Acute rhabdomyolysis after high-dose chemotherapy and circulating progenitor cell autografting for breast cancer

We describe a case of acute rhabdomyolysis developing after high-dose chemotherapy followed by circulating progenitor cell (CPC) transplantation in a woman with breast cancer treated in an adjuvant setting for high risk disease, who recovered completely.

Sir,

drug overdose, seizure and infection may be associated with non-traumatic rhabdomyolysis.[1,2] This feature has also been described in association with the administration of lovostatin in cardiac transplant recipients[3] and after interleukin-2, interferon-α and chemotherapy for melanoma.[4] We describe a case of acute rhabdomyolysis occurring in the setting of high-dose chemotherapy with autologous circulating progenitor cell (CPC) transplantation. In November 1997, a 47-year old woman was diagnosed as having breast cancer at a high risk of recurrence. After surgery the patient was enrolled in a clinical trial of high-dose chemotherapy followed by CPC autografting, based on 4 courses of paclitaxel and epirubicin, followed by CPC harvest. The patients in this trial were then scheduled to receive cyclophosphamide (6 g/m^2) + granulocyte colony-stimulating factor (G-CSF), and CPC transplantation to be performed after conditioning with thiotepa (600 mg/m^2) on day -4 and melphalan (140 mg/m^2) on day -1, with CPC reinfusion (on day 0), followed by G-CSF. Our patient underwent the clinical program in a protected environment with prophylatic antibiotics (ciprofloxacin and fluconazole) plus supportive care (tropisetron, dexamethasone, total parenteral nutrition and transfusion of platelets). She developed febrile neutropenia on day +5 and was treated with amikacin and ceftriaxone. Neutropenic fever persisted for 48 hours when vancomycin was added. On day +11 imipen and amphotericin B were given and patient was febrile until day +17.

Bone marrow engraftment occurred on day +12. On day +7 the patient developed fatigue and of severe myalgia. Biochemical tests documented: absolute neutrophil count = 0.2×10^9/L, platelets = 16×10^9/L, Hb = 10.7 g/dL , Na$^+$ = 128 mEq/L, K$^+$ 2.6 mEq/L , Cl$^-$ = 96 mEq/L, Mg^{++} = 1.7 mg/dL, phosphates = 3.0 mg/dL , LDH = 476 mU/mL, BUN = 26 mg/dL, creatinine = O.74 mg/dL, GOT = 65 mU/mL , CPK = 1,756 mU/mL. The finding of urinary myoglobin confirmed the diagnosis of acute rhabdomyolysis. Therapy with additional fluids and K$^+$ was initiated, by day +7. Within 48 hours after the diagnosis of rhabdomyolysis, the patient had virtually paretic lower limbs with persisting profound muscle weakness. Respiratory function was severely impaired. Chest radiography was normal as was cardiac and renal function.

Muscle enzymes and K$^+$ normalized by day +16. The patient was discharged on day +23 and remained bedbound for 2 months, but with intensive physical therapy her general clinical condition gradually improved. Eighten months after CPC transplantation, she has no functional disturbance of the lower limbs.

Rhabdomyolysis is a rare complication of hematopoietic stem cell autologous transplant.[5-7] Potentially rhabdomyolytic viruses include CMV, influenza A coxackie A9 and B5, Epstein-Barr virus, adenovirus 21, parainfluenza and Echo 9.[8] Bacterial and fungal infections may also be involved. No microbiological cultures were positive in our patient, and there was no serologic evidence of viral infection. We have, therefore, postulated on the basis of a temporal relationship that the rhabdomyolysis was caused by a direct iatrogenic myotoxic effect, triggered by vancomycine. The case described highlights that acute rabdomyolysis should be considered when managing cancer patients treated with similar high-dose chemotherapy programs who develop severe myalgia.

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Key words

Rhabdomyolysis, breast cancer, high-dose chemotherapy, circulating progenitor cell support.

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