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Delayed Onset of Bilateral Anterior Uveitis Secondary to Erlotinib

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ABSTRACT

Anterior uveitis is a rare complication associated with erlotinib. We report a unique case of delayed onset bilateral acute anterior uveitis at 21 months after commencement of erlotinib and review previous case reports in the literature on erlotinib associated anterior uveitis. Our patient was treated with frequent topical corticosteroid and a cycloplegic agent with good response whilst continued on erlotinib. Physicians should be aware of this potential complication and an urgent ophthalmology review is warranted when patients on erlotinib present with blurry vision, ocular injection and pain. Topical corticosteroid therapy often produces good clinical outcome.

Keywords: Erlotinib, Anterior uveitis, Epidermal growth factor receptor (EGFR), Tyrosine kinase inhibitor, Non-small cell lung cancer

INTRODUCTION

Erlotinib is an oral small molecule inhibitor of epidermal growth factor receptor (EGFR) tyrosine kinase. It is an approved therapy for advanced non-small cell lung cancer (NSCLCa) patients [1]. Common ocular adverse reactions with the use of erlotinib include conjunctivitis and keratoconjunctivitis sicca. Less common ocular adverse reactions include corneal perforation, corneal ulceration and episcleritis. Anterior uveitis is a rare complication associated with erlotinib that has been reported in only a few cases [2-7] **(Table 1)**.

CASE HISTORY

We present a case of a 69-year-old Middle Eastern man with stage IV EGFR mutated lung adenocarcinoma with liver, nodal and paraspinal metastasis. He underwent left upper lobectomy followed by three cycles of adjuvant cisplatin and vincristine chemotherapy. His disease progressed requiring debulking of T10-12 paraspinal metastasis and radiotherapy 60Gy to the area. He was commenced on erlotinib standard dose 150 mg daily, which he tolerated well, with only a mild acneiform rash on his face managed with oral doxycycline. There was a complete response to erlotinib with no other detectable disease apart from a stable paravertebral mass on CT.

At 21 months post commencement of erlotinib therapy, he presented with a 5-day history of blurred vision, ocular injection and photosensitivity. There was no prior history of systemic inflammatory disease or uveitis. He had an unremarkable eye assessment 5 years prior. He has type 2 diabetes, dyslipidaemia, atrial fibrillation and asthma. His other regular medications include aspirin, metformin, rosuvastatin, sotalol and ventolin.

On ophthalmic examination his corrected visual acuity was 6/7.5 bilaterally and the intraocular pressure 12 mmHg in both eyes. There was bilateral anterior chamber inflammation (2+ cells) and flare (2+) (Standardization of Uveitis Nomenclature). The vitreous was quiet and there was no evidence of macular oedema or posterior segment involvement. The patient demonstrated palmo plantar erythron dysaesthesia from erlotinib. The patient did not have signs or symptoms of sarcoidosis or spondyloarthropathy.

Screening for infectious and inflammatory causes of bilateral anterior uveitis was unremarkable. In particular syphilis and Quanti FERON gold testing were negative. The HLA-B27 and ACE level were normal. The patient was diagnosed

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with bilateral anterior uveitis secondary to erlotinib. He was commenced on topical corticosteroid drops (prednisolone acetate) hourly and a cycloplegic agent (topical atropine). The anterior inflammation improved with topical steroid therapy alone and the patient's vision remained stable. Erlotinib was continued throughout and hence not compromising his NSCLCa management.

Table 1. Summary of case reports on erlotinib related anterior uveitis.

Author	Age/Gender	Clinical Features	OcularFindings	Treatment	Outcome
Lim [2]	63F	Red watery eyes, photophobia, reduced vision, dull ache in both eyes 6 weeks post erlotinib	Bilateral severe anterior uveitis with almost complete posterior synechiae. Fine keratic precipitates, cells (3+) and flare (2).	Prednisolone acetate 1% and atropine 1%	Anterior uveitis and posterior synechiae resolved in 2 weeks
Ali [3]	68F	Bilateral red and sore eyes	VA 6/12 OD and 6/36 OS Bilateral non-granulomatous anterior uveitis with posterior synaechae.	Discontinued erlotinib. Prednisolone 1% Q1H, cyclopentolate 1% TDS and betnesol ointment.	Uveitis responded well, posteriorsynaechae resolved, symptoms improved
Kirkpartrick [4]	77F	Bilateral floaters 6 weeks post erlotinib	VA 20/30 OD and 20/40 OS Multiple, non-granulomatous keratic precipitates OD, none OS. Cells (3+) and flare (1+) OD Cells (2+) and flare (1+) OS.	Prednisolone acetate Q2H OD and 4 times daily OS, followed by 40mg posterior sub-Tenon's triamcinolone injection OD. Continued erlotinib.	Inflammation slowly resolved over 3 months; VA stable. Patient developed brain metastasis and died 3 months later.
Klein [5]	67F	Blurred vision, floaters in both eyes 3 weeks post erlotinib	VA 20/30 both eyes, diffuse small to medium sized keratic precipitates and extensive Koeppe nodules. Cells (3+) and flare (2+).	Topical steroid Q2H, continued on erlotinib.	Inflammation resolved in 3 weeks
	73F	Floaters and flashes in both eyes 6 weeks post erlotinib	VA 20/30 bilaterally. Cells (2+) and flare (1+).	Topical steroid 6 times daily. Erlotinib discontinued due to lack of systemic efficacy.	Inflammation resolved in 4 weeks
Chan [6]	67F	Reduced visual acuity and floaters in both eyes 6 weeks post erlotinib	VA 6/6 bilaterally. Bilateral AAU, fine keratic precipitates on both corneas and cells (1-2+)	Topical guttae dexamethasone 0.1% 2 hourly, guttae cyclopentolate 1% TDS Erlotinib dose reduced from 150mg to 100mg daily	Anterior uveitis resolved after 1 week.
Tamura [7]	87M	Pain and reduced vision in left eye	VA log MAR +2.0 both eyes. Left eye previously log MAR +0.10. IOP 10mmHg right eye, 33mmHg left eye. Fibrin deposited in anterior chamber. Left eye corneal ulcer.	Discontinued erlotinib. Topical antibiotics.	Left eye VA improved to log MAR 0. Patient passed away due to heart failure.

DISCUSSION

Anterior uveitis is inflammation of the iris and/or anterior part of the ciliary body. Patients may present with pain, erythema and blurred vision. Uveitis is often idiopathic, however also frequently occurs in association with systemic conditions, such as infections and inflammatory diseases. Erlotinib associated anterior uveitis is rare with only 7 cases

reported in the literature **(Table 1)**. In most cases, patients presented with ocular symptoms within 6 weeks after commencing erlotinib. Our patient did not develop ocular symptoms until 21 months into erlotinib therapy. He also had papulopustular acneiform eruptions, which are typical cutaneous side effects of EGFR inhibitors such as erlotinib [8]. Initial treatment in the literature includes topical corticosteroid drops and a mydriatic agent. One case required posterior sub-Tenon's triamcinolone injection [4]. In 3 cases erlotinib was discontinued [2,5,7]. In 1 case the dose of erlotinib was reduced [6]. All patients achieved resolution of uveitis with treatment.

Whilst a rare complication, there are increasing number of cases of erlotinib associated anterior uveitis with its growing use in cancer treatment. It is important for treating physicians and ophthalmologists to be aware of this complication and to educate their patients as to potential ocular side effects. An ophthalmology review is certainly required for all patients on erlotinib who have blurred vision, ocular pain and photophobia. Baseline ocular screening may also be considered in patients commencing erlotinib therapy, particularly those with co-existing systemic disease such as diabetes or inflammatory arthropathies.

CONCLUSION

We report a case of erlotinib associated delayed onset acute anterior uveitis. This is different to other reported cases where onset is usually within a few weeks of starting erlotinib. Similar to other cases, our patient responded well to topical corticosteroid treatment whilst being able to continue with erlotinib. We wish to highlight acute anterior uveitis as a potential complication with erlotinib use. Based on our review, clinical outcome is often favorable with treatment and in some cases with continuation of erlotinib therapy.

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