

First case of DRESS syndrome attributed to a spider bite

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Clinical Implications

- We describe the first case of drug reaction with eosinophilia and systemic symptoms due to a spider bite. Clinical manifestations included fever, a macular and nonfollicular pustular eruption, lymphadenopathy, eosinophilia, and liver function test abnormalities.

TO THE EDITOR:

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a hypersensitivity reaction that is usually drug induced. The acronym VRESS (V for viral)¹ was proposed in cases of proven viral reactivations. We describe a case that was unrelated to any drug or viral reactivation, but was triggered by a spider bite instead. Spider bites have been recently reported to cause acute generalized exanthematous pustulosis (AGEP) and other cutaneous reactions, but not DRESS.

A 64-year-old male patient presented with a febrile eruption. Two days before, he was gardening and noticed a bite on the inside of his right arm (Figure 1, A). At the bite site, there was an annular target-shaped erythematous crust. On day 3, there were fever, polymorphic erythematous macules, and nonfollicular pustules on the trunk (Figure 1, B) and target-shaped lesions on the limbs. There was centimetric diffuse lymphadenopathy. Laboratory tests revealed an increased white blood cell count (12,160 G/L) with hypereosinophilia (2,990/mm³ then 7,000/mm³), whereas renal function was normal. Hepatic

function showed elevation of the transaminases 2 times the upper limit of normal, and cholestasis (2 times greater than the normal range). Viral reactivation tests including human herpes virus 8, Epstein-Barr virus, cytomegalovirus, parvovirus B19, hepatitis A virus, hepatitis B virus, hepatitis C virus, and human immunodeficiency virus were negative. Rickettsia and Lyme disease serologies were negative. X-ray showed a bilateral pleural effusion and lymphadenopathy. The skin biopsy showed a nonspongiform unilocular pustule; this pattern was not in favor of AGEP but compatible with a pustulous DRESS (Figure 2). The lesions disappeared in a few weeks, with a progressive normalization of the biologic parameters in 2 months. A diagnosis of DRESS was made in view of a European Registry of Severe Cutaneous Adverse Reactions (REGISCAR) score of 7.² As there was no drug intake or viral primary infection or reactivation, a causative link to the spider bite was strongly suspected.

The absence of a culprit drug and viral reactivation and the presence of 2 bite marks corresponding to a spider bite established the causal link of the arthropod bite and DRESS, even if the spider was not caught. Spiders had been seen in the garden of the patient and the characteristics and size of the 2 bite marks showed that the marks could not have been made by another animal bite or prick.

A misdiagnosis or an overlap between AGEP and DRESS is possible,³ but we are confident with the diagnosis of DRESS in our case. Indeed, the widespread pustules on the back sparing the flexures, lymphadenopathy, high eosinophilia, and liver function test abnormalities are in favor of DRESS. Moreover, histology showing a nonspongiform unilocular pustule is not in favor of an AGEP but compatible with a pustulous DRESS (Figure 2). In our case, the short time gap of 2 days between the spider bite and the lesions is short, but such a short time interval has been reported in DRESS.⁴

AGEP, a well-known drug-induced reaction, has been reported several times after spider bites. To our knowledge, 11 cases were reported⁵⁻⁹ and spider identification was obtained in only 1 case (*Loxosceles rufescens*).⁶ In these cases, the flexural distribution of the pustules was in favor of an AGEP in contrast

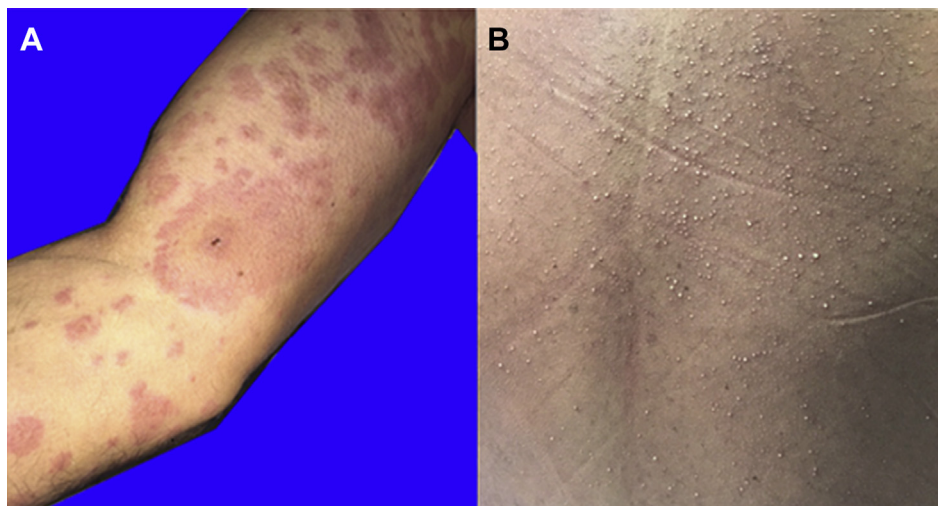


FIGURE 1. A, Prick point at the inside of the right arm and B, pustulous exanthema of the trunk.

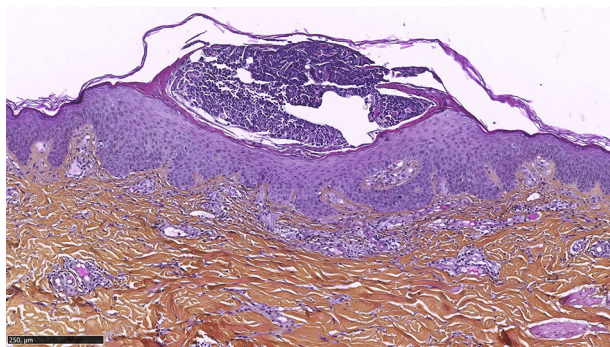


FIGURE 2. Nonspongiform unilocular pustule, not in favor of AGEP but compatible with a pustulous DRESS. AGEP, Acute generalized exanthematous pustulosis; DRESS, drug reaction with eosinophilia and systemic symptoms.

to our case with scattered nonflexural pustules. In these cases, patients presented with a marked neutrophilia, as observed commonly in AGEP, and when eosinophilia was present (5 cases), it was mild (between $650/\text{mm}^3$ and $2200/\text{mm}^3$).^{6,7} All these cases were reported in non-North European countries (Middle-East or in South Europe).

In France, most dermatological adverse events associated with spider bites are skin necrosis, attributed to the genus *Loxosceles*,¹⁰ mainly *L. rufescens*.¹¹

This case underlines the growing incidence of spider bites in Europe, probably related to an unexpected impact of climate change. So, new reports of adverse effects due to spider bites are important to describe the modified epidemiology of parasitic diseases.

This is the first case of “DRESS” related to a spider bite. We propose, after DRESS and VRESS, the new acronym SRESS (S for spider).

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