Case Report

Case report “Acute Retinal Necrosis or not?”

Abstract

Acute retinal necrosis (ARN) comprises of episcleritis or scleritis, periorbital pain, uveitis, vitreous opacity, and necrotizing retinitis. ARN is very difficult to make diagnosis if patient have several complicated ocular diseases and no views on the fundus examination. In this study, a suspicious ARN case reported here who had a left eye sudden visual loss, periorbital pain, uveitis, vitreous opacity, old choroidal hemorrhage and an area of pale retina (fundus was partially viewed due to cataract and vitreous opacity). A vitrectomy was performed and found vitreous hemorrhage (VH) and a newer choroidal hemorrhage (CH) instead of ARN. Reviews on the clinical finding and management of patients with ARN, VA and CH were discussed in this report.

Introduction

Acute retinal necrosis (ARN) is a disease including episcleritis or scleritis, periorbital pain, uveitis, vitreous opacity, and necrotizing retinitis. This case looks like ARN except lacking necrotizing retinitis. The epidemiology of ARN is either sex (a slight higher rate on male), any race or any age group (most at 20–50 years). Some patient is immunosuppression (like AIDS) or subclinical immune dysfunction. The incidence of ARN in the UK is one case per 1.6 to 2.0 million populations per year [1]. ARN is responsible for 5.5% of uveitis cases in US. The most common cause of ARN is varicella–zoster virus (VZV). It accounts for 50% to 80% cases. HSV1, HSV2 [2, 3]. And rarely cytomegalovirus (CMV) and Epstein–Barr virus (EBV) are also involved [2, 4]. Dr. Muthiah report in 2007 “The at risk population for ARN is patients who have had previous zoster viral infections: chickenpox (70.6% of cases), shingles (29.2%) and zoster opthalmicus (20.7%). The other risk factors identified in this study were previous herpes simplex cold sores (25%) and HSV encephalitis (15.4%)” [1]. The other factors might involve into the pathogenesis of ARN are HLA-DQw7, HLA-Aw33, Phenotipe Bw62, DR4, DRw6 and B44 [5]. The symptoms of ARN are: photophobia, periorbital pain or redness, decreased vision, floaters, previous varicella/herpes zoster infections. The differential diagnoses of ARN are vitritis and intermediate uveitis, Behçet’s disease, endophthalmitis, toxoplasmiasis, cytomegalovirus retinitis, Sarcoidosis, syphilis /lupus, peripheral hemorrhage exudative choriodapathy, and ocular ischemic syndrome (OIS). The treatment of ARN is antiviral therapy, prophylactic conluent laser therapy and prophylactic vitrectomy.

We report here a suspicious ARN case, including clinical history, symptoms, eye examinations, laboratory tests and antiviral treatment and vitrectomy. The final diagnosis is VH and CH instead of ARN.

Case Report

A 56 years old African American male came to our Eye Clinics for eye examination. His chief compliant was a left eye sudden loss vision with a left eye touching pain (scale 10/10) for 14 days. His ocular history included primary open-angle glaucoma OU (~-s/p trabeculectomy with mitomycin C OS with Ahmed tube shunt OS on 01/06/2012; Bleb needling OS 02/01/2012 with very low IOP, Gonioscopy: open angles all 4 quadrants); diabetes mellitus with moderate non–proliferative retinopathy 2013; early cataracts OU 2014; and follicular conjunctivitis OU secondary to chronic Brimonidine usage 2014. Family ocular history was negative for glaucoma or age-related macular degeneration or any blindness diseases. He denied past ocular trauma.

His medical history was positive for type II Diabetes mellitus (DM) 2005, Essential Hypertension 2005, Osteoarthritis and hyperlipidemia 2009, Allergic rhinitis 2009, Morbid Obesity 2009, Anemia 2009. Social history was negative for alcohol, tobacco or recreational drug abuse. He was oriented to time, person, place and was in no acute distress. His mood and affect was appropriate. His blood glucose level was 130 mg/dL recently. His eye medicines included Cosopt OU BID, 0.2% Brimonidine OU once use BID; and Latanoprost OU QHS. He was given 1% Prednisolone Acetate Ophthalmic Suspension 1 gtt OS qid for iritis treatment for the past year (not compliance).
His last ocular examination was 40 days ago with a distance best corrective visual acuity (BCVA) OD: 20/20-2, OS: 20/50-2 (PH 20/40-2; IOPs were 33, 35 / 27, 25 mmHg (not compliance on eye drops applications); macular OCT test showed: “OD normal, OS irregularity and changes within the inner retinal likely consistent with diabetic changes. ERM, no CME”; B-scan “OS area of superior temporal sub RPE fullness. Appears to be old choroidal hemorrhage. May have been related to a suture tract with AMHED. No definitive areas of erosion. No evidence of RD or tear.” His Heart rate: 74 /min, Body temperature: 98 degree; Temporal artery pulsation: palpable, no tender, no Jaw claudication (pain in jaw when chewing).

The eye examinations results were as below

The distance BCVA was 20/40 OD, Pinhole No Improvement (PHNI); OS Hand Motion (HM)/3 feet. The near visual acuity with correction was 20/20 OD and HM OS with an add of +2.50 OU. Pupils were equal, round and reactive to light; no afferent pupillary defect was noted. Confrontation fields were full to finger counting in OD (OS unable to view finger). Extraocular muscles were unrestricted in all gazes without pain or diplopia. Cover test was orthophoric at distance and near. Goldmann applanation tonometry measured intraocular pressure (IOP) 40 mmHg OD, 18 OS mmHg. (He was not compliance on eye drops applications recently)

Slit lamp biomicroscopy revealed normal adnexae, lids, lashes, and puncta OU. Palpebral conjunctivae showed follicular 3+ OD, 2+ OS. Bulbar conjunctivae showed 2–3+ diffused injection in both eyes. Left eye Superior/ Temporal bulbar conjunctivae showed a formed posterior bleb–Ahmed tube shunt. The cornea showed superficial punctate keratitis (SPK) 2+ OU. Both anterior chambers (A/C) appeared deep. No cells/ flares were detected in right eye. Trace flares and a long amhded tube (2:00 o’clock) without iris/cornea touch were noted in anterior chamber OS. The estimation of the chamber angles was 4/4 via the Von Herrick method OU. Both irides were flat and no masses, rubeosis or synechia. Lens showed 2+ nuclear sclerosis OU, and 1+ cortical opacity OU, OS PSC +1.

Patient was rejected dilation. Undilated fundus assessment OD revealed optic nerves with a cup-to-disc ratio of 0.4/ 0.4, superior sloping. There was no evidence of pallor or edema of the neuroretinal rim OD. The right macula was flat with scattered dot blot hemorrhages and microaneurysms. The vitreous was optically clear OD. The vasculature was normal and the mid retinal periphery was flat without breaks in OD. The fundus assessment OS was poor view due to cataract and cloudy vitreous body.

The assessments for this patient were

1. Sudden visual loss without trauma history OS: might have diabetic macular edema (DME) OS. Unable to view fundus due to rejected cataract and cloudy vitreous body OS.

2. Primary open-angle glaucoma (OS much worse than OD), −s/p trabeculectomy with mitomycin C OS, −s/p Ahmed tube shunt OS. OD IOP was high today (might due to not compliance on eye drops and oral steroid usage)

3. Moderate non–proliferative retinopathy OU.

4. History of chronic Uveitis OS

5. Senile cataract OU (mild)

6. Follicular conjunctivitis OU

7. Refractive Error/ presbyopia OU

The differential diagnoses for this left eye sudden visual loss without trauma history included:

- Retinal detachment (RD)
- DME
- Vitreous hemorrhage (VH)
- CH
- Vitritis
- Intermediate uveitis
- Toxoplasmosis
- Cytomegalovirus retinitis
- Sarcoidosis
- Syphilis
- Exogenous endophthalmitis (bacterial or fungal)
- Peripheral hemorrhage exudative choroidopathy
- Acute retinal necrosis (ARN)
- Ocular ischemic syndrome (OIS)

RD often has trauma history and /or high myopia history. This patient has neither history. A B–scan can diagnosis RD if retina is unable to view clearly.

DME is often painless and cause refraction statue sudden change, distorted central vision. It is rare related with A/C flare/cells.

VH (red blood cells in vitreous): might induce from diabetic retinopathy, trauma, retinal detachment and Posterior vitreous detachment, etc.

CH: It is often related with intraocular surgery (cataract surgery, etc.) or trauma. Patient reports severe pain, high IOPs and blurry visions. Hypertension or taking anticoagulants history might be found in some patients. B–scan can detect this hemorrhage.

Vitritis: White blood cells in the vitreous body. No red blood cell existed in the vitreous.
Intermediate uveitis (pars planitis): Belong to a subtype of uveitis in vitreous body and on the retina. Exudates (snowbanks like) at the pars plana or inflammatory cells (snowballs like) in the vitreous can be detected

Toxoplasmosis: Toxoplasma gondii (intracellular parasite): induce white color isolated lesions (old and new chorioretinal scars mixed on retina). Intravitreal inflammatory cells can be found close to the retinal lesion sites.

Cytomegalovirus (CMV) retinitis: Characterized with “owl’s eye” like cells. Eyes show injection, eye pain and blurry vision. Patients often have immunocompromised condition (HIV, transplants, chemotherapy) with low blood CD4 cell numbers

Sarcoidosis: Combined uveitis, uveoparotitis, and retinal inflammation. Scleral nodule and conjunctivitis might be presented.

Syphilis: Shows anterior uveitis, interstitial keratitis, iris roseola, vitritis, chorioretinitis, and papillitis. The blood test of VDRL is positive.

Exogenous endophthalmitis (bacterial or fungal): Intraocular infection from bacterial or fungus. The symptoms include eye redness, severe pain, and blurry vision. Slit Lamp exam can find hypopyon. The infectious pathogens are from intraocular surgery or penetrating trauma. The culture of aqueous or vitreous body can detect bacterial or fungal growth.

Peripheral hemorrhage exudative choroidopathy: subretinal pigment epithelial or subretinal blood and/or subretinal exudates and/or vitreous hemorrhage, retinal degeneration. This disease affects elderly persons, who have hypertension and arteriosclerotic cardiovascular disease history.

ARN includes epicleritis or scleritis, periorbital pain, uveitis, vitreous opacity, and necrotizing retinitis.

OIS is often associated with severe carotid artery occlusive disease. The symptoms and signs include ipsilateral transient visual loss, neovascularization of iris/disc, cholesterol emboli, spontaneous retinal arterial pulsations, and narrowed retinal arteries. Duplex carotid ultrasonography can detect carotid artery stenosis.

The plans

The patient was instructed to continue the present Latanoprost OU QHS and Cosopt OU BID/ Brimonidine OU BID, Tears ou PRN. Educated patient on the compliance of the eye drops administration. Referred him to a glaucoma specialty for a glaucoma evaluation/treatment. (Patient received Selective Laser Trabeculoplasty OD 2 months later after this visit. He got OD 10% IOP decrease to 20 mmHg therefore). His moderate nonproliferative retinopathy OU seemed stable; advised patient to control his blood pressure and blood glucose levels. His cataract OU (not visually significantly and symmetric OU) would be monitored yearly. The causes of his sudden OS visual loss were not clear at this visit. It might be DME, VH, vitritis, chorioretinitis, acute retinal necrosis (ARN), or other retinal/choroidal diseases, etc.

Follow-up #1

The patient returned in next day for follow-up. He reported no changes on symptoms and compliance with eye drops. His vision was stable (BCVA was 20/40 OD, PHNI; OS HM/3 feet). His left eye pain improved (scale 4/10 now). Conjunctiva: 1–2+ injection OU, Cornea: 2–3+ diffuse SPK OU; A/C: deep, no inflammation OU. IOPs were 28/7 mmHg. Vitreous: clear OD, dense vitreous, cell + OS. The rest of eye examinations showed no change comparing with last eye exam. B-scan showed no sign of retinal detachment. Continate Latanoprost OU QHS and Tears ou PRN. Increased Cosopt from OU BID to TID and increase Brimonidine from OU BID into TID. Added 1% Prednisolone Acetate Ophthalmic Suspension 1 gtt OS QIH due to the possibility of Uveitis OS.

Follow-up #2

The patient returned in 3 days for follow-up. He reported no changes on symptoms and compliance with eye drops. His vision was stable (BCVA was 20/40 OD, PHNI; OS HM/3 feet). His left eye pain stable. Conjunctiva: 1–2+ injection OU, Cornea: 2–3+ diffuse SPK OU; A/C: deep, no inflammation OU. IOPs were 23/5 mmHg. Vitreous: clear OD, very haze, + cell OS. The rest of eye examinations showed no change comparing with last eye exam. Kept the eye drops plans unchanged for OD. Added Diamox sequels 500 mg PO BID to further lower the IOP on OD. Stop all glaucoma drops for OS. Another possible diagnosis was possible chorioretinitis OS. Blood tests were ordered for Venereal Disease Research Laboratory (VDRL) test, rheumatoid factor (RF), HLA-B27, antinuclear antibody (ANA), angiotensin-converting enzyme; CH50 (complement system), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Follow-up #3

The patient returned in 2 days for follow-up. He reported no changes on symptoms and compliance with eye drops. His vision was stable. IOPs were 16/2 mmHg. The rest of eye examinations were the same as last eye exam except conjunctiva showed no injection OU. The blood test results: negative for syphilis and ANA, others pending. Kept the eye drops plans unchanged. tapered the Diamox sequels 500 mg PO BID into QD. No other change was made on treatment plans.

Follow-up #4

The patient returned in 5 days for follow-up. He reported no left eye pain. His vision was stable. IOPs were 32/9 mmHg. The eye examinations were the same as last eye exam except conjunctiva were injection OU. The causes of his sudden OS visual loss were not clear at this visit. The doctor was instructed to reduce 1%
Acute retinal necrosis (ARN) is a disease including epicleritis or scleritis, periorbital pain, uveitis, vitreous opacity, and necrotizing retinitis. This case looks like ARN except lacking necrotizing retinitis. In this case, the allergic conjunctivitis and dry eye and mild uveitis mimic the epicleritis and periorbital pain. The patient’s initial left dilated fundus assessment was poor view due to cataract and cloudy vitreous body, which made it difficult for diagnosis of sudden visual loss at the 1st visit.

After the initial topical steroid treatment, the pain and the conjunctival injection of left eye were resolved, and the anterior chamber reaction was deceased. The vitreous opacity was stable. At the 12th days follow up visit, the left retina could be viewed partially for the 1st time. The superior nasal part of left eye retina showed whitening color, which made it very suspicious for an ARN diagnosis.

The left eye retinal pale area seemed a little improvement after the antiviral treatment of Valtrex for a week. But the A/C tap didn’t detect of HSV or HZV due to insufficient aqueous quantity. Later, red blood cell showed up in the A/C. And a PPV confirmed that vitreous hemorrhage and choroidal hemorrhage in left eye. The initial suspicious diagnosis of ARN in this case was just a co-incidence of several combined eye diseases. A combination of periorbital pain, uveitis, vitreous opacity, and retinal pale is not guaranteed with a diagnosis of ARN unless with retinal necrosis and/or virus detection.

The VH of this case might derive from Diabetic retinopathy or choroidal hemorrhage. The old/new CH might due to ahmed shunt implant sutures close to that hemorrhage location.

* The logical reasons excluded other differential diagnoses were as below:
  * RD: B−scan showed no RD, but old choroidal hemorrhage.
  * DME: No refraction statue sudden change, wavy central vision.
  * Vitritis and Intermediate uveitis: No white blood cell detected in the vitreous body.
  * Behçet’s disease: Often associated with arthritis, mouth and genital ulcers, and skin lesions. No uniform distribution of peripheral retinal damages.
Toxoplasmosis: Toxoplasmosis IgG is positive, but IgM negative indicated that this patient had a history of Toxoplasmosis before, but not active infection.

Cytomegalovirus retinitis: No HIV or immunocompromised condition. This patient didn’t get blood test on HIV or CMV. He didn’t have the symptoms of HIV.

Sarcoidosis: No uveoparotid fever or Her Ferrd or syndrome or scleral nodule plus a weak uveitis

Syphilis /lupus: Blood tests of VDRL and lupus anti-coag were negative.

Endophthalmitis: Vitreous sample culture for bacterial or fungal showed negative.

Peripheral hemorrhage exudative choroidopathy: Not elderly persons, who have hypertension and arteriosclerotic cardiovascular disease history. Besides, there were no subretinal pigment epithelial or subretinal blood and/or subretinal exudates.

OIS: Palpable, no tender on temporal artery pulsation. No carotid artery occlusive disease, no ipsilateral transient visual loss, no neovascularization of iris/disc, no cholesterol emboli, no spontaneous retinal arterial pulsations, no narrowed retinal arteries.

The abnormal blood test results explanations

CH50 represented the protein level in the complement system (related with autoimmune activity). A slightly elevated CH50 test result would indicate infections, ulcerative colitis and cancer. Slightly high CPR result indicated moderate risk of developing cardiovascular disease. An elevated CPR also induced by inflammation and cancer. ESR 78 (elevated for his age) might due to infection, inflammation, autoimmune disease, or cancer. Toxoplasmosis IgG: Positive /IgM: Negative – Which indicated prior exposure or reactivation. Slight elevated Homocysteine 14.3 (refer 11.4 umol/L) might because of functional deficiency of folic acid or vitamin B12.

Below is a review of ARN

The pathological findings of ARN are: full thickness retinal necrosis, hemorrhage, retinal arteritis and choroiditis/choroidal occlusion. Optic nerve might have plasma cells infiltration and become necrosis. Immune complexes with varicella zoster viral antigens can be found in retinal vessels wall.

ARN is mainly depending on clinical finding to make diagnosis. The American Uveitis Society’s Standard diagnostic criteria for the acute retinal necrosis included: one or more foci of peripheral retinal necrosis with discrete borders; Rapid progression of disease if without treatment; occlusive vasculopathy; and inflammatory reaction in the vitreous and anterior chamber. Some supporting criteria are: pain, scleritis and optic neuropathy/atrophy [6]. The key diagnosis is retinal necrosis spreading from peripheral retina to posterior pole [7]. Around 60% of ARN patients will have bilateral ARN [8].

Differential Diagnoses: B-scan to detect Choroidal Hemorrhage, bacterial or fungal culture growth from vitreous sample to exclude exogenous endophthalmitis (previous intraocular surgery), blood IgG for Toxoplasmosis/Syphilis, Human cytomegalovirus (DNA virus), etc.

Lab tests: CBC, ANA, RF, serum protein electrophoresis, hemoglobin electrophoresis, VDRL test, and fluorescent treponemal antibody absorption, ESR and CRP. HZV and HSV (type 1 and 2) immunoglobulin G and M titers or PCR [9].

The active retina damage area will show hypofluorescence on fluorescein angiography. B-scan and CT scan may find a larger optic nerve sheath [10]. Diagnostic vitrectomy is extremely useful to differential infection or inflammation. Intraocular infection due to previous intraocular surgery might be detected by bacteria/ fungus culture from A/C tap or sample of vitreous body. Dr. Lau and colleagues reported that VZV was detected in 66.7% of eyes with vitreous biopsy and herpes HSV in 22.2% [11].

The initial management of ARN is antiviral therapy. It includes intravenous acyclovir (1500 mg/m2/day), oral acyclovir (800 mg orally five times daily), or oral produgs (Valacyclovir=1 g orally three times daily; or famciclovir – 500 mg orally three times daily; or valganciclovir-450–900 mg 2 times daily (12-14)) or intravitreal foscarnet, or valacyclovir, or famciclovir [15]. The results from oral or intravenous or intravitreal administration of antiviral treatment are controversial. Tibbetts [16] found no difference in visual outcomes by intravitreal injections or intravenous treatment. Whereas, Flaxel [17] reported that intravitreal antiviral therapy induced a better visual outcome than intravenous treatment for ARN. But intravitreal antivirals treatment has an advantage of obtaining a vitreous sampling for PCR virus detection during the injection procedure.

Other treatments are standard anti- Uveitis treatments; and retinal detachment surgeries:

1. Prophylactic confluent laser therapy (controversial results [16, 18])

2. Prophylactic vitrectomy: Some reports indicated that prophylactic vitrectomy prevented retinal detachment [18, 19]. But other report showed prophylactic vitrectomy did not improve the visual acuity in ARN [20].

The prognosis for the patient of ARN is very poor. Most ARN left untreated will demonstrate retinal detachments. The RD rate varied from 50% to 75% [11, 16, 21, 22]. The new antiviral treatment and advanced vitrectomy techniques improved the final visual function of ARN recently [23, 24].

The main cause of the sudden vision lost in this case report was VH and CH. VH is defined as blood existing in the vitreous body. The blood might derived from retinal break/ detachment, diabetic retinopathy, posterior vitreous detachment, retinal vein occlusion, exudative age-related macular degeneration, sickle cell disease, intraocular tumor, trauma, subarachnoid or subdural hemorrhage (Terson syndrome), sickle cell disease, intraocular tumor, trauma, subarachnoid or subdural hemorrhage (Terson syndrome), sickle cell disease.
The symptoms of VH are sudden visual loss (painless) and black spots (floaters). Differential Diagnosis includes: Vitritis, paras planitis, asteroid hyalosis, pigment cells, etc. B–scan can be employed to rule out retinal tear/detachment or intraocular tumor. Fluorescein Angiography can detect retinal vascular diseases.

Conservative treatments of VH include bed resting and avoiding anticlotting agents. Treatments the causes of VH (RD or proliferative diabetic retinopathy, etc.) are also necessary. Vitrectomy is indicated for the following situations: more than 3–6 months' idiopathic vitreous hemorrhage (without RD); more than 1 month diabetic vitreous hemorrhage; retinal tear/hole/detachment; and ghost cell glaucoma. The prognosis of VH is usually good [26].

CH is a vision-threatening complication often related with ocular trauma or with intraocular vascular anomalies or with ocular surgeries (cataract, glaucoma, penetrating keratoplasty, and vitreoretinal surgery (vitrectomy and laser photoocoagulation) [27–30]. CH also can happen spontaneously [31]. The risk factors include older age, hypertension, diabetes mellitus, obesity, uveitis, high myopia, arteriosclerosis and systemic anticoagulation usage [32–35].

CH happens when a fragile vessel is exposed to sudden intraocular pressure changes. CH has a massive form and a limited form. The latter form has a better prognosis than the former form. The massive CH comprises the extrusion of intraocular iris, lens, and vitreous outside the eye. The limited CH usually recovers spontaneously within 1–2 months [36].

The symptoms and ocular examination of CH included severe pain, blurry visions, a shallow A/C, mild in inflammation high intraocular pressure, dome-shaped elevation of the retina and choroid, and/or extrusion of the iris, lens, and vitreous. A scan or B–scan can detect this hemorrhage. Differential diagnosis includes RD, choroidal effusion, and choroid/ciliary body tumors.

Treatment of the serous choroidal detachment is usually non-surgical. Surgical drainage of CH is indicated for the following situations: massive CH with severe pain, high IOP, shallow A/C, CH under macula, and hemorrhage in vitreous body or sub–retinal space [9].

In this case, the CH is belonged to a limited CH form. The hemorrhage site is close to the Ahmed shunt implant sutures. PPV was performed and an endolaser panretina photoocoagulation was applied around CH and inferiorly around chorioretinal scar in this case. The BCVA of left eye was 20/40, PHNI 2 months after the PPV.

**Conclusion**

This case demonstrates the role of clinical observation, and diagnosis surgery in the diagnosis of ARN. In most cases the diagnosis can confidently be made from the retinal findings and virus detection. Since the prognosis of ARN is generally unfavorable if untreated, it is very important to get early diagnosis and treatment. The differential diagnosis can be tricky when a few eye diseases coexisting like in this case report.

**References**


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