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Case Report

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Regression of Primary Vitreoretinal Lymphoma (Pvrl) And Perivascular Flower Bud Like Lesions (Pfbls) on Octa After Intravitreal Methotrexate Injection Series

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ABSTRACT

Primary Vitreoretinal Lymphoma (PVRL) is a rare and aggressive type of intraocular lymphoma that affects the eye. PVRL is most commonly diagnosed in individuals in their sixth to eighth decade of life, but it can occur in younger, immunocompromised individuals. PVRL is challenging to diagnose due to its non-specific presentations, and a delay in diagnosis from the onset of symptoms can exceed 12 months. CNS involvement in PVRL is common, and patients may develop CNS involvement within a mean interval of 8-29 months after diagnosis.

We present a case of a 73-year-old man who presented to the emergency department with gradual decline in vision in his left eye over the past two years, with acute worsening over the past two weeks. The patient was diagnosed with PVRL with CNS involvement based on exam, imaging and biopsy findings. The patient received intravitreal injection of methotrexate in the left eye and systemic treatment with rituximab and ibrutinib. The patient's visual acuity improved in the left eye, and regression of tumor size was noted on the fundus exam, OPTOS, and OCTA.

Prompt referral to a medical center and early diagnosis are essential in managing PVRL to prevent potential vision loss. Various imaging modalities such as fluorescein angiography, optical coherence tomography, and optical coherence tomography angiography can be helpful in diagnosis and management of PVRL. However, the use of optical coherence tomography angiography has been only described in few case studies. The management of PVRL remains a challenge, with limited treatment options available, including systemic chemotherapy and/or radiation therapy.

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Background

Primary Vitreoretinal Lymphoma (PVRL) is a rare form of intraocular lymphoma that represents fewer than 1% of all intraocular tumors and approximately 1% of all non-Hodgkin lymphomas [1]. It is most commonly diagnosed in people in their sixth to eighth decade of life, but can also occur in younger, immunocompromised individuals. The disease affects both eyes in a great majority of patients, but significant asymmetry of involvement between the two eyes is often present [2].

CNS involvement in PVRL is common, with 16-34% of patients demonstrating CNS involvement at the time of diagnosis and 42-92% of patients later developing CNS involvement within a mean interval of 8-29 months after diagnosis [3]. PVRL can be challenging to diagnose due to its variable and non-specific presentations, with a delay in diagnosis from the onset of symptoms often exceeding 12 months [4].

On examination, vitreous haze is present in 92% of eyes and is the only exam finding in approximately 15% of cases [5], while cream-colored subretinal or retinal lesions are observed in around half of all cases [6,7]. Ophthalmic multimodal imaging, such as fluorescein angiography, fundus autofluorescence, optical coherence tomography, optical coherence tomography angiography can be helpful in the diagnosis of PVRL. However, the use of optical coherence tomography angiography has only been described in a few case studies. The management of PVRL remains a challenge, with limited treatment options available, including systemic chemotherapy and/or radiation therapy [8].

Case Presentation

A 73-year-old man without past medical history presented to the emergency department with a gradual decline in vision in his left eye over the past two years, with acute worsening over the past two weeks. He was referred by an outside ophthalmologist who noted suspicious retinal lesions in both eyes and vitritis in the left eye. The patient also reported floaters and flashes in both eyes, unintentional weight loss, and seborrheic keratosis over his face, chest, and back. Visual acuity was 20/40 in the right eye and 20/400 in the left eye with a central scotoma. Ophthalmic exam showed moderate nuclear sclerotic cataracts and retinal lesions in both eyes.

Initial lab workup, including complete blood count, erythrocyte sedimentation rate, and c-reactive protein, was within normal limits. Infectious workup and screening for malignancy were negative, except for MRI orbits, which showed a lesion along the lateral margin of the left eye, and MRI brain, which showed small

enhancing lesions in the corpus callosum and right frontal white matter (Figures 1,2). Lumbar puncture showed elevated protein and beta 2 microglobulin, and elevated protein of 1399 mg/L,with CSF glucose within normal limits at 53. Oligoclonal bands were not present and there was no growth of the CSF culture. Cytology and flow cytometry demonstrated a polymorphic lymphocyte population without atypical or malignant cells.

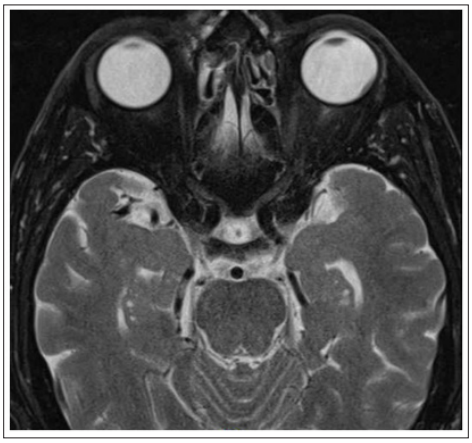

Figure 1: T2 weighted MRI orbits demonstrating an ill-defined non-enhancing curvilinear lesion along the lateral margin of the left ocular globe

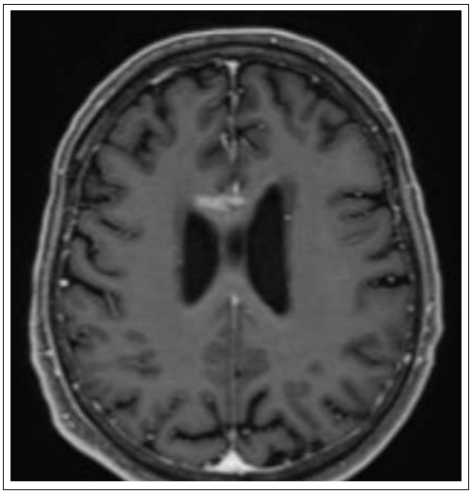

Figure 2: T1 weighted MRI brain demonstrating enhancing lesions within the body of the corpus callosum

Given the suspicious brain lesions, a vitreous biopsy of the left eye was performed. Flow cytometry of the sample did demonstrate a monotypic B-cell population (about 10% of total events) expressing CD19 (dim), CD45 (bright) and lambda light chain markers that was suspicious for a B cell lymphoproliferative disorder. Based on the constellation of exam, imaging and biopsy findings the patient was diagnosed with PVRL with CNS involvement.

The patient received intravitreal injection of methotrexate in the left eye before being discharged from the hospital. In the ophthalmology clinic, the patient received five additional intravitreal injections of methotrexate OS, each one week apart. Patient's visual acuity improved in the left eye from hand motion initially during the hospital visit to 20/60 three months later after a total of six intravitreal methotrexate injections. This marked improvement in visual acuity also corelated with the regression of tumor size noted on the fundus exam, OPTOS, and OCTA. OPTOS photographs. The patient was also seen in the oncology clinic and is on systemic treatment with rituximab and ibrutinib.

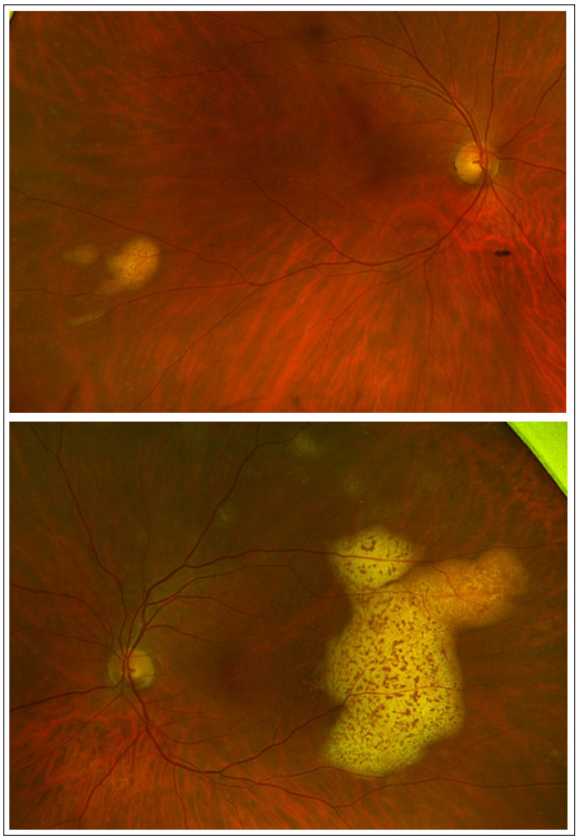

Figure 3: Initial color fundus photographs of right and left eye with elevated white lesions with leopard spotting

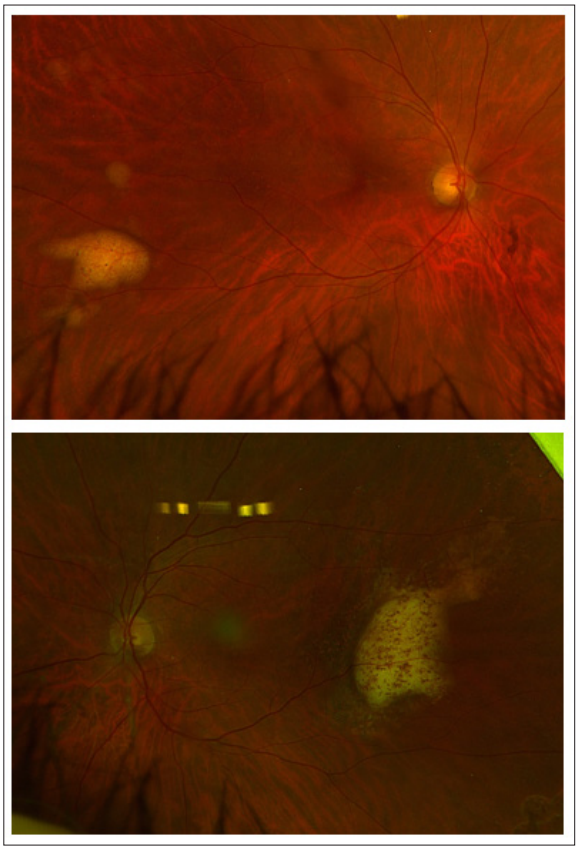

Figure 4: Color fundus photographs of right and left eye, with marked decrease in size of left eye lesion after six intravitreal methotrexate lesions for primary vitreoretinal lymphoma (PVRL)

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Discussion and conclusion

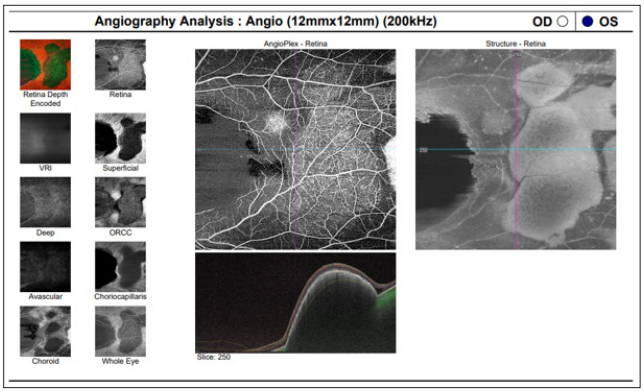
Primary vitreoretinal lymphoma (PVRL) is a rare and aggressive form of non-Hodgkin's lymphoma that affects the eye. It is a type of intraocular lymphoma that originates in the vitreous or retina of the eye and is considered a serious and challenging condition to diagnose and treat.

In our patient a prompt referral immediately to our medical center by an outside ophthalmologist enabled appropriate diagnosis and expeditious systemic work up, thus resulting in immediate start of ocular and systemic treatment.

Diagnosis of PVRL is typically made through a combination of clinical examination, imaging studies, and biopsy. The clinical presentation of PVRL can be variable, but common symptoms include floaters, visual disturbances, and progressive vision loss. It is important to diagnose PVRL early to prevent potential vision loss, and prompt referral to an ophthalmologist is essential.

Various imaging modalities such as fluorescein angiography, optical coherence tomography, and optical coherence tomography angiography can be helpful in diagnosis and management of PVRL. However, use of optical coherence tomography angiography has been only described in few case studies. Cherif et al., noted decreased signals on OCTA in choriocapillaris slab of two patients with PVRL [9] In our patient we noticed the same decreased signal in the choriocapillaris layer but also noted increased vascular density were noted in the inner retinal layer and outer retinal to choriocapillaris complex (ORCC). Interestingly, there was gross decrease in vascular density in the inner retinal layer and ORCC layers after the intravitreal methotrexate injections (Figures 5,6).

Initial OCTA retina layer



Final OCTA retina layer

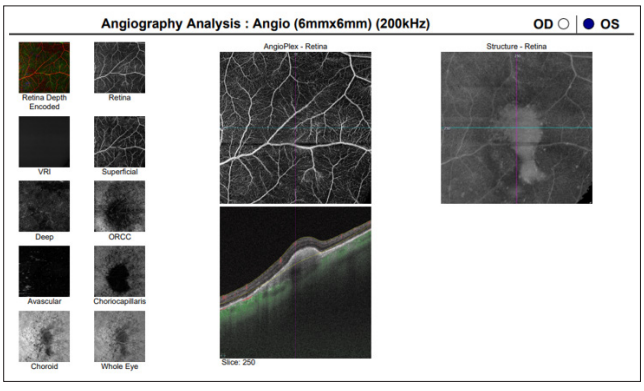
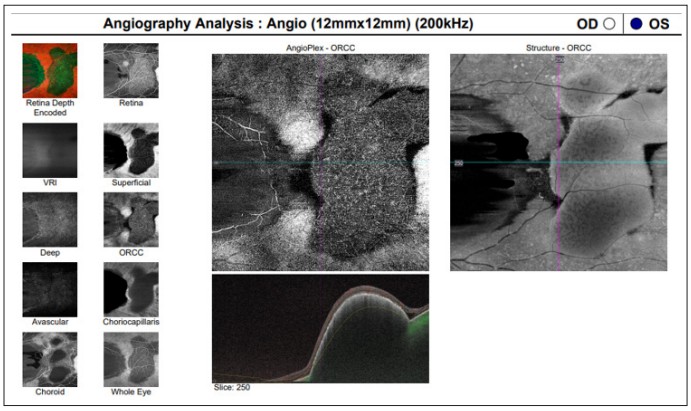


Figure 5: Initial and final OCTA images of left eye revealing decreased vascular density in the retinal layer after treatment with six intravitreal methotrexate injections

Initial OCTA ORCC layer



Final OCTA ORCC layer

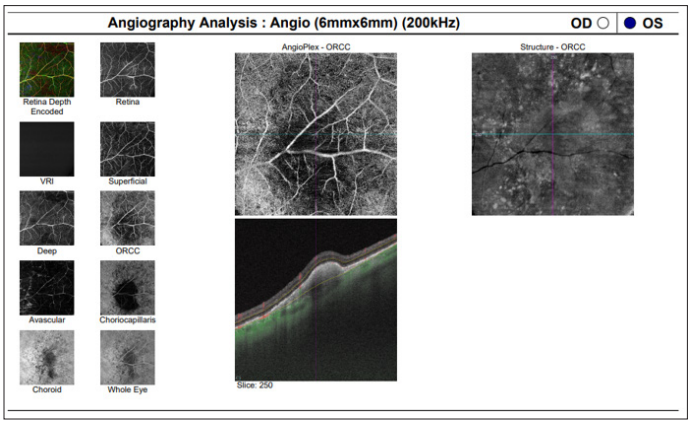


Figure 6: Initial and final OCTA images of outer retinal to choriocapillaris layer (ORCC) revealing decrease in vascular density

Chen et al, described perivascular flower-bud-like lesions (PFBLs) on en face OCTA and OCT B-scans during the initial examinations in patients with vitreoretinal lymphoma. This appeared to be different from vertical hyperreflective materials noted previously in patients with vitreoretinal lymphoma, in that vertical hyper reflective materials were noted only on OCT B scans. However, PFBLs were noted on OCTA scans as well as fundus autofluorescence. PFBLs are also noted earlier in the disease process thereby helping in early identification and treatment of PVRL[10].

In our patient, we also noted the PFBLs on en face OCTA, at various levels of retina but more clearly in the mid retina sections, and also fundus autofluorescence (Figure 7). Interestingly after treatment with intravitreal methotrexate injections there were attenuation of PFBLs noted just as noted by Chen et al in their patient series (Figure 7). Thus PFBLs can be used for early identification of PVRL and its attenuation as possible positive response to treatment. Further studies on PFBLs looking at their attenuation as a response to treatment can help with as a way for disease monitoring.

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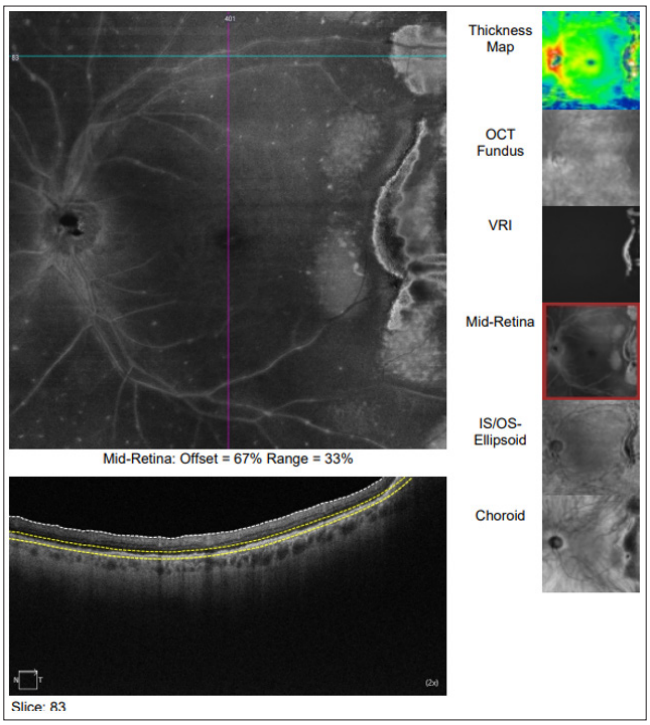
Initial enface mid retina layer



Final enface mid retinal layer

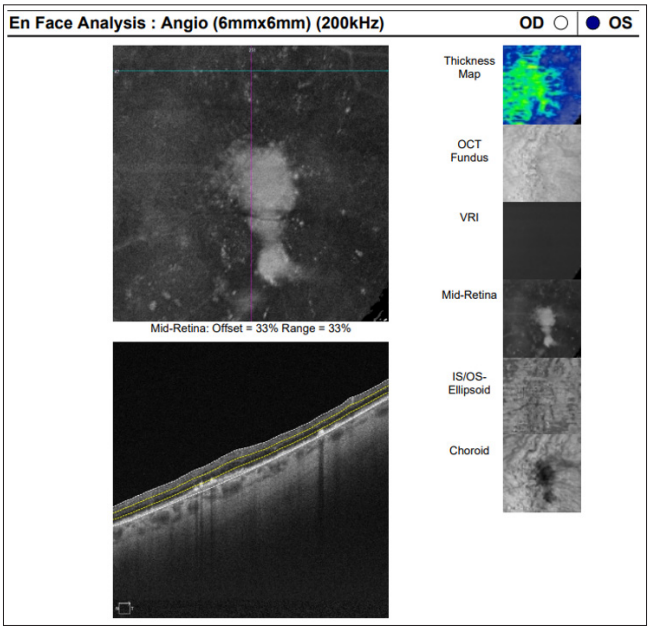


Figure 7: Decrease in perivascular flower-bud-like lesions (PFBLs) after intravitreal methotrexate injections noted on OCTA enface mid retinal layer

The treatment of PVRL can be complex and depends on several factors, including the stage and extent of the disease, the patient's overall health, and the individual's personal preferences. Treatment options typically include a combination of chemotherapy, radiation therapy, and/or local intravitreal therapy. In some cases, surgical intervention may be required to remove affected tissues.

While progress has been made in the diagnosis and treatment of PVRL, the disease remains a significant challenge for both patients and healthcare providers. Further research is needed to improve our understanding of PVRL, develop new and effective treatments, and improve outcomes for patients.

In conclusion, PVRL is a rare and aggressive form of non-Hodgkin's lymphoma that affects the eye and requires a multidisciplinary approach for diagnosis and treatment. Early diagnosis is essential to prevent potential vision loss and improve outcomes for patients. Further research is necessary to better understand and treat this disease.

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