How would you diagnose the lesion seen in Figure 1?

A. Keratoacanthoma
B. Mycosis fungoides–like eruption
C. Papulopustular rash
D. New primary melanoma
Keratoacanthoma. An unusual but frequently seen side effect in many patients being treated with BRAF inhibitor therapy is the development of new squamous cell carcinomas of the keratoacanthoma type. In the clinical trials that led to the approval of vemurafenib, this finding was seen in as many as 30% or more of patients undergoing therapy (Flaherty et al., 2010; Lacouture, O’Reilly, Rosen, & Solit, 2012). While this type of malignancy is typically not invasive, it is clearly a frightening side effect for patients who are being treated for a poor-prognosis malignancy such as advanced melanoma.

Since these lesions were first identified in patients undergoing BRAF inhibitor therapy, further research has been ongoing to better identify the etiology associated with this adverse event. It has been shown that many of these lesions are also found to have HRAS mutations and often occur in sun-damaged areas of skin. As a result, it is thought that the BRAF inhibitor may not induce these lesions de novo as much as it may serve to exacerbate progression in precancerous lesions within the skin of these patients (Su et al., 2012). Further research suggests that this side effect may be avoided by concomitant use of MAPK/ERK kinase inhibitor therapy; this hypothesis is under clinical investigation (Infante et al., 2011).

While they are very disconcerting to patients, these lesions are typically managed by surgical resection (Robert, Arnault, & Mateus, 2011). Patients should be instructed to bring these lesions to the attention of their clinician once they are identified so that prompt referral can be made to a dermatologist for ongoing management. As these lesions can become numerous, ongoing dermatologic management is critical.

Explanation of Incorrect Answers

Mycosis fungoides is the most commonly seen cutaneous T-cell lymphoma, occurring at a 50% incidence. These lesions may occur singularly but are often seen as multiple erythematous plaque–appearing lesions that subsequently progress into papular nodules. They may be treated with radiation if they cannot be completely excised (Ally et al., 2012).

Papulopustular rash, a common dermatologic toxicity seen with many targeted agents, is typically found in areas where the greatest density of sebaceous glands exist. It usually manifests in the form of pruritic papules and pustules (Balagula et al., 2011).

While patients with a primary melanoma are at risk to develop second primary melanomas at a higher rate than individuals who have never had a melanoma skin lesion, this would not be the first suspect in the diagnostic differential for this patient with stage IV disease being treated with a BRAF inhibitor. The crusty top on this lesion with a popular appearance would not be typical for a melanoma lesion.

Follow-Up

Mr. V. was referred to his dermatologist, who resected several of the suspicious lesions that were pathologically confirmed to be keratoacanthomas. He has subsequently been seeing dermatology every 3 to 4 weeks for skin evaluation and the removal of additional skin lesions. The frequency and number of new skin lesions has been decreasing over the 4 months that Mr. V. has remained on therapy.

References

Ally, M. S., Pawade, J., Tanaka, M., Morris, S., Mitchell, T., Child, F., ... Roberts, A. (2012). Solitary mycosis fungoides: A distinct clinicopathologic entity with a good prognosis: A series of 15 cases and literature review. Journal of the American Academy of Dermatology, 26, 202–215. http://dx.doi.org/10.1016/j.jaad.2012.02.039

Balagula, Y., Garbe, C., Myskowski, P. L., Hauschild, A., Rapoport, B. L., Boers-Doets, C. B., & Lacouture, M. E. (2011). Clinical presentation and management of dermatological toxicities of epidermal growth factor receptor inhibitors. International Journal of Dermatology, 50(2), 129–146. http://dx.doi.org/10.1111/j.1365-4632.2010.04791.x

Flaherty, K. T., Puzanov, I., Kim, K. B., Ribas, A., McArthur, G. A., Kosman, J. A., ... Chapman, P. B. (2010). Inhibition of mutated, activated BRAF in metastatic melanoma. New England Journal of Medicine, 369(9), 809–819. http://dx.doi.org/10.1056/NEJMoa1002011

Infante, J. R., Falchook, G. S., Lawrence, D. P., Weber, J. S., Kefford, R. F., Bendell, J. C., ... Flaherty, K. T. (2011). Phase I/II study to assess safety, pharmacokinetics, and efficacy of the oral MEK 1/2 inhibitor GSK1120212 (GSK436) [Abstract CRA8503]. Journal of Clinical Oncology, 29(suppl).

Lacouture, M. E., O’Reilly, K., Rosen, N., & Solit, D. B. (2012). Induction of cutaneous squamous cell carcinomas by RAF inhibitors: Cause for concern? Journal of Clinical Oncology, 20, 329–330. http://dx.doi.org/10.1200/JCO.2011.38.2895

Robert, C., Arnault, J. P., & Mateus, C. (2011). RAF inhibition and induction of cutaneous squamous cell carcinoma. Current Opinion in Oncology; 23(2), 177–182. http://dx.doi.org/10.1097/CCO.0b013e3283436e8c

Su, F., Viros, A., Milagre, C., Trunzer, K., Bollag, G., Spleiss, O., ... Marais, R. (2012). RAS mutations in cutaneous squamous-cell carcinomas in patients treated with BRAF inhibitors. New England Journal of Medicine, 366, 207–215. http://dx.doi.org/10.1056/NEJMoai105358

Submit your challenging case! Do you have an interesting or challenging case you’d like to share with your colleagues? Contact us at editor@advancedpractitioner.com to discuss, or submit your completed article at http://mc.manuscriptcentral.com/jadpro. Submissions should include a graphic, a brief presentation of the case, and correct/incorrect answer selections with rationales.