Dermatology Reports
https://journals.pagepress.net/dr

eISSN 2036-7406

Please cite this article as:

Guglielmo A, D'Alì L, Deotto ML, et al. Erythema nodosum-like panniculitis during BRAF inhibitor therapy for melanoma: never forget latent tuberculosis infection. *Dermatol Rep 2026 [Epub Ahead of Print] doi: 10.4081/dr.2026.10380*

Received: 31 March 2025; Accepted: 30 March 2026.

Erythema nodosum-like panniculitis during BRAF inhibitor therapy for melanoma: never forget latent tuberculosis infection

Alba Guglielmo,[1] Lorenzo D'Alì,[2] Maria Ludovica Deotto,[1] Alessia Cimadamore,[2] Gaetano Pascoletti,[3] Elena Poletto,[3] Alessandro Minisini[3]

[1]Institute of Dermatology, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [2]Institute of Pathological Anatomy, Department of Medicine, University of Udine; [3]Department of Oncology, Academic Hospital of Udine, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

Correspondence: Alba Guglielmo, Institute of Dermatology, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy. E-mail: albaguglielmo@gmail.com; Tel.: +39 0432559820.

Key words: melanoma; erythema nodosum; BRAF inhibitor therapy.

Conflict of interest: the authors have no conflict of interest to declare.

Ethics approval and consent to participate: not required.

Informed consent: the patient has given informed consent to the publication of his case details and any accompanying images.

Availability of data and materials: data are available on request from the corresponding author.

Funding: none.

Dear Editor,

Targeted therapies for melanoma play a pivotal role in the management of patients with advanced *BRAF*-mutated disease. Despite their efficacy, these treatments are associated with a spectrum of adverse events, particularly cutaneous toxicities, including photo-aggravated eruptions, increased risk of non-melanoma skin cancers, and other less frequent manifestations. Herein, we describe a clinical case and briefly review a rare and likely under-recognized adverse event: erythema nodosum (EN)-like panniculitis during BRAF inhibitor therapy.

A 64-year-old man with stage IV interscapular melanoma harboring a *BRAF* V600E mutation had been receiving dabrafenib *plus* trametinib for 2 months when he developed lower limb lesions associated with fever. Dermatological examination revealed multiple painful erythematous subcutaneous nodules on both legs, suggestive of panniculitis, prompting a skin biopsy. Histopathology showed a chronic inflammatory infiltrate of the hypodermis with histiocytes, multinucleated giant cells, membranous steatonecrosis, eosinophils, and plasma cells, without vasculitis. Findings were consistent with mixed, predominantly septal panniculitis, supporting EN (Figure 1 A-B). Oral prednisone induced initial improvement, followed by relapse during tapering. Due to persistent fever and cutaneous toxicity, dabrafenib and trametinib were discontinued. Investigations revealed a positive Quantiferon test without clinical or radiological signs of active disease, leading to a diagnosis of indeterminate latent tuberculosis. After a pulmonology consultation, no therapy was initiated. The patient was switched to encorafenib *plus* binimetinib, achieving disease control without recurrence of panniculitis. After one year, the patient developed fever of pulmonary origin and was diagnosed with active tuberculosis, treated with rifampicin, isoniazid, pyrazinamide, ethambutol, and pyridoxine. No recurrence of panniculitis occurred.

EN is an inflammatory condition characterized by painful erythematous subcutaneous nodules, usually on the lower legs. It is a form of panniculitis and a type IV delayed hypersensitivity reaction triggered by infections, drugs, autoimmune diseases, or malignancies, although sometimes idiopathic.[1-3] Immune complex deposition in subcutaneous fat is thought to play a role. EN is a rare adverse event during targeted therapy. Mossner *et al.* described 16 melanoma patients with EN-like panniculitis during BRAF inhibitor therapy, with a higher incidence for vemurafenib than dabrafenib *plus* trametinib.[4] Onset typically occurs around 8 weeks after treatment initiation and may be associated with fever and arthralgia. A recent review confirmed a higher frequency with vemurafenib monotherapy; among combinations, dabrafenib *plus* trametinib accounts for 77% of cases, while encorafenib *plus* binimetinib accounts for 5%.[5] Our case is consistent with these data regarding timing

but differs due to relapse despite corticosteroids and persistent fever, prompting a treatment switch. This resulted in melanoma control and resolution of panniculitis.

Panniculitis is classified into septal and lobular forms. EN is typically septal, whereas erythema induratum of Bazin, associated with tuberculosis, is lobular with vasculitis.[6] However, overlap exists, and EN may also be associated with tuberculosis, including latent forms.[7,8] Notably, panniculitis during targeted therapy has been reported as predominantly lobular, and latent tuberculosis was rarely investigated in prior cases. Although EN is usually diagnosed clinically, a biopsy is recommended in patients with melanoma who develop subcutaneous nodules in order to confirm the diagnosis and exclude metastatic disease, since EN-like panniculitis may closely mimic metastases on 18F-FDG PET/CT.[9] Ben-Betzalel *et al.* suggested a possible association between immune-related adverse events and favorable response to targeted therapy,[10] whereas Mossner *et al.* reported less favorable outcomes in some cases.[4] Management includes nonsteroidal anti-inflammatory drugs, corticosteroids, and potassium iodide, and treatment discontinuation is rarely necessary. In our case, resolution after therapy switch and absence of recurrence during active tuberculosis support a drug-related etiology, likely linked to dabrafenib *plus* trametinib. In conclusion, EN-like panniculitis during BRAF inhibitor therapy is usually mild to moderate and responds to standard treatment without requiring discontinuation. However, in severe or refractory cases, switching therapy may be necessary. This case also highlights the importance of evaluating alternative triggers, particularly infections such as tuberculosis, and supports histological confirmation in the diagnostic workup.

References

1. Lantto R, Jokelainen J, Huilaja L, Sinikumpu SP. Erythema nodosum in northern Finland between 1996 and 2019: A register-based study. J Dermatol 2024;51:1017-21.
2. Bardazzi F, Loi C, Clarizio G, et al. Erythema nodosum: a clinical manifestation of Neisseria gonorrhoeae infection. Int J Dermatol 2022;61:e306-7.
3. Maglie R, Genovese G, Solimani F, et al. Immune-Mediated Dermatoses in Patients with Haematological Malignancies: A Comprehensive Review. Am J Clin Dermatol 2020;21:833-54.
4. Mössner R, Zimmer L, Berking C, et al. Erythema nodosum-like lesions during BRAF inhibitor therapy: Report on 16 new cases and review of the literature. J Eur Acad Dermatol Venereol 2015;29:1797-806.
5. Kye Y, Zhao G, Guhan S, et al. Research letter: BRAF-inhibitor induced panniculitis - A systematic review. J Am Acad Dermatol 2024;90:420-3.

6. Requena L, Yus ES. Panniculitis. Part I. Mostly septal panniculitis. J Am Acad Dermatol 2001;45:163-83.
7. Boonchai W, Suthipinittharm P, Mahaisavariya P. Panniculitis in tuberculosis: a clinicopathologic study of nodular panniculitis associated with tuberculosis. Int J Dermatol 1998;37:361-3.
8. Kim KS, Kim JS, Kim SS, Kim CW. Association between erythema nodosum/ erythema induratum of Bazin and Mycobacterium tuberculosis infection in Koreans. Indian J Dermatol Venereol Leprol 2021;1-5.
9. Seban RD, Vermersch C, Champion L, et al. Immune-Related Erythema Nodosum Mimicking in Transit Melanoma Metastasis on [18F]-FDG PET/CT. Diagnostics 2021;11:747.
10. Ben-Betzalel G, Baruch EN, Boursi B, et al. Possible immune adverse events as predictors of durable response to BRAF inhibitors in patients with BRAF V600-mutant metastatic melanoma. Eur J Cancer Oxf Engl 1990 2018;101:229-35.

Figure 1. Septal panniculitis with fibrous bands and chronic lymphohistiocytic infiltrate that spills over to affect the fat lobules. No evidence of vasculitis was observed. **A**) Magnification: x4; **B**) magnification: x10.