Prenatal Diagnosis of 46,XX,der(13;21)(q10;q10),+21 and Transient Abnormal Myelopoiesis in a Fetus with Hepatosplenomegaly and Spontaneous Resolution of Fetal Ascites

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A 31-year-old, gravida 2, para 1, woman was referred for genetic counseling at 33 weeks' gestation because of fetal ascites and fetal hepatosplenomegaly detected at 32 weeks' gestation. Level II ultrasound at 33 weeks' gestation revealed a singleton fetus with fetal biometry equivalent to 31 weeks' gestation, fetal ascites and hepatosplenomegaly (Figure 1). Spontaneous resolution of fetal ascites with persistent hepatosplenomegaly was noted at 34 weeks' gestation (Figure 2). Cordocentesis at 34 weeks' gestation revealed a fetal karyotype of 46,XX,der(13;21)(q10;q10),+21 (Figure 3). The maternal karyotype was 45,XX,der(13;21)(q10;q10) (Figure 3). The full blood count revealed a marked leukocytosis with a white cell count of 24.69×10^3 μL with 30% blast cells and a hemoglobin level of 15.1 g/dL. The blood smear revealed large undifferentiated blast cells with fine granularity of the cytoplasm and large irregular nuclei representing transient abnormal myelopoiesis (TAM) (Figure 4). Intrauterine fetal death occurred at 36 weeks' gestation, and a 2,294-g dead female fetus with characteristic features of Down syndrome was delivered. Molecular analysis of the *GATA1* gene using fetal tissues revealed that there was no mutation in the *GATA1* gene.

Transient abnormal myelopoiesis (TAM), also known as transient myeloproliferative disorder or transient

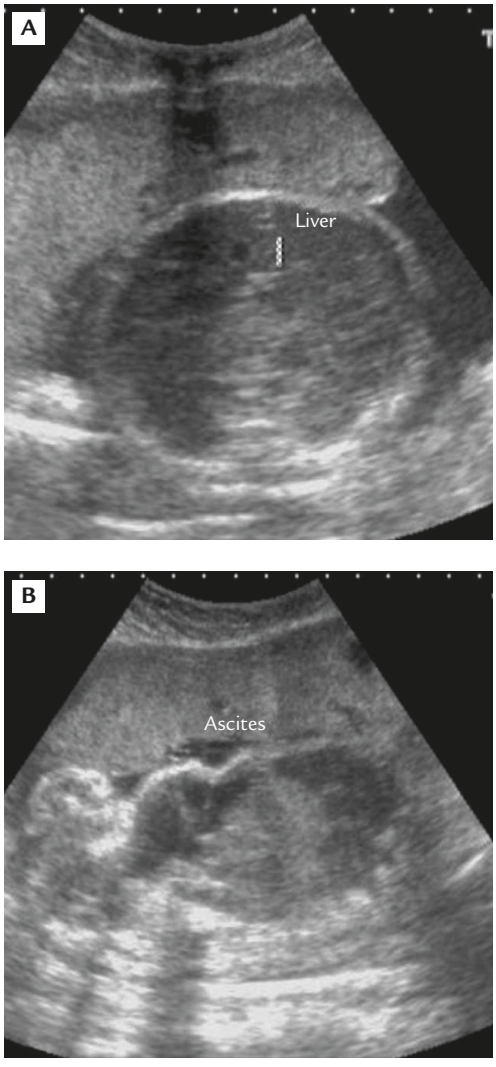

Figure 1. Prenatal ultrasound at 32 weeks' gestation shows: (A) hepatosplenomegaly, and (B) fetal ascites.

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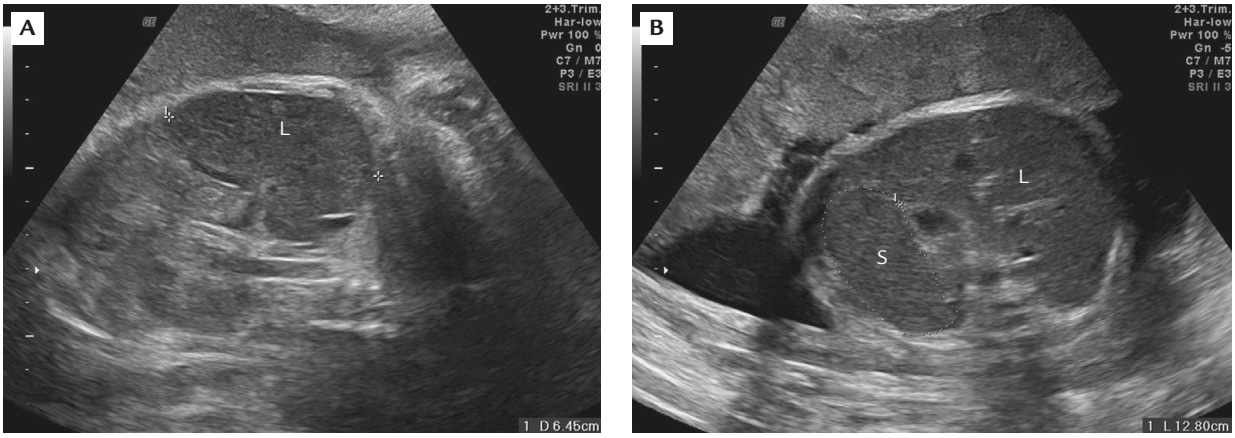

Figure 2. Prenatal ultrasound at 34 weeks' gestation shows: (A) hepatosplenomegaly in the longitudinal section, and (B) splenomegaly in the transverse section with resolution of fetal ascites. L = liver, S = spleen.

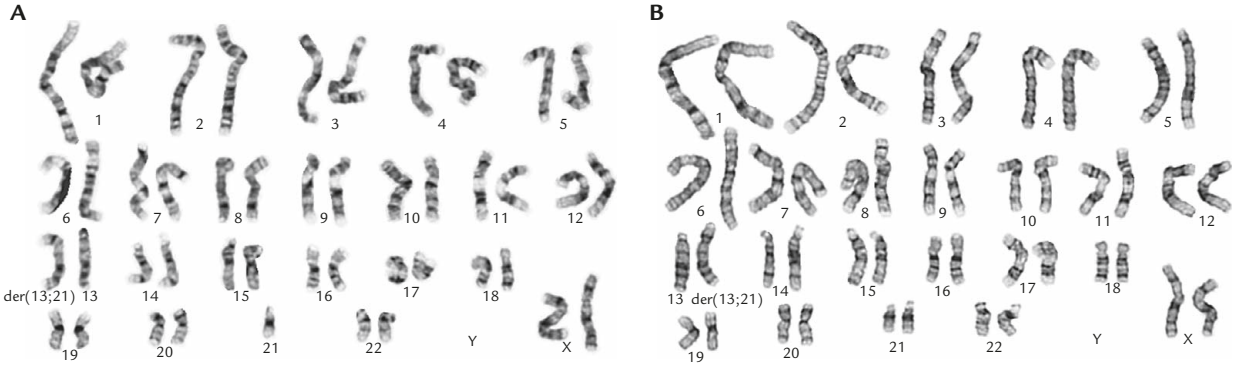

Figure 3. (A) The maternal karyotype shows a balanced robertsonian translocation of 45,XX,der(13;21)(q10;q10). (B) The fetal karyotype shows an unbalanced robertsonian translocation of 46,XX,der(13;21)(q10;q10),+21.

leukemia, is a hematologic disorder that is confined to Down syndrome and presents in the fetal or neonatal period [1]. Clinical and laboratory features of TAM in neonates with Down syndrome include pericardial effusion, ascites, pulmonary edema, hepatosplenomegaly, hepatic fibrosis, liver failure, obstructive jaundice, leukocytosis, persistent peripheral blood blast cells, abnormal platelet counts, and vesicopapular skin rashes [1]. About 10% of newborn infants with Down syndrome develop TAM [2], and 20–30% of TAM babies will develop myeloid leukemia of Down syndrome, which is an acute leukemia [3]. *GATA1* mutations have been found in Down syndrome with leukemia [4–8]. The present case was not associated with mutations in the *GATA1* gene. The sonographic findings of TAM cases diagnosed during fetal life include hepatosplenomegaly, pericardial effusion, ascites, hydrops fetalis, skin edema, polyhydramnios, and cardiomegaly [9]. Zerres et al [10] first reported the prenatal diagnosis of TAM and 47,XX,+21 in a fetus with nonimmune hydrops fetalis with ascites and pericardial effusion at 36 weeks' gestation. After birth, the neonate survived and the diagnosis of acute leukemia was confirmed by blood smear and bone marrow. Foucar et al [11] reported fetal ascites at 31 weeks' gestation in a fetus with TAM and 47,XX,+21. The fetus was delivered at 32 weeks' gestation with massive edema but survived after intensive pediatric care. Macones et al [12] reported fetal ascites, hydrops fetalis, polyhydramnios, an endocardial cushion defect, shortened femurs and hepatosplenomegaly at 28 weeks' gestation in a fetus with TAM and 47,XY,+21. Intrauterine fetal death occurred at 29 weeks' gestation. Strobelt et al [13] reported the prenatal diagnosis of pericardial effusion and hepatosplenomegaly at 31 weeks' gestation in a fetus with TAM and 47,XY,+21. At 31 weeks' gestation, worsening of pericardial effusion and a thin rim of ascites were noted. A fetal pericardiocentesis was performed to remove 40 mL of pericardial fluid. Thereafter, weekly sonographic examinations showed no re-accumulation of the pericardial effusion, disappearance of the thin rim of ascites, and stable hepatosplenomegaly. The fetus was delivered and survived at 35 weeks' gestation. Bascht et al [14] reported the prenatal diagnosis

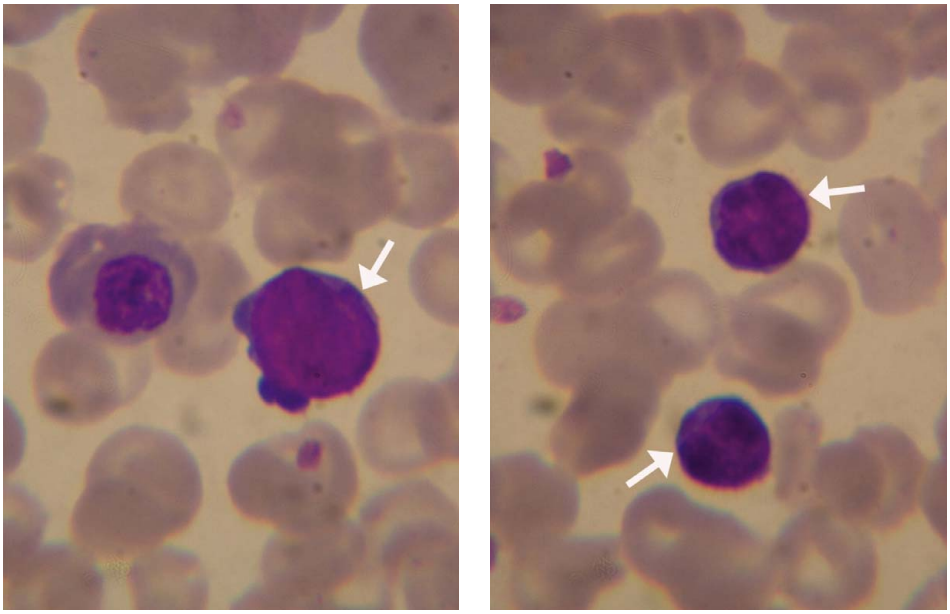

Figure 4. Blood smear obtained by cordocentesis reveals multiple, large, undifferentiated blast cells (arrows) (Wright-Giemsa stain, 400×).

of fetal hepatosplenomegaly and marked pericardial effusion at 26 weeks' gestation in a fetus with TAM and 47,XY,+21. Additional pleural effusion, ascites and skin edema were noted at 27 weeks' gestation. Fetal hydrops, hepatosplenomegaly and ascites persisted till 31 weeks' gestation when intrauterine fetal death occurred. Smrcek et al [15] reported the prenatal diagnosis of hepatosplenomegaly, ascites, skin edema, cardiomegaly and pericardial effusion at 30 weeks' gestation in a fetus with TAM and 47,XY,+21. Intrauterine fetal death occurred 10 hours after the diagnosis. The present case provides evidence that fetal ascites associated with TAM and hepatosplenomegaly may resolve spontaneously during fetal life. All reported cases of prenatally detected Down syndrome with TAM are free trisomy 21 (47,XY,+21 or 47,XX,+21). We have presented the first report of a prenatal diagnosis of an unbalanced robertsonian translocation involving chromosome 21 associated with TAM because of the abnormal sonographic findings of hepatosplenomegaly and ascites. Prenatal diagnosis of hepatosplenomegaly with or without ascites should alert the clinician to the possibility of familial trisomy 21, and prompt cytogenetic analysis and genetic counseling.

Acknowledgments

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