nique for the follow-up of Ph1 ALL patients, which may help predict clinical outcome. The value of this simple methodology should be tested in a larger trial on MRD in Ph1 ALL.

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Key words

Acute lymphoblastic leukemia, Philadelphia chromosome, FISH, minimal residual disease.

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Transformation of severe aplastic anemia into myelodysplastic syndrome with monosomy 7: monoclonal origin detected by HUMARA gene analysis during the aplastic anemia phase

A patient with aplastic anemia showed a monoclonal pattern on the HUMARA gene before the development of a myelodysplastic syndrome (MDS). The present case strongly suggests that if patients with aplastic anemia reveal monoclonality of the HUMARA gene, they should be considered to have a borderline disorder between aplastic anemia and MDS.

Sir,

Aplastic anemia is a hematopoietic disease of stem cells that causes pancytopenia and hypocellular bone marrow. Treatment with immunosuppressive agents, cytokines, and allogeneic bone marrow transplantation improves long-term survival.[1] However, long-term survivors with aplastic anemia have a high risk of developing solid tumors, acute myeloid leukemia, and myelodysplastic syndrome (MDS).[2] Recently, some patients with aplastic anemia have been reported to show clonal hematopoiesis,[3] but it is not clear whether this truly represents the clonal growth of progenitor cells, as occurs in MDS. Here, we describe an elderly woman with severe aplastic anemia and monoclonality of the human androgen receptor (HUMARA) gene who developed MDS with monosomy 7 after treatment with granulocyte-colony stimulating factor (G-CSF) and cyclosporin A.

A 77-year-old woman presented in February 1997 with purpura of the limbs. Hematological findings were as follows: hemoglobin 66 g/L, reticulocytes 6 $\times 10^9$/L, platelets 13×10^9/L, leukocytes 1.7×10^9/L, neutrophils 0.4×10^9/L. Bone marrow aspiration and biopsy revealed marked hypocellularity without proliferation of blasts and trilineage dysplastic changes. Cytogenetic analysis of bone marrow cells revealed a normal female karyotype (Table 1), and monosomy 7 was not detected by fluorescence *in situ* hybridization (FISH) using the CEP7 (D7Z1) probe (Vysis, IL, USA). She was diagnosed as having aplastic anemia, and was started on treatment with cyclosporin A and G-CSF. However, analysis of the HUMARA gene showed a monoclonal pattern in mononuclear cells obtained from the peripheral blood and bone marrow. In December 1998, bone marrow aspiration showed a hypocellular marrow with psuedo-Pelger neutrophils and megaloblastic changes. Cytogenetic analysis of her bone marrow revealed 17 abnormal mitoses [45,XX,-7,t(12,21)(q23;q22)] and only 3 normal mitoses (46,XX). The monosomy 7 was detected in 60.1% of interphase bone marrow cells by FISH. Therefore, transformation to hypoplastic MDS (refractory anemia) was diagnosed. G-CSF therapy was abandoned in January 1999, when she had been administered a total dose of 140 μg/kg over 3 months. She has now developed refractory anaemia with excess of blasts without cytotoxic agents.

In most cases of aplastic anemia, MDS may occur in the presence of monosomy 7 after long-term immunosuppressive and G-CSF therapy.[4] The cumu-

Table 1. Bone marrow findings during the clinical course.

	1997.2.26	1997.11.7	1998.12.5
Nuclear cell count (μL)	1,500	10,000	12,000
Megakaryocytes (μL)	0	0	0
Blasts (%)	0.0	0.4	0.8
Lymphocytes (%)	78.8	55.2	64.8
Erythroblasts (%)	3.6	7.6	10.4
Monosomy 7#	3.0%	2.0%	60.1%
Karyotypes	46,XX [19 cells]	46,XX [15 cells]	45,XX,-7, t(12,21) (q23; q22) [17 cells]/ 46,XX [3 cells]

Monosomy 7#: detected by FISH analysis using the CEP7 probe.

lative dose and duration of G-CSF therapy may be related to the risk of MDS arising from aplastic anemia.[5] It is interesting to note that 4/7 aplastic anemia patients showed monoclonality of the HUMARA gene, and that 3 of these 4 patients developed MDS, while all patients with polyclonality did not undergo transformation to MDS (*personal communication to Kuriya, S. et al, 1999*). Since our patient showed a monoclonal pattern on the HUMARA gene before the development of MDS and was administered a relatively low total dose of G-CSF, the present case suggests that monoclonality of the HUMARA gene in aplastic anemia is an important risk factor for MDS. Therefore, if patients with aplastic anemia reveal monoclonality of the HUMARA gene, they should be considered to have a borderline disorder between aplastic anemia and MDS.

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Key terms

Aplastic anemia, monosomy 7, G-CSF.

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Primary non-Hodgkin's lymphoma of the vagina

Primary lymphoma of the vagina can be successfully treated by pelvic radiation, but in young woman cytotoxic chemotherapy should be considered to preserve fertility. We report a case of non-Hodgkin's lymphoma of vagina (stage IE) with an optimal response to cytotoxic chemotherapy and disease-free survival for 13 years.

Sir,

Primary lymphoma of the genital tract is rare, accounting for 1% of primary extra-nodal lymphomas and localization in the vagina is ever rares; in fact only twenty-eight cases have been reported in literature,[1-6] although secondary involvement in advanced disease is found about 40% of cases.[7]

We report a case of non-Hodgkin's lymphoma (NHL) of vagina (stage IE) with an optimal response to cytotoxic chemotherapy (MACOP-B) and disease-free survival for 13 years.

A 25-year old female presented a 1-month history of vaginal discharge. Physical examination revealed an extensive tumor in the left wall of the vagina, extending into the pelvic cavity with a mass. The patient did not have fever, weight loss, or night sweats.

CT, US and MRI examinations showed a pelvic mass that measured 9 cm, with spread to the pelvic side wall. Urography showed stenosis of the left ureter. A vaginal biopsy did not show evidence of neoplasm. Because the histologic analysis was not significant despite the imaging signs and ureter is stenosis, the patient was submitted to staging laparotomy with partial exeresis of the pelvic mass and lymph node biopsy. The histologic analysis showed non-Hodgkin's centroblastic-centrocytic type lymphoma according to the Kiel classification. Ann Arbor classification was stage IEA, (Working formulation: F; Rappaport classification: DM). Bone marrow biopsy was negative.

The woman was treated with six courses of chemotherapy using the MACOP-B regimen (MTX, ADM, CTX, VCR, platinum, BLM, and leucovirin).

No hematologic toxicity was observed during chemotherapy, permitting 100% delivery of the planned dose. Grade III hair loss, grade II stomatitis and cystitis occurred.

After six cycles a complete pathologic response was achieved and the patient was disease-free at her latest follow-up in 1999. Four years after the treatment she gave birth to a female-infant.