Síndrome DRESS inducido por dabrafenib y trametinib: cambio exitoso a encorafenib y binimetinib: A propósito de un caso

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RESUMEN

Introducción
El síndrome DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) es una reacción de hipersensibilidad poco frecuente pero potencialmente mortal caracterizada por erupción cutánea, alteraciones hematológicas y afectación de órganos internos. Aunque la mayoría de los casos se han asociado a anticonvulsivantes y alopurinol, también se han descrito casos relacionados con terapias oncológicas dirigidas.

Caso clínico
Se presenta el caso de una mujer de 52 años con melanoma metastásico que desarrolló síndrome DRESS poco después de iniciar tratamiento con dabrafenib y trametinib. La paciente presentó fiebre, exantema cutáneo extenso, eosinofilia y elevación de enzimas hepáticas. Los síntomas se resolvieron tras la suspensión del tratamiento, pero reaparecieron rápidamente tras la reintroducción. Según el sistema de puntuación RegiSCAR y el algoritmo de Naranjo, la reacción se clasificó como DRESS probable inducido por dabrafenib y trametinib. El tratamiento se suspendió de forma definitiva. Posteriormente se inició tratamiento con encorafenib y binimetinib con escalada progresiva de dosis y monitorización estrecha. No se observaron nuevas reacciones de hipersensibilidad y se mantuvo el control de la enfermedad.

Conclusión
Este caso resalta la importancia de reconocer el síndrome DRESS como una reacción adversa grave asociada a inhibidores de BRAF y MEK. Asimismo, sugiere que el cambio a otros fármacos dentro de la misma clase terapéutica puede ser una opción viable en pacientes seleccionados bajo monitorización cuidadosa.

Palabras clave: síndrome DRESS, dabrafenib, trametinib, inhibidores BRAF, reacciones cutáneas adversas graves, melanoma

DRESS Syndrome Induced by Dabrafenib and Trametinib: Successful Switching to Encorafenib and Binimetinib; A Case Report

ABSTRACT

Background

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a rare but potentially life-threatening hypersensitivity reaction characterized by cutaneous eruption, hematologic abnormalities, and internal organ involvement. Although most cases have been associated with anticonvulsants and allopurinol, targeted oncologic therapies have also been implicated.

Case report

We report the case of a 52-year-old woman with metastatic melanoma who developed DRESS syndrome shortly after initiation of dabrafenib and trametinib. The patient presented with fever, extensive rash, eosinophilia, and elevated liver enzymes. Symptoms resolved after treatment discontinuation but rapidly recurred after rechallenge. According to the RegiSCAR scoring system and the Naranjo algorithm, the reaction was classified as probable DRESS induced by dabrafenib and trametinib. Treatment was permanently discontinued. The patient was subsequently switched to encorafenib and binimetinib with gradual dose escalation and close monitoring. No recurrence of hypersensitivity reactions occurred and disease control was maintained.

Conclusion

This case highlights the importance of recognizing DRESS syndrome as a rare but serious adverse reaction associated with BRAF and MEK inhibitors. It also suggests that switching to alternative agents within the same therapeutic class may be feasible in selected patients under careful monitoring.

Keywords: DRESS syndrome, dabrafenib, trametinib, BRAF inhibitors,severe cutaneous adverse reactions, melanoma

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INTRODUCTION

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a rare but potentially life-threatening hypersensitivity reaction characterized by fever, widespread rash, eosinophilia, and involvement of internal organs such as the liver or kidneys[1,2]. The syndrome usually develops two to six weeks after exposure to the causative drug[3]. The pathogenesis of DRESS involves drug-specific immune responses, genetic predisposition and viral reactivation, particularly human herpesvirus-6.[4].

DRESS has historically been associated with medications such as anticonvulsants, sulfonamides, and allopurinol[2]. However, recent evidence has reported cases associated with targeted cancer therapies, including BRAF and MEK inhibitors[5,6]. Vemurafenib has been most frequently implicated, whereas cases involving dabrafenib and trametinib are rare, suggesting molecule-specific effects[5].

Early recognition and prompt discontinuation of the offending drug are essential to reduce morbidity and mortality[1]. The mortality rate of DRESS syndrome has been estimated to range between 5% and 10%, mainly due to severe organ involvement such as hepatic failure[3,4]. In patients with advanced melanoma, preservation of therapeutic options is crucial, as withdrawal of an effective therapy without a suitable alternative may significantly limit treatment possibilities.

Hospital pharmacists play an important role in oncology teams through pharmacotherapeutic monitoring, early detection of adverse reactions and patient education.

CASE REPORT

52-year-old woman with no relevant past medical history was diagnosed with metastatic melanoma.

In September 2024, treatment with intravenous nivolumab was initiated and continued for sixteen weeks. In January 2025, the patient presented with cutaneous disease progression. Molecular testing revealed a BRAF V600 mutation and targeted therapy with dabrafenib and trametinib was initiated at standard doses (dabrafenib 150 mg twice daily and trametinib 2 mg once daily). he hospital pharmacist provided counseling on dosing, storage and potential adverse effects.

Ten days after treatment initiation, the patient developed fever that resolved with oral paracetamol. Treatment was continued; however, ten days later she presented to the emergency department with persistent fever (up to 39 °C), an edematous rash covering more than 50% of the body surface area (thorax, arms, legs and face), periorbital edema, grade 1 conjunctivitis, oral and pharyngeal candidiasis associated with grade 1 mucositis, elevated liver enzymes (grade 3 hypertransaminasemia), C-reactive protein of 186.8 mg/L, and eosinophilia of 500 cells/µL.

The patient was admitted to the hospital and treated with intravenous paracetamol and topical methylprednisolone. Because hypersensitivity was suspected, dabrafenib and trametinib were discontinued. Clinical symptoms resolved within one week and laboratory parameters returned to normal values (Figures 1, 2).

Figure 1: Evolution of Aspartate transferase (AST) and Alanine Transferase (ALT) levels during the admission period at hospital (AST normal values: 5-34 U/L; ALT normal values: 5-55 U/L)

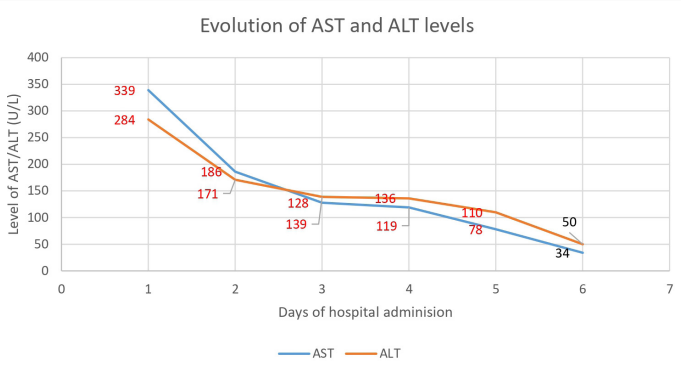
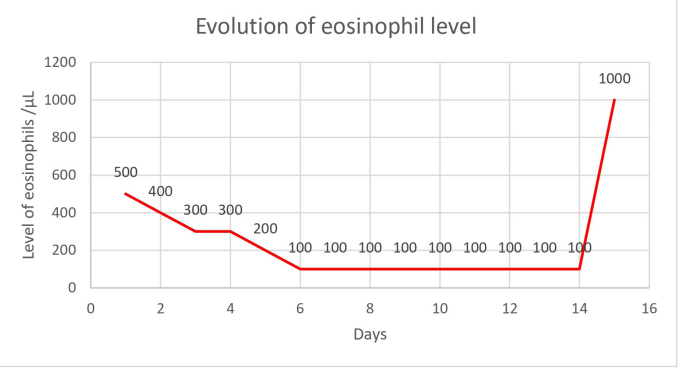


Figure 2: Evolution of eosinophil levels during the admission period (Days 1-7) and after treatment reintroduction (Day 14) (Normal value: 0-700/ µL)



One week after recovery, treatment was reintroduced at reduced doses (dabrafenib 100 mg twice daily and trametinib 1.5 mg once daily). Three hours after the first dose, the patient developed skin erythema, conjunctivitis, oral mucositis and marked eosinophilia (1000 cells/µL).

The Allergology Department was consulted. According to the RegiSCAR scoring system, the reaction was classified as probable DRESS (score 4)[1]. The Naranjo Adverse Drug Reaction Probability Scale also indicated probable causality (score 7)[7]. The adverse reaction was reported to the Spanish pharmacovigilance system.

Given the rapid recurrence and severity of symptoms, treatment with dabrafenib and trametinib was permanently discontinued. The patient was treated with topical methylprednisolone and skin lesions gradually resolved within one week.

One month later, in April 2025, treatment with encorafenib and binimetinib was initiated at reduced doses (encorafenib 225 mg once daily and binimetinib 60 mg twice daily) together with prophylactic antihistamines (ebastine 10 mg daily) and close monitoring.

In May 2025, doses were increased to encorafenib 300 mg once daily and binimetinib 90 mg twice daily. In June 2025, full therapeutic doses were achieved (encorafenib 450 mg once daily and binimetinib 90 mg twice daily), and antihistamines were discontinued. During fifteen months of follow-up, the patient tolerated treatment well without recurrence of hypersensitivity reactions and disease control was maintained.

Written informed consent for publication of this case report was obtained from the patient.

DISCUSSION

DRESS syndrome is a severe cutaneous adverse reaction characterized by delayed onset, systemic involvement and significant morbidity and mortality[1,3]. Reports describing DRESS associated with dabrafenib remain extremely limited in the literature. Although uncommon, it represents an important clinical entity requiring early recognition and prompt management.

In recent years, targeted oncologic therapies have increasingly been associated with severe cutaneous adverse reactions, including DRESS[5,8]. Among BRAF inhibitors, vemurafenib has been most frequently implicated. A retrospective study conducted in France reported 11 confirmed cases of DRESS associated with the combination of vemurafenib and cobimetinib, diagnosed using RegiSCAR criteria and frequently associated with systemic organ involvement [6].

A systematic review analyzing 31 cases of severe cutaneous adverse reactions (SCARs), including 23 cases of DRESS, reported only one case associated with dabrafenib[5]. These findings suggest that the risk of DRESS may vary among individual agents rather than representing a class effect.

In previously published reports, patients who developed DRESS with vemurafenib were successfully switched to dabrafenib without recurrence of hypersensitivity reactions[5,8]. In contrast, our patient developed DRESS shortly after initiation of dabrafenib and trametinib, with rapid recurrence upon rechallenge, strongly supporting the causal relationship between treatment and the hypersensitivity reaction.

Interestingly, switching to encorafenib combined with binimetinib was well tolerated in our patient, even after escalation to full therapeutic doses. This observation suggests that cross-reactivity among BRAF inhibitors may not be universal and that switching to alternative agents within the same therapeutic class may be a feasible option in selected patients.

These findings highlight the importance of pharmacovigilance and multidisciplinary collaboration in managing rare adverse reactions to targeted therapies.

Our case therefore contributes additional evidence supporting individualized treatment strategies in oncology patients who develop severe hypersensitivity reactions to targeted therapies. Careful multidisciplinary management and close monitoring are essential when considering rechallenge or switching strategies.

CONCLUSION

This case report provides further evidence of DRESS syndrome associated with dabrafenib and trametinib. It also suggests that switching to alternative BRAF and MEK inhibitors, such as encorafenib and binimetinib, may represent a safe therapeutic strategy in selected patients when careful monitoring is implemented, allowing continuation of targeted therapy without compromising patient safety.

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None

DECLARATION OF CONFLICTING INTEREST

The authors declare that they have no conflict of interest.

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No funding has been received.

ETHICAL APPROVAL AND INFORMED CONSENT STATEMENTS

The work was carried out in accordance with the standards of good clinical practice (GCP). This study describes a single clinical case and did not involve any experimental intervention. According to local regulations and institutional policies, approval from an Ethics Committee or Institutional Review Board was not required for the publication of this case report.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for the publication of this case report and any accompanying data. Non-essential identifying details have been omitted to protect patient confidentiality.

DATA PROTECTION

Data management complies with relevant privacy protocols, data protection policy, and local requirements for accessing medical records.

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