Fatal Acute Tumor Lysis Syndrome following Intrathecal Chemotherapy for Acute Lymphoblastic Leukemia with Meningeal Involvement

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Abstract

Acute tumor lysis syndrome (ATLS) is a well-recognized complication of systemic chemotherapy for rapidly proliferating neoplasms. ATLS has rarely occurred after intrathecal chemotherapy for the treatment of leukemia with meningeal involvement. Here, we report a case of fatal ATLS complicating intrathecal injections of methotrexate, cytarabine and hydrocortisone for acute lymphoblastic leukemia which relapsed with meningeal involvement after allogeneic stem cell transplantation. This case indicates that intrathecal chemotherapy alone may be sufficient to induce ATLS. Close monitoring and prevention of ATLS are also warranted following intrathecal chemotherapy alone.

Key words: tumor lysis syndrome, intrathecal chemotherapy, acute lymphoblastic leukemia


Introduction

Acute tumor lysis syndrome (ATLS) is a well-recognized complication that usually follows chemotherapy for rapidly proliferating neoplasms. ATLS is characterized by hyperphosphatemia, hypocalcemia, hyperuricemia and hyperkalemia and can lead rapidly to an acute renal failure (1). Although ATLS has been commonly described after systemic cytotoxic chemotherapy, it has been reported in only 2 patients after intrathecal chemotherapy (2, 3). We report a case of fatal ATLS after intrathecal injections of methotrexate, cytarabine and hydrocortisone for acute lymphoblastic leukemia (ALL) which relapsed with meningeal involvement after unrelated cord blood transplantation (CBT).

Case Report

An 18-year-old woman was diagnosed with ALL with FAB L2 morphology in January 2002. Surface marker analysis showed that the lymphoblast cells expressed CD10, CD19, CD22, CD34, CD38 and HLA-DR. Cytogenetic analysis revealed a complex abnormal karyotype. She received a conventional combination chemotherapy and achieved complete remission (CR). Thereafter, consolidation therapy was given. But she relapsed in January 2003 and achieved second CR after salvage chemotherapy. Since 16 courses of prophylactic intrathecal chemotherapy were given concurrently with systemic chemotherapy, there was no evidence of meningeal involvement before CBT. Thereafter, she underwent unrelated CBT following a conditioning regimen with total body irradiation and cyclophosphamide in November 2003. Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporine alone. Complete donor chimerism in bone marrow using short tandem repeats was achieved. Grade II acute GVHD and limited chronic GVHD occurred. One year after CBT, she complained of headache and visual disturbance with retinal detachment. Lumbar puncture revealed a lymphocytic pleocytosis (14 cells/mm³), including mainly leukemic lymphoblasts (Fig. 1A), and chimerism analysis in bone marrow revealed 8% of recipient cells. These data suggest that she relapsed with meningeal involvement after CBT. Because she developed convulsion due to meningeal involvement of leukemia, intrathecal injec-
tions of methotrexate 15 mg, cytarabine 40 mg and hydrocortisone 50 mg were given following hydration. Her renal function was almost normal before intrathecal chemotherapy. After 3 days of intrathecal chemotherapy, serum creatinine level increased to 3.3 mg/dL, uric acid to 14.4 mg/dL, phosphorus to 5.5 mg/dL, and calcium and potassium were normal. On the same day, bone marrow aspiration showed hypercellular marrow with 60.8% lymphoblast cells (Fig. 1B). A diagnosis of ATLS was made. The patient developed oliguria and congestive heart failure, and symptomatic treatment with a loop diuretic, low dose dopamine and dobutamine were started. After 5 days of intrathecal chemotherapy, serum creatinine level increased to 6.7 mg/dL, uric acid to 22.0 mg/dL, phosphorus to 8.0 mg/dL, and calcium decreased to 7.5 mg/dL, but potassium was normal. Her coagulation test results had been normal before intrathecal chemotherapy, however, the results were deranged with a prothrombin time ratio of 1.35 (normal range, 0.85-1.15), fibrinogen 923 mg/dL (normal range, 158-278) and FDP 13.7 microg/mL (normal range, 0-5) after intrathecal chemotherapy. Although the patient developed aura despite the symptomatic treatment, hemodialysis could not be performed due to severe cardiac dysfunction with low ejection fraction (23%). Ten days after intrathecal chemotherapy, the patient died of uremia with congestive heart failure.

Discussion
To the best of our knowledge, this is the third case of ATLS to be described following intrathecal chemotherapy. The systemic effect of intrathecal chemotherapy has been reported. The anatomic relationship between the medulla spinalis and the bone marrow is likely to provide major part of the cerebrospinal fluid (CSF) transport to the systemic circulation (4, 5). Methotrexate is not metabolized in the CSF and released into the systemic circulation with prolonged cytotoxic levels (3, 6). Based on these reports, tumor lysis syndrome can occur after intrathecal chemotherapy. In fact, the high tumor burden in the bone marrow might have been associated with the development of ATLS after intrathecal chemotherapy in our patient. This case indicates that intrathecal chemotherapy alone may be sufficient to induce ATLS. Close monitoring and the prevention of ATLS are warranted following intrathecal chemotherapy alone.

References