

White dot syndrome like presentation secondary to Ibrutinib therapy: A Case Report

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BACKGROUND

- Targeted anticancer agents such as small molecule kinase inhibitors have revolutionised cancer treatment
- However, the effectiveness of these drugs is limited by the growing evidence of adverse reactions
- Small molecule kinase inhibitors and monoclonal antibodies have previously been associated with uveitis
- Ibrutinib is an irreversible small molecule Bruton-tyrosine kinase inhibitor that is licensed for the treatment of certain leukaemias and lymphomas
- We report a case of Ibrutinib-associated panuveitis and white retinal opacities in a 48-year-old gentleman of Indian origin

CASE REPORT

- A 49-year-old male of Indian heritage with a history of Waldenstrom's macroglobulinaemia presented with red, painful eyes and blurred vision 2 months after starting Ibrutinib treatment.
- No significant past ocular history
- Clinical findings on initial presentation (Aug21)
 - 10/7 Hx red, painful eyes; 5/7 blurred vision
 - RE 6/12, LE 6/5
 - BE: Grade 4 AC cells and flare.
 - Bioscore 1 with some vitreous cells
 - Fundus: Peripheral white spots on retina with small retinal haemorrhages in periphery (Figure 1)
- Investigations including infectious and autoimmune screening: NAD
- Working diagnosis: *Panuveitis secondary to Ibrutinib*
- Sep21: Ibrutinib was stopped, and PO prednisolone commenced
- Late Sep21: Some vitreous activity, white opacities resolved
- Admitted for rising IgM paraprotein levels a few days later and restarted on a lower dose of Ibrutinib
- Oct21: White opacities seen again on retina

Currently the patient is on full dose Ibrutinib with a reducing regime of prednisolone. There are no white opacities on the retina.



Figure 1: (Left) White opacities in peripheral retina highlighted, (right) White opacities did not autofluoresce

DISCUSSION

- There are only a small number of cases in literature detailing uveitis in relation to Ibrutinib
- Additional ocular adverse effects that have been identified in association with Ibrutinib therapy include cataracts, red/dry eyes, subconjunctival haemorrhage, branch retinal artery occlusion and cystoid macular oedema
- This is the first case to mention white retinal opacities associated with Ibrutinib
- We have proved a direct relationship between Ibrutinib and these white opacities (Figure 2)
- Proposed theories to explain the mechanism of adverse ocular reactions secondary to Ibrutinib:
 - Ibrutinib displays inhibitory off-target effects on other receptor tyrosine kinases
 - Ibrutinib's inhibition of interleukin-2-inducible T-cell kinase, causes a Th1 shift, and therefore a pro-inflammatory Th1-based immune response
- Patients with pre-existing ocular conditions have been found to be at higher risk of developing ocular adverse effects from kinase inhibitors and monoclonal antibodies
- Thus, there may be a potential role for routine ophthalmic reviews and/or screening of patients with pre-existing ocular conditions placed on Ibrutinib

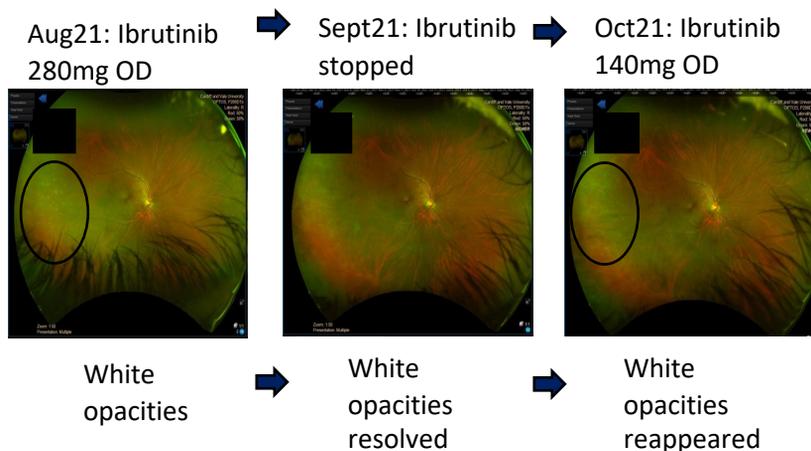


Figure 2: Timeline of Ibrutinib therapy with the corresponding Optos images

CONCLUSION

- Our case has highlighted that the possibility of drug-induced uveitis in the setting of Ibrutinib should be considered following exclusion of other causes
- This is the first case in literature to report white retinal opacities in association with Ibrutinib

REFERENCES

Scan QR code for references

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BARS BRITISH ASSOCIATION OF RETINAL SCREENING

