PRESENTATION
A complication of cancer chemotherapy led to a prolonged hospitalization for a 49-year-old man. The patient presented via the dermatology clinic with chills and a progressing diffuse body rash. His medical history was significant for a diagnosis of grade IV glioblastoma made 4 months prior at the time of a new-onset seizure. He had recently been treated with vandetanib and temozolomide for the glioblastoma. His other medications included acetaminophen with oxycodone, omeprazole, levetiracetam, and dexamethasone.

The patient first noticed a diffuse erythematous rash during the sixth week of chemotherapy. His outpatient dermatologist, in consultation with his neuro-oncologist, discontinued all medications, including vandetanib, and increased the patient’s dosage of dexamethasone, which was being used to control tumor-related edema. His symptoms remained stable for the next 3 weeks but then progressed, and urgent re-evaluation by his dermatologist revealed an extensive rash over more than 50% of his body. The patient also reported chills, swollen glands, and generalized pain. He was directly admitted to the medical step-down unit (MDSU) for further evaluation and management.

ASSESSMENT
Upon arrival to the MDSU, the patient’s vital signs were unremarkable. Physical examination revealed a middle-aged man with an extensive rash. He was in no distress despite confluent erythema and skin sloughing of the face, trunk, and upper extremities, desquamation of the ears and palms, conjunctival injection, perinasal and perioral erosions with hemorrhagic and serous crusting, small bullae on the bilateral dorsal fingers, and numerous scattered pink-red macules, papules, and plaques (Figure 1).

Approximately 65% of the patient’s body surface area was affected, and Nikolsky’s sign was positive; that is, applied lateral force caused epidermal separation from the dermis. Laboratory investigation, including a complete blood count, was unremarkable. A peripheral blood smear did not reveal atypical lymphocytes. Skin biopsy demonstrated prominent epidermal necrosis, suggestive of toxic epidermal necrolysis (skin sloughing > 30% of the body surface area) or Stevens-Johnson syndrome (skin sloughing < 10% of the body surface area).1

DIAGNOSIS
Given the widespread skin detachment, the patient’s clinical picture was most consistent with toxic epidermal necrolysis, a rare life-threatening mucocutaneous eruption, with up to 95% of cases attributed to a drug-induced hypersensitivity reaction.1-4 Consensus on the exact mechanism by which keratinocyte necrosis occurs has yet to be reached, but it is believed to be initiated by drug-specific CD8+ cytotoxic T-cells and natural killer cells. Any medication can potentially cause toxic epidermal necrolysis, but the most frequent perpetrators are allopurinol (most common), antibiotics, antiepileptics, antipsychotics, antiretrovirals, and nonsteroidal anti-inflammatory drugs.2-4

Vandetanib, temozolomide, omeprazole, and levetiracetam were potential initiating agents in our patient’s case, and all had been stopped. While no definitive means of determining the responsible medication exists, vandetanib was judged to be the most likely cause as it has an extended half life of 19 days, and symptoms continued to evolve long after other medications were discontinued. The patient manifested the most significant signs and symptoms less than 30 days after his last dose.

An oral drug, vandetanib inhibits the activity of the enzyme tyrosine kinase at a number of receptors, including those for vascular endothelial growth factor, epidermal growth factor, and the rearranged during transfection or RET proto-oncogene. In this way, it obstructs signaling that
spurs tumor cell growth and angiogenesis. Potential complications of therapy include gastrointestinal symptoms, ischemic events, transaminitis, hypertension, QT prolongation, heart failure, hemorrhage, interstitial lung disease, reversible posterior leukoencephalopathy syndrome, and skin toxicity. Vandetanib has previously been associated with Stevens-Johnson syndrome in a 71-year-old man undergoing treatment for non-small cell lung carcinoma, but to the best of our knowledge, no cases of toxic epidermal necrolysis have been reported.

The diagnosis of toxic epidermal necrolysis can usually be made clinically, but skin biopsy can be useful in equivocal cases. Patients typically present with a 1-3-day prodrome of influenza-like symptoms and mucocutaneous lesions, followed by confluent erythema, skin necrosis, and eventual sloughing. Conditions to consider in the differential diagnosis are other drug reactions, including the so-called DRESS syndrome—drug reaction with eosinophilia and systemic symptoms—and erythema multiforme/Stevens-Johnson syndrome, cutaneous T-cell lymphoma, toxic shock syndrome, staphylococcal scalded skin syndrome, and Kawasaki disease in children.2

**MANAGEMENT**

Treatment for toxic epidermal necrolysis involves discontinuing the offending medication and providing intensive supportive care, particularly infection control, wound care, and fluid management.3 Systemic corticosteroids, intravenous gamma globulin, cyclosporine, biologic agents, and plasmapheresis have been used with some success, although there is no definitive guidance for managing the condition with systemic therapy.6 The mortality rate is up to 30%, with sepsis being the most common cause of death.6

Our patient was started on intravenous gamma globulin and pulse-dose methylprednisolone therapy. In addition, he received extensive topical wound care in the MDSU. His symptoms ultimately remitted over the course of a month-long hospitalization, after which he was discharged to an inpatient short-term physical rehabilitation facility. When he succumbed to his cancer approximately 12 months later, he had no evidence of any ongoing dermatologic sequelae.

References


