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Acute myeloid leukemia with near-triploid karyotype and extramedullary involvement of mediastinum

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A 22-year-old man presented with dyspnea and left chest pain in November 2003. Complete blood counts revealed WBC: 18.2×10^9/l (35% blasts, 31% neutrophils), hemoglobin 119 g/l and platelets 166×10^9/l. CT scan showed extensive mediastinal lymphadenopathy, left sided pleural effusion (cytologically malignant) and a pericardial effusion. Lymph node biopsy was first interpreted as high-grade lymphoma after conventional stains. However, bone-marrow cytology demonstrated 85% infiltration with basophil blasts with intermediate size (15% with peroxidase-positive granulation). Lymph node immunohistology, flow cytometry and bone-marrow histology confirmed acute myeloid leukemia (AML). The blasts coexpressed CD56. Chromosome analysis revealed a near-triploid karyotype (64 XY, −X, −1, −2, −7, −16).

The patient received induction chemotherapy (two cycles standard-dose cytarabine, idarubicin and etoposide, trial: AML-HD98A). In the bone marrow, partial remission was achieved after the first and complete remission after the second cycle. Mediastinal lymph nodes and effusions decreased markedly but didnot resolve. Immediately before consolidation therapy, mediastinal lymph nodes enlarged again. Inferior vena cava syndrome and renal function impairment developed. Since these symptoms improved rapidly during consolidation therapy with high-dose cytarabine and mitoxantrone they were interpreted as signs of disease progression. In April 2004, allogeneic stem-cell-transplantation (allo-SCT) from a nonrelated donor after conditioning with total body irradiation (8 Gy), thiotepa and fludarabine was performed. Graft-versus-host disease (GvHD) prophylaxis included cyclosporine A and methotrexate, although moderate GvHD involving the liver developed.

In October 2004, CNS relapse occurred and was treated successfully with intrathecal chemotherapy (cytarabine, methotrexate and dexamethasone). Unfortunately, the patient discontinued further treatment. In February 2005, a second CNS relapse occurred. Again, intrathecal chemotherapy led to a blast-free CSF and radiation of the neuroaxis was given. However, 1 month later, AML relapsed again in CNS and in the bone marrow. In April 2005, the patient died from progression of AML 18 months after diagnosis.

High hyperdiploidy is reported in 0.5–3% of hematological malignancies, but reports of near-triploidy (58–80 chromosomes) and near-tetraploidy (81–103 chromosomes), are rare.[1] There seems to be a close association of these chromosomal abnormalities with mediastinal extramedullary myeloid tumors.[2] Rarely, near-tetraploidy has also been reported in AML without extramedullary manifestations.[3] To our knowledge, only five cases of AML with extramedullary manifestations and near-triploidy/tetraploidy have been published.[2,4,5] Although four of them entered complete remission after induction chemotherapy, all patients died of their disease.[2] Only one received allo-SCT. We report on a second patient with AML, a near-triploid/tetraploid karyotype and extramedullary involvement, treated by allo-SCT and the first case with CNS involvement. The disease was controlled for approximately 1 year after allo-SCT with a relatively good quality of life. AML with near-triploid/tetraploid karyotype and extramedullary involvement of mediastinum is a rare, highly aggressive subtype which may be initially misinterpreted as high-grade lymphoma. The prognosis is poor even with allo-SCT.

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