The patient is now working full time and continues to be asymptomatic, but has mild liver function abnormalities and serologic evidence of hepatitis C, possibly related to platelet transfusions given at the time of splenectomy. His blood counts remain normal, and a peripheral-blood analysis in June 2006 showed no evidence of an abnormal lymphocyte clone.

Because of the patient's young age, his initial pathology specimens were reviewed by pathologists at University of California, San Francisco (M.E.K.; San Francisco, CA); Stanford University (Stanford, CA); University of Chicago (Chicago, IL); and Harvard Medical School (Boston, MA), and were believed to be typical of HCL. To our knowledge, this patient is the youngest presenting with HCL yet recorded.[3-5] Although purine analogs are now the usual first-line treatment for HCL, this patient's clinical course demonstrates again the possibility of prolonged remissions after splenectomy and interferon treatment.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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# Erythema Multiforme/Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis in Lenalidomide-Treated Patients

**To the Editor:** Stevens-Johnson syndrome (SJS) is a rare but life-threatening cutaneous adverse reaction. While SJS may sometimes be admixed with diagnoses of erythema multiforme (EM) minor or major,[1] SJS and toxic epidermal necrolysis (TEN) are considered to be severity variants of the same disease with drug exposure the primary etiologic factor.[2] The incidence of SJS has been estimated at 1.1 to 7.1 cases per million person-years, and that of TEN at 0.4 to 1.2 per million person-years.[1] Mortality among patients with SJS or TEN has been reported to be between 1% to 3% and 10% to 70%, respectively.[1]

Risk factors for SJS include infection, vaccination, drugs, systemic diseases, physical agents, and food.[1] SJS has been associated with more than 100 drugs through case reports and studies, including drugs such as allopurinol,[3] quinolones,[3] corticosteroids (including dexamethasone),[3,4] rituximab,[5] imatinib,[6] and bortezomib.[7] Risk was greatest in the first 2 months of treatment.

Celgene Corporation has received 12 reports of SJS, three reports of EM and one report of TEN among approximately 57,000 patients who received lenalidomide from market launch on December 27, 2005, through June 26, 2008. The majority (83%; 10 of 12) of the SJS cases were spontaneous reports from US health care professionals. Two reports were received from US investigator-initiated trials. The 12 cases occurred in seven women and five men with a median age of 63.5 years (range, 50 to 83 years). Lenalidomide was prescribed for the approved indication of multiple myeloma (MM; 10), as well as for myelofibrosis (1) and amyloidosis (1).

One SJS case was confirmed by a skin biopsy in a patient with amyloidosis on lenalidomide, cyclophosphamide, and dexamethasone treatment who received levofloxacin one week before the onset of a localized rash that became generalized. The patient developed pneumonia and sepsis and died from septicemia 11 days following hospitalization.

Clinical information quality was variable. In four cases, it was too limited for further interpretation of the diagnoses provided by the reporters. Generalized rash was noted in five patients of which one was characterized as maculopapular and the others as erythematous. Some patients had urticaria, pruritus, swelling of the face or lips, weeping blisters, sores in the mouth, and dysphagia. One patient had a history of rash with thalidomide. The median time to onset of event from start of lenalidomide was 24 days with a range of 3 to 45 days (n = 9). Medications implicated in SJS received concomitantly by these patients included dexamethasone (eight), allopurinol (two), moxifloxacin (one), levofloxacin (one), and bortezomib (two). In one report of SJS, the prescriber attributed the event to bortezomib, which was discontinued while lenalidomide was continued. Seven patients were hospitalized. At the time of the report, six patients recovered from the event, one had not recovered, and two were unknown. Two patients later died, one from disease progression and the other of unknown cause.

Three cases of EM were reported in the United States among patients who received lenalidomide with dexamethasone for MM. There were two women and one man age 85, 74, and 70 years, respectively. The times to onset of EM from start of lenalidomide were 7, 24, and 112 days. The patients presented with lesions or rash associated with blistering, sores, mucosal involvement, crusting, fever, and erythema of the skin. In one patient, herpes simplex of the mouth preceded the EM. Two patients were hospitalized. The patients recovered from EM but one eventually died due to disease progression 59 days following hospitalization and 62 days after discontinuing lenalidomide. Concomitant medications included allopurinol and sulfamethoxazole/trimethoprim.

TEN was reported in an 85-year-old woman hospitalized 18 days after initiating lenalidomide with dexamethasone for MM. Concomitant medications were tamoxifen and alendronate. She developed a florid, patchy, erythematous, pruritic rash that was confluent in many areas and with mild exfoliation and somewhat weepy appearance. The patient recovered.

  

Most cases were postmarketing reports and as such had inadequate information, making confirmation of the reporters' diagnoses difficult and hampering causality assessment. The temporal relationship between the events and lenalidomide initiation in many reports cannot exclude a causal relationship. The company is updating the prescribing information for lenalidomide to include guidance on these rare events.

A study of the dermatologic effects of lenalidomide alone or in combination with dexamethasone reported an incidence of skin eruptions of 29% in MM patients, which in most cases were mild.[8] Physicians prescribing lenalidomide should monitor their patients for possible dermatologic adverse effects, and particular care should be given to patients with a history of thalidomide rash. In most instances, complete discontinuation of the therapy is not necessary, but may require temporary interruption of therapy or drug dosage reduction and close scrutiny.[8]

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# Cultural Challenges in Caring for Our Patients in Advanced Stages of Cancer

**To the Editor:** The August 10, 2008, issue of *Journal of Clinical Oncology* is entirely dedicated to palliative medicine. *European Journal of Cancer* also published in May 2008 an issue entitled "Palliative Medicine: The Art and the Science." Editorial choices underline how oncology is concerned with palliative and end-of-life care, not only in terms of progress in symptom control, but also in regard to basic science aspects and the many medical, psychological, social, and ethical ramifications of this field of medicine. All articles in *JCO* are extremely interesting, as they contribute to clarifying key issues and encourage discussion toward the establishment of common guidelines.

A few points, however, may benefit from further clarification. First, is palliative medicine a specialty or an aggregate of different specialties? Supportive care, palliative care, and end-of-life care are sometimes used as if they were interchangeable terms. Though at times overlapping, they denote different domains.[1] The use of nonuniform language can easily generate confusion, given that diverse terminologies refer to different areas of expertise. The need for multidisciplinary teams, for example, is widely acknowledged in this field of medicine as a means of integrating medical and psychosocial care, yet different teams require different disciplinary expertise. Supportive care may be provided by an internist or oncologist; palliative care often requires anestheologists or other specialists in pain management; and end-of-life care entails particular expertise in assessing and responding to the spiritual and religious concerns and needs of dying cancer patients. Different terms thus refer to special areas of research and intervention in different stages and phases of the patient's illness.

Second, it is important to clarify how teams are best composed and to what extent different sociocultural contexts and local logistics influence the way in which problems are managed most effectively. For example, the choice of hospice or home care may not depend so much on individual preference as on service availability, geographic closeness to specialized centers, and various socioeconomic factors. The use of clear terminology also helps in deciding the composition of different teams and in identifying roles and responsibilities within them.[2] It is critical that the team leader have a clear, broad, and flexible outlook regarding the spectrum of problems involved. The operational modalities of each team within different local facilities also need to be defined clearly in order for working groups to have a tangible effect on the quality of care delivered to cancer patients. Reaching a balance between ideal and feasible goals is often a delicate, complex process, especially if we consider that competing expertises may correspond to competing interests within groups and institutions.

The *JCO* and *European Journal of Cancer* issues demonstrate that we have greatly advanced in our ability to control symptoms such as pain, fatigue, and malnutrition. Now we need to improve our ability to positively affect other aspects of our cancer patients'