruption risk is premature placental separation in prior pregnancy [1]. The clinical presentation of abruptio placentae can range from the classical well described clinical picture to asymptomatic retro-placental hematoma [2]. Macaques have been used as an experimental model of abruptio placentae; however, recurrent cases have not been described in any non-human primates yet. We describe the first case of recurrent abruptio placentae in a *Macaca fascicularis*.

CASE REPORT

Routine daily observation discovered a 13-year-old, pregnant *M. fascicularis* at term gestation with general weakness and lack of physical activity. External examination revealed pale mucous membranes and a body temperature of 95.2°F. Blood analysis showed absence of antibodies for B-virus, Simian Immunodeficiency Virus and Simian T-Cell Leukemia Virus, but presence of antibodies for measles and Simian Respiratory Virus. Emergency cesarean section was performed, and a female fetus was delivered without life signs. Placental weight was 89.1 g. The dam was euthanized due to poor prognosis. Eight months prior, this animal had a cesarean section due to sustained dystocia. The stillborn female offspring weighed 92 grams. The placenta weighed 49 grams and showed retro-placental hematoma. Two prior deliveries were unremarkable.

Gross examination of the fetus revealed a non-macerated, fully developed female (Fig. 1A) with weight of 321.1 grams, body length of 25.5 cm; chest circumference of 11.5 cm; waist circumference of 10.5 cm; hip circumference of 9 cm; abdominal distance of 3 cm; femur length of 5.5 cm. The lungs were not inflated, the colonic contents had not passed, and the stomach was empty.

Grossly, the placenta contained a single disc; the transparent fetal membranes were marginally inserted (Fig 1B). The placental diameter was 11.11cm, placental thickness was 1.2 cm, and umbilical cord length was 31 cm. The umbilical cord was hypercoiled with venous dilatation and congestion and eccentrically inserted. The fetal surface showed marked vascular congestion. The maternal surface had a 5-6 cm in diameter, deeply and eccentrically compressed thin area covered by tan-gray membranous necrotic tissue, occupying approximately 60% of the maternal surface, and surrounded by a zone of vascular congestion (Fig. 1C). Detached blood clots weighed 18.4 grams. Microscopically, the development of the villi was age-appropriate; no inflammation was identified. The compressed area showed significant loss of parenchyma with intraplacental hemorrhage, decidual necrosis and areas of infarction involving the placental villi (Fig 1D, 1E, 1F). The peripheral villi were congested. Placental culture revealed growth of Group D *Streptococci*, non- *Enterococci*.

The uterus was enlarged, soft and congested. The placental implantation bed demonstrated dilated blood vessels, necrosis and hemorrhage (Fig. 1 G); microscopically there was necrosis and thrombosis with predominantly neutrophil infiltrates. The adjacent stromal connective tissue contained clots and healing elements, isolating the focus of hemorrhage (Fig 1H). The viable decidua and uterine smooth muscle contained multifocal generally perivascular collections of lymphocytes (Fig 1I). The placental membranes had neutrophil and macrophage infiltration (Fig 1J). No other significant microscopic lesions were seen. We additionally measured the myometrial thickness of the uterus in *M. Fascicularis* at term (Fig. 1K, 2 mm). This animal died from dystocia and underwent routine pathological examination.

DISCUSSION

A history of abruption in prior pregnancies is the major risk factor for future abruptio placentae in humans [1]. The “anti-abruption forces” [3] are proportional to the flow rate in the intervillous space, which is determined by, among other things, the diameter of spiral arteries and veins [4]. Pathologic venous drainage has been suggested contribute to the risk for abruption [5]. In the macaque myometrium, multiparity has been associated with the deposition of eosinophilic hyaline substance around the veins [6]. While this change was not present in the animal in our case report, the perivascular collections of lymphocytes in the myometrium and dilated placental bed vessels support the idea that uterine drainage is an important mechanism of placental attachment. Nevertheless, it is difficult to draw a conclusion regarding cause-and-effect relationships based on this case.

The accumulation of neutrophils in the fetal membranes and decidua in our study is in agreement with published human data regarding the link between neutrophil infiltration and abruptio placentae [7]. However, in our case this infiltration was not associated with pre-term delivery. It has been suggested that neutrophil infiltration might lead to abruption and vice versa; for example, fibrin deposition during chronic abruption might trigger a neutrophil infiltration.

The pregnancy subsequent to abruptio placentae is at risk for fetal growth restriction [8]. The weight of the fetus in our case report was within the low range of birth weights published for *M. Fascicularis* [9]. The placental weight was higher than that reported in the literature for these species (58.9-72.2gm) [10]. That might represent a compensatory mechanism for the loss of almost 60% of the placental exchange area. Alternatively, this increased weight could be also at least partially associated with increased blood content resulting from the intraplacental hemorrhage. In our case, the placenta cultured positive for group D *streptococci*; in humans, such colonization has been reported in low grade systemic inflammation in full term and premature infants [11].

The parallels between the clinical and histological presentation of abruptio placentae in humans and macaques are striking, especially considering that macaque trophoblast invasion is shallow and the myometrial wall is thinner in macaques compared to humans (1-2 mm vs 6-8 mm respectively) [12].

CONCLUSION

This is the first case report of recurrent abruptio placentae in a *M. Fascicularis*. It shares many similarities to the condition in humans, including premature separation of placentae with neutrophil infiltration of the decidua and fetal membranes, and demonstrates the involvement of uterine venous drainage in the cascade of events leading to abruption placentae.

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FIGURE 1.

Placental abruption in a 13-years-old *Macaca fascicularis*. **A.** Demised fetus. **B.** Placenta. The hypercoiled umbilical cord with venous dilation and congestion is seen. Fetal surface shows vascular congestion. **C.** Placenta. Maternal side shows compressed surface covered by fibrous materials (*F*) and free blood clots (*BC*). **D.** Intraplacental hemorrhage (*IH*). **E.** Decidual neutrophil infiltration (*). **F.** Decidual necrosis with inflammation (*N*). **G.** Implantation bed in uterus (*U*) with areas of necrosis (*N*) and hemorrhage (*H*). **H.** Uterus. Note decidual clots (*), granulation tissue (**) and necrosis (***). **I.** Uterus. Blood vessel and lymphocytes in the decidua (arrow). **J.** Acute choriodecidualitis in the extra placental fetal membranes (arrow). **K.** Gross section of uterus (*U*) and placenta (*P*).