

WHITE-DOT SYNDROME LIKE PRESENTATION SECONDARY TO IBRUTINIB THERAPY: A CASE REPORT

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BACKGROUND

M DOB: 09/04/1973

- September 2018: Presented with leg weakness and numbness. MRI demonstrated transverse myelitis
- September 2018: Waldenstrom's macroglobulinaemia, MYD88 positive
- November 2019: Initiated on R-CD
 - Admitted following 2nd R-CD cycle with fever, deranged LFT and raised inflammatory markers. No infective cause found. Thought to be 2ndry to cyclophosphamide
- November 2019 – July 2021: Rx on hold due to COVID-19



BACKGROUND

M DOB: 09/04/1973

- 1st July 2021: Commenced on Ibrutinib (2nd line for WM)
- 28th August 2021: Presented to Eye Casualty with red, painful eyes and blurred vision



INITIAL PRESENTATION TO EYE CASUALTY

- HPC: 10/7 red, painful eyes, 5/7 blurred vision (R>L)
- POH: Myopia
- DH: Ibrutinib, co-trimoxazole, allopurinol, aciclovir (started 2/52 ago)
- SH: Driver, no pets, no recent travel. Heterosexual, not sexually active. Indian heritage
- ROS: Mouth ulcers (responding to aciclovir), non-resolving severe fungal toe infection

- OE: VA 6/12, 6/5
 - No RAPD, full EOM, IOP 13 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



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Jan 12, 2022 Dec 15, 2021 Dec 8, 2021 Nov 22, 2021 Nov 8, 2021 Nov 1, 2021 Oct 18, 2021 Oct 11, 2021 Oct 6, 2021 Oct 4, 2021 Sep 27, 2021 Sep 20, 2021 Sep 13, 2021 Sep 10, 2021 Sep 8, 2021 Sep 6, 2021 Sep 3, 2021 Aug 31, 2021



Presets
Presentations
View Tools
Series

CHADHA Prabhjote Mr
DOB: Apr 9, 1973
Sep 8, 2021
8:54:17 AM
4000
4000



Cardiff and Vale University
OPTOS, P200DTx
Laterality: R

Zoom: 1.28
Presentation: Multiple

1/1
15

CHADHA Prabhjote Mr
DOB: Apr 9, 1973
Sep 8, 2021
8:54:08 AM
4000
4000



Cardiff and Vale University
OPTOS, P200DTx
Laterality: R
Red: 50%
Green: 50%

Zoom: 1.50
Presentation: Multiple

1/1
15





Early-onset invasive aspergillosis and other fungal infections in patients treated with ibrutinib

David Ghez¹, Anne Calleja², Caroline Protin³, Marine Baron⁴, Marie-Pierre Ledoux⁵, Gandhi Damaj⁶, Mathieu Dupont⁷, Brigitte Dreyfus⁸, Emmanuelle Ferrant⁹, Charles Herbaux¹⁰, Kamel Laribi¹¹, Ronan Le Calloch¹², Marion Malphettes¹³, Franciane Paul¹⁴, Laetitia Souchet⁴, Malgorzata Truchan-Graczyk¹⁵, Karen Delavigne¹⁶, Caroline Dartigeas¹⁷, Loïc Ysebaert³, French Innovative Leukemia Organization (FILO) CLL group

Panuveitis Presumed Secondary to Ibrutinib Therapy

Sruthi Arepalli, Sunil K Srivastava, Kimberly Baynes, Arthi G Venkat

PMID: 34038692 DOI: 10.3928/23258160-20210302-08

Ibrutinib-related uveitis: A report of two severe cases

Marcela Bohn^{id}, Luciano Bravo-Ljubetic, Richard W J Lee, more...

First Published March 15, 2021 | Case Report | Find in PubMed

<https://doi.org/10.1177/11206721211001268>

Article information 



CLINICAL SCIENCES

Hyperviscosity-Related Retinopathy in Waldenström Macroglobulinemia

Marcel N. Menke, MD; Gilbert T. Febr, PhD; J. Wallace McMeel, MD; Andrew Bramagan, BS; Zachary Hantre, BS; Steven P. Tizon, MD, PhD

CORRECTED PROOF

Uveitis related tuberculosis presenting as bilateral panuveitis

Ignacio Lopez, MD (Res), MD, PhD, Padmini Parthasarathi, MD, PhD, L, MD, Thomas O'Hanrahan, MD, Angela Rivers, MD, Manuraj Singh, MD, PhD, MD, Mauricio Arias, PhD, MD

Journal of Intensive Care Medicine, 36(10), <https://doi.org/10.1177/08850666211001268>

October 2021 Article history 

Call for Action: Invasive Fungal Infections Associated With Ibrutinib and Other Small Molecule Kinase Inhibitors Targeting Immune Signaling Pathways

Georgios Chamilias, Michail S Lionakis, Dimitrios P Kontoyiannis

Clinical Infectious Diseases, Volume 66, Issue 1, 1 January 2018, Pages 140-148,

<https://doi.org/10.1093/cid/cix487>

Published: 27 September 2017 Article history 



DIFFERENTIALS

- Infective cause (TB/Viral/fungal e.g. aspergillus)
- Inflammatory/autoimmune/white dot syndrome
- Drug reaction to ibrutinib
- Mixed anterior uveitis from ibrutinib and posterior changes from Waldenstrom's macroglobulinaemia



INVESTIGATIONS

- ❖ Infectious screen negative (incl HIV, TB, Hep C, toxoplasma, parvovirus and HTLV)
- ❖ *Positive IgG for CMV (but PCR negative)*
- ❖ VZV, HSV negative
- ❖ Blood cultures negative
- ❖ Aspergillus negative, TB Mantoux negative
- ❖ Autoimmune screen e.g. ANA, ANCA, HLA



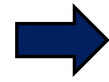
P.C

M DOB: 09/04/1973

- September 2021: Vitritis with white dot opacities in BE
 - Ibrutinib stopped by haematology
 - PO Prednisolone commenced by Ophthalmology
- Late September: White spots cleared following cessation of Ibrutinib
- 24/09/21: Admitted for rapidly rising IgM
 - Ibrutinib started at lower dose (140mg OD)



Aug21: Ibrutinib 280mg OD



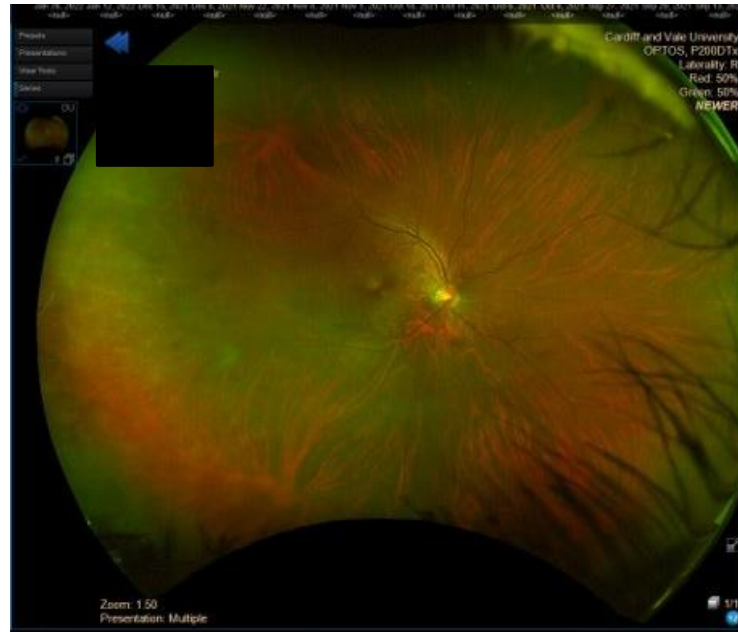
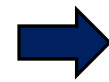
Sept21: Ibrutinib stopped



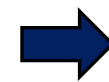
Oct21: Ibrutinib 140mg OD



White dots



White dots resolved



White dots reappeared



White dots

Ibrutinib



#2786830



Question	Scoring	Rationale
Are there previous conclusive reports on this reaction?	No (+0)	There are other reports of uveitis in literature, but this is the first report describing white dots on the retina.
Did adverse event appear after the suspected drug was given?	Yes (+2)	Symptoms first started following commencement of Ibrutinib in July 21.
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	Yes (+1)	White opacities resolved when Ibrutinib was stopped.
Did the adverse reaction appear when the drug was readministered?	Yes (+2)	White dots reappeared when drug was restarted.
Are there alternative causes that could have caused the reaction?	No (+2)	A systemic approach was taken to exclude other differential diagnoses.
Did the reaction reappear when a placebo was given?	Not known (+0)	A placebo was not given.
Was the drug detected in any body fluid in toxic concentrations?	Not known (+0)	Serum concentrations of the drug were never measured.
Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	Yes (+1)	The patient had a less severe anterior and posterior chamber reaction and fewer white dots at a lower dose of the drug.
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	Not known (+0)	The patient did not have previous exposure to this drug.
Was the adverse event confirmed by any objective evidence?	Yes (+1)	A detailed ophthalmic assessment was performed.
Total (≥9 definite, 5-8 probable, 2-4 possible, <2 doubtful)	9	



WHITE DOT SYNDROME TYPE-PICTURE



IN SUMMARY

- Pan-uveitis – **idiosyncratic drug reaction to Ibrutinib**
- 1st case of ‘white dot syndrome like picture’ to be described *worldwide* in association with Ibrutinib
- Systematic approach to bilateral uveitis



ANY QUESTIONS?



REFERENCES

1. Salmon, J. 2019 *Kanski's Clinical Ophthalmology* 9th edition, Elsevier Health Sciences
2. Bohn, M. et al. (2021) Ibrutinib-related uveitis: A report of two severe cases. *European Journal of Ophthalmology*. Pp 1-4
3. Arepalli, S. et al. (2021) Panuveitis presumed secondary to Ibrutinib Therapy. *Ophthalmic Surgery, Laser and Imaging Retina*. 52 (3) pp 160-164
4. Mehraban, P. et al. (2021) Recurrent uveitis related to Ibrutinib for treatment of chronic lymphocytic leukaemia. *Ocular Immunology and Inflammation*. Pp 1-4
5. Chiu, Z. et al. (2022) Ibrutinib-related uveitis: A case series. *American Journal of Ophthalmology Case Reports*. 25 pp 1- 6

Informed consent

Informed consent was obtained for the use of the case and imaging from the patient

