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Amantadine-Associated Bullous Pemphigoid

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Amantadine-Associated Bullous Pemphigoid

To the Editors:

Bullous pemphigoid (BP) is an autoimmune dermatological condition characterized by subepidermal blistering.[1] Triggers of BP include trauma, radiation, burns, and vaccines.[2] It is also associated with several medications and neurologic disorders; for example, an increased incidence of BP in patients with Parkinson disease (PD) has been noted.[2–4] However, the relationship between BP and antiparkinsonian drugs is less well-defined. Herein we present a patient whose BP may have been precipitated by amantadine use.

CASE REPORT

Mr D, a 77-year-old male, was admitted to inpatient psychiatry for depressive symptoms. He provided written informed consent for publication of this case report. His past medical history included major depressive disorder, a penetrating wound due to a suicide attempt requiring laparotomy and colectomy, type 2 diabetes mellitus, dyslipidemia, hypertension, and recurrent falls. He was noted to have parkinsonian symptoms at the time of admission. He also had a 4-year history of BP triggered by furosemide, confirmed by histopathology examination, and treated with systemic corticosteroids and mycophenolate mofetil. Medications upon admission included citalopram (20 mg/d), mirtazapine (30 mg qhs), quetiapine (75 mg qhs), olanzapine (2.5 mg/d), metformin (1000 mg/d), ramipril (2.5 mg/d), rosuvastatin (20 mg/d), vitamin D (2000 units/d), and mycophenolate mofetil (1000 mg bid). Mycophenolate mofetil was discontinued upon admission because there had been no recurrence of BP-related skin lesions over the previous 4 years and because it had been associated with depressive disorder in published literature.[5] Quetiapine and olanzapine were tapered and discontinued, but it did not improve his parkinsonism.

During his admission, Mr D was eventually diagnosed with PD. One hundred milligrams of amantadine daily was started and optimized to 100 mg 3 times a day. This significantly reduced his parkinsonian symptoms. However, by week 2 of amantadine use, he began to develop urticarial areas in his distal lower extremities. This progressed into bullae, particularly on the right foot. It then involved the upper extremities, moving distal to proximal and affecting the medial aspects of his arm and forearm. He was assessed by the internal medicine service, and they initiated treatment with triamcinolone, but his rash progressed to his inner thighs and the dorsum of his feet bilaterally, predominantly on the right side. A 7-day trial of cephalexin for presumed cellulitis did not improve the lesions. A provisional diagnosis of BP recurrence was made. Given that symptoms began after introduction of amantadine, it was hypothesized that this drug may have triggered the BP episode; the medication was discontinued at week 4 of use. This halted progression of the rash; by week 5, Mr D had no new lesions and the old ones were mostly denuded. Figure 1 shows various healing stages of his lesions. He was discharged from hospital with outpatient follow-up arranged with dermatology. At 6-month psychiatric follow-up, his BP had remained in clinical remission, while he was not rechallenged with any antiparkinsonian medication.

DISCUSSION

This case is remarkable because our patient developed BP lesions after being started on amantadine. We propose that amantadine may trigger BP, which could potentially explain the increased incidence of BP in PD patients. Although our patient had a preexisting diagnosis of BP, an increased incidence of newly diagnosed BP in patients with an established diagnosis of PD has been noted.[4] If amantadine is truly a BP trigger, its use may account for the increased prevalence of BP observed in PD patients without prior skin conditions. Our hypothesis is limited in that the patient's BP was not confirmed histologically during the exacerbation (although diagnostic histology had been done during his past BP episode). In addition, his mycophenolate mofetil had been discontinued before the episode, potentially making him more susceptible to BP recurrence. However, use of the Naranjo adverse drug reaction probability scale indicated a probable relationship between the patient's development of skin lesions and amantadine therapy.[6]

Commonly reported adverse effects of amantadine include gastrointestinal complaints, mood symptoms, and sleep disturbance.[7] More adverse events, such as delusions, paranoia, corneal edema, hypertension, and urinary retention, have also been reported. A link between amantadine and BP has not been identified previously. To clarify whether amantadine contributes to the increased incidence of BP in PD patients, further exploration of the medication profiles of PD patients who develop BP is merited.

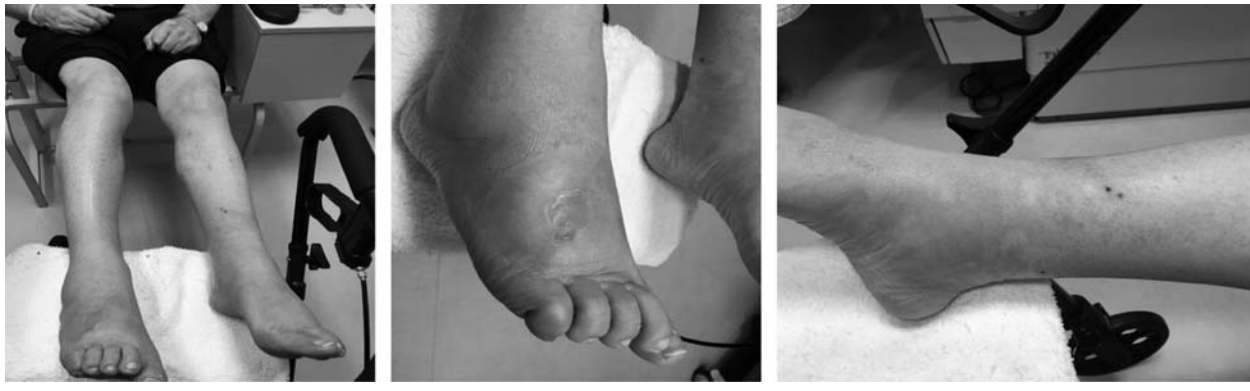

FIGURE 1. Bullous pemphigoid in a geriatric patient with PD and amantadine treatment. The patient provided written consent for use of these photographs for publication.

Given that amantadine is used off-label for several psychiatric indications, for example, for cognition in traumatic brain injury patients, antipsychotic-associated extrapyramidal symptoms, and fatigue in multiple sclerosis, an awareness of amantadine-associated BP is important for the psychiatrist who prescribes this medication.[8–10] History of PD and the use of immunomodulation therapies need to be considered in cases of apparent amantadine-associated BP.

AUTHOR DISCLOSURE INFORMATION

The authors report no relevant financial relationships and no conflict of interest.

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