

When mystery turns to misery: the challenge of investigating a Masquerade Syndrome

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Case Presentation

- 88- year old man referred by his ophthalmologist with decreased vision, elevated intraocular pressure, floaters and a retinal lesion in his left eye
- Medical history: prostate carcinoma and hairy cell leukemia (HCL), both in remission after treatment with leuporeline and cladribine
- Examination of the left eye: keratic precipitates, low anterior chamber inflammation, vitritis with non-uniform cellular infiltrate and a yellowish retinal lesion three disc diameters in size, accompanied by intraretinal hemorrhages and occlusive vasculitis
- Best-corrected visual acuity (VA): 20/25 OD and 20/30 OS
- Optical coherence tomography (OCT) of the lesion: thickening of the inner and outer retinal layers and subretinal fluid
- Fluorescein angiography: local hyperfluorescence and retinal vasculitis (Figure 1)

Diagnostic Procedure and Therapy

- Diagnostic anterior chamber tap: Epstein-Barr-virus (EBV) positive
- Treatment initiation with valacyclovir, accompanied by systemic and topical steroids one week later
- Initial follow-up: progression of the findings over a two month period while vision remained stable
- After tapering of Prednisone to 20 mg per day: VA decrease to hand movements, progression of the lesion size and a vast increase of vitreous inflammation up to grade four according to SUN-classification (Figure 2A)
- Performance of diagnostic vitrectomy with a circumscribed retinectomy and aspiration of subretinal cells allowing histological and cytological analysis with largely undamaged cells¹

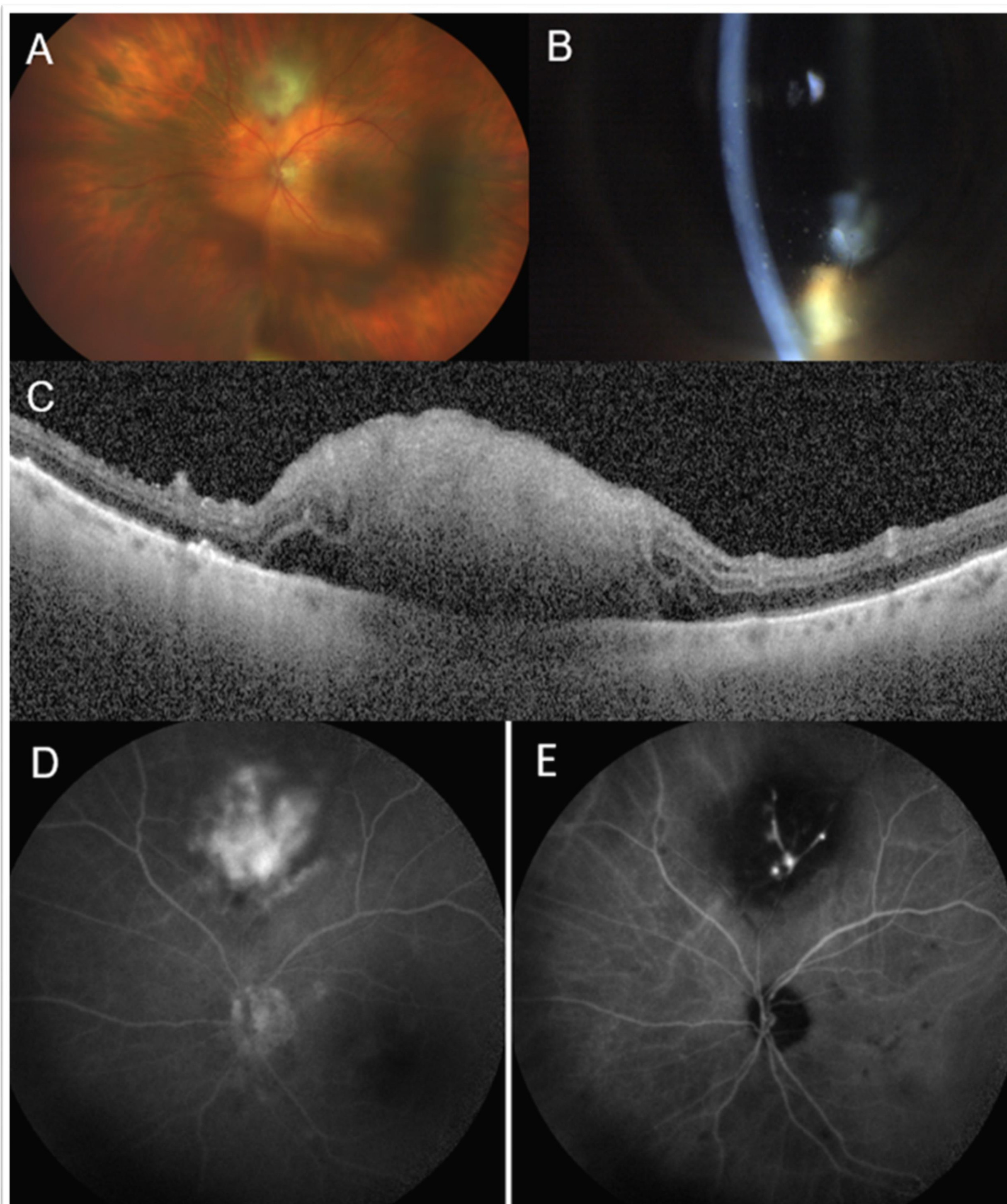


Figure 1: Left eye at first presentation: A, Color fundus photograph shows the retinal lesion with intraretinal bleedings. B, Slitlamp photograph shows keratic precipitates in Arlt's triangle. C, Optical coherence tomography section through the lesion demonstrates retinal thickening and subretinal fluid. D, Late phase fluorescein angiography reveals vasculitis. E, Late phase indocyanine green angiography with focal hyperfluorescence of the vessel walls.

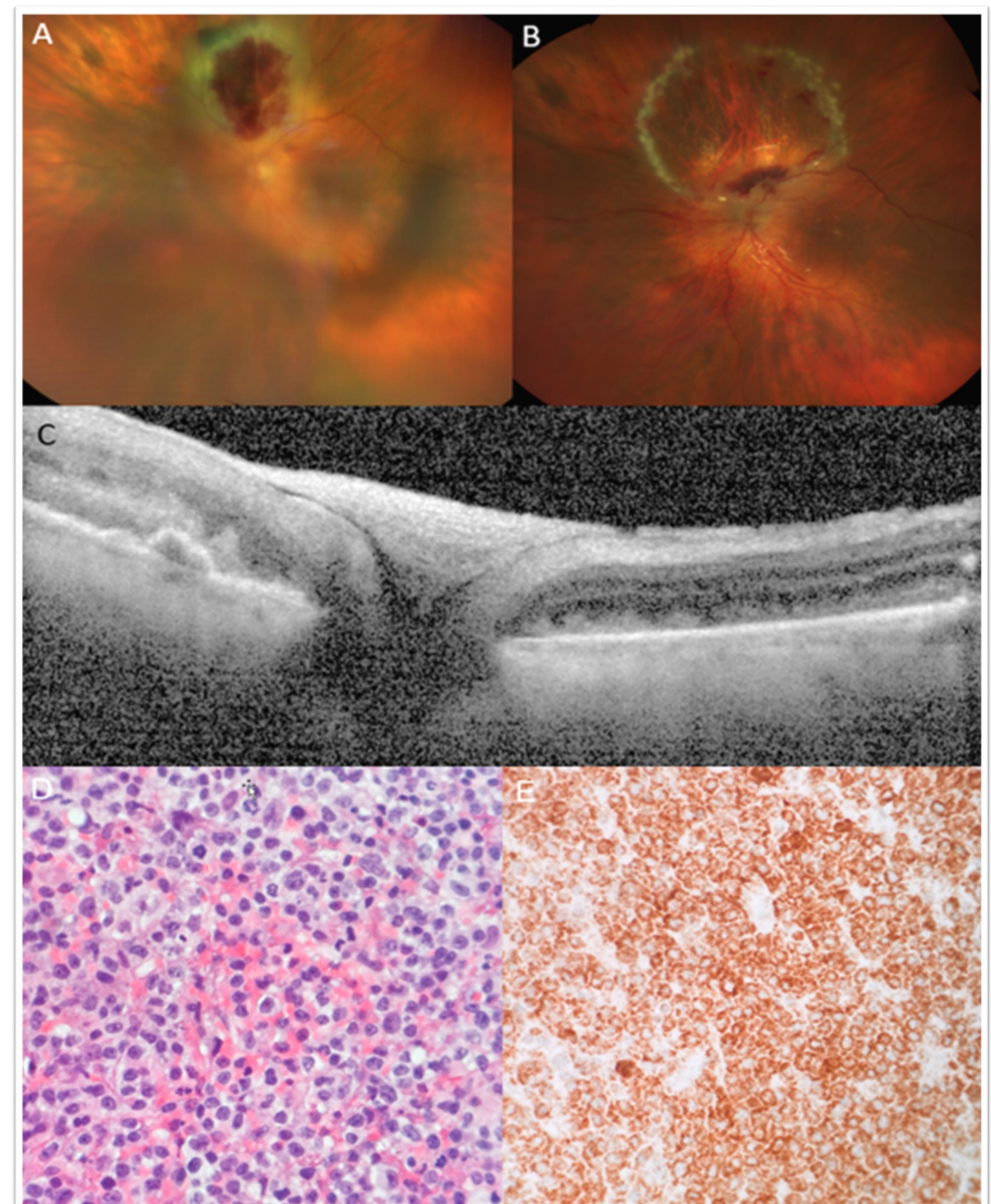


Figure 2: Retinal lesion during follow-up: A, Color fundus photograph of the lesion 8 weeks after first presentation shows increase of hemorrhage and lesion size. B and C, are images taken after surgery (diagnostic pars plana vitrectomy and retinal biopsy) 12 weeks after first presentation. B, Color fundus photography and C, optical coherence tomography demonstrate infiltration of the optic disc. D, Retinectomy specimen, hematoxyline and eosin stain, 400x magnification. Sheets of polymorphic discohesive cells with bright cytoplasm. E, Retinectomy specimen, BRAF^{VE1} mutation specific antibody Immunostain, 400x magnification, with strong cytoplasmic immunopositivity, indicative of an underlying BRAF p.V600E mutation.

Cytologic Findings and Therapeutic Implication

- Histological sample: pleomorphic clustered cells with CD20 positivity and expression of BRAF mutation specific antibody
- Favored diagnosis: manifestation of HCL
- Renewed staging via magnet resonance tomography: no intracranial involvement
- External laboratory for additional confirmatory stains: No HCL specific stains; plasmacytic marker CD 138 strongly positive and EBV association was shown by EBER-ISH, while BRAF mutation was confirmed by Sanger sequencing²
- Change of favored diagnosis: EBV associated plasma cell proliferation, most likely associated with an immunosuppressed state due to HCL and its previous therapy
- Recommendation of bone marrow biopsy was declined by the patient
- Treatment: Local radiotherapy (15 x 2 Gray)
- Diminution of the infiltrate, but no amelioration of VA

Conclusion and Discussion

- Challenging differential diagnosis due to rare publications on HCL and plasmacytic infiltration of the retina^{3, 4, 5, 6}
- In our case: after suspicion of an initial herpetic retinal necrosis due to clinical findings along with aqueous humor PCR positive for EBV, the presumptive diagnosis of HCL related infiltration based on pathological examination was abandoned in favor of the EBV associated etiology
- We highlight the value of diagnostic vitrectomy to achieve the definite diagnosis
- Our particular case demonstrates the importance of questioning a presumptive diagnosis once the course of the disease deviates from what would ordinarily be expected
- Early diagnosis in ocular malignancy can not only save vision but increase survival rate
- Ophthalmologists should preserve a high index of clinical suspicion in atypical findings in uveitis for **masquerade syndromes**

References

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