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SHORT COMMUNICATION

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Tumor lysis syndrome following docetaxel therapy for extensive metastatic prostate cancer

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Abstract Tumor Lysis Syndrome (TLS) is characterized by biochemical changes due to rapid tumor lysis of malignant cells, usually after chemotherapy. Typically it is seen in patients with hematologic malignancies sensitive to chemotherapy within days of receiving chemotherapy. Recently Baeksgaard and Sorensen reviewed the small number of cases of TLS after treatment of nonhematologic malignancies reported between 1977 and 2002. After careful review of the literature, I describe what appears to be to the first reported case of TLS associated with chemotherapeutic treatment of metastatic prostate cancer.

Keywords Tumor lysis · Prostate cancer

Case report

An 80-year-old patient with adenocarcinoma of the prostate (Gleason 3 + 3 = 6) diagnosed in January 2001 was found at that time to have enlarged pelvic lymph nodes and a serum prostate specific antigen (PSA) of 120 ng/ml (normal range 0.0–4.0 ng/ml). Leuprolide acetate was initiated and his PSA was found to have improved to 0.7 ng/ml in July 2002. However, in March 2003 his PSA was 3.3 ng/ml and 174.9 ng/ml in December 2003. A whole-body bone scan was interpreted as a ''superscan'', suggesting extensive bone metastases, and the patient developed pain in multiple bones. After 6 weeks of treatment with bicalutamide, his pain increased and his PSA rose to 348 ng/ml. Baseline chest radiograph was without evidence of pulmonary metastatic disease. Preadmission laboratory results also included: hemoglobin 9.9 g/dl (14.0–18.0 g/dl), platelets $40\times10^3/\mu l$ ($140–450\times10^3/\mu l$), white blood cell (WBC) $4.0\times10^3/\mu l$ ($4.5–10.0\times10^3/\mu l$), INR 1.1 (0.8–3), partial thromboplastin time (PTT) 26.4 s (23.6–32.4 s), a peripheral blood smear showing occasional nucleated red blood cells (RBC), but no schistocytes or RBC fragments, aspartate aminotransferase (AST) 72 U/l (8–41 U/l), alanine aminotransferase (ALT) 23 U/l (25–75 U/l) and alkaline phosphatase 1688 U/l (40–125 U/l). Preadmission medications were naproxen and morphine sulfate.

Docetaxel chemotherapy was initiated at 35 mg/m^2, after first receiving dexamethasone 8 mg by mouth, the morning and evening on the day before and again on the morning of chemotherapy. On the morning of docetaxel, laboratory results included serum creatinine 0.9 mg/dl (0.8–1.5 mg/dl), potassium 4.8 mmol/l (3.5–5.5 mmol/l), calcium 9.9 mg/dl (8.2–10.2 mg/l), phosphorus 3.5 mg/dl (2.5–4.5 mg/dl), lactate dehydrogenase (LDH) 1461 U/l (100–225 U/l) and uric acid 8.6 mg/dl (3.5–8.5 mg/dl).

The next day he had the following laboratory results: creatinine 2.3 mg/dl, potassium 5.8 mmol/l, phosphorus 5.7 mg/dl, uric acid 12.8 mg/dl, LDH 32,300 U/l, and serum calcium 8.2 mg/dl. There was no clinical evidence of an acute ischemic event affecting the heart and causing hypotension resulting in renal failure or of hypovolemia precipitating renal failure. Hemoglobin, platelet count and WBC were without significant change during his brief hospitalization, and his peripheral blood smear continued to show only occasional nucleated RBCs, without schistocytes or RBC fragments. He was treated with one dose of sodium polystyrene sulfonate for his rising serum potassium and with furosemide for fluid overload resulting from renal failure. Aggressive treatment for TLS including intervention to correct his electrolyte abnormalities was recommended and he and his family declined. He expired 40 h after receiving his first and only docetaxel treatment.

Discussion

Acute TLS has been extensively described in patients with hematologic malignancies shortly after receiving

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chemotherapy, especially after treatment of childhood malignancies or acute leukemia. The syndrome is characterized by rising serum creatinine, potassium, uric acid, phosphorus, and LDH as well as declining serum calcium after chemotherapy in patients who typically have a large tumor burden, and is usually seen within days of treatment [1].

TLS has been much less commonly associated with treatment of nonhematologic malignancies. Drakos et al. reviewed the literature in 1994, describing 13 reported cases of nonhematologic malignancies associated with TLS after treatment [2]. Baeksgaard and Sorensen reviewed the reported cases from 1977 to 2002 and documented 45 cases of nonhematologic malignancies where treatment resulted in apparent TLS [3]. After careful review of the literature, I believe this is the first case of TLS associated with chemotherapeutic treatment of prostate cancer. While it is possible that the naproxen, morphine sulfate or an unrecognized hypotensive or hypovolemic event contributed to his renal failure, tumor lysis evidenced by rapid and massive changes in the biochemical markers (in the setting of recent chemotherapy and a large tumor burden) likely represents the major precipitant for his complications. While the only radiographic evidence of a large tumor burden was the bone scan (chest radiograph showed no pulmonary metastatic disease and a CT scan was not done), his low platelet count, WBC, hemoglobin and peripheral blood smear findings were consistent with bone marrow involvement as well, particularly given his normal INR and PTT. His liver function tests were only mildly elevated, but it remains possible that he had liver involvement or involvement of abdominal/pelvic lymph nodes. It seems doubtful that disseminated intravascular coagulation (DIC) contributed to his hospital course, since his hemoglobin, platelets, WBCs, and peripheral blood smear did not significantly change over weeks before or during his brief hospitalization, and INR and PTT just prior to admission did not support DIC occurring.

The biochemical test results were very consistent with a dramatic example of TLS. A literature review revealed no evidence of an association between PSA or other serine proteases and TLS. Since prostate cancer will occasionally respond to corticosteroids, it is possible that the dexamethasone premedication contributed. However, the docetaxel would appear to be the much more likely cause of the TLS, given recent reports of high response rates to weekly docetaxel. For example, Gravis et al. reported that patients with metastatic prostate cancer achieve a 50% or greater reduction in PSA after treatment with weekly docetaxel [4]. Since reports of chemotherapy inducing high response rates in metastatic prostate cancer are a recent development, it remains to be seen how often TLS will occur. Meanwhile, clinicians should be alert to this possible complication in this setting.

References

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