

Widespread Rash with Localized Sparing: A Quiz

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A Caucasian female in her 60s had type 2 diabetes, hypertension, and schizophrenia in her medical history. Her regular medications included olanzapine, venlafaxine, rosuvastatin, bisoprolol, ramipril, and empagliflozin and had remained unchanged in the last months.

A little over a week earlier, the patient had a tick removed from her back at a primary health care facility. After 2 days, she had noticed an oval-shaped, slowly expanding erythematous macule in the right side of her lower back for which a general practitioner prescribed a course of amoxicillin. Four days later, a widespread rash with fever appeared and she sought treatment at the emergency room (ER).

In the ER, she had fever but otherwise she was in a good general condition. She was noticed to have a widespread maculopapular rash all over her skin with no mucosal lesions or bullae. A peculiar area of normal-looking skin

was noticed on the right side of her back (Fig. 1). She had leukocytosis ($12.8 \times 10^9/L$, reference $3.4\text{--}8.2 \times 10^9/L$) but no other changes in her blood cell count. Her C-reactive protein was 164 mg/L (reference $< 10 \text{ mg/L}$) and alanine aminotransferase and plasma creatinine were within normal range. Her chest X-ray was normal.

What is your diagnosis?

- 1: Phototoxic reaction with spared area under an adhesive bandage
 - 2: Drug reaction with eosinophilia and systemic symptoms
 - 3: Drug exanthem with sparing phenomenon in lesion of active erythema migrans
 - 4: Viral exanthem
- See next page for answer.

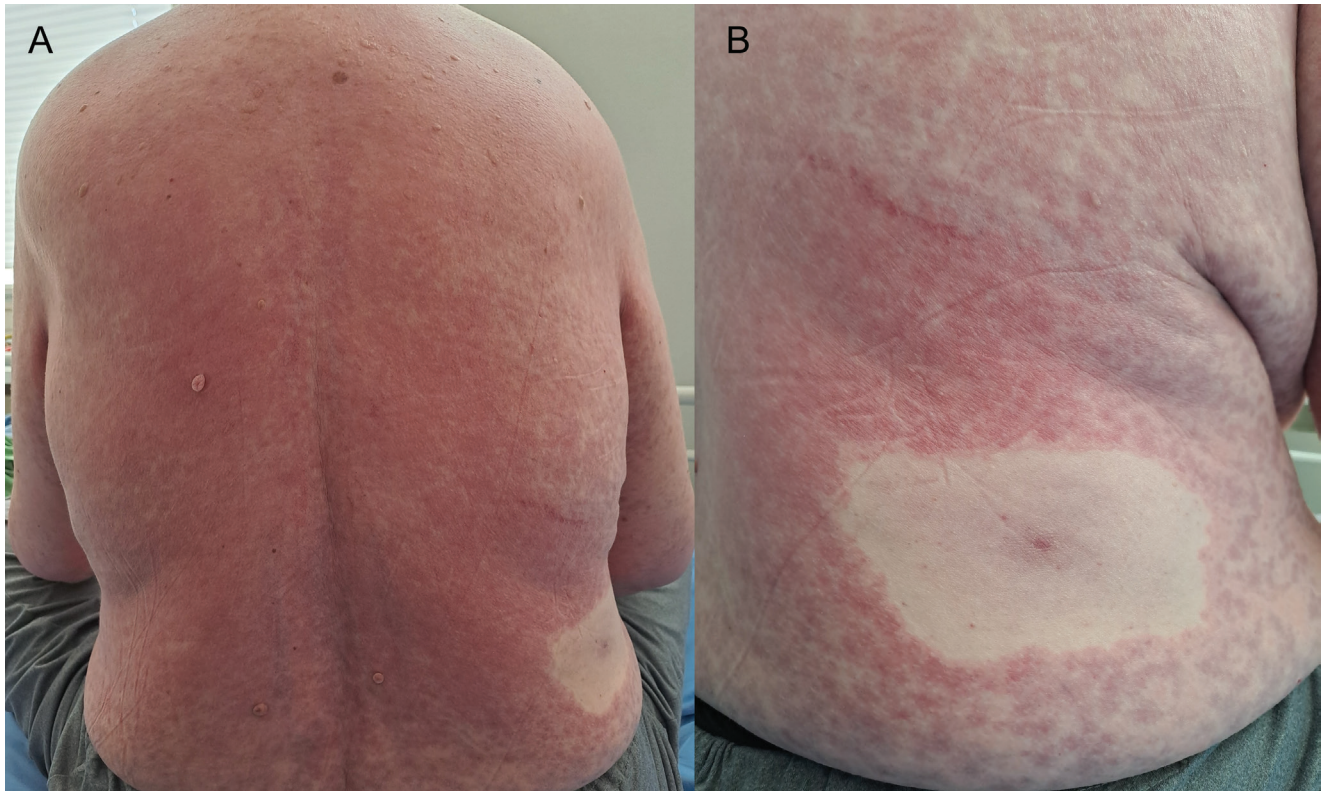


Fig. 1. (A) A widespread exanthem due to amoxicillin with (B) a sharply spared lesion on the right side.

ANSWERS TO QUIZ

Widespread Rash with Localized Sparing: A Commentary

Acta Derm Venereol 2025; 105: adv43058.
DOI: 10.2340/actadv.v105.43058

Diagnosis: Drug exanthem with sparing phenomenon in lesion of active erythema migrans

The Köbner phenomenon (KP) refers to the development of skin lesions of a certain dermatological condition at a previously healthy site due to trauma or other irritant factors (1). KP is probably best known and most often seen in psoriasis, lichen planus, and vitiligo (1). The phenomenon where a previous skin condition has already healed and another, unrelated dermatosis appears in the exact same location is called Wolf's isotopic response (2).

A lesser-known phenomenon is one where areas affected by 1 skin disease are spared of another, unrelated skin condition. This is called the reverse Köbner (Renbök) phenomenon or isotopic sparing phenomenon/isotopic non-response (3). Some authors consider isotopic non-response as a situation where the previous skin condition has already healed, and the Renbök phenomenon only when the 2 skin conditions coexist, but definitive nomenclature has not been established (3, 4). Previously described examples of the Renbök phenomenon include shingles sparing from Stevens–Johnson syndrome (5) and psoriasis sparing from alopecia areata (6).

Erythema migrans (EM) is an early stage of Lyme borreliosis, a disease caused by *Borrelia* species bacteria and transmitted by the bite of a tick (7). EM is an erythematous or violaceous, slowly expanding macule which is typically diagnosed on a clinical basis and treated with a course of antibiotics (7). In the current case, a site of recent EM was sharply spared from a widespread drug exanthem. French colleagues reported on a 60-year-old patient with Renbök phenomenon while being treated for EM with amoxicillin, and comprehensively reviewed cases of other skin diseases with reported Renbök phenomenon (8). *Borrelia burgdorferi* is endemic in Finland and one case of EM spared from drug exanthem has also been previously reported from Finland (4). However, the Renbök phenomenon is more evident in the current case with more recent EM. An amoxicillin-induced urticaria-erythema multiforme-like drug exanthem sparing EM has also been reported in a paediatric patient (9).

The mechanism of EM sparing of a drug reaction-like exanthem has not been established. It is likely that the cytokine environment in active EM is changed and thus it locally suppresses the drug reaction (8).

In a dermatological consultation, the current patient denied having a history of drug hypersensitivity or any skin diseases. An exanthem due to amoxicillin and localized sparing due to EM was diagnosed. Potent topical corticosteroid was applied daily and oral cetirizine 10 mg was introduced. A polymerase chain reaction analysis from a nasopharyngeal swab for respiratory bacteria and viruses was negative, as was a blood culture. The antibiotic treatment for EM was changed from amoxicillin to ceftriaxone and after 2 days of hospitalization she was discharged in a good condition without fever. The exanthem was fading and there was no pruritus. During her hospitalization, she did not develop any symptoms of other infections and on discharge her leukocytes were also within normal range and her C-reactive protein had decreased to 50 mg/L. Thus, her fever and high infectious parameters were considered to be due to the widespread exanthem. A course of doxycycline was prescribed to finish the treatment of EM. Afterwards, serological testing of *Borrelia burgdorferi* was consistent with early Lyme disease.

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