Drug reaction with eosinophilia and systemic symptoms syndrome associated with osimertinib

To the Editor,

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare and severe adverse drug reaction, occurring generally about two to eight weeks after the introduction of a causative drug.1 Cutaneous involvement usually begins with a morbilliform eruption, with cutaneous edema, mainly involving the face, upper trunk, and extremities, spreading from the face to the entire body, with edema of the face being a characteristic finding. Other cutaneous manifestations include vesicles, pustules, erythoderma, and purpuric lesions.2 DRESS syndrome can be accompanied by different systemic symptoms including fever, lymphadenopathy, hematological abnormalities, or visceral involvement (kidney, liver, heart, lung, muscle, and even brain). Blood test abnormalities typically persist for several days. DRESS syndrome can be life-threatening and is associated with organ failure, with a described mortality up to 10%, although analysis of prospective data shows a lower mortality rate, around 2%.3 Besides causative drug discontinuation, supportive therapy is generally sufficient and may include antipyretic drugs, systemic antihistamines, and topical corticosteroids. However, in severe cases, with visceral involvement, systemic corticosteroids (0.5–2.0 mg/kg) are usually needed. Aromatic anticonvulsants (e.g. phenytoin, carbamazepine, phenobarbital) and sulfonamides are the most frequent drugs associated with DRESS syndrome.3 The authors describe a DRESS syndrome induced by osimertinib, in an advanced EGFR mutated lung cancer patient. This third-generation agent was initially associated with scarce skin toxicity in clinical trials, compared to standard agents. After FLAURA trial results showing higher efficacy of osimertinib compared to standard EGFR-tyrosine kinase inhibitors,4 osimertinib became the first-line treatment of EGFR mutation-positive advanced NSCLC,5 enhancing the number of patients potentially treated with this agent.

A sixty-year-old woman was initially admitted to the hospital with seizures. The brain scan showed intracranial space-occupying lesions. She started levitiracetam at the end of December 2018 and carbamazepine in January 2019. Investigation revealed a stage IV EGFR mutated (deletion on exon 19) lung adenocarcinoma with the involvement of the central nervous system. She was submitted to radiosurgery and she started systemic therapy with osimertinib (80 mg daily), in early March. After eight days, she was admitted to the hospital with a painful and itchy generalized skin rash on face, neck, trunk, and lower limbs, with preserved skin integrity and with no systemic symptoms. Osimertinib induced skin toxicity was assumed and the drug was stopped. She was discharged from the hospital with topic steroid therapy. But, three weeks after osimertinib suspension, she was readmitted to the hospital with widespread erythema, impaired skin integrity, with no mucosal involvement, and accompanied by fever (Fig. 1). Blood tests revealed eosinophilia (1240/μl; 12.7%)

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https://doi.org/10.1016/j.pulmoe.2020.04.019
2017;12.
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Figure 1  (A, B) — Osimertinib-induced skin lesions. Residual skin desquamation after acute dermatosis.
Further, skin involvement had worsened after osimertinib suspension and the patient was under carbamazepine, a frequently DRESS syndrome associated drug, which made it difficult to associate osimertinib to this clinical situation. It is important to notice that skin toxicity can prevail after discontinuation of a target agent. To the best of our knowledge, this is the first case of DRESS syndrome induced by osimertinib described in literature till now.

**Conflicts of interest**

The authors have no conflicts of interest to declare.

**References**


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31 March 2020

https://doi.org/10.1016/j.pulmoe.2020.07.010

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