Tumor lysis syndrome in a multiple myeloma treated with thalidomide

A 60-year-old male with progressive high burden non-secretory multiple myeloma (NSMM) presented with tumor lysis syndrome (TLS) after starting thalidomide. He was diagnosed in 1998 with NSMM stage IIIA according to Durie and Salmon’s classification. Initial treatment consisted of six cycles of vincristine, doxorubicin and dexamethasone (VAD), and double high doses of melphalan supported by autologous peripheral blood progenitor cell transplantation with complete response. Fifteen months later he relapsed and was retreated with six cycles of VAD with progression. Consecutively he received multiple courses of standard therapy (melphalan–prednisone, high doses of dexamethasone) with progressive disease.

At that time, the patient presented with multiple osteolytic lesions, multiple plasmacytomas and 80% plasma cells in bone marrow. Serum creatinine, calcemia and uric acid levels were within normal limits. He started treatment with thalidomide (200 mg/24 h).

After 3 days of therapy the patient developed anuria. Serum creatinine level increased to 5.1 mg/dl [normal range (NR) 0.5–1.25 mg/dl], uric acid to 16.8 mg/dl (NR 2–7 mg/dl), phosphorexia to 6.5 mg/dl (NR 2.5–4.7 mg/dl), kaliemia to 6.3 mg/dl (NR 3.5–5 mg/dl) and calcemia was normal. Thalidomide was stopped, and treatment with hydration, furosemide, alcalinization and allopurinol was administered for 4 days. Serum creatinine level and uric acid decreased to 1.6 and 6.5 mg/dl, respectively. After renal function resolution, the patient again started thalidomide at a lower dose (100 mg/24 h), with allopurinol, bicarbonate and hydration. Thalidomide was escalated to the initial dose in 1 week with no further complications. Two months later the patient continues with thalidomide.

The use of thalidomide is one of the most significant advances in the treatment of myeloma since the introduction of high-dose melphalan and autologous stem cell transplantation [1]. The optimal dose of thalidomide has yet to be defined. Some investigators have observed response rates (30%–40%) with doses varying from 50 to 200 mg/24 h, and similar rates with the highest doses [2]. The reported adverse effects of thalidomide at a dose of 200 mg/24 h were constipation in 100% of patients, sedation in 87%, ankle edema in 70%, dry skin and dry mouth in 65% and deep venous thrombosis in 2%, and peripheral neuropathy as a dose-limiting side-effect [3]. Thalidomide is not eliminated by the kidney. The excretion rate is 0.7% [4].

TLS occurs in bulky disease treated with cytotoxic agents and leads to cell death with subsequent acidosis, hyperuricemia, hyperkalemia, hyperphosphatemia and renal failure. Renal insufficiency in multiple myeloma may occur for multiple reasons.

In our case, the patient did not receive intravenous contrast and had normal calcemia. He developed acute renal failure with hyperphosphatemia, and hyperuricemia that improved with hydration and allopurinol; this case therefore suggests TLS.

To our knowledge only one other case of TLS has been observed soon after beginning treatment with thalidomide [5]. In the only case described, response with reduction of plasma cell infiltration (90% to 40%) was seen, but survival was poor.

In conclusion, thalidomide has shown efficacy in refractory and relapse multiple myeloma with tolerable adverse effects, but TLS must be prevented in patients with bulky disease.

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References

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Intravenous ibandronate reduces the incidence of skeletal complications in patients with breast cancer and bone metastases

In their randomized study on the efficacy of ibandronate to reduce the incidence of skeletal complications in breast cancer patients with bone metastases, Body et al. [1] included a placebo group, while acknowledging in the same paper that biphosphonate treat-