Clinical notes

Immune thrombocytopenia in a case of trisomy 18

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Trisomy 18 is a genetic disorder associated with chromosomal abnormalities that has unclear long-term prognosis. Frequency of hematological disorders in patients with trisomy 18 also remains unclear. Herein, we report the case of a girl with ventricular septal defect, patent ductus arteriosus, epilepsy, and severe developmental retardation. At 3 months of age, she underwent pulmonary artery banding and ligation of patent ductus arteriosus to manage increased pulmonary blood flow. She also underwent gastrostomy with Nissen fundoplication at 10 months of age. She had no other signs or symptoms until she reached 3 years old, when the patient presented with systemic rash, eye discharge, swollen lips, and a high fever. Then, her platelet count was 15.4×10^9/L. She was administered with oral lamotrigine, tolvaptan, cilazapril hydrate, furosemide, spironolactone, pranlukast hydrate, domperidone, famotidine, magnesium oxide, sodium valproate and levocetirizine hydrochloride. She was suspected of having Stevens-Johnson syndrome caused by administration of lamotrigine, which is an antiepileptic drug. Drug lymphocyte stimulation test and histopathological examination of the skin tissue confirmed this diagnosis and administration of lamotrigine was stopped. The symptoms disappeared after administration of prednisolone (PSL) (2 mg/kg/day). Four days after initiation of PSL, the patient developed thrombocytopenia. Her laboratory test findings were as follows: white blood cell count, 7.1×10^9/L; red

blood cell count, 4.72 × 10^9/L; hematocrit, 41.3 %; hemoglobin level, 13.4 g/dL; and platelet count, 1.6×10^9/L; mean corpuscular volume (MCV), 87.5 fL; mean corpuscular hemoglobin (MCH) 28.4 pg; and mean corpuscular hemoglobin concentration (MCHC) 32.4 g/dL. There is no data about vitamin B12 and folate acid of her serum.

Microscopic examination of the bone marrow revealed normoplastic marrow with proliferation of small megakaryocytes, erythroblasts with bleb formation, and binuclear erythroblasts (Fig.1). Differential count of 500 cells in the bone marrow was as follows: promyelocytes, 6.2%; myelocytes, 11.2%; metamyelocytes, 10.6%; stab cells, 7.0%; segmented cells, 4.6%; monocytes, 2.6%; eosinophils, 4.4%; lymphocytes, 15.0%; erythroblasts, 34.2%; erythroblasts with bleb formation, 3.6%; and erythroblasts with multiple nuclei, 0.6%. The findings did not fulfill the diagnostic criteria of myelodysplastic syndrome (MDS) that was defined according to the 2016 World Health Organization classification. Chromosomal analysis of the patient's bone marrow did not reveal any additional abnormalities. She was diagnosed with immune thrombocytopenia related to Stevens-Johnson syndrome. Three days after bone marrow aspiration, that was 7 days after initiation of PSL, her platelet count increased to 9.1×10^9/L and her platelet count further increased to 34.2×10^9/L 4 days later. We gradually decreased the dose of PSL, and completely stopped it after 1 month when her platelet count was

17.4×10^9/L. She was not administered any other therapeutic agents, including intravenous injection of immunoglobulin. She has remained in a stable condition with no medications for half a year. We lacked the pportunity to perform bone marrow aspiration again. Informed consent was obtained from the parents.

There have been few reports regarding hematological disorders, including immune thrombocytopenia, leukemia, and lymphoma, in patients with trisomy 18, although presence of thrombocytopenia and neutrophilia in the first week of life was reported.[1] Therefore, the frequency of hematological disorders in patients with trisomy 18 has never been fully investigated. Regarding solid tumors, Farmakis, et al. reported that patients with trisomy 18 could be predisposed to develop hepatoblastoma and nephroblastoma.[2] Recently, the overall survival of patients with trisomy 18 is considerably prolonged by intervention for congenital heart disease and digestive tract malformations.[3,4] In this context, details of hematological disorders and solid tumors in trisomy 18 may become evident as prognosis and overall survival improves, similar to the situation in trisomy 21. It is now clear that 5%－10% of patients with trisomy 21 experience transient myeloproliferative disorder (TMD), and subsequently, 20%－30% of patients with TMD develop acute megakaryoblastic leukemia.[5] In addition, the risk of acute lymphoblastic leukemia is 20-fold higher in patients with trisomy 21 than in the

normal population. In the current case, microscopic examination of the bone marrow revealed a marginal dysplasia. We should carefully observe whether this condition can lead to bone marrow failure or leukemia in this patient. Physicians treating patients with trisomy 18 should be aware of the high index of suspicion for these disorders, particularly malignant diseases in order to make a prompt diagnosis, thereby improving overall patient prognosis.

Author contribution

M.S. wrote the manuscript; M. S. and Y. T. performed examinations; A.M., A.I, and A. T. gave technical support and conceptual advice. All authors read and approved the final manuscript.

Disclosure

The authors declare no conflict of interest.

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Figure legend

Figure 1. Microscopic test of bone marrow (May-Giemsa stain) (a) erythroblasts with bleb formation, (b) an erythroblast with multiple nuclei