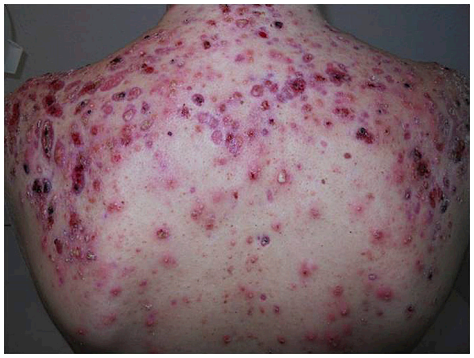

Fig 1. Acne fulminans. Initial presentation with draining pustules and crusted papules and nodules on the back.

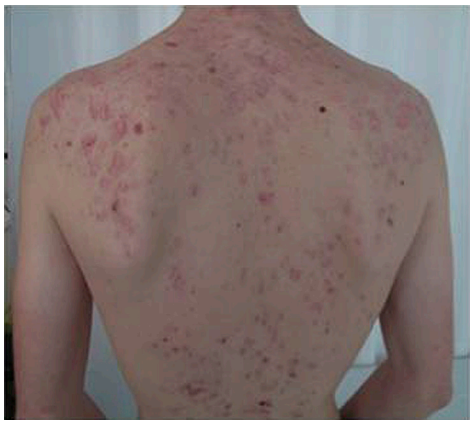

Fig 2. Acne fulminans. Complete resolution of the inflammatory lesions with residual scarring after treatment with cyclosporine and isotretinoin.

the lesions improved, and 4 months later, cyclosporine was discontinued. A total dose of isotretinoin 100 mg/kg could be completed, and he presented an almost complete resolution of the inflammatory lesions with some residual scarring (Fig 2). No significant side effects or laboratory abnormalities were observed during treatment.

AF is a rare condition that is considered the most severe form of acne. It is characterized by a sudden onset of ulcerative, crusty, painful lesions. Most patients are young teenagers with previous mild to moderate acne. It is considered a severe inflammatory disease with abscess formation and hemorrhagic crusts accompanied by high temperature, asthenia, anorexia, and often asymmetric polyarthralgias.[1] In this case, laboratory findings showed an intense neutrophilic leucocytosis and elevation of erythrocyte sedimentation rate and C-reactive protein. The etiology of AF is appears to be multifactorial.[2] The diagnosis is usually clinical. The differential diagnosis includes other disorders such as PAPA[3] syndrome and SAPHO syndrome.[4]

Oral antibiotics are usually ineffective. The combination of oral isotretinoin and systemic corticosteroids is the treatment of choice,[1] but recurrences are not unusual when steroid dose is tapered. We have found only 1 report describing a good response of AF to a combination of cyclosporine and prednisolone.[5] To our knowledge this is the first report showing a good response to cyclosporine combined with isotretinoin. Because this regimen has a very good short-term safety profile (particularly in young persons), it can be an alternative in patients with AF when systemic steroids are either ineffective or contraindicated.

Priscila Giavedoni, MD, PhD, José Manuel Mascaró-Galy, MD, Paula Aguilera, MD, PhD, and Teresa Estrach-Panella, MD, PhD

Department of Dermatology Hospital Clínic, University of Barcelona, Spain

Funding sources: None.

Conflicts of interest: None declared.

Correspondence to: Priscila Giavedoni, MD, PhD, Department of Dermatology, Hospital Clínic, C/ Villarroel 170, 08036 Barcelona, Spain

E-mail: giavedonip@gmail.com

REFERENCES

1. Zaba R, Schwartz R, Jarmuda S, Czarnecka-Operacz M, Silny W. Acne fulminans: explosive systemic form of acne. J Eur Acad Dermatol Venerol 2011;25:501-7.
2. Karvonen SL, Rasanen L, Cunliffe WJ, Holland KT, Karvonen J, Reunala T. Delayed hypersensitivity to *Propionibacterium acnes* in patients with severe nodular acne and acne fulminans. Dermatology 1994;189:344-9.
3. Geusau A, Mothes-Luksch N, Nahavandi H. Identification of a homozygous PSTPIP1 mutation in a patient with a PAPA-like syndrome responding to canakinumab treatment. JAMA Dermatol 2013;149:209-15.
4. Chua SL, Angus JE, Ravenscroft J, Perkins W. Synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome and acne fulminans: are they part of the same disease spectrum? Clin Exp Dermatol 2009;34:e241-3.
5. Tago O, Nagai Y, Matsushima Y, Ishikawa O. A case of acne fulminans successfully treated with cyclosporine A and prednisolone. Acta Derm Venerol 2011;91:337-8.

http://dx.doi.org/10.1016/j.jaad.2013.09.043

Complete pathologic response after neoadjuvant treatment with vemurafenib for malignant melanoma

To the Editor: Invasive melanoma on the left arm was diagnosed in a 32-year-old male patient. The initial diagnosis was made by skin biopsy, which revealed a nonulcerated melanoma of 3 mm depth. The patient underwent reexcision and sentinel lymph node

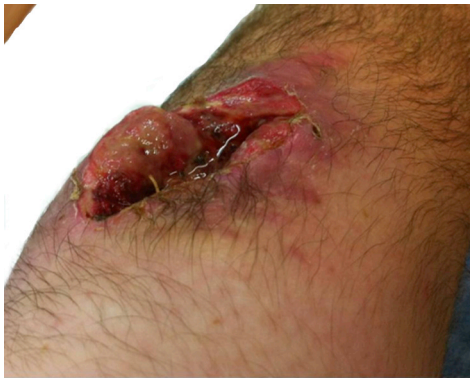

Fig 1. Melanoma before neoadjuvant vemurafenib treatment. Tru-Cut biopsy from the recurrent skin lesion was positive for melanoma and left an open wound at the site, which required prolonged hospitalization.

biopsy, both of which were negative for malignant melanoma. Two months later, the patient presented with a large mass (>7 cm) in his left arm and palpable axillary lymph nodes. Biopsy of the lesion with an 18-gauge Tru-Cut needle and automatically triggered biopsy gun was positive for melanoma and BRAF V600E mutation. After the biopsy, the tumor mass transformed to an open wound with constant bleeding (Fig 1), necessitating prolonged hospitalization. Fluorodeoxyglucose positron electron tomography (FDG-PET) examination showed uptake in the primary site and left axilla, and suspicious uptake in the left supraclavicular lymph nodes. Axillary cytology via fine-needle aspiration was positive for melanoma. The patient refused immediate surgery, which would have involved disarticulation amputation. Neoadjuvant treatment with vemurafenib (Zelboraf, Hoffmann-La Roche), 960 mg orally twice daily, was instituted. A follow-up visit 2 weeks later showed significant clinical improvement. After 8 weeks of treatment, the mass disappeared (Fig 2). There were no significant side effects of vemurafenib treatment. A multidisciplinary team decided to refer the patient to surgery. Vemurafenib was continued until 2 days before surgery. The patient underwent resection of the recurrent skin lesion and axillary lymph node dissection, all of which indicated complete pathologic response. Vemurafenib was not renewed after surgery. The patient was followed every 3 months by a physical examination and with FDG-PET every 6 months. At 18 months after surgery, he shows no evidence of disease.

Neoadjuvant treatment for resectable/unresectable stage III melanoma remains an investigational approach; there are neither large prospective randomized trials nor recommended regimens or

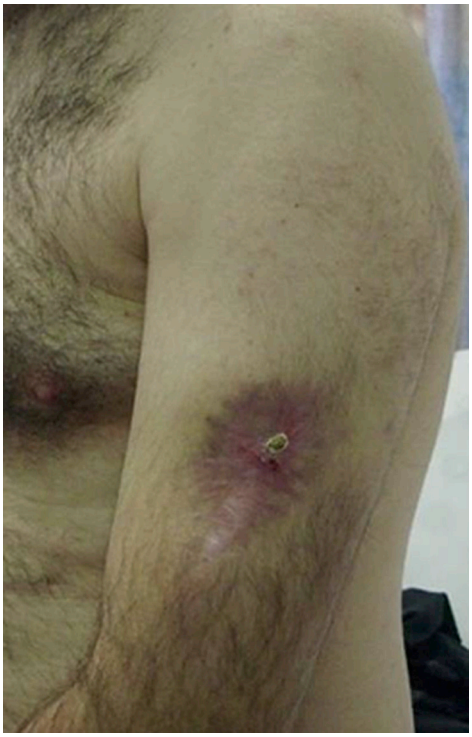

Fig 2. Site of prior melanoma, shown in Fig 1, after 8 weeks of treatment with vemurafenib.

timelines for a treatment frame, in that none of the systemic therapies or radiotherapy for melanoma were proven to be sufficiently active to support this approach.[1]

Vemurafenib was approved by the Food and Drug Administration in August 2011 for the treatment of patients with unresectable or metastatic melanoma with the BRAF V600E mutation based on a large randomized study.[2,3] The majority of the patients (95%) had metastatic disease. Subgroup analysis of overall survival indicated that the nonmetastatic patients did not benefit from vemurafenib but a significant benefit to this subgroup was shown with regard to progression-free survival. It was not stated whether these patients became operable or were referred for surgical resection. There are no ongoing trials evaluating the role of vemurafenib in the neoadjuvant setting, and a literature review reveals that there are only 2 other reports of vemurafenib in the neoadjuvant setting.[4,5]

In the case presented, there was a pathologic complete response; however, the role of vemurafenib in locally advanced disease, whether in the neoadjuvant or adjuvant setting, is yet to be determined. A major concern of this approach is the possibility of gaining resistance to BRAF inhibition and losing it as potential treatment in the metastatic setting.

Orit Kaidar-Person, MD,[a] *Ayelet Eran, MD,*[b] *and Gil Bar-Sela, MD*[a]

Division of Oncology[a] *and Department of Radiology,*[b] *Rambam Health Care Campus and Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel*

Funding sources: None.

Conflicts of interest: None declared.

Correspondence to: Dr Gil Bar-Sela, MD, Division of Oncology, Rambam Health Care Campus, POB 9602, Haifa 31096, Israel

E-mail: g_barsela@rambam.health.gov.il

REFERENCES

1. Moschos SJ, Edington HD, Land SR, Rao UN, Jukic D, Shipe-Spotloe J, et al. Neoadjuvant treatment of regional stage IIIB melanoma with high-dose interferon alfa-2b induces objective tumor regression in association with modulation of tumor infiltrating host cellular immune responses. J Clin Oncol 2006;24:3164-71.
2. Food and Drug Administration. Vemurafenib. Available from: http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm268301.htm. Accessed October 30, 2013.
3. Chapman PB, Hauschild A, Robert C, Haanen JB, Ascierto P, Larkin J, et al; , BRIM-3 Study Group. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. N Engl J Med 2011;364:2507-16.
4. Kolar GR, Miller-Thomas MM, Schmidt RE, Simpson JR, Rich KM, Linette GP. Neoadjuvant treatment of a solitary melanoma brain metastasis with vemurafenib. J Clin Oncol 2013;31:e40-3.
5. Fadaki N, Cardona-Huerta S, Martineau L, Thummala S, Cheng ST, Bunker SR, et al. Inoperable bulky melanoma responds to neoadjuvant therapy with vemurafenib. BMJ Case Rep 2012: bcr2012007034.

http://dx.doi.org/10.1016/j.jaad.2013.09.052

Nonuremic calciphylaxis in a patient with rheumatoid arthritis and osteoporosis treated with teriparatide

To the Editor: Calciphylaxis is a devastating condition in which metastatic calcification of the microvasculature results in thrombosis and ischemic necrosis of target tissues.[1-3] Calciphylaxis is well described in patients with chronic kidney disease and secondary hyperparathyroidism, however the literature describing it in the absence of these classic comorbidities is scant.

A 66-year-old woman presented with a 3-month history of painful lower extremity nodules. Her medical history included obesity, pulmonary emboli, osteoporosis, and a 20-year history of well-controlled rheumatoid arthritis. Medications included leflunomide, prednisone (2 mg daily), warfarin, and teriparatide [recombinant human parathyroid hormone (1-34)], initiated 5 months prior. Physical examination revealed a 10- × 3-cm indurated subcutaneous plaque with livedoid erythema and retiform purpura on the bilateral thighs and scattered indurated subcutaneous nodules on the bilateral lower extremities (Fig 1). A lateral thigh lesion was biopsied at an outside facility 2 months prior, leaving a nonhealing ulcer despite appropriate wound care. The biopsy specimen was consistent with thrombotic vasculopathy; however, no additional workup was performed. Von Kossa stains were ordered and read by our pathologist, but no changes of early calciphylaxis were seen. Laboratory studies demonstrated normal renal function, parathyroid hormone levels, and calcium-phosphate product. Serum and urine protein electrophoresis, antineutrophil cytoplasmic antibodies, antinuclear antibodies, and antiphospholipid antibodies were all negative.

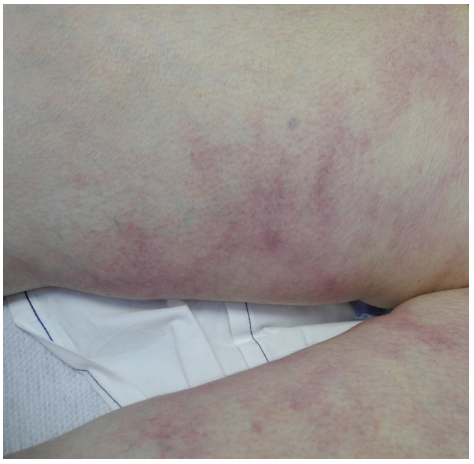

Fig 1. Nonuremic calciphylaxis in a patient treated with teriparatide: livedoid erythema and retiform purpura on the bilateral thighs.

Because of the patient's multiple risk factors, calciphylaxis was suspected clinically. Warfarin and teriparatide were discontinued and the patient was placed on low-molecular-weight heparin. Given her risk for poor wound healing, repeated biopsy was deferred. Bone scintigraphy of the thighs showed no abnormal uptake. Because of continued clinical suspicion and further lesion progression, the patient consented to repeated biopsy. Histopathology revealed intramural calcium deposition in subcutaneous arterioles with intimal hyperplasia and ischemic changes of the surrounding tissue consistent with calciphylaxis (Fig 2). Treatment with intravenous sodium thiosulfate therapy was initiated after surgical consultants determined the patient was a poor candidate for debridement. Unfortunately, her lesions progressed over the next month causing