

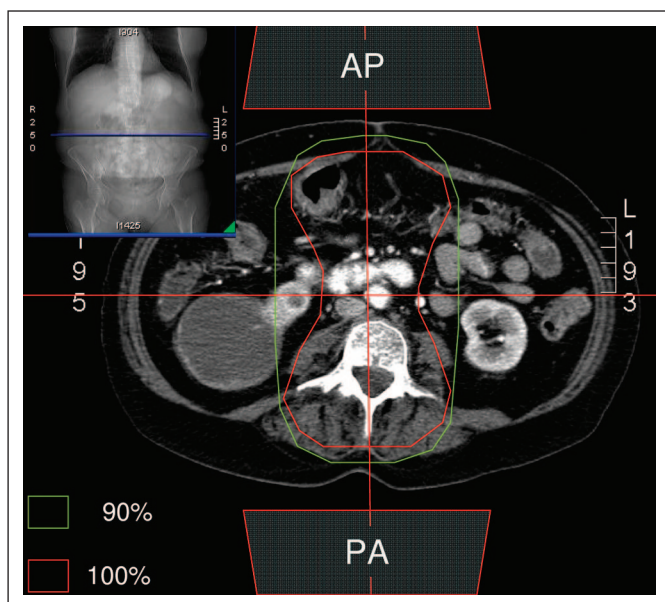


Fig 2.

an approximate half-life of 24 to 48 hours, there may have been residual sorafenib present during radiation treatment and thus normal tissue was still radiosensitized via sorafenib. This report describes a patient receiving sorafenib that developed a lumbar metastasis that required irradiation. She died of complications in the bowel—the area directly targeted by irradiation. In conclusion, this case provides evidence for potential oversensitization of normal tissue by sorafenib. Further studies combining antiangiogenic therapy with radiotherapy are warranted in order to further determine the efficacy and toxicity of combination therapy of sorafenib with radiation.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest

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DOI: 10.1200/JCO.2007.15.8451

Cetuximab-Related Tumor Lysis Syndrome in Metastatic Colon Carcinoma

This is a 64-year-old white male who was initially evaluated in December 2006 for right upper quadrant pain. Ultrasound and computed tomography scan of the abdomen revealed multiple hepatic nodules, the largest being 5.5 cm in the left lobe of the liver (Figs 1A and 1B). Liver biopsy on December 26, 2007, revealed multiple foci of adenocarcinoma consistent with metastasis (Figs 2A and 2B). Subsequent colonoscopy showed a mass in the mid-transverse colon, and the biopsy confirmed a moderately differentiated adenocarcinoma of the colon. He had no other medical problems. In the next 4 weeks, the patient developed obstructive jaundice. Symptoms included nausea, reduced oral intake, and clay-colored stools with narrow caliber. Repeat computed tomography scans of the chest abdomen and pelvis

without contrast revealed conglomerate adenopathy in the mediastinum with bilateral pleural effusions. The CBC showed elevated leukocytes of 18,000/ μ L (up from 11,000 4 weeks previously) with 80% neutrophils, hemoglobin of 12.4 g/dL, and platelet count of 318,000/ μ L. Transaminases were elevated (ALT, 150 U/L; AST, 279 U/L). Alkaline phosphatase was also elevated to 1,000 U/L with direct bilirubinemia of 14 mg/dL (total bilirubin was 17 mg/dL). He underwent gastroduodenoscopy and endoscopic retrograde colangiopancreatography with a biliary stent placement. There was no obvious biliary ductal dilation noted during this procedure. Chemotherapy was not considered, due to extensive liver metastasis causing hyperbilirubinemia and transaminitis. Single agent cetuximab was planned with the intention of adding standard chemotherapy when the patient's liver function improved. He received single agent cetuximab at 400 mg/m². He tolerated the infusion well without any major complications. After 18 hours, his renal function started to deteriorate. In that

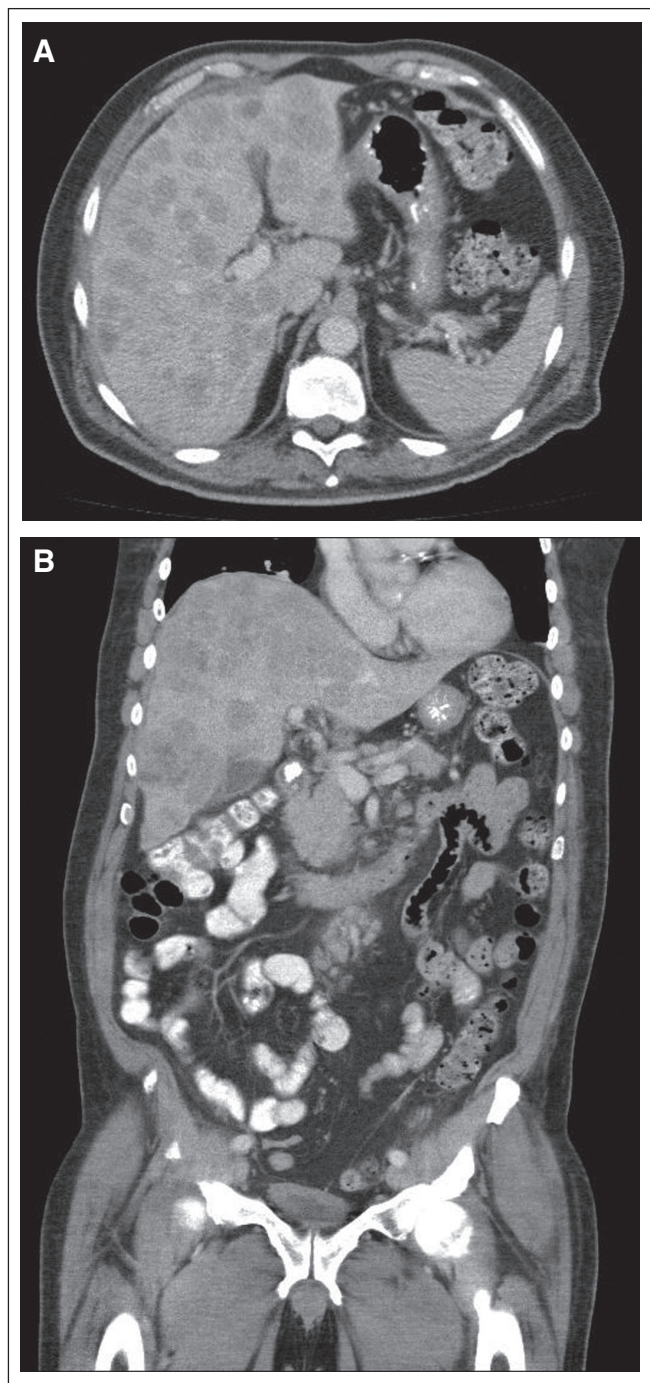


Fig 1.

time period, his blood urea nitrogen went up from 24 to 36 mg/dL, creatinine has increased from 0.9 to 1.8 mg/dL, and potassium went up from 4.2 to 7.4 meq/L. Phosphorous increased from 2.1 to 5.7 to 10 mg/dL. His calcium went down from 7.9 to 6.2 mg/dL, and during that time his albumin was 2.2 g/dL. His uric acid was elevated to 12 mg/dL, creatine phosphokinase to 4,200 U/L, and lactate dehydrogenase to 59,000 U/L. His bilirubin was slightly elevated. He also developed hypotension and respiratory failure requiring intubation. His biochemical profile was consistent with acute tumor lysis syn-

drome (TLS). Approximately 6 hours later, he had further deterioration of his renal function with blood urea nitrogen of 44 mg/dL, creatinine of 3.1 mg/dL, and phosphorous of 10 mg/dL. His lactate level was elevated to 15 mmol/L. Transaminases were elevated significantly (ALT, 3,600 U/L; AST, 17,000 U/L). Hemodialysis was recommended. The patient's family decided against it. He did receive a dose of rasburicase and his uric acid came down to 8.3 mg/dL about 20 hours later. The patient eventually died due to complications of TLS.

TLS is an oncologic emergency characterized by hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia, and uremia that are results of the rapid destruction of malignant cells and the abrupt release of nucleic acids, intracellular ions, proteins, and their metabolites into the extracellular space. High uric acid and calcium phosphate crystals can deposit in the renal tubules and may lead to acute renal failure. TLS has been reported mostly with hematological malignancies. Solid malignancies that can cause TLS include small-cell lung carcinoma and breast carcinoma. TLS can occur following initiation of chemotherapy or spontaneously in the absence of treatment.¹ Laboratory TLS is much more common in the early acute phase (40% to 60%) than clinical TLS (3% to 6%).¹ On the other hand, TLS is an extremely rare complication in patients treated with biologic therapies. Several cases of imatinib mesylate-associated TLS were reported in the literature.²⁻⁴ TLS was also reported with rituximab⁵ in lymphomas, with sunitinib⁶ in gastrointestinal stromal tumor, and with bortezomib⁷ in multiple myeloma. In the past decade, several targeted biologic therapeutic agents revolutionized the field of cancer therapeutics. Cetuximab is widely used in the treatment of metastatic colorectal carcinoma and squamous cell carcinoma of the head and neck. In the phase II European randomized BOND (EMR-007) trial, single-agent cetuximab and cetuximab in combination with irinotecan were examined in patients with irinotecan-resistant tumors.⁸ The overall response (OR) rate for the combination of cetuximab and irinotecan was 22.9% compared with 10.8% for cetuximab monotherapy. Based on these observations, cetuximab was approved by the US Food and Drug Administration in February 2004, both in combination with irinotecan and as a single agent for the treatment of patients with epidermal growth factor receptor-expressing metastatic colorectal carcinoma who are intolerant to irinotecan-based chemotherapy. Another nonrandomized, single arm study confirmed the antitumor activity of cetuximab as a single agent.⁹ Detailed subgroup analysis revealed that cetuximab was equally active in all patient subgroups regardless of numbers of prior therapy or the sequence of prior agents including irinotecan and oxaliplatin.¹⁰ The safety and efficacy of combined biologics (ie, cetuximab and bevacizumab), with or without irinotecan, were evaluated in the randomized BOND-2 study.¹¹ Patients receiving cetuximab, bevacizumab, and irinotecan experienced a 38% OR rate, and patients on cetuximab and bevacizumab experienced a 23% OR rate. Cetuximab was also studied in combination with fluorouracil/leucovorin/oxaliplatin¹² and fluorouracil/leucovorin/irinotecan¹³ with significant efficacy and safety in metastatic colon cancer patients. In the previously mentioned clinical trials involving cetuximab, dermatological adverse effects in the form of acne or allergic skin reactions were more prevalent. Other adverse effects include asthenia, atrial fibrillation, diarrhea, nausea, vomiting, headache, and hypokalemia. There was also a positive correlation between the severity of the skin rash and survival. Adverse events like TLS were never reported to be associated with cetuximab. Our patient

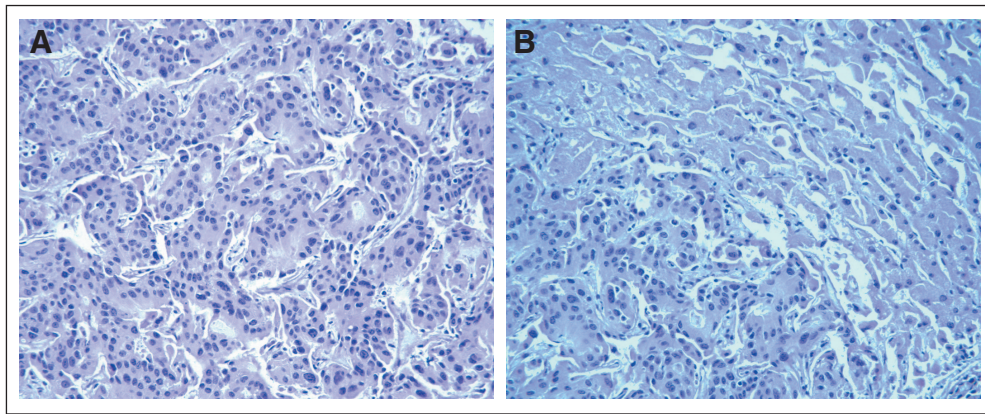


Fig 2.

developed TLS within 24 hours after the first dose of the cetuximab. To our knowledge, this is the first case of TLS associated with cetuximab treatment in the literature. In the light of our observation, we conclude that TLS should be taken into account as a rare complication of cetuximab, and renal function should be monitored in patients receiving cetuximab treatment.

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DOI: 10.1200/JCO.2007.14.7603

Phenotypic Evolution of Waldenstrom's Macroglobulinemia to Extramedullary Plasmacytoma

A 61-year-old Hispanic man who had no significant past medical history presented in April 2007 with a month-long history of progressive fatigue, right flank pain, and acute renal failure. Evaluation at the Myeloma and Amyloidosis Program at the University of Colorado Health Sciences Center showed a pale skin without other physical abnormalities. Laboratory data revealed a hemoglobin of 8.0 g/dL (normal range [normal], 14.3 to 18.1 g/dL), serum creatinine of 8.9 mg/dL (normal, 0.4 to 1.2 mg/dL), blood urea nitrogen of 58 mg/dL (normal, 6 to 23 mg/dL) and normal electrolytes including calcium of 9.3 mg/dL (normal, 8.5 to 10.3 mg/dL); lactate dehydrogenase of 98 u/L (normal, 98 to 192 u/L), total protein 10.3 g/dL (normal, 6.4 to 8.3

g/dL), albumin of 3.0 g/dL (normal, 3.4 to 5.0 g/dL), immunoglobulin (Ig) G of 1,340 mg/dL (normal, 791 to 1643 mg/dL), IgA of 81 mg/dL (normal, 66 to 436 mg/dL), IgM of 4,240 mg/dL (normal, 43 to 279 mg/dL), IgM kappa monoclonal protein of 2,600 mg/dL, serum viscosity of 2.23 cP (normal, 1.1 to 1.8 cP), serum free kappa and lambda light chain of 153 mg/dL (normal, 0.33 to 1.94 mg/dL) and 3.73 mg/dL (normal, 0.57 to 2.63 mg/dL) (by nephelometry), respectively; a 24-hour urine protein of 3,598 mg (normal, 0 to 150 mg) of which 1,500 mg came from Bence-Jones proteinuria of free kappa light chain. A positron emission tomography/computed tomography (CT) scan showed a large right-sided perinephric mass of 14 cm × 16 cm with an standard unit of value (SUV) of 5.7 (Fig 1), one left upper lobe lung nodule of 1.5 cm × 1.4 cm with an SUV of 3.9 and an enlarged right perihilar lymph node with an SUV of 3.4. No lytic changes of the bone were noted. A diagnostic CT-guided needle biopsy of the perinephric mass showed a dense lymphoid infiltrate with aggregates of small