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CASE REPORT

Successful azacitidine therapy for myelodysplastic syndrome associated with VEXAS syndrome

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Abstract

VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is caused by *UBA1* somatic mutations and is characterized by late-onset systemic autoimmune inflammation and blood abnormalities such as cytopenia, vacuolation of myeloid/erythroblastic cells, and myelodysplastic syndrome (MDS). It is often resistant to immunosuppressive therapy, and no treatment strategy has been established. A 65-year-old man presented with palpable erythema, fever, macrocytic anemia, and arthralgia. He was subsequently diagnosed with MDS complicated by Sweet's disease. Treatment with azacitidine was initiated due to suspected skin invasion by MDS cells and resistance of the skin rash to steroid therapy. Next-generation sequencing of bone marrow samples prior to treatment initiation revealed the presence of *UBA1* p.M41L (VAF 0.38) and *DNMT3A* p.L605fs mutations (VAF 0.184). Based on the findings of systemic inflammation, a diagnosis of VEXAS syndrome was made. The fever and skin rash improved with azacitidine therapy. In conclusion, somatic mutations in *UBA1* should be explored in patients with MDS exhibiting systemic autoimmune inflammation. Furthermore, azacitidine may be a good treatment option for systemic autoinflammation in MDS associated with VEXAS syndrome.

Keywords VEXAS syndrome · Myelodysplastic syndrome · Azacitidine · *UBA1* mutation · *DNMT3A* mutation

Introduction

The VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome, a new disease concept proposed by Beck et al. (2020), is a treatment-resistant autoinflammatory disease that develops in late adulthood owing to somatic mutations in *UBA1*, causing fever, neutrophilic dermatitis/pneumonia, arthritis, and hematologic abnormalities, such as cytopenia, vacuolation of myeloid/erythroblastic cells, and myelodysplastic syndrome (MDS) [1]. VEXAS syndrome is caused by *UBA1* mutations in hematopoietic stem cells, which induce systemic inflammation. This new disease concept was discovered by analyzing 25 patients with *UBA1* p.Met41 mutations identified by exome sequencing. The disease was named VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome as an acronym for the disease characteristics. All patients were male and had old-onset systemic inflammatory and hematological abnormalities. The effects of steroids are often limited, and no disease-specific treatment has been proposed [1, 2]. Herein,

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