CASE REPORT

A rapidly fluctuating rash in a stuporous patient

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INTRODUCTION

There is a range of skin changes that are transient in nature, from urticaria to vasomotor disturbances such as Raynaud phenomenon and flushing. However, rapidly fluctuating lesions that appear then disappear in a matter of seconds to a minute are rarely observed and are not well documented in the dermatologic literature. Herein, we describe an unresponsive young man with rapidly fluctuating patches of erythema in whom the neurologic and cutaneous symptoms improved following treatment for benzodiazepine withdrawal-induced catatonia (BWC).

CASE REPORT

A 27-year-old man presented to the emergency department with altered mental status, diaphoresis, and a rapidly fluctuating, blotchy rash. Two days prior, he had abruptly discontinued his long-term use of alprazolam and oxycodone/acetaminophen. His past medical history was significant for benzodiazepine and opioid use disorder, including hospitalization 3 years prior for severe abdominal pain after sudden discontinuation of alprazolam.

On presentation, his blood pressure was 157/93 mm Hg, and he was febrile at 37.9 °C. Laboratory evaluation was notable for a mildly elevated white blood cell count and a serum glucose level of 125 mg/dL (Table I lists all laboratory values). A urine toxicology screen was positive for benzodiazepines and cannabinoids. Noncontrast computed tomography of the head and magnetic resonance imaging of the brain showed no acute changes. An electroencephalogram did not reveal seizure activity. Laboratory

receiving diazepam 5 mg orally and 10 mg intravenously in the emergency department. He was subsequently admitted to the inpatient medicine service for further evaluation.

After admission, he became stuporous and lost control of bowel and bladder functions. Further laboratory evaluation was remarkable for slightly elevated protein and glucose levels in the cerebrospinal fluid (Table 1). Other tests for metabolic and infectious causes as well as toxic drug or alcohol ingestion as the etiology of his neurologic status was negative (Table I). On the third day after admission, the dermatology service was consulted for a blotchy erythematous rash on his face and chest. Ancillary history showed no recent history of fish ingestion, which might implicate scombroid poisoning.

Clinical examination revealed a young man who was completely unresponsive to physical or verbal stimuli. Cutaneous examination was significant for multiple blotchy pink macules and patches varying in size from 3 mm to several centimeters. They were distributed symmetrically on the face, neck, and upper portion of the trunk, with fewer lesions on the upper portion of the thighs. Notably, the blotchy patches appeared then disappeared in a matter of seconds to 1-2 minutes (Fig 1 and Video 1). Based upon a literature review,1,2 the possibility of central nervous system (CNS)-driven autonomic neurovascular dysregulation was raised. Laboratory

Abbreviations used:
BWC: benzodiazepine withdrawal—induced catatonia
CNS: central nervous system

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evaluation for metabolic causes of flushing was also conducted (Table I).

By the next day, the differential diagnosis for his neurologic dysfunction had narrowed to include a toxic ingestion driven by synthetic cannabinoids, BWC, and viral encephalitis. Based upon additional consultation by the psychiatry service and toxicology team, the clinical diagnosis of BWC was favored, and the patient was started on 2 mg of intravenous lorazepam every 8 hours, which led to rapid clinical improvement in his neurologic status and more gradual resolution of the fluctuating erythema. Given his response, the final clinical diagnosis was BWC. He was discharged 5 days after his first

Table I. Laboratory evaluation studies performed to screen for metabolic, infectious, and toxic etiologies for the patient’s neurologic and cutaneous findings

| Test                                      | Result     | Reference range       |
|-------------------------------------------|------------|-----------------------|
| **Metabolic**                             |            |                       |
| White blood cell count                    | 14.6 × 10^3/L | 4–10 × 10^3/L         |
| Serum glucose (mg/dL)                     | 125        | 70–100                |
| Aspartate aminotransferase (U/L)          | 39         | 11–33                 |
| Alanine aminotransferase (U/L)            | 17         | 6–34                  |
| Creatine kinase (U/L)                     | 111        | 11–204                |
| Ammonia (µmol/L)                          | 23         | 11–35                 |
| TSH (µIU/mL)                              | 0.997      | 0.270–4.200           |
| ESR (mm/h)                                | 8          | 0–20                  |
| CRP (mg/L)                                | 0.3        | >1                    |
| Ferritin (ng/mL)                          | 264        | 30–400                |
| Vitamin B₁₂ (µg/mL)                       | 1218       | 232–1245              |
| Copper (µg/dL)                            | 127        | 70–175                |
| Total plasma porphyrins (µg/dL)           | <1         | <1                    |
| Anti-nuclear antibody titer               | <1:80      | <1:80                 |
| CSF glucose (mg/dL)                       | 76         | 40–70                 |
| CSF protein (mg/dL)                       | 52         | <45                   |
| Serum tryptase (µg/L)                     | 2.5        | <11                   |
| Serum chromogranin A (ng/mL)              | 75         | 25–140                |
| Timed urine 5-HIAA                        | 0.5 mg/24 h| <6 mg/24 h            |
| Timed urine metanephrines*                | 354 µg/24 h| 25–222 µg/24 h        |
| Timed urine normetanephrines              | 388 µg/24 h| 40–412 µg/24 h        |
| Timed urine metanephrines and normetanephrines* | 742 µg/24 h| 94–604 µg/24 h        |
| Timed plasma metanephrines (pg/mL)        | 50         | <57                   |
| Timed plasma normetanephrines (pg/mL)     | 64         | <148                  |
| Timed plasma metanephrines and normetanephrines (pg/mL) | 114 | <205 |

**Infections**

Negative or within normal limits:
- Respiratory viral panel, SARS-CoV-2 (nasopharyngeal swab specimens)
- PCR of blood for hepatitis C virus, HHV-6, HIV-1; PCR of CSF for enterovirus, HSV-1, HSV-2, VZV, WNV
- Serology for EBV, SARS-CoV-2, and WNV infections
- Anti-*Treponema pallidum* antibody (serum)
- Bacterial cultures of blood, CSF, lower respiratory tract sputum, and urine

**Toxicity**

Toxicology screen of urine:
- Positive: benzodiazepines and cannabinoids
- Negative: acetaminophen, amphetamines, barbiturates, cocaine, ethanol, fentanyl, ketamine, methadone, opiates, oxycodone, phenycyclidine, phenobarbital, salicylates, and tricyclic antidepressants

CRP, C-reactive protein; CSF, cerebrospinal fluid; EBV, Epstein-Barr virus; ESR, erythrocyte sedimentation rate; HHV, human herpes virus; 5-HIAA, 5-hydroxyindoleacetic acid; HSV, herpes simplex virus; PCR, polymerase chain reaction; TSH, thyroid-stimulating hormone; VZV, varicella zoster virus; WNV, West Nile virus.

*Although a modest elevation in these two urine values was noted, plasma metanephrine and normetanephrine levels were within normal limits and were viewed as more reliable diagnostic assays.*
intravenous lorazepam dose on 5.5 mg of oral lorazepam daily to be tapered by 0.5 mg each week.

DISCUSSION

Rapidly fluctuating blotchy patches that appear then disappear in a matter of seconds to a minute are a striking clinical presentation that is not well documented in the dermatologic literature. A broader literature review found descriptions of six patients with similar cutaneous findings.1,2 Five patients (between 9 and 15 years of age) had an acute elevation in intracranial pressure due to hydrocephalus, head trauma, or intraventricular hemorrhage; the sixth patient was a 42-year-old man with head trauma.1,2 The cutaneous findings described in all six cases were attributed to an unclear mechanism linking the CNS pathology to the rapidly fluctuating rash.

We propose CNS-driven autonomic neurovascular dysregulation of arteriolar sphincters as the underlying mechanism leading to the rapidly fluctuating erythema. The distribution of dermal arterioles that control ascending umbrella-like cascades of capillaries would explain the observed pattern.3 Drawing attention to this rather unique clinical presentation and its association with underlying CNS abnormalities beyond head trauma and elevated intracranial pressure should prove useful to dermatologists asked to evaluate such patients.

Conflicts of interest

None disclosed.

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