Review Article

VITREOUS HEMORRHAGE

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Vitreous hemorrhage is defined as the presence of extravasated blood within the space defined by internal limiting membrane of retina posteriorly and laterally, the non-pigmented epithelium of ciliary body laterally and the lens zonular fibers and posterior lens capsule anteriorly.¹

Vitreous hemorrhage does not just include Intra-gel hemorrhage but is a term which also includes hemorrhage within:
- Berger's space
- Canal of Petit
- Cloquet's canal
- Bursa premacularis
- Subhyaloid hemorrhage

Although hemorrhage within these space display different features as compared to hemorrhage within formed vitreous.

CLINICAL FEATURES

Patient with acute vitreous hemorrhage complains of visual haze, floaters, smoke signals, photophobia and perception of shadows and cobwebs.²

1. Intra-Gel Hemorrhage
   - Features depend on the amount of blood in the vitreous cavity
   - Profuse vitreous hemorrhage if diffuse anteriorly and centrally; it obscures the view of peripheral retina and ora (since the subhyaloid hemorrhage is limited by vitreous base anteriorly, thus a peripheral rim of retina can be visualized on indirect ophthalmoscopy).

   - Slit lamp examination will show extensive hemorrhagic debris in the anterior vitreous and on posterior lens capsule.
   - Blood in the formed vitreous clots rapidly (due to platelet activation by collagen) and finger like projections can be seen from the site of bleeding into the vitreous gel.
   - Blood generally remains stationary in vitreous cavity except to the extent that the formed vitreous gel itself moves with the movement of globe.
   - Blood in formed vitreous gel tends to stay longer and resolve more slowly.
   - Organized vitreous hemorrhage appears as yellowish fluffy vitreous opacity and dense yellowish-white vitreous membranes.

2. Pre retinal/ Sub hyaloid hemorrhage
   - Hemorrhage is located between internal limiting membrane of the retina and detached posterior hyaloid membrane.
   - Blood in this location does not clot, moves freely on head movements and settles down on gravity forming a boat shaped figure (although this appearance can be altered by vitreo retinal adhesions)
   - The blood may settle down as layers of red blood cells and plasma
   - Since the subhyaloid hemorrhage is limited by vitreous thus a peripheral rim of retina can be visualized on indirect ophthalmoscopy.
   - Visual impairment in the patient with pre retinal hemorrhage depends on the amount of bleeding and location (involvement of macular region)
   - Bleeding in this location resolves and reabsorb rapidly (due to close proximity of blood to retinal circulation)

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COMPARISON WITH SUB ILM HEMORRHAGE

- In sub ILM hemorrhage, the blood is under tension and does not shift with change in the position of patient’s head as observed in sub hyaloid hemorrhage.
- Hemorrhages can break through ILM into sub retinal space.

ETIOLOGY

Children

- Trauma
  a. Birth trauma
  b. Shaken baby syndrome
  c. Traumatic child abuse
- Retinopathy of prematurity
- Retinal break
- Retinal detachment
- Retinoblastoma
- Congenital Retinoschisis
- Pars planitis
- PHPV
- Terson’s syndrome

Adult

A. Bleeding from diseased retinal vessels or abnormal new vessels
   - Diabetic retinopathy
   - Eale’s disease
   - Retinal vein occlusion
   - Sickle cell retinopathy
   - Retinal capillary angioma
   - Hypertensive retinopathy
   - Radiation retinopathy
   - Macraneurysm
B. Rupture of normal retinal vessels
   - Retinal breaks
   - Retinal detachment
   - Posterior vitreous detachment
   - Trauma

C. Extension of hemorrhage from other sources
   - ARMD with CNVM
   - Intraocular tumour- choroidal melanoma

D. Miscellaneous
   - Terson’s syndrome
   - Bleeding diathesis

PROLIFERATIVE DIABETIC RETINOPATHY

- Most common cause of vitreous hemorrhage overall in epidemiological studies
- Accounts for 63% of patients with bilateral vitreous hemorrhage.
- In NIDDM, proliferative diabetic retinopathy accounts for 64% cases of vitreous hemorrhage while in IDDM it accounted for 89% of vitreous hemorrhage.
- Characterized by growth of fibroglial and neovascular tissue in response to the underlying ischemia.
- Vitreous traction on the neovascular membrane is the cause of hemorrhage.

TRAUMA

- Represents the leading cause of vitreous hemorrhage among patients younger than 40 years
- More common in males
- Blunt trauma can lead to vitreous hemorrhage due to retinal detachment with retinal break, choroidal tears with an overlying retinal tear (retinitis sclopetaria) and optic nerve avulsion
- Cause of late vitreous hemorrhage after trauma can be retinitis proliferance with contraction of fibrovascular bands and sub retinal neovascularisation
- Penetrating injury with or without intraocular foreign body may also be associated with vitreous hemorrhage.

RETINAL VASCULAR OCCLUSION

- Most of the studies report retinal vascular occlusion as the third common cause of vitreous hemorrhage.
- Mean age of the patient is 64 years and upto 88% of these have hypertension.
• Branch retinal vein occlusion account for upto 59% of cases while hemiretinal and central vein occlusion accounts for 35% and 6% cases respectively

• Vitreous hemorrhage occurs usually from NVE or NVD during the late stages of the disease. It may also occur as a result of rupture of the blood through the internal limiting membrane, particularly in the eyes with many sub-internal limiting membrane hemorrhages.

• Sometimes the vitreous hameorrhage can occur from intraretinal microvascular abnormalities (IRMA) secondary to BRVO or development of posterior vitreous detachment (PVD).

ACUTE POSTERIOR VITREOUS DETACHMENT

• Posterior vitreous detachment is the separation of cortical vitreous form internal limiting membrane and retina.

• It can be partial or total. It occurs from weakening of the vitreous cortex- ILM adhesions i.e. liquefaction. Dissolution of vitreous ILM adhesion allows liquid vitreous to enter the retro-vitreal space via peripapillary hole and perhaps the premacular vitreous cortex as well. With sudden eye or head movement's liquid vitreous dissects a plane as a wedge between vitreous cortex and ILM leading to PVD.

• In the presence of strong vitreo-retinal adhesions, the instability of liquefied vitreous exerts undue traction on the retina resulting in retinal tears. Tears are usually U shaped, symptomatic and located in the upper fundus. They are often associated with vitreous hemorrhage.

• When such a sudden traction force develops then it may avulse a peripheral retinal vessel and lead to vitreous hemorrhage with or without retinal tear.

• 15% patients with acute PVD have vitreous hemorrhage and 70% of those have associated retinal tears.

OTHER CAUSES

i. Blood dyscrasias (leukemia, thrombocytopenia) and hemostatic disorders are important causes of vitreous hemorrhage; however, there is not a very high rate of vitreous hemorrhage in these patients.

ii. Anti-coagulation therapy is not a risk factor for the development of vitreous hemorrhage, even in severe vascular occlusions but with the possible exception of patients with preexisting nonvascular changes.

iii. Terson's Syndrome: Terson described occurrence of vitreous hemorrhage in patients of sub arachnoid hemorrhage. Such a hemorrhage is usually sub ILM although it may rarely break through into the vitreous cavity. The currently accepted hypothesis is a threefold mechanism.

a. Sudden increase in intra cranial tension leads to effusion of clear or bloody CSF into optic nerve sheath through optic canal's, sub arachnoid communication compresses and obstruction of retinochoroidal outflow cause retinal venous hypertension and hemorrhage.

b. Severe rise in intra cranial tension causes reflex systemic hypertension.

c. Dilation of optic nerve sheath causes rupture of intradural bridging vessels running from dura to the pia mater of the optic nerve.

SEQUELAE FOLLOWING VITREOUS HEMORRHAGE

• Lamellae of aggregated platelets and vitreous collagen form membranes (Ochre membranes) with in the clot.

• Vitreous membranes outside the clot may get formed as a result of inflammation incited by the presence of iron (ferrous ions) and macrophages in the vitreous cavity which may lead to traction on vitreoretinal interfaces and can lead to retinal detachment.

• Vitreous undergoes liquefaction and sometimes cholesterol deposits may be seen after resolved vitreous hemorrhage.

• Hemoglobin spherulosis is a term given to a rare occurrence of brown colored aggregations of hemoglobin, instead of breakdown of hemoglobin to ferritin.

• Cylindroid structures may get formed in the vitreous as a result of degenerative influence of degradation products of hemoglobin. (Vitreous cylinders)
COMPLICATIONS OF VITREOUS HEMORRHAGE

Hemosiderosis Bulbi and Retinal damage

- Iron (Fe³⁺) is liberated during catabolism of hemoglobin which is toxic to the retina especially to the photoreceptors and Muller's cells.
- Iron related toxicity becomes clinically manifest in extensive long standing vitreous hemorrhage.
- The morphological retinal changes with acute iron toxicity consist of pyknosis and degeneration of photoreceptor cells, along with inner retinal edema.
- Iron especially in its ferrous form, binds to the acid mucopolysaccharides at the posterior hyaloid face, perivascular tissue, optic nerve head and trabecular meshwork. Toxic effects are first noticed around these structures. Choroids and ciliary muscle remain largely unaffected.
- Patients may complain of decreased vision especially at night and xanthopsia. Peripheral fields get constricted and later, the central field defects also appear.
- In case of subretinal hemorrhage, damage to photoreceptors is extensive, with signs of choroidal inflammation on histopathology.

PROLIFERATIVE RETINOPATHY

- Haemoglobin or iron in the vitreous may cause fibrovascular or glial proliferation internal to the retinal internal limiting membrane with secondary retinal detachment.
- The degree of retinal proliferation is dependent on the amount of bleed.
- Direct stimulation of fibroblastic elements by iron or possible deletion of an inhibitory factor which normally prevents the growth of fibrous tissue was responsible for the observed proliferations.
- Once preretinal proliferation is established recurrent bleeding may cause vitreous collapse with traction on newly formed and normal vessels and subsequent recurrent hemorrhage which may perpetuate and repeat the problems.

Glaucoma related to vitreous hemorrhage

a. Ghost Cell Glaucoma

Following vitreous hemorrhage, fresh red blood cells (biconcave, pliable cells) degenerate into ghost cell forms (smaller, khaki-colored, spherical, more rigid cells) usually within 1-3 weeks. Ghost cells contain intra-cellular, denatured hemoglobin adherent to the red cell membrane (Heinz body).

- G host cells pass forward into the anterior chamber after disruption of the anterior hyaloid face following accidental trauma, cataract extraction, or vitrectomy.

- Being more rigid and less pliable than fresh RBC's, ghost cells can lower the aqueous outflow much more significantly.

- AC is deep and filled with multiple, small, tan colored cells. Angle is open, with a discolored trabecular meshwork, ghost cells form a typical tan colored precipitate inferiorly which mimics hypopyon. Also known as HEMOPHTHALMITIS. If fresh RBC's also coexist, a double layered precipitate of light khaki on top of red is present, known as CANDY STRIPE sign.

b. Hemolytic Glaucoma

- Trabecular meshwork is obstructed by the red blood cell debris, free hemoglobin and hemoglobin laden macrophages.

- Clinical features are indistinguishable from ghost cell glaucoma.

c. Hemosiderotic Glaucoma

- Very rare, presents years after recurrent vitreous hemorrhage. Mucopolysaccharides of the trabecular meshwork have a high affinity for iron and this high concentration of iron may damage endothelial cells in the human trabecular meshwork, which may cause secondary degenerative changes such as sclerosis and obliteration of the inter trabecular spaces.

- Other associated signs of ocular hemosiderosis such as cataract, iris discoloration and ERG changes are present.

INVESTIGATIONS

1) A detailed history and general physical examination should be done in each case. History of ocular and systemic disease especially diabetes, hypertension, trauma, retinal break or
detachment in the other eye, family history of detachment.

2) Base line visual acuity and projection of rays should be assessed.

3) Careful ocular examination to assess:
   a. Corneal status: corneal edema, opacities and any evidence of trauma.
   b. Iris should be examined for rubeosis, synechiae, tears and holes (may indicate penetrating ocular injury, sectoral ischemia or atrophy).
   c. Gonioscopy should be done for any evidence of neovascularization and status of angles. It may also reveal a ciliary body tumour.
   d. Fluorescein angiography of iris can detect early rubeosis.
   e. Pupil examination for light reflex and relative afferent pupillary defect. Posterior synechiae, pupillary membrane and iris atrophy may prevent pupillary dilation which hampers the fundus visualization during surgery and examination.
   f. Lenticular changes also interfere with fundus evaluation.
   g. Pre-operative IOP should be taken.

   ➢ This may be supplemented by slit lamp biomicroscopy with 78D or 90D lens or fundus contact lens.
   ➢ Contralateral eye examination is often diagnostic eg. Diabetes, ARMD, Eale’s, ROP. Presence of peripheral retinal lesions in the other eye should alert one for the possibility of retinal break.

4) Indirect ophthalmoscopy is used primarily to study the fundus. An attempt should be made to determine whether the underlying retina is attached or detached and whether bleeding is from a retinal tear or neovascular frond. In most cases, vitreous hemorrhage is less dense superiorly and in the periphery, so scleral depression will reveal any retinal breaks or a retinal detachment extending into that area. In traumatic vitreous hemorrhage (esp. open globe injuries) scleral depression is avoided for the first 3- weeks.

5) Certain baseline investigations are helpful in detecting and diagnosing systemic conditions associated with vitreous hemorrhage.
   a. Complete hemogram including platelet count, BT, CT (for bleeding diathesis) and peripheral smear examination.
   b. ESR, chest X ray, Montoux test (tuberculosis, Eale’s disease).
   c. Blood sugar profile.
   d. Carotid Doppler and echocardiography in patients with retinal vascular occlusion.
   e. If choroidal metastasis are suspected then relevant investigations to look for primary malignancy are a must. Also in a case of primary choroidal and ciliary body tumour (melanoma) patients should be investigated for any systemic metastasis.

6) Ultrasonography:
   Main indication in vitreous hemorrhage:
   • To assess nature of bleed
   • Detection of PVD
   • Detection of RD (tractional or rhegmatogenous)
   • RIO FB
   • Fibrovascular frond
   • Intraocular tumour
   • Scleral rupture
   a. Vitreous hemorrhage (recent/ dispersed)
      Shape: Multiple small opacities, blood aggregates to form a large interface
      Reflectivity: Low to medium (10-60%)
      Mobility: Marked after movements (vertical> horizontal)
      Sound Attenuation: weak to medium
   b. Vitreous hemorrhage (long standing/ dispersed)
      Shape: Multiple small opacities + membranes, aggregates break down into small interfaces
      Reflectivity: Extremely low (2 to 5%)
      Mobility: after movements+
      Sound Attenuation: weak to strong
   c. Vitreous hemorrhage (Long standing/organised)
      Shape: Multiple membranes, blood organizes to form multiple membranes
      Reflectivity: High (60 to 100%)
      Mobility: slight after movement+
      Sound Attenuation: weak
Optical examination and ultrasonography help to delineate ocular structures. Functional tests are important for diagnosis and prognosis in patients with opaque media eg. Vitreous hemorrhage.

**MOS T I MP ORTA N T TR EA TMEN T I S**
**TO  E L I M I N A T E  T H E  C A U S E  O F**
**HEMORRHAGE.**

**Treatment options include**
Observation fresh vitreous hemorrhage often clears in days to weeks to allow evaluation of retina. In vitreous hemorrhage of unknown etiology and attached retina on USG, the patient is asked to rest with the head in elevated position (some surgeons advice binocular patching also) to be reevaluated after 3-7 days to find the cause of hemorrhage. Eyes with attached retina and known etiology, which do not need to be treated, are evaluated after 3-4 weeks.

No medication is of proven benefit during this period. Oral ascorbic acid (Vitamin C) may be given for faster clearance. This treatment offers two advantages.

- Hemorrhage in retro-hyaloid space clears more rapidly as it allows blood to settle.
- Allow visualization and treatment of retina at least in some quadrants (specially superior) and
- Aspirin, NSAIDS and anti-clotting agents should be stopped unless necessary.

**SURGICAL TREATMENT**
Nonclearing vitreous hemorrhage requires vitrectomy and treatment of the underlying pathology. The surgery may be delayed up to three months or more. However, the surgical decision depends on the merit of individual cases. Early vitrectomy is considered in case of bilateral vitreous hemorrhage causing blindness, tight preretinal macular hemorrhage, chronically recurring hemorrhage, acute vitreous hemorrhage with retinal detachment, and vitreous hemorrhage with known tractional retinal detachment close to the macula.

**ANTERIOR RETINAL CRYOTHERAPY**
Has been successfully tried in eyes with relatively fresh hemorrhage. It acts by-
- Breakdown of blood retinal barrier by inciting inflammation and hence increased levels of tissue plasminogen and
- Activation of fibrinolysis via extra-cellular pathway.
- Ablates peripheral ischaemia and neo-vascular areas in DM and Eales disease.

But it promotes the formation of pre-retinal fibrin and contraction of vitreous gel and may lead to tractional RD, so it should not be used in case with TRD and vitreous hemorrhage of unknown etiology.

The best indication for ARC is:
1. Post vitrectomy eye with recurrent vitreous hemorrhage from sclerotomy sites and
2. Anterior hyaoid proliferation.

**LASER PHOTOCOAGULATION**
In proliferative vasculopathies laser photo-coagulation should start as soon as any part of the retina is visible. Similarly, after partial clearing of haemorrhage, one visualize the tear and the avulsed vessel and can be barraged with the help of laser.

**POSTERIOR HYALOIDOTOMY**
Hemorrhage located between the ILM and retina may cause permanent damage to macular before spontaneous resolution occurs. In these cases posterior hyaloidotomy can be done using Nd- YAG laser, which disrupts the ILM and releases blood into vitreous cavity.

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