

# Carbamazepine-Induced Generalized Pustular Eruption

Gayathri Bhagwath, MD

Michael DiSalle, MD

**A**llergic cutaneous reactions to drugs are well-known adverse effects of pharmacologic therapy. Several drugs, including antiepileptic medications, can cause generalized pustular reactions, which can be either mild or more severe. Examples of severe pustular reactions include acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson syndrome, and toxic epidermal necrolysis. This article discusses a case of AGEP that developed after a patient with complex partial seizures was given carbamazepine. The salient features of the presentation, diagnosis, and management of this condition will be discussed.

## CASE PRESENTATION

### Initial Presentation

A 40-year-old white man admitted to the inpatient psychiatric unit was found to have a fever and a diffuse erythematous rash. The patient subsequently developed obtundation with generalized swelling and was transferred to the medical intensive care unit (ICU).

### History

The patient's medical history included chronic schizophrenia. He had no history of psoriasis or other skin disorders. He had developed complex partial seizures 2 days after being admitted to the psychiatric unit and was treated with carbamazepine. Approximately 48 hours after initiation of treatment, however, the patient became febrile and developed a rash. Significantly, neuroleptic therapy had been discontinued on the day of his admission to the psychiatric unit because of adverse effects (primarily rigidity).

### Physical Examination

On admission to the ICU, the patient had a temperature of 40.5°C (104.9°F) and was hypotensive. A generalized erythematous maculopapular rash was noted on the palms, groin, axillae, head, and chest. During the next

several hours, nonconfluent pustular lesions appeared over the generalized erythematous base (**Figure 1**); in addition, purpuric lesions developed over the extremities (**Figure 2**). A few bullae were seen, but there was no mucosal or conjunctival involvement. After facial edema developed, the patient was electively intubated and given supportive treatment.

### Laboratory Studies

Laboratory studies at the time of admission to the ICU revealed a hematocrit of 42%, a leukocyte count of  $23.7 \times 10^3/\text{mm}^3$ , and a platelet count of  $237 \times 10^3/\text{mm}^3$ . Results of serum electrolyte measurement and liver function tests were within normal limits. Because of his history of fever and hypotension, urine and blood cultures were obtained, and a lumbar puncture was performed; results of these studies were again within normal limits. No pathogen was identified on Gram stain or culture of pustular material. Results of viral serologies, determination of antistreptolysin O titer, and rapid plasmin reagin testing similarly revealed no abnormalities.

### Treatment

The patient's hypotension responded to intravenous administration of fluids, and he was extubated after 2 days. The rash was treated with topical hydrocortisone cream and emollients. Exfoliation of the involved areas began 4 to 5 days after onset of symptoms, followed by complete resolution of both the rash and the fever. Based on the patient's history and clinical presentation, a tentative diagnosis of AGEP was made.

---

*Dr. Bhagwath completed her residency in Internal Medicine at St. Mary's Hospital/Unity Health System, Rochester, NY. Dr. DiSalle is the Internal Medicine Residency Program Director at Unity Health System and a Clinical Assistant Professor of Medicine, University of Rochester, Rochester, NY.*



**Figure 1.** Discreet and confluent pustules on the case patient's scalp.



**Figure 2.** Erythema involving the hand of the case patient, with papules and crusted vesicles in the interdigital areas.

## **DISCUSSION**

### **Etiology**

Described in the literature as toxic pustuloderma or pustular drug rash, AGEP is a pustular cutaneous reaction precipitated by infection or exposure to certain drugs or toxins. Causative agents include bacteria, viruses, drugs (most commonly, penicillins and sulfonamides), and toxic chemicals (eg, mercury)<sup>1,2,3</sup> (**Table 1**). Carbamazepine likewise has been known to cause AGEP, although rarely.<sup>1,4</sup> Many patients who develop AGEP after carbamazepine administration have a history of prior adverse reaction to drugs. Prior carbamazepine exposure might hasten the onset of the pustular rash as a result of sensitization.

### **Clinical Features**

AGEP is characterized by an acute or subacute onset, fever, neutrophilia, and spontaneous resolution. Peripheral eosinophilia and target lesions also are sometimes observed. The onset of rash after drug exposure can vary from a few hours to a few days. In addition to pustules, patients can develop petechiae, purpura, vesicles, or blisters; the case patient developed all of these lesions. The presence of target lesions can cause this condition to be confused with erythema multiforme.

Skin biopsy most consistently reveals intraepidermal or subcorneal pustules. Dermal edema, perivascular eosinophils, and focal necrosis of keratinocytes can also be seen.<sup>1</sup>

### **Management**

A review of the literature does not reveal a consensus about any specific treatment plan except for sup-

portive care and avoidance of the causative agent. Symptomatic topical care with emollients and corticosteroids is a commonly observed practice. However, there is a case report describing successful treatment of AGEP with intravenously administered corticosteroids.<sup>5</sup> Spontaneous resolution of the disorder generally occurs, as it did with the case patient.

Determination of the offending agent causing AGEP can be made with either a drug lymphocyte stimulation test<sup>2</sup> or a patch test. Patch testing seems to be more reliable in diagnosing acute drug reactions such as AGEP, with less benefit shown in diagnosing Stevens-Johnson syndrome or toxic epidermal necrolysis.<sup>6,7</sup> Rechallenge with the suspected drug is dangerous and should be avoided.

### **Differential Diagnosis**

Besides erythema multiforme, several other disorders comprise the differential diagnosis of AGEP (**Table 2**). Infectious conditions such as candidiasis, folliculitis, and septic vasculitis can manifest as generalized pustular eruptions in adults; candidiasis is characterized by satellite pustules, whereas the pustules of folliculitis and septic vasculitis have a follicular locus. Either a Gram stain or use of a potassium hydroxide preparation, followed by appropriate culturing techniques, can confirm the diagnosis. Additionally, Sneddon-Wilkinson disease is a pustular disorder that is chronic in nature and manifests similarly to AGEP; it generally can be diagnosed by skin biopsy. AGEP also can be confused with generalized pustular psoriasis (von Zumbusch's type), especially when large areas of skin are involved. In most cases, pustular eruption in psoriasis surrounds plaques in acral, crural, and flexural areas of the body. Arthritis

**Table 1.** Causes of Acute Generalized Exanthematous Pustulosis

---

Infections
Bacterial
Viral
Drugs
$\beta$ -Lactams
Macrolides
Sulfonamides
Acetaminophen
Carbamazepine
Metronidazole
Nifedipine
Toxins (eg, mercury)
Unknown agents

---

and fever generally accompany this type of psoriasis, and diagnosis is based on skin biopsy. Biopsy of a psoriatic lesion reveals spongiform superficial pustules but not the papillary edema and vasculitis seen in AGEP.

#### SUMMARY

The keys to making the diagnosis of AGEP are obtaining a detailed history and performing a thorough clinical examination. Although biopsy might not be required in patients with a classic presentation (such as the case patient), it can help to narrow the differential diagnosis in ambiguous cases. The absence of a history of drug reaction is especially helpful in reaching the appropriate diagnosis. Prompt discontinuation

**Table 2.** Differential Diagnosis of Acute Generalized Exanthematous Pustulosis

---

Erythema multiforme
Infections
Candidiasis
Folliculitis
Septic vasculitis
Pustular psoriasis (von Zumbusch's type)
Sneddon-Wilkinson disease

---

of exposure to the causative agent will lead to rapid resolution of signs and symptoms of AGEP. **HP**

#### REFERENCES

1. Roujeau JC, Bioulac-Sage P, Bourseau C, et al. Acute generalized exanthematous pustulosis. Analysis of 63 cases. *Arch Dermatol* 1991;127:1333-8.
2. Katagiri K, Takayasu S. Drug induced acute generalized exanthematous pustulosis. *J Dermatol* 1996;23:623-7.
3. Commens CA, Fischer GO. Toxic pustuloderma following carbamazepine therapy [letter]. *Arch Dermatol* 1988;124:178-9.
4. Manders SM, Heymann WR. Acute generalized exanthematous pustulosis. *Cutis* 1994;54:194-6.
5. Watsky KL. Acute generalized exanthematous pustulosis induced by metronidazole: the role of patch testing [letter]. *Arch Dermatol* 1999;135:93-4.
6. Wolkenstein P, Chosidow O, Flechet ML, et al. Patch testing in severe cutaneous adverse drug reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis. *Contact Dermatitis* 1996;35:234-6.
7. Alanko K. Patch testing in cutaneous reactions caused by carbamazepine. *Contact Dermatitis* 1993;29:254-7.

Copyright 2001 by Turner White Communications Inc., Wayne, PA. All rights reserved.