Severe Cutaneous Adverse Reactions in the Setting of Antineoplastic Therapy: A Single-Institution Retrospective Study

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PRACTICE **POINTS**

- Clinicians should be aware of the occurrence of severe cutaneous adverse reactions (SCARs) in patients on antineoplastic therapy to prevent delays in treatment and improve patient outcomes.
- Rapid initiation of treatment can be effective in resolving SCARs and ensuring full recovery.
- Close coordination between dermatology and oncology teams is crucial to manage SCARs while minimizing cancer treatment interruptions.

To the Editor:

Severe cutaneous adverse reactions (SCARs) are rare, life-threatening reactions that include acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), and Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN).[1] In addition to being associated with commonly implicated medications, SCARs also may occur in the setting of antineoplastic therapy.[2,3] Although antineoplastic-associated SCARs have been described, diagnosis can be difficult due to varying latency periods and atypical clinical features, such as those observed with BRAF inhibitor–related DRESS during immunotherapy.[4] Severe cutaneous adverse reactions can increase morbidity and mortality in the oncologic patient population due to both the clinical sequelae from the cutaneous reaction and the potential to interrupt cancer treatment.

The aim of this study was to evaluate the clinical characteristics, outcomes, and impact on cancer treatment among patients diagnosed with a SCAR while receiving active therapy for malignancy. We conducted a retrospective chart review of electronic medical records at Yale New Haven Hospital (New Haven, Connecticut) from 2013 to 2023, identifying patients receiving antineoplastic therapy who were diagnosed with a SCAR. Cases were identified through a search of the electronic medical record performed by the joint data analytics team using the keywords *DRESS, SJS, TEN, AGEP,* and *generalized bullous fixed drug eruption,* along with spelling variations (both abbreviations and full terms), in addition to manual review by one of the authors (K.V.) of the inpatient dermatology consultation log and dermatopathology database. Only patients for whom an antineoplastic agent was identified as a high-probability culprit by the dermatology and/or oncology teams were included.

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TABLE 1. Patient Demographics and Clinical Characteristics

Characteristic	Total cohort (N=20)
Mean age, y (SD)	60.8 (11.0)
Sex, n (%)	
Female	11 (55.0)
Male	9 (45.0)
Cancer type, n (%)	
Leukemia/lymphoma	4 (20.0)
Lung cancer	4 (20.0)
Melanoma	4 (20.0)
Breast cancer	2 (10.0)
Glioblastoma	2 (10.0)
Multiple myeloma	2 (10.0)
Oral cancer	1 (5.0)
Prostate cancer	1 (5.0)
SCAR type, n (%)	
AGEP	2 (9.5)
DRESS	13 (61.9)
DRESS (second hit)[a]	3 (14.3)
SJS/TEN	3 (14.3)
Median latency period, d (IQR)	
AGEP	7.5 (4.0-11.0)
DRESS	14 (10.0-32.0)
DRESS (second hit)	IO: 122 (96.0-426.0); drug culprit: 28 (21.0-52.0)
SJS/TEN	23 (20.0-27.0)
SCAR treatment, n (%)	
Systemic corticosteroids + topical corticosteroids	13 (65.0)
Systemic corticosteroids monotherapy	6 (30.0)
Systemic corticosteroids + etanercept	1 (5.0)
Cancer treatment interruption, n (%)	17 (85.0)

Abbreviations: AGEP, acute generalized exanthematous pustulosis; DRESS, drug reaction with eosinophilia and systemic symptoms; IO, immunotherapy; IQR, interquartile range; SCAR, severe cutaneous adverse reaction; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis.

Given that 1 patient on immunotherapy had 2 distinct SCARs (AGEP, DRESS) at different time points, the number of SCAR cases was 21.

[a]Drug culprits for patients with a potential second-hit phenomenon included trimethoprim-sulfamethoxazole (n=2), and phenobarbital (n=1).

TABLE 2. Implicated Antineoplastic Therapy and Associated SCARs

Antineoplastic therapy	SCAR
Chemotherapy	
Bendamustine	DRESS
Cladribine	DRESS
Cytarabine + daunorubicin	SJS/TEN
ICE regimen	DRESS
Hormonal therapy	
Enzalutamide	DRESS
Immunotherapy	
Ipilimumab	AGEP, DRESS[a]
Ipilimumab + nivolumab	DRESS
Nivolumab	DRESS
Pembrolizumab	DRESS
Targeted therapy	
Adagrasib + afatinib	SJS/TEN
Afatinib + cetuximab	SJS/TEN
Akt + MEK inhibitor (clinical trial)[b]	DRESS
Alpelisib	DRESS
Bevacizumab	AGEP
Carfilzomib + lenalidomide	DRESS
Crizotinib	DRESS
Lenalidomide	DRESS
Vemurafenib	DRESS[c]

Abbreviations: AGEP, acute generalized exanthematous pustulosis; ICE, ifosfamide, carboplatin, and etoposide; MEK, mitogen-activated protein kinase; SCAR, severe cutaneous adverse reaction; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis.

[a]This patient had distinct episodes of AGEP and DRESS on ipilimumab.

[b]This patient was participating in a clinical trial and received combination Akt and MEK inhibitor.

[c]There were 3 cases of DRESS in patients on vemurafenib.

In total, 20 patients (11 female, 9 male) were identified as having an antineoplastic-associated SCAR. All patients had metastatic or advanced disease. We identified 2 (10%) cases of AGEP, 16 (80%) cases of DRESS, and 3 (15%) cases of SJS/TEN. One patient on immunotherapy had 2 distinct SCARs (AGEP, DRESS) at different time points. Table 1 describes patient and SCAR characteristics as well as impact on cancer treatment. The median (interquartile range [IQR]) latency period for AGEP was 7.5 (4-11) days. The median (IQR) latency period for 13 of the 16 (81%) DRESS cases was 14 (10-32) days. For 3 DRESS cases with a potential second-hit phenomenon in the setting of current or antecedent immunotherapy,[5] the median (IQR) latency period was 122 (96-426) days for the immunotherapy drug and 28 (21-52) days for the drug culprit. The median (IQR) latency period for SJS/TEN was 23 (20-27) days.

Patients received treatment with combination systemic corticosteroids and topical corticosteroids in 13 (65%) cases, systemic corticosteroid monotherapy in 6 (30%) cases, or combination systemic corticosteroids and etanercept in 1 (5%) case. All patients experienced resolution of the SCAR and survived to hospital discharge. Most (17/20 [85%]) patients experienced interruption or discontinuation of cancer treatment. Table 2 describes the implicated antineoplastic therapies, which included chemotherapy (3 DRESS, 1 SJS/TEN), hormonal therapy (1 DRESS), immunotherapy (1 AGEP, 4 DRESS), and targeted therapy (1 AGEP, 8 DRESS, 2 SJS/TEN).

Limitations of this study include the retrospective study design, the small sample size, and the challenge of drug culprit identification in oncologic patients on multiple high-probability medications.

Though rare, SCARs can be encountered in patients on antineoplastic therapy with a wide range of drug culprits. In our cohort, SCARs occurred with various antineoplastic agents, including chemotherapy, hormonal therapy, immunotherapy, and targeted therapy. The most common antineoplastic-associated SCAR was DRESS, which had the widest latency period in the setting of a potential second-hit phenomenon with another drug culprit. Although we did not observe any cases of SJS/TEN in the immunotherapy category, it is important to consider progressive immunotherapy-related mucocutaneous eruption in the differential diagnosis. Fortunately, all patients survived to hospital discharge and experienced SCAR resolution with systemic treatment; however, most patients experienced interruption of cancer therapy, which has the potential to affect oncologic outcomes. This interruption is not uncommon, as rechallenge of an antineoplastic agent in patients with a therapy-related SCAR generally is not recommended. The awareness and prompt management of SCARs in a patient on treatment for malignancy are critical in order to minimize negative outcomes in this vulnerable patient population.

REFERENCES

1. Duong TA, Valeyrie-Allanore L, Wolkenstein P, et al. Severe cutaneous adverse reactions to drugs. *Lancet.* 2017;390:1996-2011.
2. Chen CB, Wu MY, Ng CY, et al. Severe cutaneous adverse reactions induced by targeted anticancer therapies and immunotherapies. *Cancer Manag Res.* 2018;10:1259-1273.
3. Ng CY, Chen CB, Wu MY, et al. Anticancer drugs induced severe adverse cutaneous drug reactions: an updated review on the risks associated with anticancer targeted therapy or immunotherapies. *J Immunol Res.* 2018;2018:5376476.
4. Maloney NJ, Rana J, Yang JJ, et al. Clinical features of drug-induced hypersensitivity syndrome to BRAF inhibitors with and without previous immune checkpoint inhibition: a review. *Support Care Cancer.* 2022;30:2839-2851.
5. Hammond S, Olsson-Brown A, Grice S, et al. Does immune checkpoint inhibitor therapy increase the frequency of adverse reactions to concomitant medications? *Clin Exp Allergy.* 2022;52:600-603.