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Urticarial Systemic Allergic Dermatitis Following Mitomycin C Instillation

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We report a case of systemic allergic dermatitis (SAD) caused by mitomycin C characterised by persistent urticaria and dermographism.

1 | Case Report

In 2018, a 63-year-old female patient received 12 intravesical instillations of mitomycin C (MMC; CAS-50-07-7) for the treatment of carcinoma of the bladder, which were tolerated well. Six years later, she was given another two instillations because of a recurrence of the tumour. A few hours after the first treatment session in 2024, the patient developed pruritic blisters on the palms of her hands (Figure 1). Hours after the second instillation, she presented to us with itching over the entire body, vesicles on the palms, and urticarial papules and plaques in the neck (Figure 2). Linear urticarial lesions and plaques appeared at every site where the patient scratched on the body (Figure 3). The patient reported no prior history of urticaria.

The vesicles on her hands disappeared within 2 days, but the itch and urticarial reactions persisted for several months and are ongoing, despite the fact that no more treatments with mitomycin were given. Symptomatic treatment with desloratadine provided some improvement.

Patch testing was performed according to the recommendations of the European Society of Contact Dermatitis with readings on day (D)2, D4 and D7 [1]. Removal of the adhesives (Medipore tape, Maplewood, Minnesota) and patch test materials (Van der Bend square chambers, Brielle, the Netherlands) resulted in a

localised erythematous reaction which subsided within 30 min. Positive reactions were observed to MMC 0.06%, 0.13% and 0.2% in aqua (concentrations prepared by Maastricht university hospital pharmacist) on D4 (+) and D7 (+) (Figure 4). We diagnosed systemic allergic dermatitis (SAD) from mitomycin C.

2 | Discussion

Systemic allergic dermatitis (SAD; previously known as systemic contact dermatitis) is a condition that occurs when an individual sensitised to an allergen (hapten) from contact with the skin, mucosa, or both, is exposed to that same allergen or a cross-reacting molecule through a systemic (haematogenous) route. Systemic exposure may occur from transcutaneous, transmucosal, enteral, intravenous, intramuscular, intra-articular, subcutaneous, intralesional, intravesical and inhalational routes as well as implants. Possible manifestations of SAD include reactivation of previous eczema, acrovesicular (dyshidrotic) dermatitis, various drug eruptions including dermatitis/eczema, maculopapular eruption, urticaria, erythema multiforme-like reactions, photoallergic dermatitis, and, sometimes, systemic symptoms such as fever, malaise, nausea, vomiting, diarrhoea, headache and arthralgia [2]. Patch tests can be used to confirm SAD to mitomycin C.

SAD from mitomycin C is well known and has been reported in (at least) 32 patients in 16 publications ([2–4]). Most had vesicular dermatitis of the hands, feet, or both, with or without genital dermatitis; six had SDRIFE (systemic drug-related intertriginous and flexural exanthema)/baboon syndrome, and some

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FIGURE 1 | Pruritic vesicles on the palm of the left hand a few hours after the first MMC instillation.



FIGURE 3 | Urticarial linear plaques on the left leg with positive dermographism a few hours after the second MMC instillation.



FIGURE 2 | Urticarial papules and plaques in the neck a couple of hours after the second MMC instillation.

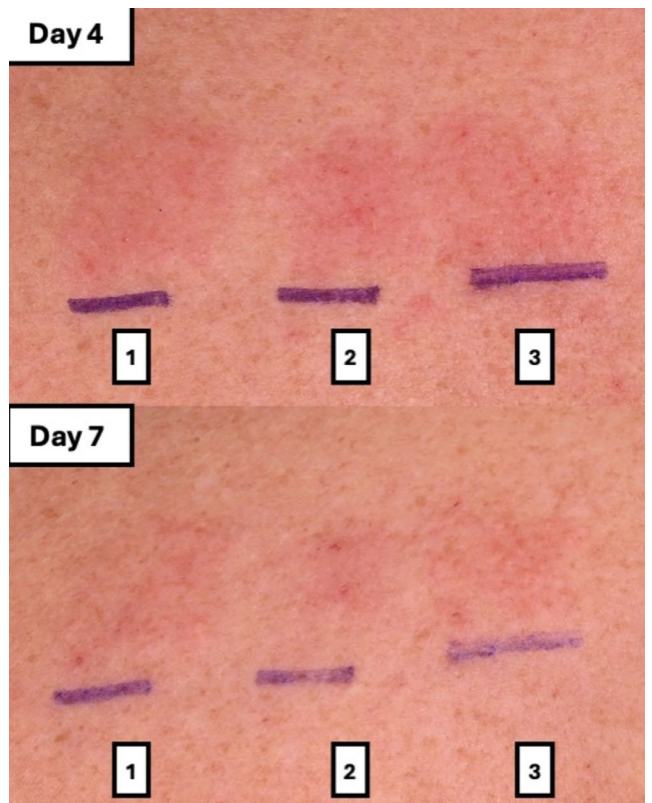


FIGURE 4 | Patch test for mitomycin C in aqua (1 = 0.06%, 2 = 0.13%, 3 = 0.2%) at Day 4 and 7.

a 'generalised rash' [2]. There have also been single cases of maculopapular eruption [5] and Henoch-Schönlein purpura [6] that could be reproduced by patch testing.

Our patient had SAD from intravesical instillation of MMC with persistent urticaria and dermographism as key features. SAD with urticarial lesions has been previously described following systemic delivery of various drugs such as acyclovir, disulfiram, pristinamycin and trimebutine [2]. Urticaria in SAD to MMC may have been reported only once. In that case report, the patient developed a vesicular eruption with oedema on the palms and soles and generalised urticaria 6 h after the fourth MMC instillation given for transitional cell carcinoma of the bladder. Treatment with oral corticosteroids and antihistamines was initiated until total recovery [7].

The exact pathomechanisms of SAD are unknown, but it is thought that both the humoral and the cellular immune systems are activated in SAD [8]. At least in one case, both Type 3 and Type 4 hypersensitivity may have been involved [6]. The pathomechanisms of the urticarial manifestations in SAD have not been investigated and are therefore unknown.

The administration of MMC may have induced or contributed to the formation of autoantibodies, which, upon binding to an autoallergen, IgE, or the high-affinity IgE receptor, has resulted in the activation of mast cells with prolonged release of histamine—a mechanism well known to occur in chronic spontaneous urticaria [9]. Furthermore, in chronic inducible urticaria, such as symptomatic dermographism, which our patient had, autoallergen binding via the autoallergic pathway is thought to play a role in mast cell activation [10]. Alternatively, the bladder cancer itself may have been responsible, as malignancies, albeit rarely, can trigger urticaria [9].

Author Contributions

Dani Heuts: investigation, writing – original draft. **Bashar Razoki:** investigation, writing – review and editing. **Frank van Leersum:** writing – review and editing. **Valerie Verstraeten:** investigation, writing – review and editing, supervision. **Anton de Groot:** writing – review and editing.

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Consent

The patient in this manuscript has given permission for publication of her case details and photographs.

Conflicts of Interest

The authors declare no conflicts of interest.

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