and sorafenib therapy was restarted without further sequelae. Unlike other cases reported in the literature, the patient described herein and the one described by Bilaç et al² had clinically EM-like eruptions with targetoid lesions, nondiagnostic histopathologic findings, and successful reintiation of sorafenib treatment. Thus, we recommend biopsy of targetoid eruptions during sorafenib therapy to differentiate between a diagnosis of EM and EM-like sorafenib reaction to minimize discontinuation of an antineoplastic agent shown to prolong progression-free survival.

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Conflict of Interest Disclosures: None reported.

Funding/Support: This study was supported by the Intramural Research Program of the National Institutes of Health, Center for Cancer Research, National Cancer Institute.

Role of the Funder/Sponsor: None.

Additional Contributions: The authors would like to acknowledge Edward W. Cowen, MD, MHSc, and Mark C. Udey, MD, PhD, for helpful comments regarding this article.

BRAF Inhibition in a Lung Transplant Recipient With Metastatic Melanoma

New treatment options like the BRAF inhibitors have been established for immunocompetent patients with metastatic melanoma, but experience in organ transplant recipients is lacking.

Report of a Case | A female double lung transplant recipient in her 60s with a standard triple immunosuppressive regimen (cyclosporine, mycophenolate mofetil, prednisolone) and chronic lung allograft dysfunction was diagnosed with metastatic melanoma and pulmonary (Figure 1A), mediastinal, hepatic, osseous, subcutaneous, and cerebral metastases (Figure 2A). A primary tumor could not be detected, and tumor cells harbored
BRAF V600E mutation. Tumor marker S100 was elevated to 0.545 μg/L (reference value, <0.105 μg/L).

Therapy with the BRAF inhibitor vemurafenib was initiated 38 months after transplantation. Initial vemurafenib dose was 480 mg twice daily with a projected increase to the target dose of 960 mg twice daily. Because several potential interactions with her existing medication regimen were likely, itraconazole and azithromycin treatments were stopped, and the immunosuppressive regimen was changed from cyclosporine to everolimus. To reach stable levels of the immunosuppressive drugs, doses had to be monitored and adjusted frequently.

Within 3 weeks, the vemurafenib dose was increased to 960 mg twice daily, which was accompanied by a variety of well-known adverse effects, in particular joint pain, erythema, verrucalike lesions, diarrhea, and taste disturbances. Despite symptomatic treatment with loperamide and etoricoxib, vemurafenib dose reduction to 720 mg twice daily was necessary. Simultaneously, lung function continued to decrease, and laboratory tests revealed anemia that required transfusion of packed red blood cells.

After 2 months of vemurafenib treatment, the S100 marker dropped to 0.115 μg/L. Fluorodeoxyglucose–positron emission tomography, computed tomography and cerebral magnetic resonance imaging showed a partial extracerebral response but over 30 new cerebral lesions (Figures 1B, 2B). On a very low level, the graft function stayed stable, but laboratory findings showed a decline in renal function and iron deficiency anemia.

In addition to vemurafenib treatment, whole-brain radiotherapy was planned. However, our patient was hospitalized owing to progressive deterioration and died without additional tumor-specific treatments 3.5 months after initiation of vemurafenib therapy.

Discussion | In immunocompetent patients, metastatic melanomas are known for their poor prognosis, which is even worse in immunocompromised organ transplant recipients. New treatment options for metastatic melanoma have been established, leading to a significant improvement in recurrence-free and overall survival. These therapies, especially immunotherapies based on cytotoxic T-lymphocyte-associated protein 4 blockade with ipilimumab and targeted therapies inhibiting BRAF V600E mutations with vemurafenib and dabrafenib, have not been investigated in immunocompromised patients such as lung transplant recipients. In our patient with unstable lung allograft function, we considered an immunotherapy with ipilimumab to be inappropriate. Since molecular analysis of the melanoma showed a BRAF V600E mutation, our treatment strategy consisted of adjustment of the immunosuppression (ie, switch of calcineurin to mammalian target of rapamycin [mTOR] inhibition) and BRAF inhibition with vemurafenib. Several clinical trials have shown a beneficial effect of mTOR inhibitors in organ transplant recipients, particularly with regard to the development of nonmela-noma skin cancer.

In immunocompetent patients with metastatic melanoma harboring a BRAF V600E mutation (excluding patients with brain metastases), vemurafenib and dabrafenib treatment results in a response rate of 59%, with a median progression-free survival (PFS) of 6.9 months. In patients with brain metastases, the response rates to dabrafenib were lower (39%), and the PFS was shorter (median 16.1 weeks). There is a possibility that the melanoma was of donor origin, but the donor had no history of cancer.

The limiting factor in our patient was the progression of the intracerebral metastases, leading to a PFS of 9 weeks and an overall survival of 16 weeks. However, noncerebral metastases were regressing, and adverse effects were manageable. This indicates that BRAF inhibitor therapy is feasible in these patients if an intense monitoring of possible drug interactions is performed.

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Conflict of Interest Disclosures: Dr David has received funds and grants for research and fees for consultancy and speaking from Silence Therapeutics AG unrelated to the topic of this report. Dr Gutzmer has received honoraria and research and fees for consultancy and speaking from Silencetherapeutics AG.

NOTABLE NOTES

Crazy in Love

Deshan F. Sebaratnam, MBBS, Patricia M. Lowe, FACC

Every February brings with it St Valentine’s Day, and while expressions of love abound during this month, on any given day throughout the year there are ample romantic descriptions to be found in dermatology.

Drawing on classical mythology, the hypopigmented macules of syphilis are known as the necklace of Venus, and the vermiform border of the upper lip is referred to as Cupid’s bow.

Infectious mononucleosis is known as “kissing disease,” “kissing” lesions have been described in Zoon balanitis and electrical burns, and the ideal apposition of wound edges has been described as that of a “social kiss.” Ecchymoses on the neck are known as “love bites,” and, somewhat less desirably, those with excess abdominal adiposity are said to have “love handles.”

Part of the tradition of Valentine’s Day is the exchange of gifts, and plenty of inspiration can be drawn from the dermatological realm. While the rose is perhaps the most popular gift, it is also a popular descriptor of cutaneous lesions, such as “dew drops on a rose petal” for the vesicles of varicella, roseola infantum, and the “rose spots” of Salmonella typhi infection. The rossette is a widely used dermatology descriptor, clinically as in linear IgA disease, dermoscopically as in keratinizing tumors and histologically as in cyclindromas.

Chocolates are always a favorite, and chocolate agar is also the desired medium for growth of Mycobacterium chelonae. Champagne is liberally consumed on Valentine’s Day, and once the bottle is overturned, it resembles the leg of a patient with advanced lipodermatosclerosis. Oysters and caviar may feature on the romantic dinner menu, conjuring images of rupioid psoriatic plaques and “caviar tongues” (sublingual varicosities). For dessert, strawberries, as in the “strawberry tongue” of Kawasaki disease, are often coupled with cream, the ubiquitous medium for delivery of topical medicaments. Followed by port of course, as in port-wine stains (best referred to as capillary malformations).

The luckiest among us will receive jewelry, be it silver, as in the scale of psoriasis, or gold, as in lichen aureus or Staphylococcus aureus infection (with special mention of the Panton-Valentine leucocidin strain). Pearls for some, hopefully rarer types than the common “pearly” surface of nodular basal cell carcinomas, and diamonds for others, such as the rhomboid structures seen dermoscopically in lentigo maligna.

While skin remains the love of all dermatologists, the universal symbol of St Valentine’s Day is of course the heart, and a wide range of cutaneous abnormalities with heart-shaped morphologic characteristics have been reported.

So this February, let us all remember that dermatology is more than skin deep and that caring for patients with cutaneous disease remains at the heart of dermatology.

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