Apremilast-induced rise in intraocular pressure in a chronic plaque psoriasis patient

Dear Editor,

A 52-year-old man with chronic plaque psoriasis on topical steroids presented with unsatisfactory disease control. He had large, erythematous scaly plaques over the lower limbs and a few small plaques over the back, with on-and-off joint pain and knee joint swelling. The psoriasis area and severity index (PASI) was 13.8. After routine investigations he was started on oral apremilast, the dose being gradually increased to 30 mg twice a day. After about two months, he complained of redness and watering from eyes. There was no associated headache, nor a significant family history. Ocular examination showed conjunctival congestion. Intraocular pressure (IOP) measured using Goldmann Applanation Tonometry was 22.7 and 25.2 mmHg (normal range: 10–21 mmHg) in his right and left eyes, respectively. Cold compresses, carboxymethyl cellulose drops, acyclovir ointment, and dexamethasone-moxifloxacin eye drops were advised which were tapered off in a week. His symptoms subsided within a few days, and he was continued on topical steroids and oral apremilast for psoriasis. However, the relief in ocular symptoms was transient and he presented with similar complaints after three weeks; IOP was still elevated: 25.9 and 26.1 mmHg, and at four weeks, 25.3 and 27.9 mmHg in the right and left eyes, respectively. It raised suspicion that the IOP rise could be drug induced. On further probing, he reported similar eye symptoms in the past when he received apremilast from another practitioner. As the only new drug added and continued was oral apremilast, and symptoms increased with increasing doses of apremilast, it was suspected as the culprit agent and stopped. It led to symptomatic relief within days. His IOP decreased to 23 and 26 mmHg on the 4th day and was normal on the 26th day. The patient has been symptom-free for the last six months after the withdrawal of the apremilast.

The Food and Drug Administration has approved apremilast for plaque psoriasis and psoriatic arthritis management.[1] Compared to other systemic agents, this drug has fewer side effects, the most common being gastric upset and the most severe being mood disorders and suicidal tendencies. In a case series, 45 cases of increased tearing, possibly due to apremilast, were noted at standard dosing of 30 mg twice daily.[2] Of these, the dechallenge was positive in 10 cases, the rechallenge was positive in three cases and one had a double-positive rechallenge. There are no details of IOP measurement in those cases and it is possible that a apremilast-induced rise in IOP might be implicated. The Naranjo adverse drug reaction probability scale supports the assumption, which scored +9 in our case.[3] Although we did not do the rechallenge test, indirectly, increasing the dose from 20 mg to 30 mg, leading to increased symptoms, also reiterates it.

Unilateral glaucoma alerts the wary physician to seek secondary etiologies, which were ruled out in our patient. Thus, the unilateral slight rise in pressure was initially attributed to mechanical error, and the patient was treated empirically in the line of conjunctivitis. However, symptom relapse and increasing IOP trend pointed towards an alternate etiology, leading to our suspicion. Further, evidence for raised IOP following short-duration topical steroids is lacking.[4] In our patient, a high-potent topical steroid was applied for < 5% of the body surface area over the thick psoriatic lesions only over the legs. Nevertheless, a suspected topical steroid-induced glaucoma was reported in a patient with chronic use for facial atopic eczema.[5] The site's nearness to the eyes, the high absorption rate of facial skin, and the chronic use might have caused it.

Phosphodiesterase (PDE) inhibitors have shown cross-reactivity within receptor subtypes in different organs, for example, PDE-5 inhibitors may increase blood flow to the ciliary body, increasing IOP.[6] Apremilast, a PDE-4 inhibitor, showed some cross-reactivity with other PDE subtypes.[7] Thus, there is a good chance that apremilast cross-reacts with PDE receptors in the ciliary body, inhibiting them, leading to vasodilation, increasing ciliary blood flow and thus raising IOP.

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To conclude, there might be a temporal association between oral apremilast administration and the rise in IOP, and patients should be educated to seek ophthalmology consultation for new-onset eye discomfort or pain and watering.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of AI-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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References

1. Norris MR, Bielory L. Chronic tearing induced by apremilast. Ann Allergy Asthma Immunol 2018;121:375.
2. Fraunfelder FT, Fraunfelder FW. Possible association between apremilast therapy and increased tearing. Ophthalmic Plast Reconstr Surg 2021;37:S31–S32.
3. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al*. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239–45.
4. Daniel BS, Orchard D. Ocular side-effects of topical corticosteroids: What a dermatologist needs to know. Australas J Dermatol 2015;56:164–9.
5. Ross JJ, Jacob A, Batterbury M. Facial eczema and sight-threatening glaucoma. J R Soc Med 2004;97:485–6.
6. Kerr NM, Danesh-Meyer HV. Phosphodiesterase inhibitors and the eye. Clin Exp Ophthalmol 2009;37:514–23.
7. Andersson KE. PDE5 inhibitors – pharmacology and clinical applications 20 years after sildenafil discovery. Br J Pharmacol 2018;175:2554–65.