Acta Oncologica Turcica 2010;43:88-90

Myelodysplastic Syndrome with Complex Cytogenetic Abnormalities and Immunocompromised in Two Siblings

Miyelodisplastik Sendromlu İki Kardeşte Kompleks Sitogenetik Anormallik ve Ağır İmmün Yetmezlik

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Dear Editör,

Myelodysplastic syndrome (MDS) is a clonal hematological disorder leading to impaired proliferation and differentiation of the multipotent hematopoietic stem cells (1). Cytogenetic abnormalities are reported in about half of the patients. The most common chromosomal defects are partial or complete deletions of chromosome 5, 7, 20, and trisomy of chromosome 8 (2). Patients with MDS frequently have immune abnormalities (IA) including autoimmune disorders, functional and quantitative abnormalities of T-cells, B-cells, and natural killer lymphocytes. Decreased total T-cells and CD4+ cells, reduced ratio of CD4+/CD8+ cells, impaired production of lymphokines, impaired T-cell and B-cell interactions, reduced T-cell response to mitogens, impaired natural killer cell activity, defective adherence, locomotion, diapedesis, and chemotaxis of granulocytes, impaired antibody dependent and lectin induced polymorphonuclear cytotoxicity, and both hypergammaglobulinemia and hypogammaglobulinemia are observed in patients with MDS (3-8). IA may contribute significantly to the development of disseminated infections. Recurrent infections and transformation to acute leukemia are the major causes of death in patients with MDS (9,10). In this report, we describe MDS with complex cytogenetic abnormalities/*del(ll)(q23)* in two immunocompromised siblings. Patients' characteristics are summarized in Table 1.

They had to be hospitalized for intravenous antibiotic therapy because of recurrent infections. They had persistent pancytopenia and required several blood cell transfusions and intravenous immunoglobulin. They were diagnosed with MDS refractory cytopenia with multi-lineage dysplasia (RC-MLD) (11). Any matched donor for bone marrow transplantation couldn't be found. The male patient and his sister died four and three months after the diagnosis, respectively. The chromosome abnormality at *del(11)(q23)* involving the mixed lineage leukemia (MLL) gene has been observed in acute lymphoblastic leukemia, acute myeloid leukemia, chronic lymphocytic leukemia, and myelodysplastic syndrome. It is suggested that *del(11)(q23)* band/MLL gene has an important role in normal hematopoietic cell growth and the differentiation and the rearrangement of MLL gene lead to the dysregulation of

Table 1. Characterization of patients.

	Sibling 1	Sibling 2
Sex	**Male**	**Female**
Age (year)	30	42
Symptoms	Neutropenic fever, weakness, epistaxis	Neutropenic fever, skin lesion on her face
Physical exam	Multiple infective skin lesions on extremities, no organomegaly	Infective skin lesion on her face, no organomegaly
HB g/dL	8.2	10.2
WBC x109/l	2.05	1.0
NEU x109/l	1.43	0.2
PLT x109/l	20	28
IgG g/l (7-16)	1.4	2.0
IgM g/l (0.4-2.3)	0.2	0.18
IgA g/l (0.7-4)	0.18	0.24
MDS Subtype*	** RC-MLD	** RC-MLD
Cytogenetic abnormalities	*trp(1)(q25qter), del(11)(q23)*	*der(1), del(6)(p22), del(11)(q23), der(20)*
Survey (Month)	4	3
Cause of death	Sepsis	Sepsis

* Myelodysplastic syndrome.
** Refractory cytopenia with multi-lineage dysplasia.

differentiation along both lymphoid and myeloid pathways. *del(11)(q23)* abnormalities are associated with unfavorable prognosis. Patients with *del(11)(q23)* chromosomal deletions often exhibit a more severe disease course and shortened survival (12). Harbott et al. reported that 15/16 AML and 5/12 MDS patients with deletion *del(11)(q23)* died with a median overall survival of 14.1 months (13). Both of the siblings were living in central Anatolia region (Corum) and survived on farming. They had no exposure to the industrial and chemical substances. Nevertheless, herbicides and white soil (involving asbestos or zeolite) may play a role in the development of MDS. Immunocompromised state associated with MDS and certain chromosomal abnormalities seemed to be related with unfavorable prognosis. These cases presented here draw attention to the importance of IA and cytogenetic abnormality of *del(11)(q23)* in MDS. Studies including large amounts of cases are required to evaluate the familial association of cytogenetic abnormality of *del(11)(q23)* and immunocompromised state in MDS.

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