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CASE REPORT

Identification of an asymptomatic Shwachman–Bodian–Diamond syndrome mutation in a patient with acute myeloid leukemia

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Abstract

Shwachman–Diamond syndrome (SDS) is an autosomal recessive inherited disorder characterized by bone marrow failure, exocrine pancreatic dysfunction, and skeletal abnormalities. SDS is typically caused by a pathogenic mutation in the Shwachman–Bodian–Diamond Syndrome (SBDS) gene. Patients with SDS have an increased risk of developing acute myeloid leukemia (AML) and myelodysplastic syndromes. We identified germline biallelic SBDS mutations (p.K62X and p.I167M) in a 50-year-old AML patient who had never experienced the typical symptoms of SDS. The K62X mutation is one of the most common pathogenic mutations, whereas the significance of the I167M mutation was unclear. Based on cellular experiments, we concluded that the I167M mutation contributed to the development of AML, and chemotherapy including topoisomerase inhibitors, which induce DNA double-strand breaks, may have been toxic to this patient. Our experience indicates that some asymptomatic Shwachman–Bodian–Diamond syndrome mutations contribute to the development of leukemia, and that careful treatment selection may be warranted for patients harboring these mutations.

Keywords Shwachman–Diamond syndrome · Acute myeloid leukemia · DNA double-strand break repair

Introduction

Shwachman–Diamond syndrome (SDS) is an autosomal recessive inherited disorder characterized by bone marrow (BM) failure, exocrine pancreatic dysfunction, and skeletal abnormalities. SDS is typically caused by a pathogenic mutation in the Shwachman–Bodian–Diamond Syndrome (*SBDS*) gene. Patients with SDS have an increased risk of developing acute myeloid leukemia (AML) and myelodysplastic syndromes [1].

Case report

A 50-year-old female visited our hospital with chest pain. She had a history of cervical cancer since the age of 41 but no signs of SDS nor relevant family history. Though macrocytic anemia (hemoglobin [Hb], 9.1 g/dL; mean corpuscular volume, 118) was observed during the treatment of cervical cancer, she did not wish to have any further inspection. Laboratory data on admission showed that anemia (Hb, 5.2 g/dL), thrombocytopenia (40,000/μL), and about 90% of white blood cells (3000/μL) were myeloperoxidase (MPO)-positive blasts. The serum amylase level was normal (48U/L), without symptoms indicating deficiency in pancreatic exocrine function. BM aspiration demonstrated that 80% of the nucleated cells were blasts positive for CD13, CD33, CD34, CD38, and CD117, and she was diagnosed with AML. Immunohistochemistry revealed that leukemic cells in the BM were strongly positive for p53 (Fig. 1a).

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