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CASE REPORT

A Rare Case of Acute Promyelocytic Leukemia with ider(17)(q10)t(15;17)(q22;q21) and *FLT3*-ITD Mutation

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SUMMARY

Background: **Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia characterized by the t(15;17)(q22;q21) translocation. Although it typically responds well to therapy, certain genetic aberrations, including ider(17)(q10)t(15;17)(q22;q21) and FLT3-ITD mutations, have unclear prognostic implications.**
Methods: **A 61-year-old female patient presented with dizziness and persistent bruising. Laboratory and imaging studies revealed coagulopathy and intracranial hemorrhage. Morphological, immunophenotypic, cytogenetic, molecular, and FISH analyses confirmed APL with both ider(17)(q10)t(15;17)(q22;q21) and FLT3-ITD mutation.**
Results: **Despite standard ATRA and idarubicin induction therapy, there was no improvement in leukemic burden, and the patient succumbed to worsening hemorrhage one week after emergency surgery.**
Conclusions: **This case of APL with coexisting ider(17) and FLT3-ITD mutations exhibited an aggressive course and resistance to standard treatment. These findings suggest that such patients may require intensified therapeutic strategies and closer monitoring.**
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KEYWORDS

acute promyelocytic leukemia, ider(17)(q10)t(15;17), FLT3-ITD, poor prognosis, case report

CASE PRESENTATION

In September 2023, a 61-year-old female patient without any significant underlying conditions was brought to the Yeungnam Medical Center with a chief complaint of dizziness. A week prior to her visit, she had a fall, and the bruising did not subside. On the day of the visit, she had experienced dizziness and nausea since the morning. The patient did not exhibit any communication difficulties, and her vital signs were stable with a blood pressure of 100/80 mmHg, body temperature of 36.4 degrees Celsius, pulse rate of 70 beats per minute, and respiratory rate of 18 breaths per minute. The complete blood count test yielded a hemoglobin (Hb) level of 8.1 g/dL, a white blood cell count of 4,540/μL, and a platelet count of 430,000/μL. Coagulation tests showed a prolonged prothrombin time of 18.5 seconds, and an international normalized ratio of 1.68.

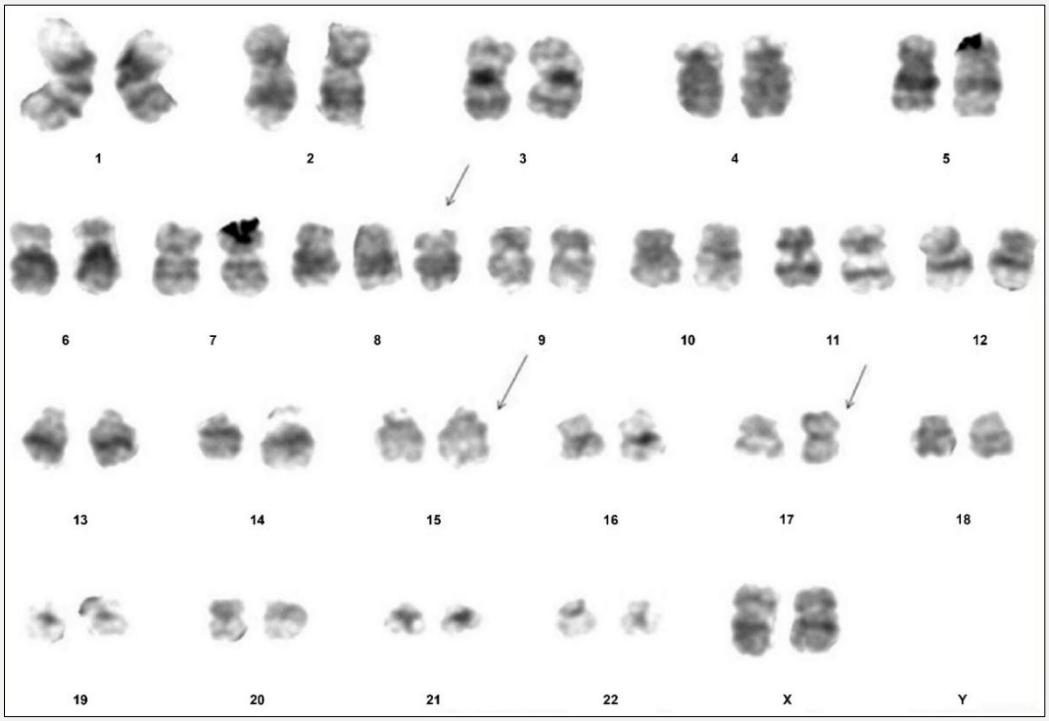

Figure 1. G-banded bone marrow karyotype showing 46, XX, +8, der(15)t(15;17)(q24;q21), ider(17)(q10)t(15;17).

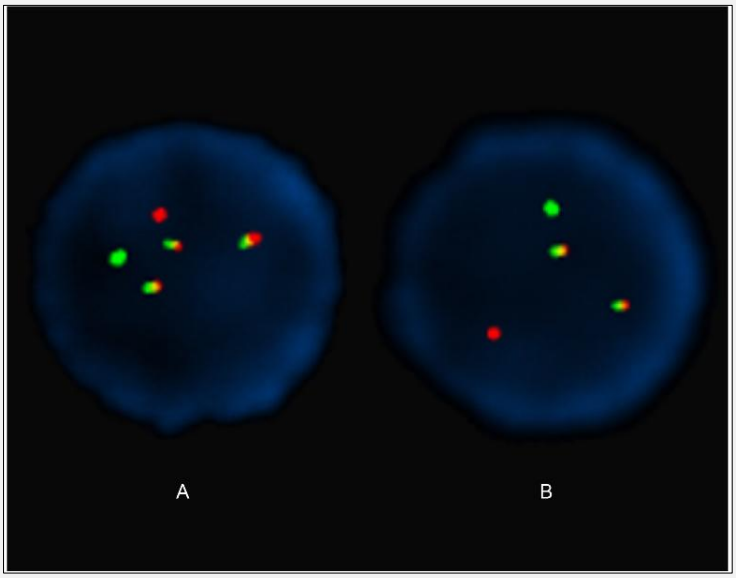

Figure 2. Interphase FISH (*PML::RARA* dual color, dual fusion translocation probe, red *PML* signal and green *RARA* signal) showing the variant 3 fusion pattern (A) and the typical 2 fusion pattern (B). (A) Variant fusion pattern with one fusion signal on the der(15)t(15;17), two fusion signals on the ider(17q), one red signal on the normal chromosome 15, and one green signal on the normal chromosome 17.

The serum D-dimer level was elevated at 18.34 g/L, and the fibrinogen level decreased to 63 mg/dL, suggesting disseminated intravascular coagulation (DIC). On brain CT, a 22 mm-sized hemorrhage was observed in the cerebellar vermis; however, immediate surgery was not deemed necessary.

Upon examination of a peripheral blood smear, abnormal promyelocytes were observed in > 70% of white blood cells, prompting an immediate bone marrow aspiration test. Bone marrow aspiration revealed hypercellular marrow with 71.2% abnormal promyelocytes. Flow cytometric analysis of the bone marrow showed that 65.31% of promyelocytes were strongly positive for CD13, CD33, CD64, CD117, and cMPO, whereas they were negative for CD34 and HLA-DR. RT-PCR analysis confirmed the presence of the PML::RARA rearrangement. Chromosomal karyotyping revealed a 46, XX,der(15)t(15;17)(q24;q21),ider(17)(q10)t(15;17)[15]/47,idem+8[2]/46,XX[3] karyotype (Figure 1). Interphase fluorescence in situ hybridization (FISH) signals from PML::RARA probes indicated nuc ish(PML, RARA)x4,(PML con RARA)x3[440/500],(PML,RARA)x3,(PML con RARA)x2[20/500] (Figure 2). One fusion pattern was identified for PML::RARA, while the other two were thought to correspond to the RARA::PML gene. This finding corresponded to that of the ider clone (17). Next-generation sequencing analysis of AML-related genes revealed c.1752_1784-dup in the FLT3 gene, indicating a mutation corresponding to FLT3 internal tandem duplication (ITD) mutation.

Upon confirming PML::RARA, the patient was treated with ATRA and idarubicin following the NCCN guidelines. On the 8th day of induction therapy, the patient complained of severe headaches, which prompted brain CT, CBC, and peripheral blood smear (PBS) examinations. The brain CT revealed a worsening of hemorrhage, and the WBC count was 14,880/μL. PBS showed that abnormal promyelocytes remained at 70%, indicating no improvement compared with before treatment. The patient underwent emergency surgery and received intensive care in the ICU; however, there was no improvement in consciousness. Unfortunately, the patient passed away one week after the emergency surgery.

DISCUSSION

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML) characterized by the morphology of leukemic cells and the chromosomal rearrangement t(15;17)(q22;q21). APL is considered a serious form of acute leukemia because of disseminated intravascular coagulopathy and hemorrhage, which cause early mortality. However, nowadays it is a curable leukemia with chemotherapies such as all-trans retinoic acid (ATRA) in combination with arsenic trioxide, amongst others [1].

A rare cytogenetic abnormality, ider(17)(q10)t(15;17)(q22;q21), has an abnormal karyotype and its prognostic significance is unclear [2-6]. FLT3-ITD mutation, the most frequent genetic variant in APL, occurs in 20 - 40% of patients with APL. While there are claims of a relationship between FLT3-ITD and early death rates in APL, its role as an overall prognostic factor remains unclear [6-9].

APL responds well to standard treatment with ATRA and is recognized as a subtype of AML with a favorable prognosis [1]. The impact of ider(17)(q10)t(15;17)(q22;q21) on APL remains unclear. It has been suggested that this additional cytogenetic abnormality, potentially involving the loss of TP53, provides an advantage in tumor growth compared to cells with the typical t(15;17) [3]. However, as the reported cases are still limited and there are also reports suggesting that it does not impact prognosis, a definite conclusion has not been reached. The case we encountered belonged to a low-risk group according to the NCCN guidelines [10]. Despite this classification, the number of abnormal promyelocytes did not decrease even after a week of standard treatment, and the patient died. Based on our experience, we argue that patients with ider(17)(q10)t(15;17)(q22;q21) and FLT3-ITD mutations may require more intensive observation and care compared to typical APL cases without the coexistence of ider(17) and FLT3-ITD mutations.

CONCLUSION

To the best of our knowledge, the case of APL with both ider(17)(q10)t(15;17)(q22;q21) and FLT3-ITD mutation has not yet been reported in the literature. Here, we report a rare case of APL with ider(17)(q10)t(15;17)(q22;q21) and FLT3-ITD mutation, which showed an unfavorable outcome.

Declaration of Interest:

The author declares no conflicts of interest.

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