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The novel translocation of t (1;21) in multiple myeloma with poor prognosis

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Abstract

Objective: Multiple myeloma (MM) is characterized as the neoplastic proliferation of plasma cells producing a monoclonal paraprotein. The aim of this paper is to report complex karyotype that leads to a fatal clinical course in a patient with MM.

Case: A 48-year-old male patient was diagnosed as MM free lambda. The karyotype of the patient was 46, XY, t(1;21) (p11;p11), del(3) (q25;q29), del(6) (q24;q26), t(11;14) (q13;q32), del(13) (q14;q21) in cytogenetic evaluation. Vincristine, doxorubicin and dexamethasone were started. The creatinine levels increased after the second course of chemotherapy, the chemotherapy protocol was switched to bortezomib and dexamethasone. Patient was admitted to the emergency department with pneumonia after the second chemotherapy cycle. Despite using broad spectrum antibiotics and oxygen support, he died after the development of sepsis syndrome.

Conclusion: The anomaly of t (1;21) (p11;p11), that we detected in this case was detected in a case with MM for the first time and this anomaly has not been detected between these breaking points in any malignancies before. Although the prognostic impact of this unique anomaly may be unclear, further studies are needed to evaluate the effect of cytogenetic anomalies on prognosis of multiple myeloma.

Keywords: multiple myeloma, karyotyping, chromosome aberrations

Introduction

Multiple myeloma (MM) is characterized as the neoplastic proliferation of plasma cells producing a monoclonal paraprotein (1, 2). Multiple myeloma is a heterogeneous disease with overall survival less than 1 year or more than 10 years. The staging, patient factors, disease biology and response to therapy are the factors affecting prognosis (1). The cytogenetic anomalies of patients have prognostic significance. In studies, it was stated that cytogenetic abnormalities were very important in the diagnosis and follow-up (3). According to high-risk and standard-risk cytogenetic abnormalities, response to treatment and resistance can be estimated (4, 5). There are numerous cytogenetic abnormalities in the literature (6, 7). The aim of this paper is to report a new translocation with complex karyotype in a patient with MM.

Case report

A 48-year-old male patient was admitted to our emergency department with the symptom of black stool. The hemoglobin value was 7.3 g/dl, platelet count was 37×103/µl and leukocyte count was normal at admission. The patient was consulted to hematology department due to the presence of bicytopenia, high creatinine level and hypercalcemia. Monoclonal free lambda band was observed in the serum immunofixation electrophoresis. The serum free lambda level was 13,050 mg/l. His serum calcium level was 15 mg/dl. The patient was hospitalized. Bone marrow biopsy showed diffuse neoplastic plasma cell infiltration.

The bone marrow sample of the patient was cultured for 24 hours and then GTG (Giemsa-Trypsin) banding was performed. Twenty metaphases of the patient were analyzed and karyotype was generated according to the 2013 International System for Human Cytogenetic Nomenclature (ISCN) (8). Complex karyotype was detected in all of 20 metaphases. The karyotype of the patient was 46, XY, t(1;21) (p11;p11), del(3) (q25;q29), del(6) (q24;q26), t(11;14) (q13;q32), del(13) (q14;q21). Translocations between chromosomes 1 and 21, deletions in the long arms of chromosomes 6 and 13 and translocations between chromosomes 11 and 14 were identified in all analyzed metaphases (Figure 1).

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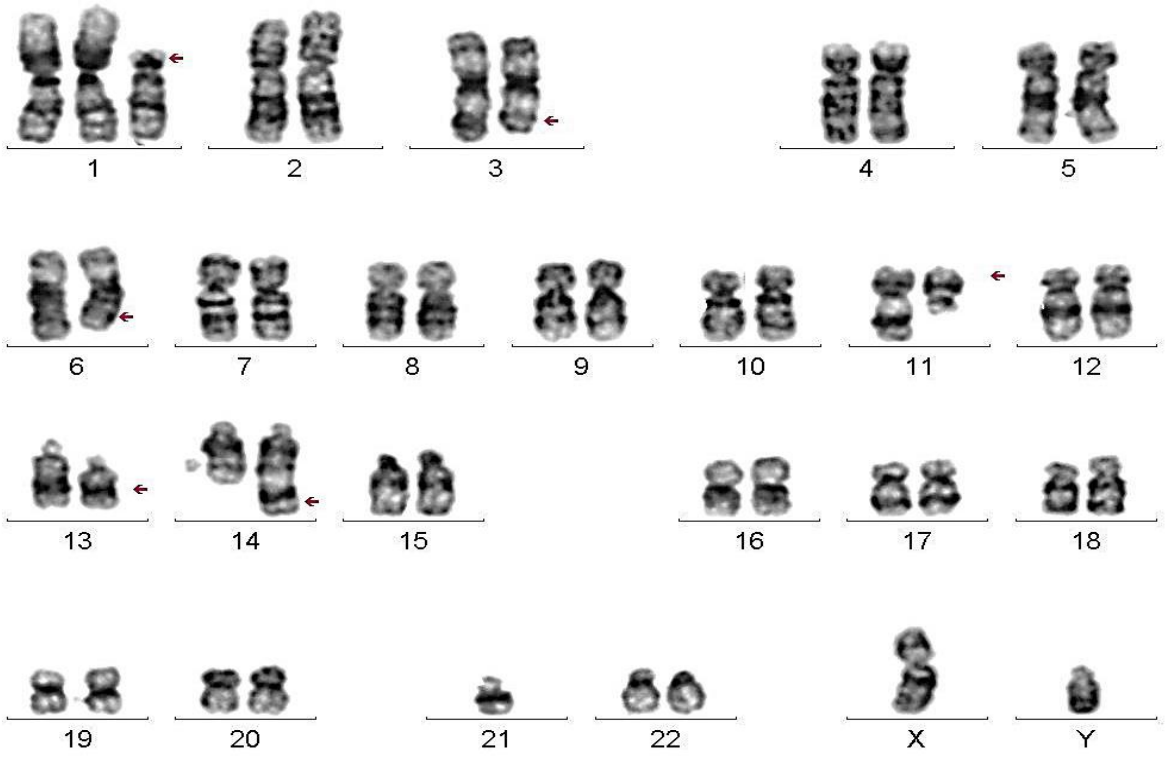

Figure 1. Karyotype of the patient (G-banding with Giemsa-Trypsin 358x316 mm (72 x 72 DPI)).

The patient was diagnosed with MM and the treatment of vincristine, doxorubicin, dexamethasone (vincristine 0.4 mg/day on day 1, 2, 3, 4, intravenously, doxorubicin 9 mg/m2 on day 1, 2, 3, 4, intravenously, dexamethasone 40 mg/day on day 1-4, 9-12 and 17-20, peroral) was initiated. A minimal decrease was observed in the creatinine levels during follow-up in first chemotherapy cycle. When the creatinine levels increased again after the second course of chemotherapy, hemodialysis was initiated. The chemotherapy protocol was switched to bortezomib and dexamethasone (bortezomib 1.3 mg/m2/day on day 1, 4, 8, 11, subcutaneous and dexamethasone 40 mg/day on days 1-4, 9-12, peroral). After 4 cycles, autologous stem cell transplantation was planned. After the second chemotherapy cycle, the patient was admitted to the emergency department with the complaints of coughing and producing sputum. He was diagnosed as pneumonia. He was hospitalized again and moxifloxacin was started. After 2 days, the oxygen saturation level decreased. Creatinine levels showed progressive elevation. Despite the broad spectrum antibiotics and oxygen support, he died because of sepsis syndrome. The patient's informed consent form was obtained according to local ethic commission rules.

Discussion

New treatment modalities have become available for the patients with MM (9). Several cytogenetic abnormalities [t(4;14), del(17/17p), t(14;16), t(14;20), nonhyperdiploidy, gain(1q)] were associated with poor prognosis. Treatment recommendations were different in high-risk and standard risk MM (9). In this case, we reported a new translocation of t(1;21) (p11;p11), which did not occur between these points previously according to the databases that we have searched (Atlas of Genetics and Cytogenetics in Oncology and Hematology and Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer). When we evaluated the other anomalies of the patient, we saw that t(11;14) (q13;q32) is one of the most common translocations of MM (9). Translocation t(11;14) was identified as neutral in some studies or favorable in other studies (9). When t(11;14) (q13;q32) was included in the complex karyotype, del(3)(q) and the anomalies of chromosome 1 can be detected together (10, 11). Also in our case, t(11;14) (q13;q32) was accompanied by both del(13) (q14;q21) and dic(1;21) (p11;p11) that we reported as a new translocation. The anomaly of del (3)(q) is associated with short overall survival. The other anomaly was detected in our patient which was del (6)(q) occurs in 2-5% of MM patients (12-14).

This anomaly indicates a favorable prognosis in adult acute lymphoblastic leukemia. The same deletion is associated poor prognosis in MM (15). In the literature, it was also reported another rare cytogenetic abnormality t(3;16) (q21; q22) which detected in MM, associated with poor prognosis (16).

Conclusion

The anomaly of t(1;21) (p11;p11) is a new entity which has not been detected between these breaking points in any malignancies before. It was detected in a case with MM for the first time. Although, the prognostic impact of this unique anomaly may be unclear. Since the complex karyotype was detected in this patient, it was difficult to say t(1;21) (p11;p11) is associated with poor prognosis.

Further studies are needed to evaluate the effect of cytogenetic anomalies on prognosis of multiple myeloma.

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: **M.O., S.B., İ.C.H.,** were contributed to planning the research, patient examination, **S.B.** was contributed to cytogenetic analysis and result**, M.O. and M.Ö.** were contributed to preparation of the article.

Ethical issues: All Authors declare, originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities.

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