Viral anterior uveitis

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Viral anterior uveitis (VAU) needs to be suspected in anterior uveitis (AU) associated with elevated intraocular pressure, corneal involvement, and iris atrophic changes. Common etiologies of VAU include herpes simplex, varicella-zoster, cytomegalovirus, and rubella virus. Clinical presentations can vary from granulomatous AU with corneal involvement, Posner-Schlossman syndrome, Fuchs uveitis syndrome, and endothelitis. Due to overlapping clinical manifestations between the different viruses, diagnostic tests like polymerase chain reaction and Goldmann-Witmer coefficient analysis on the aqueous humor may help in identifying etiology to plan and monitor treatment.

Key words: Cytomegalovirus, herpes simplex virus, ocular hypertension, rubella virus, varicella-zoster virus, viral anterior uveitis

Viral anterior uveitis (VAU) is characterized by anterior uveitis (AU) with elevated intraocular pressure (IOP) diffuse stellate keratic precipitates (KPs), presence of pigmentation in active KPs and iris atrophic changes.[1-4] The most commonly implicated viruses include herpes simplex (HSV), varicella-zoster (VZV), cytomegalovirus (CMV), and rubella (RV).[5-8] Herpetic AU is the most common cause of VAU accounting for 5–10% of all uveitis cases in the western world and 0.9–8.3% of all infectious uveitis in India.[7,10] The severity and outcome of VAU depend on the type of the virus, clinical characteristics of the disease, immune status, and genetic makeup of the individual. In an aqueous-based polymerase chain reaction (PCR) study from South India, 2/3rd of cases were VZV, 19.4% were HSV-1, and 8.3% were CMV.[9] This review will focus on syndromes associated with viral etiology, different viruses causing AU, clinical features, diagnostic tools, and management of viral anterior uveitis.

Methods

Literature search pertaining to VAU published in PubMed, EMBASE, and MEDLINE. For PubMed related search, MESH terms “viral anterior uveitis” and “Herpetic”/“Cytomegalovirus”/“Rubella”/“Fuchs heterochromic iridocyclitis”/“Posner Schlossman syndrome”/“Diagnosis”, and “Therapy”. A manual search of references cited by retrieved articles for additional references was also done. All authors independently conducted a systematic review of the literature and extracted data.

 Syndromes Associated with Viral Aetiology

Posner Schlossman syndrome (PSS)
PSS is characterized by recurrent, acute attacks of unilateral mild AU with few granulomatous KPs, and severely elevated intraocular pressure (IOP). [12] Symptoms include mild blurring of vision and haloes. It affects young adults more frequently in the 3rd decade in the European population but later in the Asian population (3–5th decade).[13,17] Males are at a higher risk of developing PSS (50.5–71.4%).[18] CMV appears to be a major cause of PSS, especially in Asia.[14,15,19] HSV is also known to cause PSS.[20] Posterior synechiae and vitritis are absent. Mild iris atrophic changes may occur. Glaucoma develops in 26% of which 17% require filtration surgery.[14] The course is recurrent and often unpredictable.

Fuchs uveitis syndrome (FUS)
FUS is a chronic low-grade inflammation involving the anterior uveal tract and vitreous and is most commonly unilateral (90%).[1,21] Fuchs initially described this condition as Fuchs heterochromic iridocyclitis, characterized by

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Common Etiologies of Viral Anterior Uveitis

Herpes simplex virus

HSV AU is characterized by small to medium-sized KPs, some of these fresh KPs may be pigmented. The location may be central, paracentral, or diffuse. In keratouveitis, they are located in the same distribution as the inflamed cornea. Elevated intraocular pressures occur due to trabeculitis and this can be episodic. These may cause secondary glaucomatous optic neuropathy. Iris atrophy occurs in 41–48%. During acute HSV, sectoral iridoplegia and flattening of the pupillary border occur in the affected area [Fig. 1]. The presence of patchy or sectoral iris atrophy is seen in recurrent or chronic disease and may be absent in very early disease. Spiral atrophy is typically associated with HSV. Diffuse iris atrophy is rather uncommon finding and noted in 10% cases. HSV AU causes iris pigment epithelitis. In severe inflammation, hypopyon, transient hypHEMA, posterior synechiae (38%), and vitritis (43%) may occur. Focal iris stromal hemorrhage may be seen in acute HSV. Cataract occurs later in the disease course.

Varicella Zoster virus

VZV lies dormant in the neural sensory ganglia following primary infection usually in childhood and reactivates when VZV specific immunity wanes, typically during the 6th or 7th decade of life. Alternatively, it may occur in young immunocompetent individuals, conditions causing immunosuppression like acquired immunodeficiency syndrome and immunosuppressive drugs. Herpes zoster ophthalmicus (HZO) presents with severe pain followed by a vesicular eruption in the dermatome of the ophthalmic division of the trigeminal nerve. If the tip of the nose is involved, it is a predictor for ocular inflammation (Hutchinson’s sign). VZV AU occurs in 40–60% of HZO in immunocompetent patients and may be present for many months.

Typically, VZV AU presents 2 weeks following dermatological manifestations in the form of acute hypertensive AU with granulomatous or nongranulomatous uveitis. The inflammation in VZV is generally more severe than in HSV AU, possibly because VZV invades the root of iris epithelium and causes occlusive vasculitis. Segmental iris atrophy (triangular sectoral loss of iris pigment epithelium with the base at the iris root) may develop after the acute episode resolves causing transillumination defect (88%). It has been postulated that the severity of iris atrophy and pupil distortion is closely related to the viral load in aqueous. Corneal involvement has been reported in 25% of cases and includes nummular keratitis, limbal keratitis, and ring infiltrates. Profound reduced corneal sensation and coarse pseudo dendrites with an elevated appearance that lacks terminal bulbs may be seen. There may be associated episcleritis, scleritis, and choroidal vitiligo. Posterior synechiae (40%) and vitritis (83%) can occur in VAV AU. Secondary glaucoma is noted in 15–43% of cases. A detailed posterior segment examination is mandatory in all cases of herpetic uveitis.

Zoster sine herpete AU: At times, patients present with AU typical of viral AU in the absence of dermatological manifestations.

Cytomegalovirus

CMV is an important cause of hypertensive AU in immunocompetent individuals and there is likely a prominent immunological component as it is not seen in immunocompromised individuals. Ocular tissues like iris and ciliary body may be a site of CMV latency as suggested
by murine studies. An intraocular immunocompromised state with impairment of both innate and adaptive immunity, especially the virus-specific T-cell response, may trigger CMV reactivation (Example: ocular corticosteroid implants, topical cyclosporine A 0.05% ophthalmic emulsion, topical prostaglandin analogs, ophthalmic surgery). 

Most cases have been reported from Asia, particularly from Chinese and Japanese populations, which could be due to the higher seroprevalence of CMV in Asia. CMV has been identified as the causative virus for 75% of hypertensive AU in Singapore, 67% of the chronic idiopathic recurrent AU and ocular hypertension in Korea, 33% of the viral AU in Thailand, 8.3% of viral AU in south India and only 2% of viral AU in the United States of America. CMV AU usually affects individuals from the 3rd decade onwards, particularly Asians and males, those in their 3rd-5th decade present with PSS while those in their 5th-7th decade present with chronic CMV AU resembling FUS. It is acute and recurrent in patients
younger than 40 years of age or chronic in those above 40 years of age. It is unilateral in most of the cases and bilateral in 7% cases.\cite{16,17,74,79} The clinical manifestations of CMV AU vary.

**Acute relapsing hypertensive anterior uveitis (Posner-Schlossman Syndrome)**

CMV is thought to be the cause of PSS in Asian and western populations.\cite{18,19,22,40,77,78} The typical presentation is a patient in the 3rd–5th decade with an acute onset of haloes, unilateral mild blurring of vision associated with an ipsilateral headache, possibly with a history of similar episodes. The IOP often exceeds 50 mm Hg during the attack in the presence of subtle subepithelial edema. The severely elevated IOP is often out of proportion to the findings of mild anterior segment inflammation. KPs are medium to large (39%), white or gray colored, and few located centrally or in the peripheral cornea.\cite{16}

**Chronic hypertensive CMV anterior uveitis**

Chronic CMV AU more commonly affects older patients in the 5th–7th decade, at a mean of 65 years of age, who may present with ocular discomfort and blurring of vision. A geographic disparity is seen in the clinical presentation of chronic CMV AU in Asian and western populations. CMV is a major cause of FUS in East Asia, especially in Singapore, Taiwan and Japan.\cite{14,15,18,19} It presents with mild ocular injection, mild-to-moderate anterior chamber activity and diffuse, fine, stellate uniformly distributed KPs. Chronic CMV AU in eyes of European patients has fewer KPs that are brown (pigmented) and located inferiorly, with minimal flare. The IOP is typically persistently elevated in chronic CMV AU. The iris may appear moth-eaten due to stromal atrophy, which is more commonly diffuse, although patchy and rarely sectoral atrophy have been reported, and the posterior pigment epithelium is often relatively intact with no transillumination defects.\cite{79} Although findings of CMV in the smooth muscle cells of the iris led some to postulate that the iris stromal atrophy was due to ischemic necrosis of the iris stroma as a result of the direct viral invasion, Sakai et al. have suggested that the diffuse iris atrophy which is not associated with dyscoria may develop as a consequence of persistently elevated IOP rather than tissue damage by CMV.\cite{58} Heterochromia (in which a naturally darker iris appears lighter, and lighter irides, particularly blue or light green, appear darker) is uncommon but may be present.\cite{80} The diffuse iris atrophy may also result in fragile iris vasculature, which can be visualized on gonioscopy in the iris and trabecular meshwork or iridocorneal angle. These fragile vessels may be prone to bleeding easily, giving rise to Amster’s sign.

A posterior subcapsular cataract occurs in 81.3% of eyes later in the disease course. Unlike RV, vitritis is rare in CMV infection. Unlike in PSS, the inflammation tends to recur when topical corticosteroids are tapered.

**Recurrent or chronic iridocyclitis**

Unlike Asian patients who present similarly to FUS or PSS, patients in the West often present with less distinct syndromes, or overlap of features from both syndromes, manifesting as a mild unilateral recurrent or chronic iridocyclitis.\cite{14}

**Corneal endotheliitis**

Corneal endotheliitis is the inflammation of the corneal endothelium characterized by localized corneal stromal edema and KPs.\cite{81} It can involve a focal area or even the entire endothelium that presents similarly to diffuse bullous keratopathy with severe stromal edema. An immune ring formation similar to that seen in HSV-related keratitis may sometimes be present. The IOP may be elevated.\cite{82} CMV corneal endotheliitis may be associated with AU in 30% of Asian or European patients or may occur in isolation.\cite{19,80}

**Other characteristic clinical signs**

Coin-shaped lesions in which small-sized KPs are distributed in a ring pattern are pathognomonic of CMV with a positive predictive value of 90.9% and, maybe seen in both acute and chronic infection.\cite{71} These coin-shaped KPs were seen in 53% of CMV AU cases in a recent Japanese study.\cite{58} KPs may also be seen in a linear pattern in the peripheral cornea.\cite{58}

Nodular endothelial lesions, which possibly represent swollen endothelial cells, are white medium-sized nodular lesions with a surrounding translucent halo and may become pigmented over time. They are more common in chronic CMV AU and are significantly associated with CMV infection in eyes with presumed FUS [Fig. 3].\cite{75} The endothelial cell count is significantly reduced in CMV positive eyes, a feature that is less commonly seen in other AU in the absence of frank keratitis.\cite{83,80}

The pupil is usually round and posterior synchiae are notably absent. Associated posterior segment abnormalities are uncommon and include peripheral fibrovascular disc, and macular edema and epiretinal membrane. Prolonged arm to retina time on fluorescein angiography has been hypothesized to reflect subclinical vascularity.\cite{84}

**Rubella virus**

RV AU is chronic, often unilateral but may be bilateral (14%) in the presentation.\cite{85} It is a common cause of FUS in the western population. The definitive finding of anti-RV antibodies in the anterior chamber fluid of FUS patients clearly shows that rubella may be participating in the pathogenesis.\cite{24,16,85,86} On the other side, the very rare finding of RV-PCR may be a sign that FUS is less an infectious but more an immune response to rubella. The hypothesis of FUS as a RV-induced disease was supported by the decreased number of FUS patients after the introduction of the rubella vaccination program in the United States (from 4.48% to 1% FUS patients/year).\cite{25} However, the question rises if a living attenuated vaccine or a subclinical RV infection before vaccination may induce FUS.\cite{59} Analysis of the aqueous humor in FUS patients also showed elevated levels of the inflammatory cytokine (IL-6, IL-10), interferon-γ, and low IL-12 levels suggesting a Th1-type response.\cite{87,88}

RV AU usually presents in relatively younger patients (mean age 35 ± 12 years) with posterior subcapsular cataract (47%) with a chronic blurring of vision and or floaters with minimal redness and pain.\cite{86} It has a chronic course and presents with diffuse stellate KPs (do not become pigmented and persist despite treatment), diffuse iris atrophy, and mild anterior chamber reaction. Koeppen nodules may be present. Low-grade vitritis is often present and frequently mistaken for intermediate uveitis [Fig. 4].

Absence of redness, pain, posterior synchiae, and cystoid macular edema are characteristic features. RV AU can be complicated by ocular hypertension (25%) leading to secondary glaucoma.

**Other viral etiologies**

Less common causes include, human T-cell lymphotropic virus-type 1 (Seen in southern Japan and Africa and frequently
Anterior chamber tap

Aqueous humor analysis is a useful method to determine the etiology and estimate the viral load as it may difficult to differentiate the etiology based on clinical manifestations in all cases. Tests done include PCR, Goldmann–Witmer coefficient (GWC) analysis, metagenome sequencing.\cite{6,25,77,98,99}Polymerase chain reaction

PCR can detect minimal amounts of viral DNA and enable rapid confirmation of diagnosis. Aqueous tap for PCR should be done during the IOP spike, preferably before initiation of therapy especially in CMV.\cite{10} A negative PCR does not exclude a viral etiology. This could be due to the limited volume of aqueous sample, low intraocular viral load, transient rapid rise in IOP, and self-limiting tendency of ocular inflammation with rapid elimination of viral DNA and presence of inhibitory compounds in the sample or microorganism polymorphism.\cite{89} In some cases, a positive result may only be obtained after repeated aqueous taps. Conversely, PCR may give a false positive result by detecting DNA from latent viruses in leukocytes present in the anterior chamber during inflammation. A qualitative multiplex PCR can be done to screen for viruses and subsequent real-time PCR can help to identify the causative virus and quantify the viral load as a marker of severity of the infection. Real-time PCR can also be used to monitor response to therapy and any drug resistance.\cite{77,83}

Goldmann–Witmer coefficient analysis

GWC helps to determine pathogen-specific intraocular antibody production. Unlike PCR which tends to be positive at the early reactivation, when the viral load is higher, GWC analysis may take up to 2 weeks to become positive but remains positive for longer periods and hence more useful when patients present later (chronic) as in RV AU. RV is commonly detected via positive GWC results but only sporadically by PCR. However, it is less specific than PCR due to possible cross-reactivity of antibodies. As the diagnostic utility of the above tests depends on the patient’s immune status, the chronicity of infection and the time of aqueous sampling, it is best to perform both the tests in parallel to increase the diagnostic yield. GWC analysis is not widely available in most countries and hence most countries rely solely on PCR.\cite{6,40,98}

Viral cultures are difficult and time-consuming. It is not commonly done.

Other investigations

Anterior segment imaging includes specular microscopy to demonstrate lowered endothelial cell counts (ECC) compared to the fellow eye is known to occur in CMV AU. The extent of endothelial cell loss is correlated with the viral disease burden.\cite{60,83} Anterior segment optical coherence tomography can demonstrate the nodular endothelial lesions as thickened, highly reflective endothelial cells layer. Confocal microscopy demonstrates the oval eye cells (large endothelial cells containing nuclei with a high reflection area surrounded by a halo of low reflection within the cornea) and to monitor the response to therapy.\cite{108,109} Serology has limited value as most adults have had prior exposure to the viruses. Metagenomic deep sequencing can detect deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) viruses in as little as 20 μL of intraocular fluid samples in a single assay and holds promise in diagnosis of infectious uveitis.\cite{102}

Treatment

Treatment of HSV AU

Though the management of HSV keratitis is well studied, the role of acyclovir in the treatment of HSV AU is not evaluated. Studies suggest that the duration of AU may be shortened by the prompt use of therapeutic doses of antiviral therapy and, maintenance therapy is effective in decreasing disease recurrence.\cite{51}

Oral acyclovir 400 mg five times daily for 4 weeks in conjunction with topical corticosteroids that reduce the anterior segment inflammation, cycloplegics/mydriatic agents that reduce the pain and prevent posterior synechiae. In severe and recurrent disease, maintenance therapy of oral acyclovir 400 mg twice daily is useful to prevent a relapse. Alternatively, valacyclovir, which is a prodrug with better bioavailability, may also be used at a dose of 500 mg three times a day for 4 weeks followed by 500 mg twice a day for maintenance.\cite{107} Systemic antiviral therapy combined with low-dose corticosteroid drops may have to be used for several years, to prevent relapses. In eyes with raised IOP, antiglaucoma medications are given topically. Severe elevation of IOP may require oral carbonic anhydrase inhibitors and filtration surgery. When preparing the eye with a viral AU for cataract surgery, the eye should be quiescent and prophylactic oral antiviral therapy is found to be useful. Lucy M Lu et al. noted the recurrence of herpes zoster in 23 (40.4%) patients after phacoemulsification cataract surgery. An increased risk for recurrence was associated with shorter periods of quiescence and a greater number of recurrences before surgery. Acyclovir prophylaxis protected against recurrences after cataract surgery and, may be required in cases with a history of multiple disease recurrences.\cite{103}

Treatment of VZV AU

Acyclovir given 800 mg five times daily for 10 days given within 72 h of the onset of skin lesions in HZO reduces the incidence and severity of episcleritis, dendritiform keratopathy, stromal keratitis, and anterior uveitis. Topical steroids and cycloplegics/mydriatic agents are used to alleviate inflammation and pain. However, the duration of treatment for chronic VZV AU should be as long as the uveitis is active. Oral acyclovir 400 mg twice a day is used as prophylaxis for recurrent uveitis. Owing to the predictability of its resorption, oral valacyclovir is generally
| Variables                      | Herpes simplex virus (HSV) | Varicella-zoster virus (VZV) | Cytomegalovirus (CMV) | Rubella virus (RV) Rubella associated FUS |
|-------------------------------|---------------------------|-------------------------------|-----------------------|------------------------------------------|
|                               |                           |                               | Acute (Posner Schlossman like syndrome) | Chronic CMV anterior uveitis | CMV-associated Fuchs uveitis syndrome (FUS) |
| Age                           | 40-50 years               | >60 years                     | 30-50 years           | 40-70 years                              | 40-70 years                                      |
|                               |                           | Immunocompromised patients (any age) |                       |                                         | (Mean: 35±12 years)                               |
| Gender                        | No predilection          | No predilection               | Males (65%)           | Males (80%)                              | No predilection                                  |
|                               | All                       | All                           | Predominantly Asian population | Predominantly Asian population | Predominantly Western population                 |
| Race                          | Mostly unilateral (bilateral in 18%) | Unilateral                     | Unilateral            | Mostly unilateral (bilateral in 7%)      | Mostly unilateral (bilateral in 14%)             |
| Laterality                    | Acute, recurrent         | Acute spikes (38-90%)         | Acute, recurrent      | Chronic                                  | Chronic                                          |
| Course                        | h/o fever or blisters/grouped vesicles occurring at the border of the eyelids with diffuse edema | Vesicular rash involving the ophthalmic division of the trigeminal nerve | Very high (up to 50 mmHg) during acute episodes (100%) | Very high (43.5±9.8 mmHg); persistently elevated | Very high (43.5±9.8 mmHg); persistently elevated (73.3%) |
| Dermal manifestations         | Moderate to severe       | Moderate to severe            | Mild                  | Mild                                     | Mild                                             |
| Conjunctival injection        | May be reduced           | May be reduced                | Intact                | Intact                                   | Intact                                           |
| Corneal sensation             | May be reduced           | May be reduced                | Intact                | Intact                                   | Intact                                           |
| Epithelial keratitis          | Dendritic ulcers (usually branching, with well-developed terminal bulb) | Pseudodendritic ulcers (less regular branching, few terminal dilatations) | None                   | None                                     | None                                             |
| Stromal keratitis             | Disciform keratitis; Interstitial keratitis; Immune ring keratitis | Nummular keratitis; Limbal keratitis; Immune ring keratitis | Immune ring keratitis | None                                     | None                                             |
| Corneal scars                 | Present (33%)            | Present (25%)                 | Rare                  | May be present                           | Nodular endothelial lesions surrounded by a translucent halo and occasional pigmentation |
| Endotheliitis                 | May be present           | May be present                | May be present        | May be present                           | None                                             |
| Keratic precipitates          | Small to medium          | Small to medium               | Medium to large (39%) | Small                                    | Fine and stellate (44%)                          |
| Size                          | Central, paracentral, diffuse, may be in Arlt’s triangle or in the same distribution as inflamed cornea | Central, paracentral, diffuse, may be in Arlt’s triangle or in the same distribution as inflamed cornea | Single or few, distributed centrally or in peripheral cornea; may have coin like lesions | May have a coin like lesions | Diffusely distributed; may have a coin like lesions (ring or linear pattern) |
| Distribution                  |                           |                               |                       |                                         | Diffuse                                          |
Table 1: Contd...

| Variables                        | Herpes simplex virus (HSV)                           | Varicella-zoster virus (VZV)                          | Cytomegalovirus (CMV)                                                                                                                                 |
|----------------------------------|------------------------------------------------------|-------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                  | White, may be pigmented                              | White, may be pigmented                               | Acute (Posner Schlossman like syndrome)                                                                                                               |
|                                  |                                                     |                                                       | Chronic CMV anterior uveitis                                                                                                                                 |
|                                  |                                                     |                                                       | CMV-associated Fuchs uveitis (FUS)                                                                                                                     |
| Colour                           | White or gray                                        | White or gray, may be brown                           | White or gray, may have pigmentation                                                                                                                  |
| Endothelial cell count           | Normal                                               | Reduced                                               | Reduced                                                                                                                                               |
| Anterior chamber inflammation    | Moderate to severe                                   | Mild                                                  | Mild                                                                                                                                                 |
| Iris                              | May be present during acute phase causing pupil flattening or D shaped pupil | Absent                                               | Absent                                                                                                                                               |
| Iris atrophy                     | Sectoral or patchy atrophy with transillumination defects, spiral iris atrophy | Mostly absent, rarely diffuse stromal iris atrophy | Mostly absent, rarely diffuse stromal iris atrophy, no transillumination defects                                                                   |
| Iris atrophy                     | Sectoral atrophy with transillumination defects, rarely massive iris atrophy with gross sphincter damage | Rarely sectoral, stromal iris atrophy, no transillumination defects | Rarely sectoral, stromal iris atrophy, no transillumination defects                                                                                   |
| Posterior synechiae              | May be present                                      | Absent                                               | Absent                                                                                                                                               |
| Pupil shape                      | May be irregular                                     | Round                                                | Round                                                                                                                                               |
| Elevated IOP                     | Elevated (38-90%)                                    | Elevated (100%)                                      | Elevated (69%)                                                                                                                                   |
| Cataract                          | Present in 28-35%, later in onset                    | 23%, later in onset                                   | 75%, later in onset                                                                                                                                |
| Glaucoma                         | Present in 18-54%                                    | 36%                                                  | At the time of presentation (47%)                                                                                                                   |
| Vitritis                          | 43%                                                  | 83%                                                  | 0%                                                                                                                                                    |

is a direct inhibitor of the viral DNA polymerase and does not require phosphorylation.

At present, there are no clear guidelines regarding the management of CMV AU. Studies have evaluated the efficacy of systemic (intravenous ganciclovir or foscarnet, oral ganciclovir) and local therapy (intravitreal ganciclovir, topical ganciclovir drops and gel) and have compared the various forms of antiviral therapy.

The induction regimen of oral ganciclovir followed is, 900 mg twice daily for 3 weeks followed by, a maintenance regimen of 450 mg twice daily for a minimum of 4 weeks. CMV AU may require long term antiviral therapy to reduce the risk of recurrences. Regular laboratory monitoring for bone marrow suppression, renal and hepatic toxicity and the cost of treatment makes it less feasible as long-term therapy in developing countries. Intravitreal ganciclovir has a lower risk of systemic toxicity and has been explored as an alternative to systemic ganciclovir. However, the recurrence rates were high. Topical ganciclovir is an alternative form of antiviral therapy in CMV AU. The topical concentration ranged between 0.15%–2% and applied 6–8 times/day for induction and 1–4 times/day for maintenance. Ganciclovir 2% eye drops
have reported good results in CMV corneal endothelitis and AU. Ganciclovir ophthalmic gel 0.15% is well tolerated with minimal toxicity. As this is less expensive and does not require laboratory monitoring, this may be a more viable option for long term antiviral therapy. The systemic and topical control of CMV anterior uveitis-treatment outcomes (STACCATO) is an ongoing randomized trial comparing the efficacy of oral ganciclovir and 2% topical ganciclovir along with placebo which, may provide further insight of effective routes of antiviral therapy in CMV AU.[110] Some authors favor the administration of intravitreal ganciclovir. An injection of 2 mg/0.05–0.1 ml is given weekly for 3 months either with or without adjunctive oral ganciclovir. The treatment of CMV induced endothelitis with either topical or systemic ganciclovir has been reported to be partially successful.[23] Topical nonsteroidal anti-inflammatory drugs (NSAIDs) may also be considered in CMV AU recalcitrant to topical steroids.[208]

Treatment of Rubella AU
Topical steroids may not be necessary due to the low-grade inflammation. Prolonged use can hasten cataract and glaucoma formation. Systemic immunosuppressive therapy is not recommended. Topical NSAIDs are considered to retard progression especially if required long term. Antiglaucoma medications may be used for secondary glaucoma. In glaucoma cases resistant to topical treatment, filtration surgeries are recommended.

Conclusion
A high index of suspicion for a viral etiology is required in the presence of the following features: Raised IOP at presentation, corneal scars, fresh pigmented KPs, and iris atrophy. HSV, VZV, CMV, RV are common etiologies. Variable clinical presentations with overlapping manifestations in different viruses may require diagnostic tests like PCR, GWC analysis for confirmation of etiology. This is important for planning therapy. Glaucoma is the most common vision-threatening complication of VAU.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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