Unexpected outcome (positive or negative) including adverse drug reactions

Tacrolimus-induced unilateral ischaemic optic neuropathy in a non-transplant patient

Monika Gupta, Reema Bansal, Nikhil Beke, Amod Gupta

Department of Advanced Eye Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Correspondence to Professor Amod Gupta, dramodgupta@gmail.com

Summary

Tacrolimus is commonly used as an immunosuppressant in organ transplantation. Although it is well tolerated, visual loss has been known as a rare but serious complication of this drug. We report a woman developing visual complaints while on tacrolimus therapy for nephrotic syndrome. Omission of the drug led to partial visual field recovery. Visual complications in patients receiving tacrolimus should alert the treating physicians for timely discontinuation of the drug.

BACKGROUND

We report the first case of tacrolimus-induced optic neuropathy in a non-transplant patient who received it for maintaining remission of nephrotic syndrome. Tacrolimus (FK-506, Prograf; Fujisawa USA, Inc, Deerfield, Illinois, USA) is an immunosuppressive agent approved for use in patients receiving solid organ transplantation to prevent graft rejection. While corticosteroids remain the mainstay of therapy, due to its effect on cytokines such as interleukin-2 and interferon- γ , tacrolimus is increasingly

being used as an off-label drug in nephrotic syndrome in patients who show steroid resistance or steroid dependence. While visual loss following cortical blindness or optic neuropathy due to tacrolimus use has been reported in transplant patients,^{1–7} there is no report of visual loss when it is used as an off-label drug.

CASE PRESENTATION

A 35-year-old woman presented with decreased vision in the left eye since 2 weeks. She had been diagnosed to have

Figure 1 Fundus photograph of left eye showing optic disc oedema (A), Humphrey visual field showing an inferior altitudinal field defect in the left eye (B), fundus fluorescein angiography showing delayed perfusion of the superior half of the disc in the early phase (C) and with diffuse disc staining in the late phase (D).

nephrotic syndrome 2 years earlier and was receiving tacrolimus 1 mg twice a day orally for maintaining immunosuppression. The best corrected visual acuity (BCVA) was 6/6 in both eyes. The intraocular pressures were 19 mm Hg in both eyes. The right eye examination was unremarkable. The left eye had a relative afferent pupillary defect (RAPD). There was no associated pain on eye movements. The left eye showed optic disc oedema (figure 1A). There was no vitreous activity or retinal infiltrates. The visual field examination by Humphrey visual field analyser showed an inferonasal altitudinal field defect in the left eye (figure 1B). The fundus fluorescein angiography showed a delayed perfusion of the superior half of the disc in the early phase with diffuse disc staining in the late phase (figures 1C,D). A diagnosis of anterior ischaemic optic neuropathy (AION) was made. There was no history of hypertension or smoking.

INVESTIGATIONS

The blood pressure was 120/80 mm Hg. She underwent relevant investigations including complete blood counts,

erythrocyte sedimentation rate, coagulation profile, lipid profile, serum homocysteine levels, renal and liver function tests, along with peripheral blood film examination. None of the investigations was contributory.

TREATMENT

Considering the possibility of tacrolimus-induced optic neuropathy, tacrolimus was discontinued and oral prednisolone (1 mg/kg/day) was started. An alternative immunosuppressive agent was not considered as her disease was in remission.

OUTCOME AND FOLLOW-UP

During follow-up, the left eye optic disc oedema resolved and oral corticosteroids were gradually tapered. The Humphrey visual field performed at 4 months of follow-up showed improvement of the inferonasal altitudinal field defect (figure 2). At 6 months of follow-up, the BCVA was 6/6 in left eye and RAPD was present. The disc oedema had subsided with pallor of optic disc and retinal nerve fibre layer defect along the superotemporal arcade (figure 3A,B).

Figure 2 Humphrey visual field showing mild improvement of the inferior altitudinal field defect in the left eye at 4 months of follow-up.

Figure 3 Fundus photograph of left eye at 6 months follow-up showing optic disc pallor (A) and red-free photograph showing retinal nerve fibre layer defect in superotemporal quadrant (B).

DISCUSSION

Bilateral optic neuropathy secondary to tacrolimus has been previously reported in three cases.^{4 5 7} Another report could not confirm bilaterality as the fellow eye was affected severely by diabetic retinopathy.⁶ Our patient had a unilateral involvement. A direct neurotoxic effect of tacrolimus therapy has been postulated that causes axonal swelling, increased water content and oedema of neural tissues. The breakdown of blood–brain barrier may enhance the passage of lipophilic agents such as tacrolimus and cyclosporine. The myelin sheath becomes an attractive site for binding of these drugs due to its high lipid content.¹ Vasoconstriction and tissue ischaemia following tacrolimus therapy have also been hypothesised to cause anterior ischaemic optic neuropathies.⁷

Tacrolimus is primarily used after allogenic organ transplantation, in atopic dermatitis and inflammatory bowel disease. It has also been reported to be an effective, well-tolerated treatment in children with nephrotic syndrome who developed resistance, dependence or intolerable side effects from other therapies.⁸ In a non-transplant patient, acute tacrolimus toxicity has been reported in the form of renal failure and metabolic acidosis.⁹ Visual loss following ischaemic optic neuropathy due to tacrolimus in patients of nephrotic syndrome may occur similar to that seen in transplant patients. Clinicians should be aware of this rare, but sight-threatening, complication of tacrolimus and reserve it only for selected cases of nephrotic syndrome. It is highly likely that this patient developed the AION in association with the drug tacrolimus given the remission state and the absence of hypertension. However, a chance occurrence of AION in a potentially vasculopathic individual with nephrotic syndrome cannot be completely discounted.

Learning points

- ▶ Tacrolimus-induced optic neuropathy has not been reported in non-transplant patients.
- ▶ Visual loss due to tacrolimus can be significant.
- ▶ Clinicians should be aware of this sight-threatening complication that may revert following timely discontinuation of the offending drug.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Gupta M, Bansal R, Beke N, Gupta A. Tacrolimus-induced unilateral ischaemic optic neuropathy in a non-transplant patient. *BMJ Case Reports* 2012;10.1136/bcr-2012-006718, Published XXX

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