supported the diagnosis of IP. Since his respiratory symptoms were mild without hypoxaemia, IP was carefully monitored without treatment. Skin lesions were severe and painful, therefore treatment was started with ustekinumab (UST). UST induction treatment (45 mg per month) improved not only the skin lesions (assessed by PASI), but also IP (assessed by extent of GGO on CT and serum KL-6), although IP itself was not treated. After recurrence of skin lesions during UST maintenance treatment (45 mg every three months), IP also worsened. Increased dose of UST (90 mg every three months) without other immunomodulating agents improved both the cutaneous and pulmonary lesions. Intriguingly, in parallel with further relapse of psoriasis skin lesions, IP worsened again, and newly administered secukinumab (which demonstrated efficacy for skin lesions) also suppressed IP activity, as shown by the decrease in KL-6 levels.

In the present case, IP activity fluctuated in parallel with psoriasis severity (measured by PASI), suggesting that common mechanisms were underlying both the lung and skin lesions. UST (and secukinumab) was effective against both organ lesions, suggesting that IL-12, IL-23, and IL-17 were involved in the pathogenesis of both lesions. The coexistence of other connective tissue diseases that may cause IP was excluded clinically, supporting the possible causal link between psoriasis and IP. However, a single case is not sufficient to prove a causal association between psoriasis and IP. To clearly confirm this, lung lesions in psoriasis patients should be more extensively investigated using CT in larger studies. Since IP itself may regress without specific treatment, as in our case, the incidence of IP in psoriasis patients could be underestimated. Careful observation of lung and skin lesions is key for diagnosis of psoriasis-associated pneumonia.

If IP is diagnosed as psoriasis-associated inflammatory disease, treatment for psoriasis with UST or other biologic agents could be effective not only for skin lesions, but also for IP. To avoid unnecessary therapy for IP associated with psoriasis, clinicians should be aware of the presence of IP responding to psoriasis treatment. ■

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Is gliclazide a new antidiabetic drug implicated in the pathogenesis of ocular mucous membrane pemphigoid?

Induced mucous membrane pemphigoid (MMP) is an autoimmune blistering disorder characterized by subepithelial bullae with predominant involvement of mucous membranes. It is clinically, immunologically and histopathologically indistinguishable from idiopathic MMP. In most cases, induced MMP is due to topical agents, whereas systemic drugs are rarely involved. We report the first case of ocular MMP (OMMP) in a diabetic patient treated with gliclazide, a second-generation oral hypoglycaemic agent, belonging to the sulfonamide drugs group. Gliclazide-induced adverse cutaneous reactions are uncommon; in fact, only one case of erythroderma and another of acute generalized exanthematous pustulosis have been reported [1, 2].

An 84-year-old woman was admitted to the Ophthalmology Department because of recurrent conjunctivitis and adhesions of the right ocular plica. One month later, dermatological examination revealed symblepharon lower conjunctiva, tear deficiency, and eyelid malposition (*figure 1A*). The patient had been treated with an ACE inhibitor and metformin (1 g/d) for diabetes mellitus type 2 for 10 years; she had not used ocular topical drugs, and had no prior history of skin diseases. However, a new treatment with gliclazide had been introduced six weeks prior to the dermatological evaluation. Histopathology of the conjunctiva biopsy revealed hyperkeratosis with acanthosis and subepidermal blister formation, necrotic keratinocytes, and moderate inflammation with eosinophils in both the blister area and the underlying dermis (*figure 1B*). Direct immunofluorescence of the peri-lesional mucosa revealed linear deposits of C3 at the basement membrane zone (BMZ) (*figure 1C*). Indirect immunofluorescence and ELISA for BPAg2 and BPAg1 were negative. Western blotting with keratinocyte extracts demonstrated IgG reactivity to BPAg2 and its shed ectodomain (LAD1) (*figure 1D*). The medical history, pharmacological anamnesis (Naranjo algorithm score: 9), clinical features, and immunohistological findings suggested the diagnosis of glicazide-induced OMMP. Gliclazide was discontinued and treatment with topical tacrolimus 0.1% (twice daily), associated with dapsone (50 mg/d), was started. After two months, dapsone was discontinued because of increasing methemoglobinaemia (1.8 mg/dL) and substituted with mycophenolate mofetil (2 g/d). Nine months later, the OMMP partially improved.

OMMP has been associated with topical ocular drug administration, particularly with echothiophate iodide, pilocarpine, idoxuridine, and epinephrine [3, 4]. Different systemic agents have been implicated as a cause of drug-induced bullous pemphigoid, including diuretics, ACE inhibitors, antibiotics, and gliptine (a different group of antidiabetic drugs compared to gliclazide) [5-7]. To our knowledge, no case of OMMP or bullous pemphigoid induced by gliclazide has so far been reported. Our patient is the first case of glicazide-induced OMMP, not associated with gliptin treatment. Gliclazide is a sulphonylurea that stimulates insulin secretion through the beta-cell

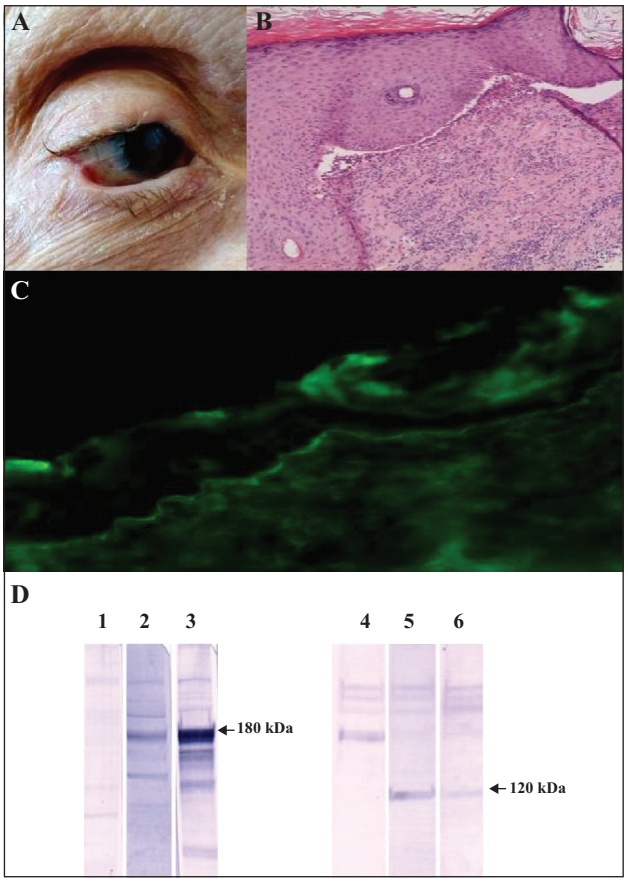

Figure 1. **A**) Clinical features: evidence of symblepharon formation, entropion, and trichiasis with partial keratinization of the entire ocular surface. **B**) Histopathology: hyperkeratosis with acanthosis and subepidermal blister formation, necrotic keratinocytes, and moderate inflammation consisting of eosinophils in both the blister area and underlying dermis (10×). **C**) Direct immunofluorescence: linear deposit of C3 at the basement membrane zone. **D**) Western blot: direct IgG reactivity to BPAg2 (180 KDa) (1: normal healthy serum; 2: OMMP serum; 3: anti-BPAg2 polyclonal antibody) and its shed ectodomain LAD1 (120 KDa) (4: normal healthy serum; 5: bullous pemphigoid patient; 6: OMMP serum).

sulphonylurea receptor, and possibly through a direct effect on intracellular calcium transport [8]. It could be speculated that in patients predisposed to develop autoimmune bullous diseases, an increase in the intracellular calcium levels could stimulate metalloproteinase activity (ADAM-9, ADAM-10) with a consequent stimulation of BPAg2 shedding [9, 10]. In this case, the abnormal abundance of ectodomain shedding (LAD1) could induce the production of specific autoantibodies detected by western blotting, both with keratinocyte culture medium enriched for LAD1 and keratinocyte extracts. Regarding the prognosis of drug-induced OMMP, we speculate that it is similar to that of drug-induced bullous pemphigoid (DIBP). Two types of DIBP have been described in the literature [6]: the first type is referred to as "proper DIBP" and is an acute and self-limited condition which responds promptly when the culprit drug is withdrawn. The second type is referred to as "drug-triggered BP" and follows a more chronic, persistent and severe course, resembling that of classic bullous pemphigoid. Our case could be a "drug-triggered MMOBP" that did not improve after discontinuation of the inducing drug. In conclusion, the clinical presentation of idiopathic and drug-induced OMMP forms are indistinguishable. A detailed pharmacological anamnesis and the Adverse Drug Reaction Probability Scale (Naranjo score) are mandatory to differentiate between these two forms. Many drugs can be involved in the pathogenesis of OMMP, but as far as we know, this is the first report of OMMP induced by gliclazide. Further studies and case reports are needed to confirm the triggering role of gliclazide on OMMP. This drug should nevertheless be considered as a possible inducing agent of OMMP. ■

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