



# Perinatal Stroke Associated with Placental Chorioangioma: A Rare Case and Review of Literature

Nam Rri Kim, MD<sup>1</sup>,  
Soo Hyun Kim, MD<sup>1</sup>,  
Suk-Joo Choi, MD, PhD<sup>1</sup>,  
Soo-young Oh, MD, PhD<sup>1</sup>,  
Jung-sun Kim, MD, PhD<sup>2</sup>,  
Cheong-Rae Roh, MD, PhD<sup>1</sup>,  
Jong-Hwa Kim, MD, PhD<sup>1</sup>

Departments of <sup>1</sup>Obstetrics and  
Gynecology, <sup>2</sup>Pathology, Samsung  
Medical Center, Sungkyunkwan  
University School of Medicine,  
Seoul, Korea

Placental chorioangioma is the most common non-trophoblastic and hamartoma-like tumor and has generally good prognosis if the size is small. The incidence of a placental chorioangioma is an estimated 1% of all deliveries. The size of a chorioangioma is considered significant if it is larger than 4 cm, since fetal compromise can occur due to circulatory overload. Very rarely, a placental chorioangioma can directly exert fetal circulation to cause fetal cerebral ischemic stroke, especially in giant placental chorioangiomas which are defined as more than 4-5 cm in diameter. Here, we report a case of a huge chorioangioma, sized 7×5 cm with thrombo-occlusion in the placenta associated with neonatal stroke. Perinatal stroke and giant placental chorioangioma are each very rare. Moreover, the combination is extremely rare as is expected. Our case implicates that placental examination should be considered as an important diagnostic workup in cases of perinatal stroke with unknown etiology.

**Key Words:** Placental chorioangioma, Perinatal stroke, Perinatal cerebral infarction

## Introduction

Placental chorioangioma is the most common non-trophoblastic and hamartoma-like tumor originating from capillaries or larger vessels. Its incidence is in 1% of all placentas<sup>1,2</sup> and its size is significant because if a chorioangioma is larger than 4 cm, circulation can be affected, resulting in fetal compromise. For example, polyhydramnios, preterm delivery, fetal anemia or thrombocytopenia, pre-eclampsia and fetal hydrops can be seen.<sup>3,4</sup> Especially giant placental chorioangiomas, which are defined as more than 4-5 cm with an estimated prevalence varying from 0.002% to 0.01%, are associated with high prevalence of pregnancy complications and poor perinatal outcomes.<sup>5</sup>

A perinatal stroke refers to a stroke occurring in a period up to the 28th day of life and its incidence is about 0.025%.<sup>4,6,7</sup> In addition, a chorioangioma can cause fetal cerebral ischemic stroke so obstetrician and pediatrician should aware of it.<sup>8</sup> Chorioangioma can be the cause of the tendency of thrombosis due to the characteristics of a tortuous vascular system. We report a case of a huge chorioangioma with thrombo-occlusion in the placenta associated with neonatal stroke.

## Case

A 31-year-old pregnant woman with gravida 0 para 0 was transferred from a local clinic to this hospital for delivery due to a large placental mass at 36 weeks of gestation. During antenatal check-up at the local clinic, there were no abnormal findings at screening ultraso-

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### Corresponding author

Soo-young Oh, MD, PhD  
Department of Obstetrics and  
Gynecology, Samsung Medical  
Center, Sungkyunkwan University  
School of Medicine, 81 Irwon-ro,  
Gangnam-gu, Seoul 06351, Korea

**Tel:** +82-2-3410-3517

**Fax:** +82-2-3410-0630

**E-mail:** ohsymd.oh@samsung.com

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nography in the second trimester, serum screening test, gestational diabetes and routine laboratory test. Through ultrasonography, large for gestational age with polyhydramnios, estimated fetal weight was 3,561 g (>90 percentile) and amniotic fluid index was 26.46 cm (deepest 9.52 cm), a 7×5 cm-sized placental mass (Fig. 1) was found. We considered fetal Beckwith-Wiedemann syndrome as one differential diagnosis. Because cephalopelvic disproportion was clinically suspected, elective cesarean delivery was planned after careful counseling with the patient.

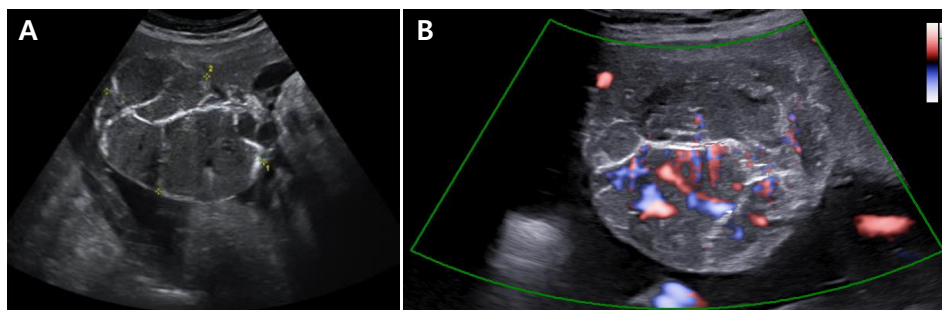
A 3,740 g female infant was born by elective cesarean section at 39 weeks of gestation with Apgar score of 8 and 8 at 1 and 5 minutes, respectively. The baby showed no gross anomaly and in the fetal side of the placenta, there was a 7×7 cm-sized round and well circumscribed mass suggesting chorioangioma.

The arterial pH of cord blood at birth was 7.298 and base excess was negative 2.3 mmol/L. The baby was moved to a nursery room and the only abnormal finding from physical examination by a pediatrician was increased head circumference (37.5 cm, >90 percentile). Overall her activity was good and oral feeding was appropriate.

Thirty hours after birth, unexpectedly, the baby manifested tonic-clonic movement at right upper and lower limb twice and thus an anticonvulsive agent (phenobarbital) was initially infused, there were no risk factors of epilepsy at neonatal period, and no familial history of epilepsy. The brain ultrasonography taken at the day after birth showed asymmetrical ventricles with irregular choroid plexus contour, otherwise no abnormal findings associated with this event (Fig. 2A). An echocardiogram

showed just a small patent ductus arteriosus and physiologic atrial septal defect. Abdominal ultrasonography showed no specific findings. On day 3 after birth, electroencephalography was done and showed normal. After the phenobarbital treatment, no more seizures occurred.

As for a diagnostic workup for perinatal stroke, the platelet count was 260,000/ $\mu$ L, Hemoglobin and hematocrit were 17.2 g/dL and 50.7%, respectively. A blood culture showed no microorganism. Coagulation studies showed a serum fibrinogen level of 347 mg/dL within normal range. International normalized ratio (INR) INR level of 0.85, antithrombin III level of 68% (60–89%), protein C activity level of 40% (28–54%) and protein S activity level of 67% (33–67%) were within normal limits. Serum ammonia increased to a level of 93.1  $\mu$ mol/L (11.2–48.2  $\mu$ mol/L). Brain magnetic resonance (MR) imaging was done on day 7 after birth and showed acute infarction in the left temporo-parieto-occipital area that was supposed to be a venous infarct due to a superior sagittal sinus thrombus or arterial infarcts on the posterior division of middle cerebral artery territory and diffuse excessive high signal intensity of white matter on T2W1 (Fig. 2B). Follow-up brain ultrasound was done on day 8 and showed no demonstrable superior sagittal sinus thrombosis or hemorrhage, but mild asymmetrical parenchymal swelling with slightly increased echogenicity involving the left temporo-parietal area due to acute infarct. A further workup was done for the etiology of cerebral infarction. Serum examination for toxoplasmosis, rubella, cytomegalovirus, and herpes simplex type 1 & 2 IgM were negative. Ammonia level was normalized to 47.0  $\mu$ mol/L on day 7 after birth and newborn screening test

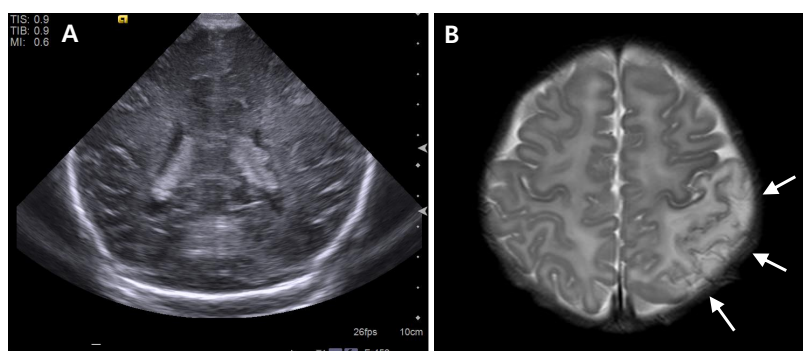


**Fig. 1.** (A) In ultrasonographic examination at 36 weeks of gestation, a 7×5 cm sized well circumscribed, round, heterogeneous mixed echoic mass along the fetal surface of the placenta was seen. (B) It looks chorioangioma and with color Doppler sonography increased blood flow was seen along the hypoechoic portion of mass. Giant chorioangioma measuring more than 4 cm has a risk of shunting of blood flow from fetus to mass.

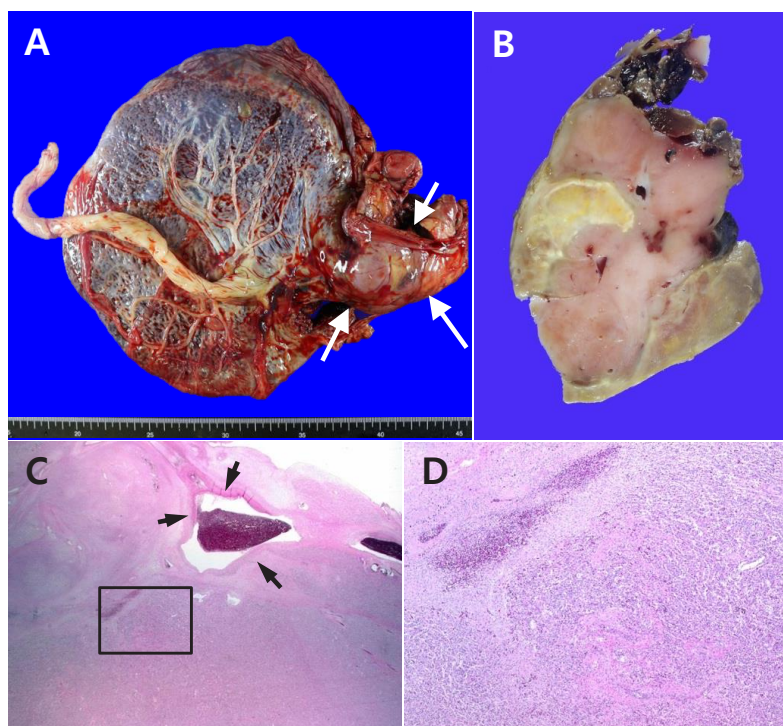
was negative. Cerebrospinal fluid analysis and culture were done and showed no specific findings.

A thorough placental pathologic exam was requested and per-

formed by a pathologist (JSK). Microscopically, the placental mass was mainly composed of benign capillary proliferation, characteristic of chorioangioma. Multifocal infarcts and calcifi-



**Fig. 2.** (A) The brain ultrasonography taken at the day after birth showed asymmetrical ventricles with irregular choroid plexus contour, otherwise no abnormal findings associated with this event. (B) Seven days after birth, brain magnetic resonance imaging was done and the arrow indicates acute infarction in left temporo-parieto-occipital area (arrows) that supposed venous infarcts due to superior sagittal sinus thrombus or arterial infarct on posterior division of middle cerebral artery territory.



**Fig. 3.** Pathological findings of the placental mass. (A) A lobulated solid mass (arrows) is present at the periphery of the placental disc. (B) The cut surface of the mass is pinkish brown with multifocal tan brown or yellow degenerating areas. (C) Microscopically, the mass is composed of proliferating capillaries (lower area) with multifocal infarction (upper left area). The adjacent large vessels show fibrin deposition in the wall with early thrombi (arrows). (D) The magnified image of the inset in (C). Original magnification in (C) 10 $\times$ , (D) 50 $\times$ .

cations were identified in the mass. Adjacent vessels showed intimal fibrin deposition and early thrombi (Fig. 3).

Two months after birth, brain MR imaging and MR angiography follow up were done and showed attenuation of left distal middle cerebral artery branch due to previous arterial obstruction or secondary changes after infarction. In addition, progression of encephalomalacia of the left parietal lobe was seen (Fig. 4). Fortunately her performance was good without any problem and she grew up normally till 6 months after birth. She took phenobarbital 10 mg twice a day and stopped taking anticonvulsant at 4 months after birth.

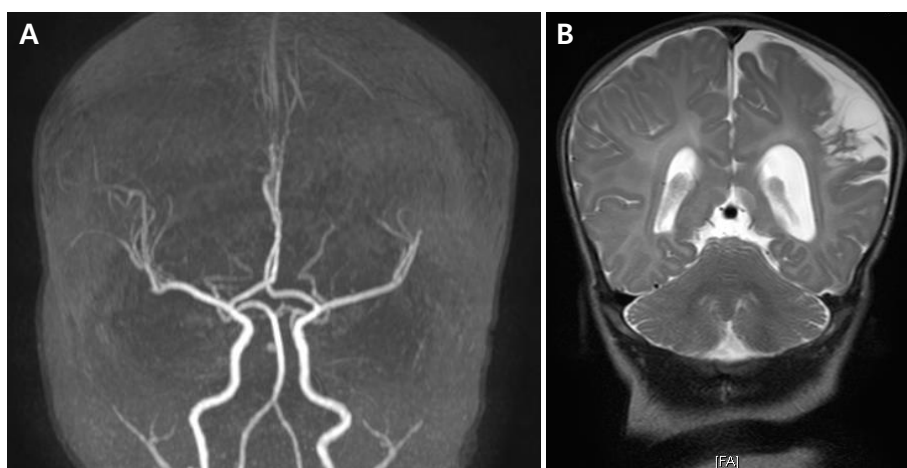
## Discussion

If placental chorioangioma was found prenatally, small size of tumor (usual cut-off is 4 cm), has a good prognosis, and can be managed conservatively. However, larger size chorioangiomas should be managed considering risk of fetal compromise.<sup>5,8</sup> Without any sign of fetal compromise, term delivery is reasonable.<sup>8</sup> Otherwise, when hemodynamically unstable condition or fetal hydrops develop, and if in early 3rd trimester or late 2nd trimester, delivery is acceptable; but at an even earlier gestational age, fetal intervention should be considered.<sup>8</sup> Intervention for ligation of vessels using fetoscopic devascularization, laser or alcohol ablation can interrupt blood supply from tumor to

fetus.<sup>1,2,5</sup>

We reviewed all cases and articles of perinatal stroke associated with placental chorioangioma and according to one review article of 99 cases, rate of placental chorioangioma at less than 4 cm, between 4 and 5 cm, more than 5 cm is 9.0%, 12.2%, 78.8%, respectively. As expected, the rate of perinatal complications increases as the size of the placenta increases. When placental chorioangioma is less than 4 cm, 44% of these had co-existing fetal complications, but all had a good perinatal outcome. When the placental tumor was reported as measuring between 4 and 5 cm, all had perinatal complications and 25% of these were associated with a stillborn baby. In 78 cases, the "tumor" was reported to be >5 cm, there was a reported fetal and perinatal mortality of 28.2% (13 fetal deaths and 9 stillbirths).<sup>9</sup> Fifty to 94% were associated with a wide variety of fetal complications, including polyhydramnios, growth restriction, anemia and non-immune hydrops.<sup>10</sup>

Since a chorioangioma is characterized through being in numerous narrow and tortuous vascular systems, thrombotic tendency can complicate and manifest as perinatal stroke.<sup>11</sup> In this case, there is no evidence for coagulation abnormality which can be attributed for causes of perinatal stroke. Instead, placental pathologic examination showed obvious focal infarction and fibrin cushions near the vessels that did not allow enough perfusion to fetus. Therefore, we posit that those lead to the consequence of perinatal stroke.



**Fig. 4.** (A) Two months after birth, brain magnetic resonance (MR) imaging and MR angiography follow up was done and showed attenuation of left distal middle cerebral artery branch due to previous arterial obstruction or secondary changes after infarction. (B) Progression of encephalomalacia of the left parietal lobe was seen.



We found two similar cases where emboli originating from chorioangioma caused multiple neonatal cerebral infarcts. One was born at 40 weeks by cesarean section due to decreased fetal movement repeatedly and low biophysical profile. The other was born at 36 weeks due to preterm premature rupture of membranes.<sup>5,11</sup>

A perinatal ischemic stroke was defined as a group of heterogeneous conditions in which there is focal disruption of cerebral blood flow secondary to arterial or cerebral venous thrombosis or embolization, between 20 weeks of fetal life through to the 28th postnatal day, confirmed by neuroimaging or neuropathological studies.<sup>6</sup> Ischemic perinatal stroke causes neurological disability in childhood, and 1/3 of all strokes in children occur during the perinatal period.<sup>7,12</sup> The incidence of perinatal stroke is 1:4,000, indicating rarity. Nevertheless, perinatal stroke is recognized as a cause of neurological disability in children, which is why there should be more awareness.<sup>7,12</sup> Usually, non-specific clinical symptoms are seen in this age group and common presentations are seizure, encephalopathy, apnea and abnormal tone. The only relatively specific symptom is seizure during the first 3 days to 1 week of life.<sup>7,13</sup> Unfortunately, focal neurological deficit was seen in only 30% of patients, and 95% of whom demonstrated a lateralizing hemiparesis.<sup>13</sup> Therefore, stroke should be ruled out by brain imaging.<sup>7</sup>

There are various risk factors of perinatal stroke and they are classified as maternal, fetal and placental factors. Maternal factors are preeclampsia, chorioamnionitis, coagulation disorder, etc. Fetal factors are congenital heart disease. In addition, gender, race and dehydration can also be risk factors of perinatal stroke. Lastly, placental factors include placental thrombosis, abruption or infection.<sup>12,13</sup> Likewise ischemic strokes are caused by arterial occlusion due to thrombosis or embolism, in which case we suggest placental thrombosis due to chorioangioma as a risk factor of perinatal stroke.<sup>7</sup>

Perinatal stroke and giant placental chorioangioma are rare individually, and in combination exceedingly so. Our case implicates that placental examination should be considered as an

important diagnostic workup in cases of perinatal stroke with unknown etiology.

## Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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