Case Report

Sea-Blue Histiocytosis of Bone Marrow in a Patient with t(8;22) Acute Myeloid Leukemia

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Keywords

Acute myeloid leukemia · Histiocytosis · Bone marrow · t(8;22)

Abstract

An 80-year-old Japanese male was treated with chemotherapy consisting of cyclophosphamide, doxorubicin, vincristine, and prednisolone, for non-Hodgkin lymphoma. Nine months after the chemotherapy, he was diagnosed with acute myeloid leukemia (AML) (M4) with translocation 8p11 and 22q13. The patient bone marrow indicated a remarkable degree of sea-blue histiocytosis. His disease was aggressive, and he died of the disease. Sea-blue histiocytes are macrophages harboring blue vacuoles and granular deposition, which results from the phagocytosis of dead cells and the subsequent deposition of phospholipids. AML with the t(8; 22) (p11; q13) translocation is a rare subtype of AML, which is a rare translocation with a prevalence of less than 1.0% among all AML cases. The oncogenesis of t(8; 22) (p11; q13) is caused by the fusion protein monocytic leukemia zinc finger protein (MOZ) and transcription factor p300. MOZ can be fused to various translocation targets including CBT, TIF2, and p300, corresponding to t(8; 16), inv(8), and t(8; 22), respectively. This subgroup of AML reveals the hallmarks of the disease, including monocytic arrest and erythro/hemophagocytosis by blasts. A substantial proportion of the AML M4/M5 subtype harboring MOZ as an aberrant fusion gene represents erythrophagocytosis. Although rare, t(8; 22) is very specific to the AML M4/M5 subtype and seems to represent sea-blue histiocytosis as one of the characteristic features of monocytic AML with macrophage activation. Thus, sea-blue histiocytes are considered to be one of hallmarks in monocytic AML with MOZ translocation.

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Introduction

Acute myeloid leukemia (AML) with the t(8; 22) (p11; q13) translocation is a rare subtype of AML. t(8; 22) (p11; q13) is a novel chromosomal translocation whose function has not been fully elucidated. The oncogenesis of AML with the t(8; 22) (p11; q13) translocation was demonstrated to be caused by the fusion protein monocytic leukemia zinc finger protein (MOZ) and transcription factor p300 [1]. MOZ encodes a potential histone acetyltransferase and was identified as the gene that is located at the breakpoint of t(8; 16). The chromosomal translocation t(8; 16) has been found in AML [2], and it is one of the most common causes of aberrant cytogenesis in AML. MOZ can be fused to various translocation targets including CBT, TIF2, and p300, corresponding to t(8; 16), inv(8), and t(8; 22), respectively. Indeed, t(8; 22) is a novel chromosomal translocation [3, 4], and the leukemogenesis has been investigated only over the past decade.

Case Report

An 80-year-old Japanese male was diagnosed with therapy-related myelodysplastic syndrome (MDS) 9 months after chemotherapy for non-Hodgkin lymphoma. An unrecovered anemia was detected after chemotherapy. His bone marrow revealed a substantial degree of sea-blue histiocytosis at 1.0%.

After several months of follow-up, his white blood cell count increased up to $52.73 \times 10^3/\mu\text{L}$ with 16.0% of immature myeloid cells. He underwent bone marrow aspiration. He was then diagnosed with AML, M4 according to the FAB classification along with myelodysplastic/myeloproliferative neoplasm (MDS/MPN)-type marrow proliferative disease (Fig. 1a, b). His karyotype revealed translocation between chromosomes 8p11 and 22q13, which is a rare translocation with a prevalence of less than 1.0% among all AML cases [3, 4]. The patient received chemotherapy consisting of low-dose cytarabine 20 mg/kg body weight for 10 days, but eventually died of the disease.

Fig. 1. The patient's bone marrow revealed AML with monocytic proliferation featuring myelodysplastic/myeloproliferative neoplasm; $\times 40$ (a) and $\times 100$ (b). Concomitantly, a remarkable degree of sea-blue histiocytosis was found in his bone marrow; $\times 40$ (c) and $\times 100$ (d).

Discussion

Erythro- or hemophagocytosis by blasts is the hallmark of leukemia associated with t(8;16) and was noted to various degrees in most of the patients (22 out of 24) examined by Stark et al. [5]. This subgroup of AML reveals other hallmarks of the disease, including monocytic arrest and erythrophagocytosis [6]. These morphological features are sometimes observed as various degrees of phagocytosis-associated monograms including erythrophagocytosis [5] that represent aberrant biological behavior. Although erythro-/hemophagocytosis was limited in our AML patient, a remarkable degree of sea-blue histiocytosis was found in his bone marrow (Fig. 1c, d). Sea-blue histiocytes are macrophages harboring blue vacuoles and granular deposition, which is caused by the phagocytosis of increased numbers of dead cells and the subsequent deposition of phospholipids [7]. Sea-blue histiocytosis has been reported to be associated with chronic myeloid leukemia [8], MDS [9] and lymphoma [10]. However, as the previous report describes, a substantial proportion of the AML M4/M5 subtype harboring MOZ as an aberrant fusion gene represent erythrophagocytosis [5]. Although rare, t(8; 22) is very specific to the AML M4/M5 subtype [1]. We speculate that as in many cases of classical monocytic leukemia, sea-blue histiocytosis should be added as one of the characteristic features of monocytic AML with macrophage activation in AMLs with genetic abnormalities including t(8; 22).

Statement of Ethics

The Institutional Review Board approved the case report and submission of medical literature. We obtained written informed consent from the patient to publish his case including his images.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

O.I. wrote the manuscript and made substantial contributions to the concept and design; M.U. suggested important intellectual content and took part in the critical discussion; M.U. managed the study and reviewed the manuscript; all authors read and approved the final version of the manuscript.

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