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Case Report

An isolated der(1;21)(q10;q10) translocation in a patient with myelodysplastic syndrome: a case report

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Abstract: Whole-arm translocations are relatively rare among hematological malignancies. There are a few reports on myeloid malignancies harboring der(1;21)(q10;q10). A 65-year-old male was referred to our hospital due to squamous cell carcinoma of the lung. Pembrolizumab monotherapy resulted in progression, and so chemotherapy involving nab-paclitaxel and carboplatin was administered thereafter. The patient developed cytopenia, and his bone marrow exhibited dysplasia. Chromosomal analysis revealed a whole-arm translocation, der(1;21)(q10;q10). Thus, the patient was diagnosed with myelodysplastic syndrome. The der(1;21)(q10;q10) translocation is a rare variant of the der(1;7)(q10;p10) translocation, which is an adverse prognostic factor for myeloid neoplasms. Clarifying the clinical features of myeloid neoplasms in patients with der(1;21)(q10;q10) would facilitate the elucidation of their tumorigenic mechanisms.

Keywords: der(1;21)(q10;q10), myelodysplastic syndrome, whole-arm translocation

Introduction

Unbalanced whole-arm translocations (WAT), which involve the breakage and reunion of non-homologous chromosomes at their centromeres, are acquired cytogenetic abnormalities and are relatively rare among hematological malignancies [1]. In previous studies of myeloid malignancies, der(1;21)(q10;q10), which is an unbalanced WAT, was reported to be a recurrent, but rare, chromosomal abnormality [2-6]. Here, we present the case of a patient with myelodysplastic syndrome (MDS) involving solely der(1;21)(q10;q10).

Case presentation

A 65-year-old male without any history of prior illness was referred to our hospital due to the detection of an abnormal shadow on a chest X-ray in March 2017. Computed tomography revealed an irregular mass in his right lung and swelling of the paratracheal (#2R) and tracheobronchial (#4R) lymph nodes. A transbronchial lung biopsy examination of the mass revealed squamous cell carcinoma (70% of the tumor cells were positive for programmed cell death-1 ligand 1). As the patient had swollen lymph nodes, the disease was diagnosed as clinical stage T3N2M0, stage III, according to the Union for International Cancer Control classification. At this time, the patient's laboratory data included a white blood cell count of 4.5×10^9/L and a platelet count of 153×10^9/L. In addition, although mild anemia was observed (a hemoglobin concentration of 9.1 g/dL), it was considered to have been caused by chronic inflammation associated with the carcinoma. Due to the patient's poor performance status (2 according to the Eastern Cooperative Oncology Group classification), he was started on pembrolizumab monotherapy (200 mg/body, every three weeks). After the third course of treatment, disease progression was detected; hence, second-line chemotherapy, involving carboplatin (area under the curve: 5.5) and nab-paclitaxel (100 mg/m^2), was administrated in June 2017. Before the chemotherapy, a laboratory examination detected a white blood cell count of 4.8×10^9/L, a hemoglobin concentration of 7.8 g/dL, and a platelet count of 179×10^9/L. Un-

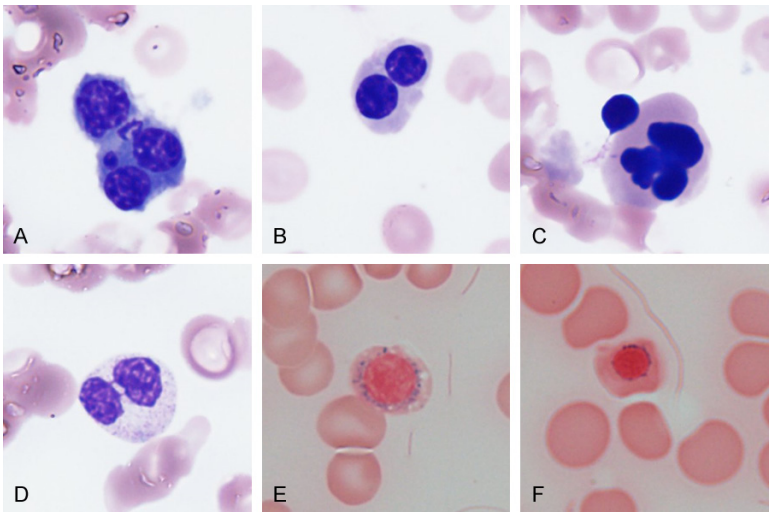

Figure 1. Bone marrow cells seen at the diagnosis of myelodysplastic syndrome. Various types of dysplasia, such as erythroblast multinucleation (A, B) and karyorrhexis (C), neutrophils exhibiting the pseudo-Pelger-Huët anomaly (D), and ringed sideroblasts (E, F), were observed (A-E: original magnification: ×1000, May-Giemsa stain; E and F: original magnification: ×1000, Prussian blue stain).

expectedly, the patient developed marked anemia (hemoglobin: 5.6 g/dL), thrombocytopenia (platelet count: 26×10^9/L), and leukocytopenia (white blood cell count: 2.1×10^9/L) in spite of the administration of granulocyte-colony-stimulating factor on day 27. Bone marrow aspiration was conducted to investigate the etiology of the patient's cytopenia since it was too severe and had lasted too long to have been a hematotoxicity of the chemotherapy. The aspirate was hypocellular (blast cell frequency: 0.4%), and the erythroid and myeloid cells were dysplastic (**Figure 1**), resulting in a diagnosis of MDS. A chromosomal analysis of the patient's bone marrow cells revealed the following karyotype: 46, XY, +1, der(1;21)(q10;q10) [3]/46, XY [17] (**Figure 2**). While the carboplatin and nab-paclitaxel-based chemotherapy shrunk his pulmonary carcinoma, which seemed to represent a partial response, the anemia persisted, and the patient remained red blood cell transfusion-dependent. Therefore, azacitidine monotherapy (75 mg/m^2 for 7 days every 4 weeks) was administered as a treatment for his MDS; however, his pancytopenia did not improve after two courses of azacitidine therapy. Although his pulmonary carcinoma unfortunately recurred, only palliative radiotherapy was administered because it was considered that treating two malignancies simultaneously would be difficult. Eventually, he died of respiratory insufficiency due to pulmonary carcinoma in December 2017.

Discussion

WAT are considered to be rare in hematological malignancies [1]. Various types of WAT have been reported to be recurrent abnormalities. The der(1;7)(q10;p10) translocation is representative of these WAT and is the most well documented, especially with regard to its clinical and prognostic characteristics. However, other types of WAT have not been fully analyzed because of their rarity.

It has been reported that the centromere of chromosome 1 is the centromere that is most often involved in WAT, as is the case for der(1;7)(q10;p10) [2]. However, as far as we know, only two cases of myeloid neoplasms harboring der(1;21)(q10;q10) as a sole anomaly have been reported [2, 3]. Furthermore, only three cases of myeloid malignancies involving complex abnormalities that included der(1;21)(q10;q10) have been reported [4-6]. Hence, the occurrence of der(1;21)(q10;q10) as an isolated abnormality is considered to be extremely rare in myeloid malignancies.

As for WAT involving the long arm of chromosome 1, it has been reported that WAT that result in the gain of 1q frequently involve the acrocentric chromosomes [2]. However, while D1Z7 and D7Z1, which are responsible for the formation of the der(1;7)(q10;p10) translocation and are from the same suprachromosomal family, exhibited marked homology during alpha-satellite sequence analysis, chromosomes 1 and 21 are not from the same suprachromosomal family [7, 8]. In addition, no common alphoid subset, such as that including chromosomes 1 and 15, is known to exist among the acrocentric chromosomes [9]. Therefore, the further accumulation of cases harboring der(1;21)(q10;q10) is necessary in order to clarify why WAT involving chromosomes 1 and 21, which do not exhibit clear centromeric homology, occur.

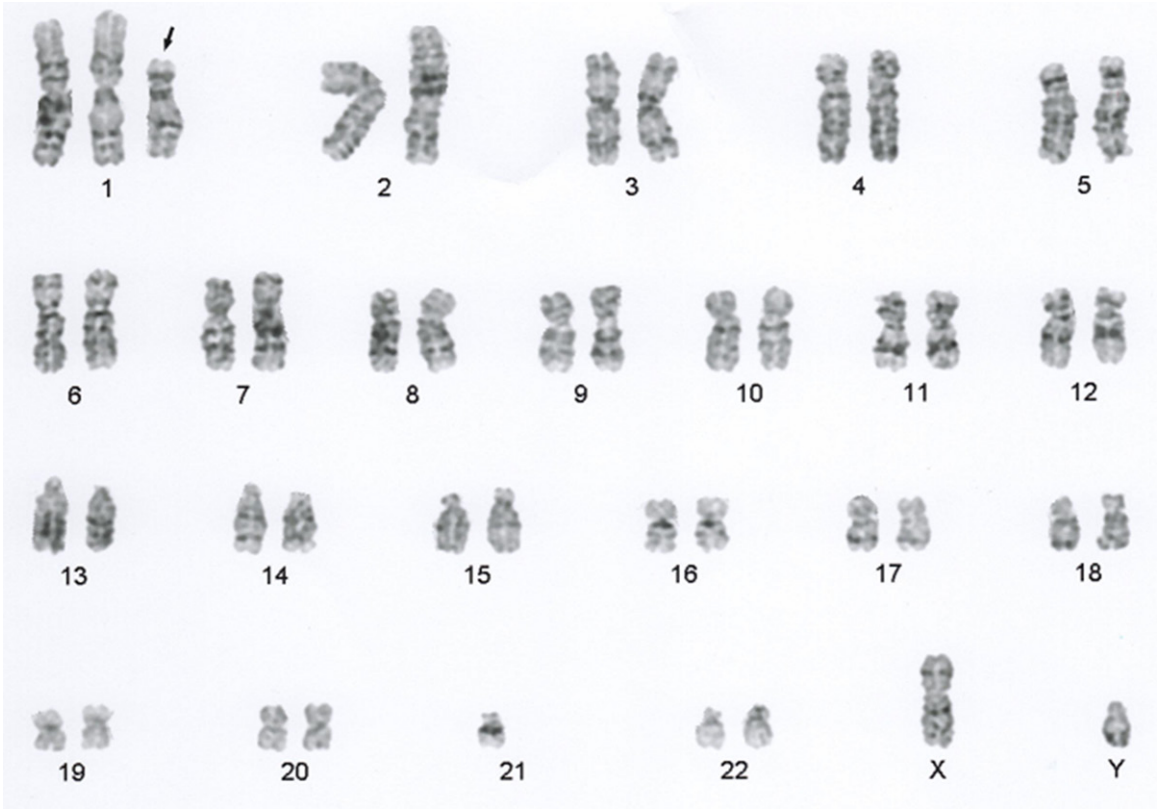

Figure 2. Results of the G-banding karyotype analysis. G-banding karyotype analysis performed at the diagnosis of myelodysplastic syndrome revealed the following karyotype: 46, XY, +1, der(1;21)(q10;q10).

Concerning diagnosis, the present case corresponds to therapy-related MDS, according to the strict definition, because the patient had a history of chemotherapy before being diagnosed with MDS. If so, regarding the treatment that caused the therapy-related MDS, the patient was treated with pembrolizumab (an immune-checkpoint inhibitor), nab-paclitaxel (a microtubule depolymerization inhibitor), carboplatin (a bifunctional alkylator), and granulocyte-colony-stimulating factor. However, pembrolizumab, which has no direct effect on nucleic acids or cell differentiation, is not considered to be a cause of therapy-related MDS. Additionally, as for the remaining three agents, nab-paclitaxel, carboplatin, and granulocyte-colony-stimulating factor, they were only administered for a month, which is shorter than the period that is normally associated with therapy-related MDS [10]. Considering a short latent period between the chemotherapy and diagnosis of MDS, we finally diagnoses occult *de novo* MDS coexistent with lung cancer rather than therapy-related MDS after chemotherapy.

When considered in correlation between the chromosomal aberration, Adeyinka et al. reported that, apart from der(1;7)(q10;p10), the WAT that result in the gain of 1q are variants of the der(1;7)(q10;p10) and have similar molecular consequences due to the gain of 1q [2]. In addition, der(1;7)(q10;p10) is closely associated with therapy-related myeloid neoplasms [11-13]. Certainly, among the reported case involving the der(1;21)(q10;q10), there was a therapy-related AML case [6]. On the other hand, cases of other settings, such as pediatric *de novo* acute myeloid leukemias harboring complex chromosomal abnormality involving der (1;21)(q10;q10) [5], or myeloproliferative neoplasms harboring der(1;21)(q10;q10) as isolated chromosomal abnormality and also had a diploid clone such as seen in present case [2]. Accordingly, it seems that the der(1;21)(q10;q10) is not restricted to therapy-related myeloid neoplasms, and might play an important role in tumorigenesis in hematological neoplasms.

One limitation of our case study is the lack of detailed cytogenetic data, such as data from

centromeric breakpoint analyses [8]. Obtaining such information through the accumulation of cases involving the der(1;21)(q10;q10) translocation might be helpful for further elucidating the molecular biology of the der(1;21)(q10;q10) translocation.

Disclosure of conflict of interest

None.

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