

A case of lichenoid and pigmented drug eruption to acetazolamide confirmed by a lichenoid patch test



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Clinical Implications

- Cutaneous adverse drug reactions to acetazolamide are uncommon. Lichenoid drug reaction are rarely described with sulphonamides. We described the first lichenoid drug eruption due to acetazolamide with a pigmented evolution of the lesions and confirmed by a lichenoid patch test.

TO THE EDITOR:

Allergy and adverse reactions to sulphonamide agents are quite common. Cutaneous adverse drug reactions (CADRs) to oral acetazolamide have been occasionally reported, including maculopapular exanthemas, acute generalized exanthematous pustulosis (AGEP), and Stevens-Johnson syndrome.¹ Two cases of contact dermatitis have been described with topical acetazolamide.² We report here the first lichenoid and pigmented eruption due to oral acetazolamide confirmed by a lichenoid patch test.

A 76-year-old patient was hospitalized in the department of dermatology for a suspicion of AGEP 2 days after receiving oral acetazolamide (2 tablets of 250 mg) for the prevention of vitreous loss during cataract surgery. A pruriginous maculopapular rash of the large folds, initially localized in submammary, inguinal, and axillary areas, was noted without mucosal involvement. Although no pustules were observed, the skin lesions evolved to a fine “collar shape” desquamation as observed in healing of AGEP (Figure 1, A). On clinical examination, the patient remained afebrile and presented bilateral axillary lymphadenopathy and a mild edema of the face. Laboratory investigations showed hyperleukocytosis (10.8 G/L) associated with increased eosinophil count (2.81 G/L). A first skin biopsy revealed vacuolar changes, necrotic keratinocytes in the epidermis, and a band-like cell infiltrate of lymphocytes in the upper dermis compatible with a lichenoid pattern, without the presence of eosinophils (Figure 2, A). Healing occurred in 1 week with emollients. On follow-up, 2 months later, the patient developed hyperpigmented skin patches localized on previous affected areas of the large skin folds with an extension to the face, the upper and lower limbs, and the abdomen (Figure 1, B). A new skin biopsy was performed on the pigmented lesions showing a more marked lichenoid pattern associated with dermal melanophages (Figure 2, B). Six months later, we conducted drug patch tests according to the European Society of Contact Dermatitis guidelines for skin testing in CADRs.^{3,4} Acetazolamide patch tests were prepared with commercial acetazolamide (Diamox, Sanofi, France), diluted at 30% in

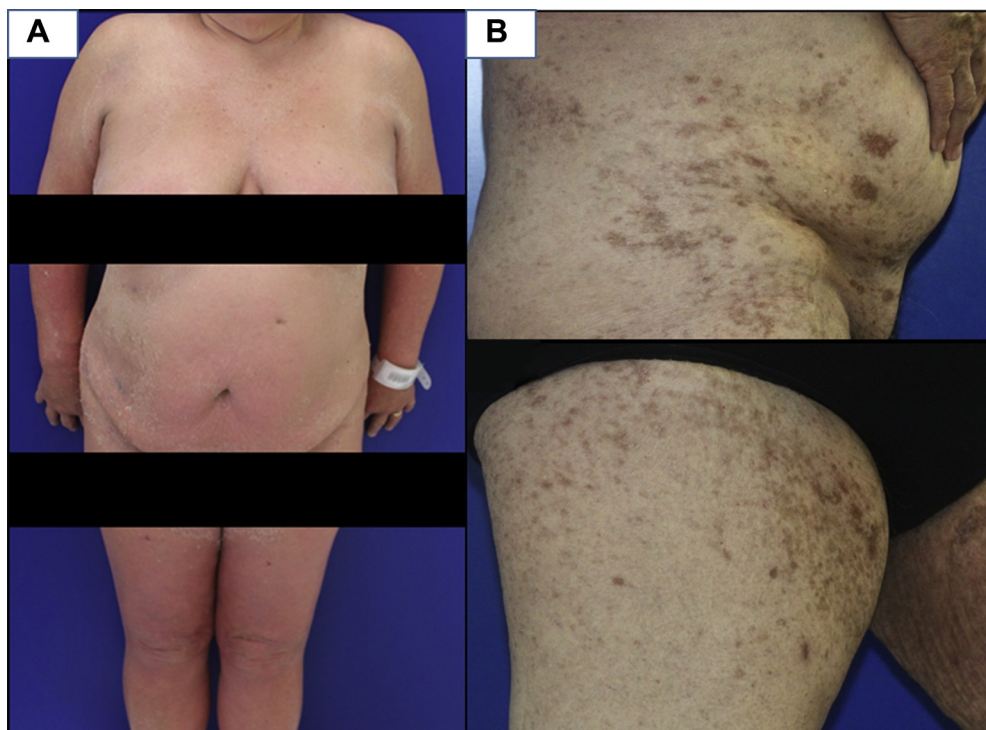


FIGURE 1. Clinical presentation. A, First clinical presentation. B, Pigmented evolution of the skin lesion, at 2 months.

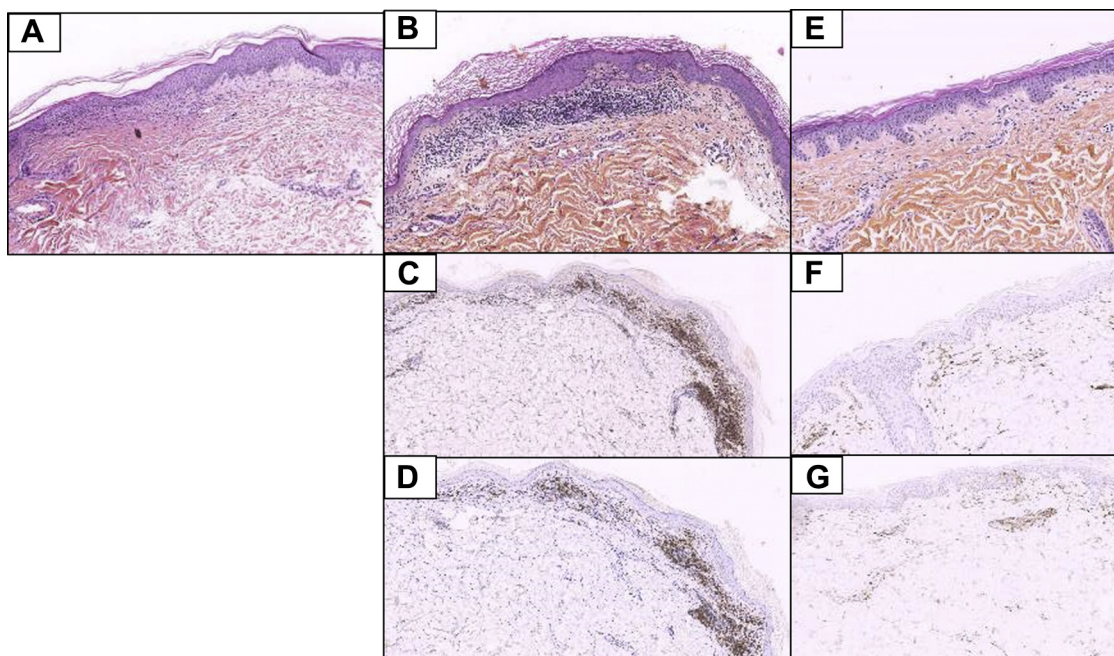


FIGURE 2. Histopathological findings (hematoxylin/eosin and immunohistochemistry). **A**, Initial lichenoid pattern (×25). **B**, Biopsy of a pigmented lesion: more marked lichenoid pattern. T CD4 lymphocytes (**C**) and CD8 (**D**) (×25, ×75, and 75). **E**, Biopsy of the patch test pigmented lesion: same histological findings as the pigmented skin evolution. T CD4 lymphocytes (**F**) and T CD8 (**G**) (×30, ×75, and ×75).

petrolatum and in water. Patch tests were applied both on the healthy skin of the upper back and on a postpigmented thigh skin lesion. Readings were performed on day 2 and day 3. Patch tests were positive for all the preparations of acetazolamide both in healthy skin and in the residual pigmented skin lesion. Interestingly, on follow-up, patch tests presented an hyperpigmented evolution. A skin biopsy of the patch test on the back (healthy skin) revealed the same histological findings as the clinical hyperpigmented drug evolution, associating band-like cell infiltration in the upper dermis and melanophages without eosinophils (Figure 2, E). The lymphocytic infiltrate was characterized on the pigmented skin lesion and on the pigmented patch test by exocytosis of CD4 and CD8 T lymphocytes (Figure 2, C, D, F, and G).

We report to our knowledge the first case of pigmented lichenoid drug reaction to acetazolamide. Acetazolamide is a carbonic anhydrase inhibitor that belongs to the sulphonamide class. Indications for acetazolamide are the treatment of hypercapnia due to chronic obstructive pulmonary disease, idiopathic intracranial hypertension, prevention or treatment of postoperative intraocular pressure after cataract surgery, and prophylaxis of acute mountain sickness. Only a few cases of CADR due to acetazolamide have been previously reported including maculopapular exanthemas, AGEP, Stevens-Johnson syndrome, and contact dermatitis.^{1,2} No specific pigmented evolution had been notified in the literature and no lichenoid infiltrate has been described in biopsies.^{1,2} The time of onset of drug eruptions caused by

acetazolamide varies from several hours to few days after drug intake. This short delay suggests, as in AGEP, a prior sensitization. In our case, the delay was short, but the patient did not report previous systemic use of acetazolamide or other sulphonamides. It was her first cataract surgery. In addition, she did not report previous topical (eye-drops or cream) treatment by acetazolamide. In most of the reported cases, positive patch test results support the diagnosis of delayed-type CADR, as in our case. The clinical presentation is unusual in our case. First, the clinical aspect and the delay was compatible with an AGEP⁵ because lesions were predominantly found in the large folds with a collar-shaped desquamation. We could also consider a drug rash with eosinophilia and systemic symptoms syndrome because of the hyper-eosinophilia, but there was no fever, no visceral involvement, and the delay of onset and the rapid spontaneous improvement did not support this diagnosis. However, the progression toward hyperpigmented skin after resolution of the skin rash is not classically seen in AGEP. Moreover, histopathology did not show classical features of AGEP such as subcorneal spongiform pustules. Strikingly, the lichenoid pattern characterizing the initial skin lesions was similarly observed on the positive skin patch test performed with acetazolamide, confirming the diagnosis of lichenoid drug eruption. Lichenoid drug eruptions are induced by various drugs, such as antimalarials, diuretics, antihypertensive agents, nonsteroidal anti-inflammatory drugs, and anticonvulsants.⁶ Some cases of lichenoid drug eruption caused by other

sulphonamides such as sildenafil and hydrochlorothiazide have been described.⁷⁻⁹

We report the first case of pigmented lichenoid drug eruption due to acetazolamide confirmed by a positive lichenoid patch test result. Hence, we emphasize the usefulness of patch testing in assessing drug imputability. This particular cutaneous side reaction could be added to the spectrum of the cutaneous side effects of acetazolamide.

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Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

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