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Case Report
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A Case Report of Neonatal Death due to Transient Myeloproliferative Disorder with Hepatic Fibrosis in Trisomy 21

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Abstract

Objective: We present a case of neonatal death due to transient myeloproliferative disorder with hepatic fibrosis in trisomy 21.

Case Report: Transient Myelodysplastic Disorder (TMD) occurs in 3% to 10% of newborns with trisomy 21 (DS) and is characterized by clonal proliferation of maternal cells in the blood/bone marrow, with most newborns being asymptomatic. However, in rare cases, die prematurely from organ failure, including liver fibrosis. In this report, we present a non-dysmorphic neonate, with a negative noninvasive prenatal screening of maternal blood for trisomy 21, who with ruddy skin and good birth score then he was dead within one day genetic testing suggesting trisomy 21 chimerism (mos, x3, ~50%) and an autopsy pathology report suggesting extramedullary hemopoiesis and liver fibrosis.

Conclusion: Transient myeloproliferative disorder with hepatic fibrosis in trisomy 21 is an uncommon clinical condition in which accurate diagnosis is difficult and Sudden onset. With the increasing prevalence of NIPT detection, clinicians need to be vigilant about chromosome chimerism, and pay attention to the occurrence of liver fibrosis and DIC when neonatal test indicators indicate extramedullary hematopoiesis.

Keywords: 21-trisomy; Transient myeloproliferative disorder; Liver fibrosis; Case Report

Introduction

Down's Syndrome (DS), also known as congenital dysmorphism, has become one of the most serious congenital disabilities, manifesting as severe mental retardation and developmental abnormalities, with an incidence of about 1/600 to 1/800 in newborns. There are three common types of karyotype: Standard, translocation, and chimeric.

Transient Myelodysplasia Disorder (TMD) is unique clonal myelodysplasia occurring in the neonatal period in trisomy 21 or 21-trisomy chimeras characterized by the fetal liver, peripheral blood, and bone marrow [1]. The presence of immature megakaryocytes in [2] most newborns are asymptomatic. Still, many have elevated White Blood Cell (WBC) counts or liver [3-5] enlargement. About 20% of patients with TMD die prematurely from organ failure, including liver disease [6,7]. When TMD is combined with liver fibrosis, the outcome is fatal [8,9]. The most common cause of death is extensive liver fibrosis, organ and cardiopulmonary failure due to massive primitive megakaryocyte infiltration of the liver [10].

Case Presentation

A male, 18 min, was admitted to the hospital with a "mother 36 weeks three days pregnant, born with pale skin and moaning for 18 min". The baby was born in our hospital on 2022-01-12 at 18:51 as a G2P1 IVF baby, with premature rupture of membranes for 18 h. She had no history of rubella or other viral infections and no history of exposure to radiation or toxins in early menopause. A non-invasive DNA test at midterm showed low risk. No significant abnormalities were found on routine ultrasound at the maternity hospital. Blood glucose and blood pressure were average during pregnancy. She denied any history of intrauterine distress, birth injury, or asphyxia during labor. He had a general bruised face, pale skin all over the body, flat and soft fontanelle, about 1.0 cm × 1.0 cm, blue lips, soft and unresisting neck, 54 breaths/min, coarse breath sounds in both lungs, coarse wet rales could be heard.

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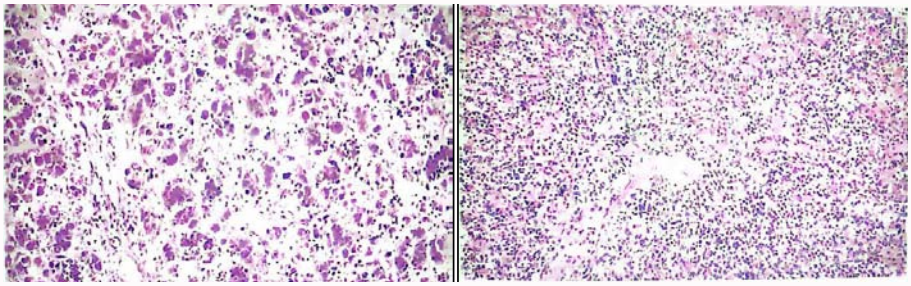

Figure 1: Pathological anatomical diagnosis.

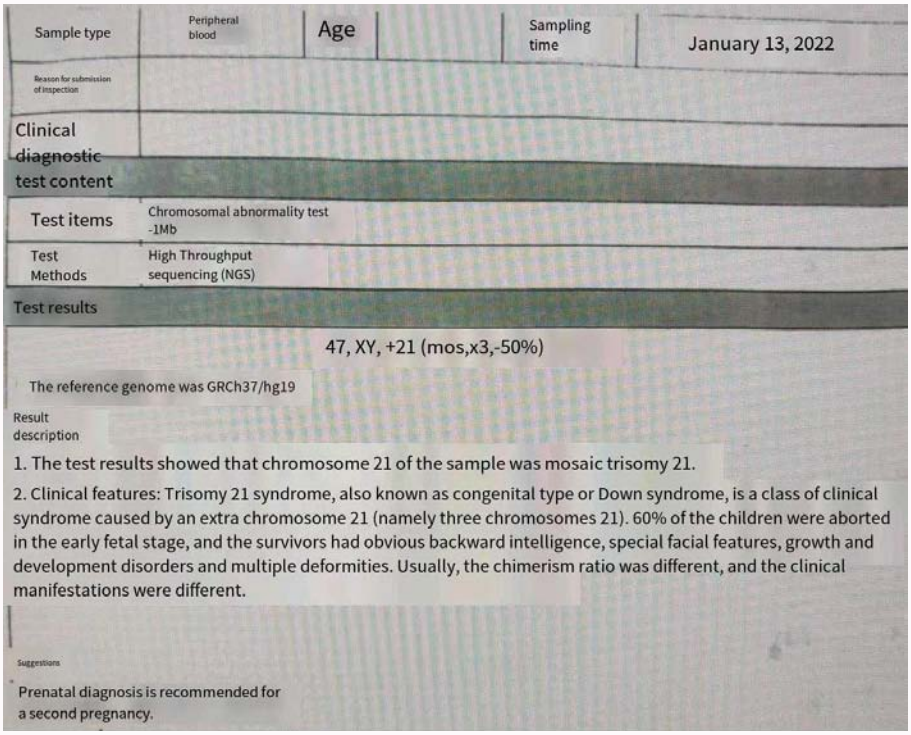

Figure 2: Mosaic trisomy 21.

Heart rhythm was uniform; intense heart sounds, normal muscle tone in all limbs, and incomplete primitive reflexes were elicited. After consultation with the neonatology department, he was immediately transferred to the neonatal unit. After admission, he was given warmth, monitoring, oxygen, sputum, cefoperazone sulbactam, anti-infection, sodium phosphate for myocardial nutrition, saline for volume expansion, fasting, acid correction, rehydration, and other symptomatic treatment. Erythrocytes 0.5 u, laboratory indicators suggest: Glutathione transaminase: 51 U/L↑; glutamic oxaloacetic transmigrate: 66 U↑; lactate, deaminase: 1155 U/L↑; emergency fibrinolytic function test: Prothrombin time: Non-coagulation seconds; fibrinogen: Non-coagulation g/L; activated partial thromboplastin time: Non-coagulation seconds; prothrombin time: 46.4 sec ↑; antithrombin activity: 14.8% ↓; Fibrin (original) degradation products: 93.7 ug/mL↑; D-dimer: 65.16 mg/L↑. At 20:40, oxygen saturation and heart rate decreased, and resuscitation treatment, such as mechanically assisted ventilation with tracheal intubation, epinephrine, and acid rehydration, was given. The cause of the neonatal hemorrhage was diagnosed as pending investigation, and the baby was immediately referred to the neonatal surgery department of Jiangsu Provincial People's Hospital at 23:00 on 2022-01-12. On 2022-01-13 at 4:20, the family brought the newborn back to our department, and the baby showed no signs of life. The cause of intra-abdominal hemorrhage in newborns was unknown. After communication with the patient and family, an autopsy was performed, and the pathological anatomical diagnosis was (Figure 1): 1. Diffuse hepatocellular perisinusoidal fibrosis with hepatic sinusoidal histiocytosis, hepatocyte atrophy with megakaryocytic transformation and extramedullary hemopoiesis of the liver; 2. Pancreatic alveolar atrophy with interstitial fibrosis; 3. Incomplete dilatation of the alveolar cavity with partial pulmonary atelectasis; 4. Significant extramedullary hemopoiesis of multiple organs including spleen, lung and adrenal glands; 5. Macrocytosis and clustered aggregates in multiple organs, including the liver, spleen, lung, and thyroid gland; 6. Hematochezia in the abdominal cavity, approximately 100 ml Immunohistochemical findings: CD117 (individually positive), CD34 (individually positive), CD61 (megakaryocyte pack +) (a) SMA (+). Exceptional staining results: Masson (perihepatic sinusoid +), PAS (-), VG (perihepatic sinusoid +), iron staining (individual +, reticulocyte staining (not showing the

collapse of reticulocutaneous scaffold). The possibility of potential low-level or tissue-specific mosaicism missed by prenatal screening, NGS (Next Generation Sequencing) was performed on an uncultured blood sample, performed mosaic trisomy 21 (Figure 2).

Discussion

Few cases have been reported nationally or internationally of transient myelodysplastic disorder with liver fibrosis in newborns with trisomy 21 that progresses rapidly and results in death.

This child apparently has a mosaic trisomy 21 patient, and no other recognizable features of Down syndrome. It is known that varying degrees of mosaicism for trisomy 21 exist in apparently healthy individuals [11,12]. Although NIPS has up to 99.3% sensitivity for trisomy 21 [13], mosaicism in the fetus can reduce this sensitivity then resulting in a false-negative NIPS [14]. AMKL (Acute Megakaryoblastic Leukemia) is a unique category of ML-DS (Myeloid Leukemia associated with Down syndrome) [15]. TMD may be indistinguishable from ML-DS. So, it would be interesting to determine whether myelofibrosis (a common complication of AMKL) is also present in TMD. There was no myelofibrosis but diffuse intralobular hepatic fibrosis as observed on autopsy pathology. It is also unlikely that viral hepatitis due to intrauterine infection was the cause of liver fibrosis in our patient, as neither the hepatitis virus nor TORCH titers were elevated. Due to the rapid progression of the child's condition, we were unable to further refine the relevant imaging studies at our hospital.

GATA1 plays a central role in TMD [16,17]. GATA1 mutations detectable only by sensitive methods with no clinical or hematologic manifestations (*i.e.*, silent TAM) [18]. NGS undetected GATA1 mutations in TMD may be due to technical.

In summary, the cause of neonatal death is currently considered to be related to transient myelodysplasia combined with severe liver fibrosis in neonates with trisomy 21 chimerism, leading to liver failure and induction of DIC, based on autopsy pathology and associated tests and clinical signs. Although patients whose mothers are at low risk for NIPT, NIPT also has limitations for the detection of fetal/placental chimerism [19,20]. Although it is a low probability event and the child's family has given full informed consent and signed an informed consent form beforehand, it still places a burden on the child's family and society. Pregnancy management and pregnancy monitoring need to be strengthened during pregnancy. Therefore, ensuring a high level of suspicion despite a negative screening test is imperative in clinical practice.

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