Yuka Otera, Yasuo Yumoto*, Masayuki Ochiai, Koji Yamashita and Kiyoko Kato

# Prenatal diagnosis of periventricular venous infarction *in utero*: a case with hereditary protein C deficiency

**Abstract**: A 36-year-old primigravida woman with a normal pregnancy course presented with fetal unilateral focal ventriculomegaly on routine ultrasonography performed at 28 weeks of gestation. Periventricular venous infarction (PVI) *in utero* was diagnosed with fetal magnetic resonance imaging (MRI). The neonate was born at term uneventfully and *in utero* PVI was confirmed by MRI after birth. The neonate was diagnosed with hereditary protein C deficiency after coagulation laboratory studies. At 10 months of age, the infant presented with mild retardation of motor development. This is the first report about prenatally diagnosed PVI *in utero* by fetal MRI. When focal, unilateral enlargement of the ventricles is detected *in utero* by prenatal ultrasonography, it is important to consider PVI and perform confirmatory fetal MRI.

**Keywords:** Cerebral palsy; fetal MRI; periventricular venous infarction; prenatal ultrasonography; unilateral focal ventriculomegaly.

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## Introduction

A 36-year-old primigravida woman with a normal pregnancy course underwent routine ultrasonography at 28 weeks of gestation. Subsequently, she was referred to our department because of fetal unilateral ventriculomegaly. Fetal neurosonography revealed a focal enlargement in the right lateral ventricle (Figure 1). Maternal findings from general blood laboratory tests and toxoplasma, rubella, cytomegalovirus, and herpes simplex screening were unremarkable. Fetal magnetic resonance imaging (MRI) at 28 weeks of gestation identified focal enlargement of the right lateral ventricle and a linear low signal intensity along the right lateral ventricle on axial and coronal T2-weighted images (WI) (Figure 2). Both the cerebral cortex and basal ganglia seemed to be spared. Periventricular venous infarction (PVI) *in utero* was diagnosed based on fetal MRI findings. The focally enlarged right lateral ventricle did not vary in size and no other abnormal findings appeared by term.

## Case report

The infant was delivered vaginally at 38 weeks of gestation and weighed 2750 g with the Apgar score of 8 and 9 at 1 and 5 min, respectively. No abnormal physical findings were observed. Postnatal neurosonography showed focal enlargement of the right lateral ventricle, but no additional abnormal findings, such as intraventricular hemorrhage, on the day of his birth. On day 1 of life, he developed apnea and experienced a seizure. Computed tomography revealed bilateral intraventricular and subarachnoid hemorrhages. Neonatal MRI at 8 days showed focal enlargement of the right lateral ventricle and a linear low signal intensity along the right lateral ventricle on T2*-WI (Figure 3). These findings were consistent with those of fetal MRI, thereby confirming the diagnosis of PVI *in utero*. Laboratory investigation for coagulation abnormalities indicated hereditary protein C (PC) deficiency in the neonate. In addition to the PVI lesion, diffusion WI demonstrated multiple, bilateral hyperintense lesions in the cerebral white matter, posterior limb of the left internal capsule, and corpus callosum. On

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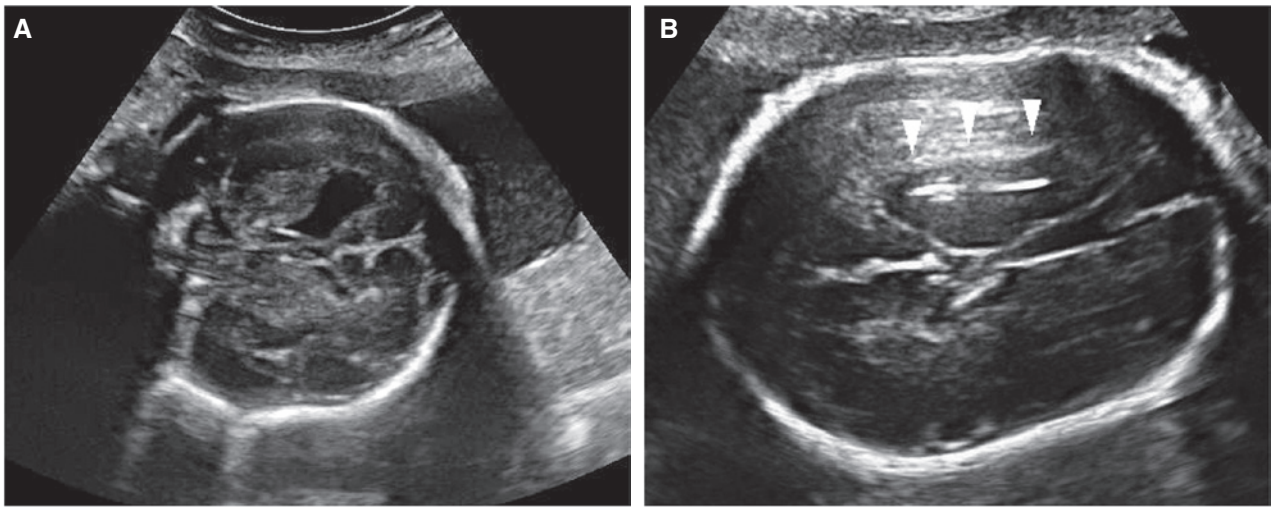


**Figure 1:** Fetal neurosonography at 28 weeks of gestation. (A) Coronal section of fetal head. Comparing to the left ventricle, see enlarged right lateral ventricle expanding into the hemisphere. (B) Unilateral focal enlargement of the right lateral ventricle on transversal section (white arrowheads).

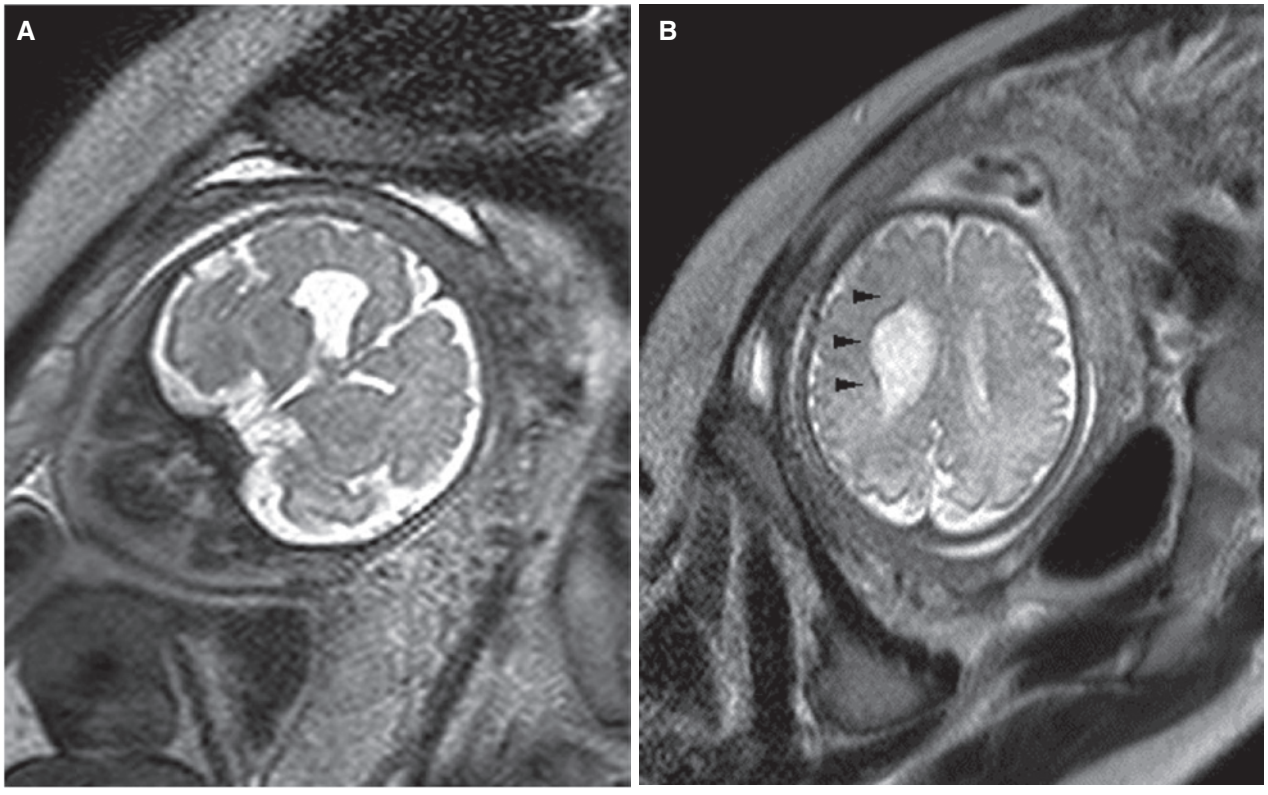


**Figure 2:** Fetal magnetic resonance imaging at 34 weeks of gestation. (A) Enlarged right lateral ventricle and spared cerebral cortex on coronal T2-WI. (B) Liner low signal intensity along the focally enlarged right lateral ventricle on axial T2-WI (black arrowheads).

neurological examination at 10 months of age, the infant presented with a slightly activated deep tendon reflex and lack of disjunctive movements in his lower extremities that reflected a mild retardation of motor development.

## Discussion

PVI is well described in preterm infants with germinal matrix hemorrhage, which results in compressive

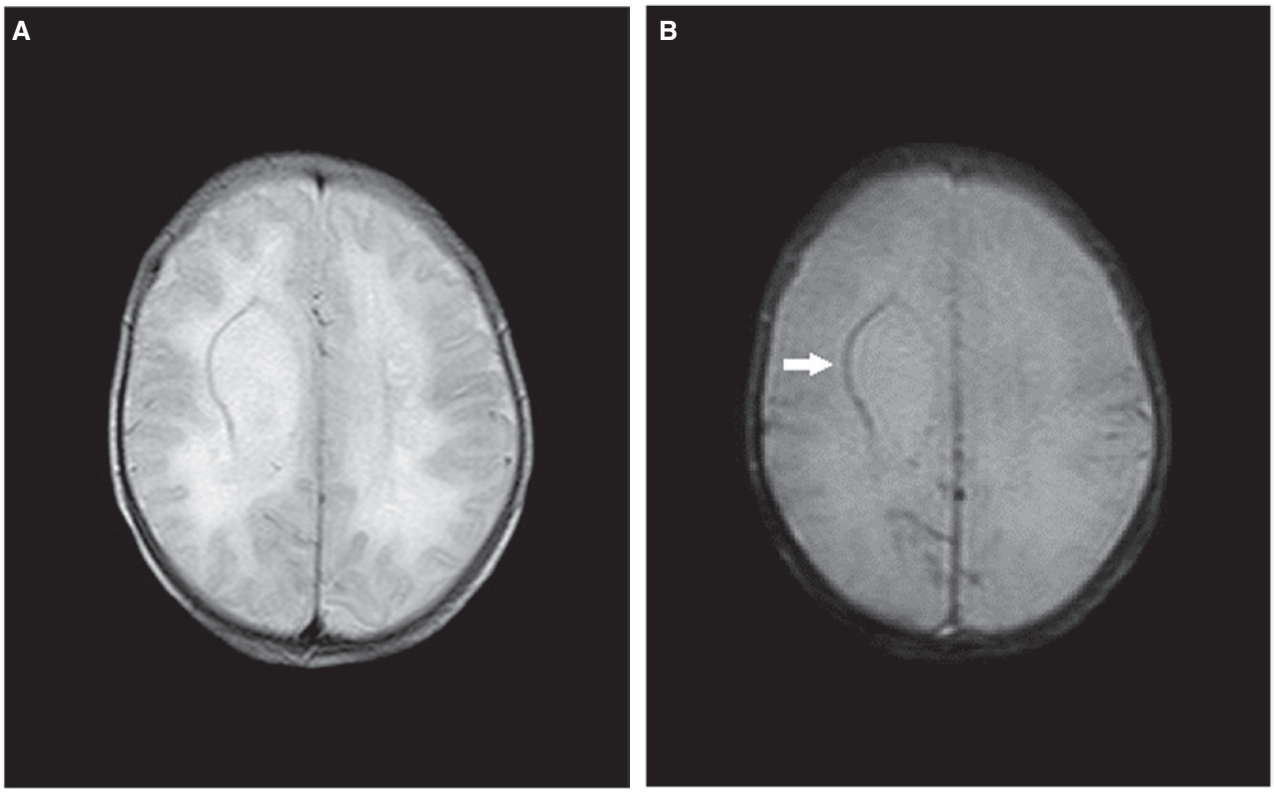


**Figure 3:** Magnetic resonance imaging at 8 days of age. (A) Focally enlarged right lateral ventricle on T2-WI and (B) liner low signal intensity along the right ventricle on T2*-WI (white arrow).

obstruction of medullary vein drainage into the periventricular white matter and venous infarction of the periventricular parenchyma [1, 2]. PVI can cause cerebral palsy in infants born at term with uneventful pre-, peri-, and postnatal courses in the same manner as in preterm infants. Reportedly, PVI *in utero* has been presumed by MRI after birth [2, 3]. However, to the best of our knowledge, there are no reports of PVI diagnosed *in utero* by fetal MRI. Herein, we report a case of unilateral focal ventriculomegaly incidentally detected by a routine prenatal ultrasonography and PVI diagnosed *in utero* by fetal MRI.

The criteria for diagnosis include the presence of unilateral periventricular white matter infarction in the medullary venous territory with four or more of the following: (i) focal periventricular encephalomalacia; (ii) T2 prolongation in the posterior limb of the internal capsule; (iii) cortical sparing; (iv) hemosiderin (within lesion, ventricle, and/or germinal matrix) on susceptible sequences; and (v) relative sparing of the basal ganglia (lesser volume than cranial white matter lesion) [4]. Fetal MRI findings in our case matched criteria listed as (i), (iii), (iv), and (v); therefore, we arrived at the diagnosis of PVI *in utero*, which was subsequently confirmed by MRI at 8 days of age. In this case, fetal MRI played a leading role in the diagnosis of PVI *in utero*. Takanashi et al. reported a case of an infant born at term with suspected PVI *in utero* on neonatal MRI [3]. According to this report, the neonate did not have prenatal and perinatal events, but showed an enlarged right lateral ventricle on routine postnatal neurosonography and PVI *in utero* was later confirmed by MRI at 5 days of age. However, fetal MRI findings for PVI *in utero* have not been reported.

The hemorrhagic infarcted region in PVI is slowly resorbed, resulting in liquefaction of the area. The infarcted region may then shrink, causing adjacent ventricle expansion (*ex vacuo*) into the affected region of the hemisphere, usually in communication with the adjacent ventricle [5]. In our case, focal periventricular encephalomalacia resulted from PVI was observed as the focal enlargement of the right lateral ventricle on prenatal ultrasonography. Although no abnormal findings were identified on routine ultrasonography performed at 25 weeks of gestation, unilateral focal enlargement of the right ventricle became visible at 28 weeks. A characteristic echogenic lesion, a fan-shaped echogenicity following the distributions of medullary veins, appeared in periventricular white matter and became less echogenic when the lesion subsequently progressed into an enlargement of the

affected lateral ventricle within approximately 14 days [2]. Thus, the pathogenetic onset of PVI *in utero* was thought to occur between 25 and 28 weeks of gestation.

PVI may damage the descending corticospinal tracts resulting in cerebral palsy [2, 6]. Our patient, at 10 months of age, presented with a slightly activated deep tendon reflex and a lack of disjunctive movements in his lower extremities. We speculated that the multiple hemorrhagic strokes, which were observed on MRI at 8 days of age, may be attributed to the neonatal seizure and might be responsible for the retardation of motor development.

Our infant had low PC activity and he was diagnosed with hereditary PC deficiency. Kirton et al. investigated prothrombotic risk factors associated with PVI; however, no children with PVI in his study showed low PC activity [7]. Fong et al. reported siblings with familial PVI caused by hereditary PC deficiency [8]. In our case, low PC activity in fetal blood may possibly be the cause of PVI *in utero*.

This is the first report of PVI *in utero* diagnosed with fetal MRI. Our findings confirm and support those of previous reports about presumed PVI *in utero* using MRI findings after birth. Further, it is important to consider PVI *in utero* and perform fetal MRI when unilateral focal ventriculomegaly is detected on fetal ultrasonography.

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