

Case Report

Erythroblastosis of the Donor Twin of Twin Anemia-Polycythemia Sequence

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Twin anemia-polycythemia sequence (TAPS) is a group of disorders in monochorionic twins characterized by a large intertwin hemoglobin difference without amniotic fluid discordance. Reticulocyte count is used to diagnose this condition, but little is known about the role of erythroblasts, which are the prior stage of reticulocytes. In the present case of TAPS, the 25-yr-old Japanese mother showed no signs of oligohydramnios or polyhydramnios throughout gestation. The twins were born at 36 weeks and 6 days, weighing 2,648 g and 1,994 g. The intertwin hemoglobin difference in umbilical cord blood was (21.1 – 5.0 =) 16.1 g/dL and the donor twin showed signs of chronic anemia, including myocardial hypertrophy and pericardial effusion. Erythroblastosis of the donor twin was prolonged (53,088.5, 42,114.8 and 44,217.9/ μ L on days 0, 1 and 2, respectively). Erythroblastosis, which indicates chronic anemia, is also a good diagnostic indicator of TAPS.

Key words: anastomosis, erythroblast, monochorionic diamniotic twin, reticulocyte, twin anemia-polycythemia sequence

Twin anemia-polycythemia sequence (TAPS) is a group of disorders characterized by a large intertwin hemoglobin difference without amniotic fluid discordance in monochorionic twins [1]. TAPS is thought to be caused by chronic intertwin blood transfusion through small placental atriovenous (AV) anastomoses [1]. The two forms of TAPS are the spontaneous form and the post-laser surgery form [1]. The spontaneous form complicates approx. 3–5% of monochorionic twin pregnancies, and the post-laser surgery form occurs in 2–13% of twin-to-twin transfusion syndrome (TTTS) cases following fetoscopic laser photocoagulation [2–5].

Erythroblasts (EBLs) are reportedly cleared quickly from the bloodstream after birth in normal neonates.

By 12 h of age, the EBL count falls by approx. 50%; by 48 h only 20–30/ μ L are found, and virtually no EBLs are found after the third or fourth day of life [6]. Premature newborns may have up to 10,000 EBL/ μ L [6]. The main known causes of erythroblastosis include preterm birth, chronic hypoxia, anemia, maternal diabetes, acute stress, and postnatal hypoxia [6]. Reticulocytosis in the donor twin is used to diagnose TAPS, but little is known about the role of erythroblastosis, which would occur in the prior stage of reticulocytes.

Here, we document our experiences with a spontaneous TAPS case, focusing on erythroblastosis. Written informed consent was obtained for publication of this report.

Case Report

The mother was a 25-year-old Japanese woman with no remarkable medical history. Her spontaneous pregnancy (monochorionic diamniotic [MD] twins) was managed at our hospital beginning at 10 gestational weeks. We identified no signs of oligohydramnios or polyhydramnios, but after 33 gestational weeks, the twin fetal body weights differed: Twin 1 showed normal growth, and Twin 2 showed reduced growth (-1.5 SD level). The mother was hospitalized at 34 weeks and 1 day due to pregnancy-induced hypertension. An emergency caesarean section was performed at 36 weeks and 6 days, following the premature rupture of membranes in Twin 1. No signs of infection (*e.g.*, maternal fever or dirty amniotic fluid) were evident.

Twin 1. Twin 1, a male, had a birth weight (BW) of 2,648 g ($+0.10$ SD), birth height (BH) of 46.0 cm (-0.53 SD), and birth head circumference (HC) of 32.0 cm (-0.41 SD). His Apgar scores at 1 and 5 min were 8 and 9, respectively. His skin was red, but he had no dyspnea. Blood taken from the umbilical artery showed the following: pH 7.293, PCO_2 38.9 mmHg, base excess (BE) -7.6 mmol/L, hemoglobin (Hb) 21.1 g/dL, and hematocrit (Ht) 64%. Given his good general status, he received care in the maternity ward on day 0. On day 1, he was admitted to the neonatal intensive care unit (NICU) due to worsening polycythemia (Hb 24.9 g/dL and Ht 73.8%).

Despite fluid administration, the polycythemia worsened (Hb 26.3 g/dL and Ht 76.7%) and thus a partial exchange transfusion was performed on day 1. The polycythemia improved thereafter (Hb 20.2 g/dL and Ht 60.7%). Upon admission to the NICU, Twin 1's counts were as follows: WBC was 18,280/ μ L, RBC 658×10^4 /dL, platelets 20.6×10^4 / μ L, and EBLs 2,376.4/ μ L (Fig. 1). Phototherapy was started on day 2 due to elevated the total bilirubin (TB), and was completed on day 3.

Echocardiography performed on day 1 showed a left ventricle end-diastolic diameter (LVDd) of 16.2 mm (0 SD), an ejection fraction (EF) of 68.9%, and the intraventricular septum diameter (IVSd) 2.8 mm (-1.7 SD). Patent ductus arteriosus and pericardial effusion were evident. On day 2, the ductus arteriosus closed spontaneously, and the resolution of the pericardial effusion was confirmed on day 5.

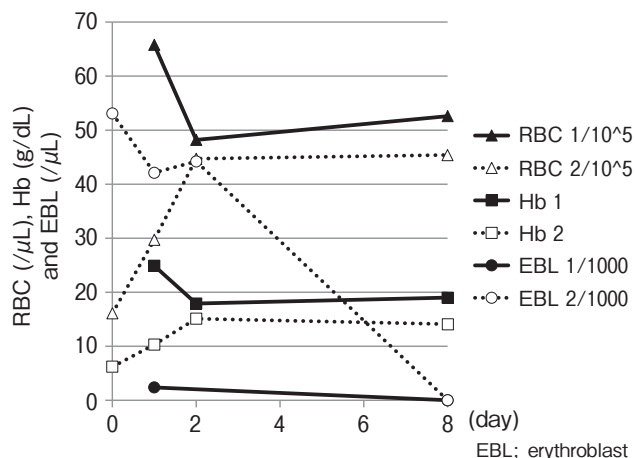


Fig. 1 Trend of RBC, Hb and erythroblasts (EBLs). Solid line: Twin 1's data. Dotted line: Twin 2's data. Triangles: RBC. Squares: Hb. Circles: EBLs.

Twin 2. Twin 2, also male, had a BW of 1,994 g (-1.93 SD), BH of 44.5 cm (-1.17 SD), and HC of 32.0 cm (-0.41 SD). His Apgar scores at 1 and 5 min were 8 and 8, respectively. His skin was pale, and he had a poor general appearance. Blood taken from the umbilical artery had a pH of 7.150, PCO_2 of 54.3 mmHg, BE of -9.3 mmol/L, Hb of 5.0 g/dL, and Ht of 16%. He was admitted to the NICU. He required 10 mL/kg of red cell concentrate transfusion. Hypoglycemia was also evident (blood sugar [BS] level, 13 mg/dL). Upon his NICU admission, the WBC was 11,930/ μ L, the RBC was 161×10^4 /dL, the platelet count was 20.2×10^4 / μ L, and the EBL count was 53,088.5/ μ L (Fig. 1).

On day 1, an additional 10 mL/kg of red cell concentrate transfusion was needed due to his Hb of 10.3 mg/dL. He showed prolonged hypoglycemia, with the serum insulin level of 3.14 μ U/mL, BS 58 mg/dL, WBC 12,460/ μ L, and EBL 42,114.8/ μ L. On day 2, phototherapy was performed due to the rapid elevation in TB. The WBC was 14,310/ μ L and the EBL count was 44,217.9/ μ L. Phototherapy was completed on day 3. On day 8, the WBC was 19,100/ μ L and the EBL was 0/ μ L. Glucose infusions were finished on day 10.

Echocardiography performed on day 0 showed the LVDd of 14.8 mm ($+0.45$ SD), EF 68.5%, and IVSd 5.1 mm ($+3.2$ SD; Fig. 2). Patent ductus arteriosus and pericardial effusion were noted on day 0, but by day 8, the ductus arteriosus closed spontaneously and no pericardial effusion remained.

Placenta. The placenta weighed 1,036 g, and the umbilical cord of each twin was attached to the central part of the placenta. The placenta was congested where Twin 1's umbilical cord was attached, whereas the placenta where Twin 2's umbilical cord was attached was pale. A small arterio-arterial (AA) anastomosis was also noted (Fig. 3).

Discussion

The present case was diagnosed as TAPS because the intertwin hemoglobin difference in the umbilical cord blood was $21.1 - 5.0 = 16.1 \text{ g/dL}$ (> 8.0) [7], and because Twin 2 showed pericardial effusion and myocardial hypertrophy, both of which are signs of chronic anemia. In this case, there was an AA anastomosis at the surface of the placenta, but no AV

anastomosis, a common formation in TAPS [8]. The AV anastomoses may have been difficult to detect if they were too small. That said, AA anastomoses are rare in TAPS [1].

Based on the postnatal intertwin hemoglobin difference of 16.1 g/dL (14.0–17.0), this case is classified as stage 3 [1]. Slaghekke *et al.* reported that 90% of stage 3 TAPS cases require postnatal treatment (blood transfusion or partial exchange transfusion) for both neonates [1], and the present case was no exception.

We considered TTTS and acute fetofetal hemorrhage (AFFH) as differential diagnoses in the present case. TAPS has been described as a form of chronic fetofetal transfusion [9]. TTTS is also a form of chronic fetofetal transfusion, but TTTS leads to hypovolemia, oliguria and oligohydramnios in the donor

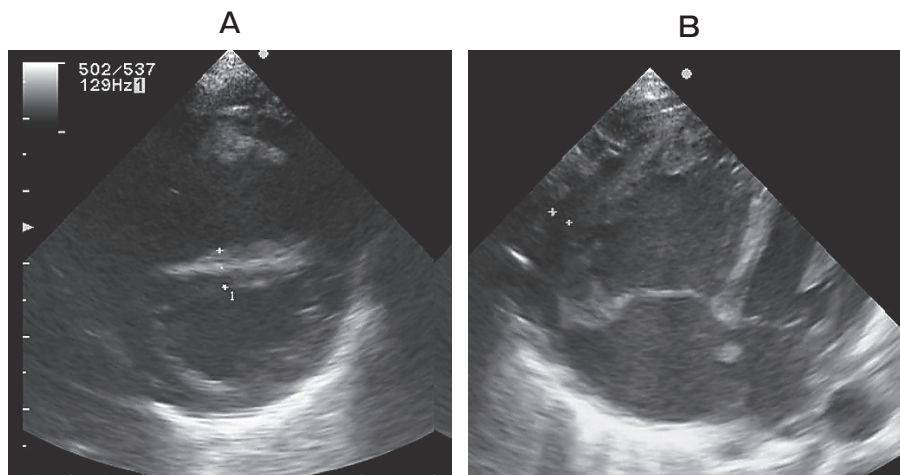


Fig. 2 Echocardiography of Twin 2 on day 0. **A**, Myocardial hypertrophy with the intraventricular septum measuring 5.1 mm ($+3.2\text{SD}$); **B**, Pericardial effusion.

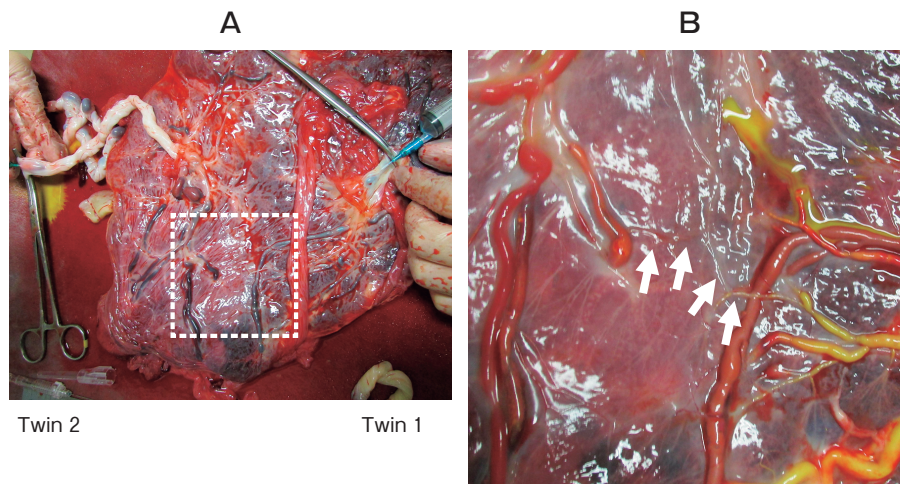


Fig. 3 Fetal side of the placenta. Image **A** reveals that Twin 1's part of the placenta (right side) was congested, whereas that for Twin 2 (left side) was pale. The arteries of Twin 1 and Twin 2 appear in yellow and red, respectively. The square surrounded by the white dotted line is magnified in Image **B**, and shows a small arterio-arterial anastomosis (white arrows).

twin and hypervolemia, polyuria and polyhydramnios in the recipient twin [10]. In the present case, TTTS was ruled out due to the absence of oligohydramnios and polyhydramnios. AFFH is thought to occur by an acute blood shift from one twin to the other as a result of uterine contractions during delivery [11]. The chronic features of the present case were inconsistent with AFFH, so that was ruled out as well.

EBLs and reticulocytes are in the process of erythropoiesis and easy to measure. The EBL count might be considered an indirect measure of liver (extramedullary) hematopoiesis, whereas reticulocytes are the product of both medullary and extramedullary erythropoiesis [12]. Nicolaidis *et al.* reported that the reticulocyte count increased linearly with fetal anemia, and that the EBL count increased exponentially [13]. That is, the fetus responds to mild or moderate degrees of anemia by developing intramedullary hematopoiesis (mainly reticulocytosis occurs), and severe anemia leads to extramedullary hematopoiesis, which results in erythroblastosis.

Nicolaidis *et al.* also wrote that not reticulocytosis but erythroblastosis was significantly related to the presence of hydrops. The donor twin in this case had pericardial effusion, one of the symptoms of fetal hydrops, which is consistent with Nicolaidis' report. We thus note that erythroblastosis is also important, although reticulocytes were used to diagnose TAPS [1, 14, 15].

The present study has two main limitations. First, we have no data regarding the blood flow through the middle cerebral artery of the fetus, which was used for the prenatal diagnosis. These data should be obtained for MD twins, even in the absence of oligohydramnios or polyhydramnios. It should also be stated that prenatal classifications of TAPS are not always fully consistent with postnatal classifications of TAPS [1]. Second, we have no data on the reticulocytes, although the reticulocyte ratio, which was calculated with the reticulocyte count of both twins, has been used for the diagnosis of TAPS [1]. Reticulocyte counts should be determined for cases such as the present case.

In conclusion, the present case of TAPS showed an AA anastomosis. We surmise that erythroblastosis in the donor twin is important in cases of TAPS, and further research into this topic could contribute to our pathophysiological understanding of TAPS.

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