Reintroduction of dabrafenib after previous vemurafenib-induced DRESS: Not always safe!

To the Editor: We read with interest the recent case report by Pinard et al[1] about the successful introduction of dabrafenib after DRESS (drug rash with eosinophilia and systemic symptoms) induced by vemurafenib and more recently the same successful experience of Tahseen et al[2] after vemurafenib-induced toxic epidermal necrolysis. However, from our own practice, we would caution that these experiences should not be extended to all patients. Indeed, we report the case of a patient with previous vemurafenib-induced DRESS in which this reintroduction has induced a recurrence of the hypersensitivity reaction.

A 68-year-old man had a surgical resection of a nodular melanoma in the left abdominal region with a left inguinal lymphadenectomy. A positron emission tomography scan showed multiple adenopathies. A *BRAF* V600E mutation was identified, and vemurafenib was started in association with cobimetinib. Fourteen days later, the patient presented with facial erythema, cheilitis, maculopapular rash, intense pruritus, hyperthermia (39°C), and axillary and inguinal supracentimetric lymphadenopathies. No other drug had been introduced. Vemurafenib and cobimetinib were immediately discontinued. Laboratory tests found moderated hepatic cytolysis with aspartate aminotransferase 2N, Alanine transaminase 1,7N, but no evidence of renal failure. Polymerase chain reaction did not identify any viral reactivation (herpes simplex virus, Epstein-Barr virus, cytomegalovirus, human herpesvirus-6, hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis E virus, and HIV). Eosinophilia appeared (1.18 g/L) after 3 days. Skin biopsy findings supported the diagnosis of DRESS, revealing a moderate dermal lymphocytic infiltrate with eosinophils. DRESS syndrome was diagnosed according to the RegiSCAR international consensus criteria[3] with a score of 6. Oral corticosteroid therapy was initiated at 0.5 mg/kg/d, and the rash and blood parameters improved within 5 days and normalized within 2 weeks. Because of the benefit of BRAF inhibitors on his metastatic disease, and the published experience of the safe use of dabrafenib after previous SCAR (severe cutaneous adverse reaction) with vemurafenib,[4] dabrafenib was initiated 1 month later at the mild dose of 75 mg/d and carried out at the hospital with informed consent. Six hours after the first intake of dabrafenib, a maculopapular rash and hypereosinophilia (0.55 g/L) occurred. To prevent a recurrent potentially life-threatening DRESS that may have probably ensued, we decided to discontinue dabrafenib immediately and definitively. Immunotherapy with an anti–programmed cell death 1 agent was then started for the ongoing treatment of his metastatic melanoma.

Contrary to what was suggested in both articles by Pinard et al[1] and Tahsen et al,[2] this case implies that the hypersensitivity reaction can be class specific rather than drug specific. Even if few cases noting the successful use of dabrafenib after vemurafenib-induced SCAR have been reported,[1,2,4] the reintroduction cannot be alleged as safe and should be considered with care. In practice we do not suggest the avoidance dabrafenib after vemurafenib SCARs, but we emphasize that this introduction should take place within a hospitalized setting.

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REFERENCES

1. Pinard C, Mignard C, Samain A, et al. Successful use of dabrafenib after the occurrence of drug rash with eosinophilia and systemic symptoms (DRESS) induced by vemurafenib. *JAAD Case Rep*. 2017;3(6):532-533.
2. Tahseen AI, Patel NB. Successful dabrafenib transition after vemurafenib-induced toxic epidermal necrolysis in a patient with metastatic melanoma. *JAAD Case Rep*. 2018;4(9):930-933.

3. Kardaun SH, Sidoroff A, Valeyrie-Allanore L. Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: does a DRESS syndrome really exist? *Br J Dermatol*. 2007;156:609-611.

4. Jeudy G, Dalac-Rat S, Bonniaud B. Successfull switch to dabrafenib after vemurafenib-induced toxic epidermal necrolysis. *Br J Dermatol*. 2015;172:1454-1455.

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