Ibrutinib-related uveitis: A case series from two tertiary centres in the United Kingdom

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Background

- Ibrutinib irreversibly inhibits Bruton's Tyrosine Kinase, disrupting B-cell receptor signalling, cell survival and proliferation
- Ibrutinib is usually used to treat B-call malignancies, including chronic lymphocytic leukaemia, mantle cell lymphoma and lymphoplasmacytic lymphoma.
- Four previous case reports to date of ibrutinib-related uveitis (IRU)

a) Sclerouveitis
b) Anterior uveitis
c) Hypertensive anterior uveitis

- Only two cases reported resolution of uveitis with discontinuation of ibrutinib

Objectives and Methods

- Retrospective case series of patients from two UK tertiary centres with ibrutinib-related uveitis

Features of ibrutinib-related uveitis (IRU)

Example Patient 2:

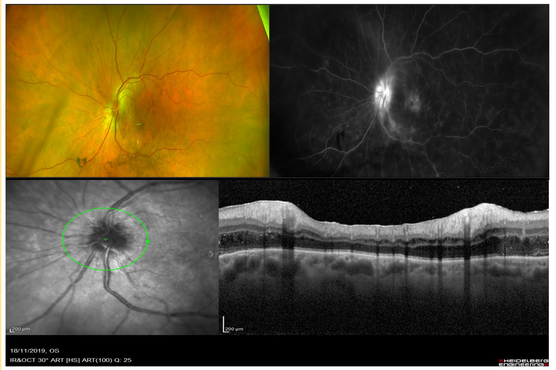


Figure 1: Papillitis left eye due to IRU

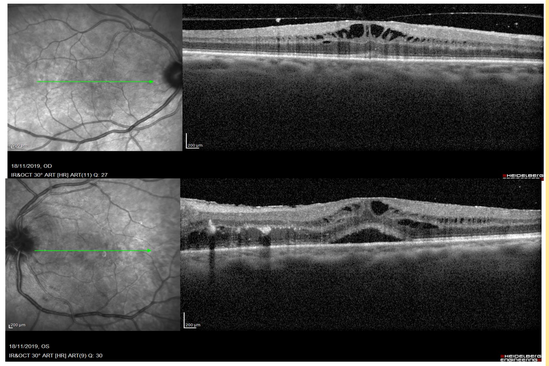


Figure 2: Bilateral macular oedema due to IRU

Discussion points

- Evidence of temporal association between ibrutinib and the development of ocular inflammation.
- IRU is a type D delayed drug response due to increase in Th1-based immune responses
- Downstream inhibition of interleukin-2-inducible T-cell kinase and Tec protein kinase, causing hyphaema and vitreous haemorrhage (bleeding events)

Results

Age	Gender	Ibrutinib dose	Time to uveitis onset	BCVA Right eye	BCVA left eye	Ophthalmic findings	Treatment	Ibrutinib cessation (time from uveitis)	Clinical outcome
68	Male	480mg	8 months	6/9	6/9	Bilateral AC cells, posterior synechiae, left moderate vitreous haze Bilateral disc swelling and macular oedema	Topical steroid and topical cycloplegics	Yes (1 month)	Resolved uveitis, disc swelling and macular oedema Recurrence of lymphoma upon stopping ibrutinib Uveitis recurred upon restarting ibrutinib (half dose), so stopped 2 weeks later and changed to Acalabrutinib
68	Female	560mg	36 months	6/12	6/60	Bilateral anterior and intermediate uveitis with papillitis and macular oedema	Oral steroid Right orbital floor triamcinolone injection Intravitreal Ozurdex Topical steroid and NSAIDs	Yes (29 months)	Improved macular oedema upon stopping ibrutinib No lymphoma recurrence
54	Male	420mg	13 months	6/6	6/9	Recurrent bilateral anterior uveitis with left hyphaema and vitreous haemorrhage	Topical steroid (2nd episode) topical steroid and then left periocular steroid injection, Topical Bimatoprost/Timolol	Yes (19 months)	Ibrutinib changed to venetoclax, but due to leukaemia progression, acalabrutinib commenced
55	Male	420mg	15 months	6/6	6/9	Right anterior uveitis with keratic precipitates and posterior synechiae	Topical steroid and topical cycloplegics	Yes (5 days)	Resolved uveitis Ibrutinib restarted at low dose, but uveitis recurred, so discontinued. Leukaemia in remission
60	Male	420mg	8 months	6/9	6/9	Bilateral anterior uveitis with keratic precipitate	Topical steroid	Yes (16 days)	Improved uveitis Venetoclax introduced first, then low dose ibrutinib gradually increasing to full dose with no uveitis recurrence
69	Male	420mg	22 months	6/6	6/12	Bilateral anterior uveitis and macular oedema	Topical steroid and NSAIDs	Yes (at presentation)	Resolved uveitis. Venetoclax commenced with no further flare-up of uveitis
76	Male	420mg	48 months	6/18	6/9	Bilateral panuveitis with macular oedema	Topical steroid	Yes (7 days)	Resolved uveitis. Ibrutinib restarted at 280mg gradually increased to 420mg. Patient died 20 months later
84	Male	420mg	9 months	6/12	6/9	Recurrent bilateral anterior uveitis	Topical steroid	Yes (12 months)	Ibrutinib dose reduced to 280mg due to acute kidney injury, then full dose when resolved. No uveitis flare up as ibrutinib stopped due to amyloidosis.
77	Female	420mg	27 months	6/6	6/12	Bilateral anterior uveitis	Topical steroid Chloramphenicol and ganciclovir eye ointment	No	Uveitis resolved No uveitis flare up on prophylactic once daily topical steroid

Conclusion

- Ibrutinib-related uveitis extends beyond simple anterior uveitis and can be vision threatening
- Ibrutinib cessation seems to be the definitive management (8 cases in our series). Ophthalmologists need to liaise with haemato-oncologist closely to help with making this decision

References

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