Review Article

"For your eyes only": ophthalmic complications following lung transplantation

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Abstract: Ophthalmic complications in the lung transplant population are a little-known entity. It includes a spectrum of diseases ranging from infections such as cytomegalovirus (CMV) retinitis, herpetic keratitis, *Pseudallescheria boydii* to non-infectious complications such as posterior subcapsular cataracts (PSCs), cyclosporine retinopathy, and post-transplant lymphoproliferative disorder (PTLD). These diseases can be attributed to high levels of immunosuppression, advanced age, and drug-specific side effects. Underlying comorbidities such as diabetes mellitus may also play a role in the pathogenesis. Patients can present with varied symptoms such as blurry vision, floaters or eye pain. Prompt diagnosis often requires a high index of suspicion. With increasing numbers of transplants being performed worldwide, it is imperative for the pulmonologist and transplant physician to recognize these often subtle symptoms. Any visual symptom should trigger an ophthalmological evaluation in order to manage these complications; some of which pose the risk of systemic dissemination and significant morbidity. The following article provides an in-depth review of the common presenting symptoms, treatments and recent advances related to common ophthalmic complications following lung transplantation. While this article focuses on the lung transplant sub-population, the authors would like to point out that some of these complications are shared by other solid-organ transplants as well, by virtue of their shared immunosuppressive therapies.

Keywords: Eye complications; lung transplantation; ophthalmological; immunosuppression; infectious *vs.* non-infectious

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Introduction

Lung transplantation has witnessed significant growth over the past decade, with as many as 4,122 adult transplants performed worldwide in 2015 (1). With the increasing donor pool, the advent of improved immunosuppressive drugs and surgical techniques, this number is expected to increase significantly in the coming years. Lifelong immunosuppression in these recipients makes them subject to a host of complications affecting multiple organ systems. Ophthalmic complications after lung transplantation are uncommon and range from infections to malignancies (*Table 1*). Some side effects are specific to the drug such as cyclosporine (CsA) induced retinopathy, while others can be attributed to systemic immunosuppression. The authors provide a detailed review of the various ophthalmic complications after lung transplantation with emphasis on early recognition of symptoms and emerging treatment options.

Table 1 Ophthalmic complications after lung transplantation

Infectious	Non-infectious	
	Non-neoplastic	Neoplastic
CMV retinitis	Cyclosporine (CsA) retinopathy	Post-transplant lymphoproliferative disorder (PTLD)
Herpetic keratitis	Posterior subcapsular cataract (PSC)	Squamous cell carcinoma (SCC) of the conjunctiva and eyelids.
Herpes Zoster ophthalmicus	Central retinal vein occlusion (CRVO)	
Rhino-orbital mucormycosis		
Disseminated pseudallescheria boydii infection		

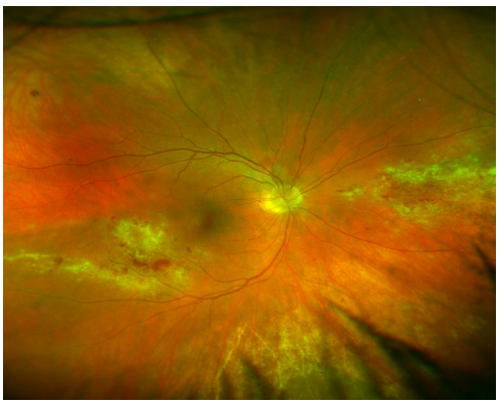

Figure 1 Cytomegalovirus retinitis. Fundus photograph showing multifocal yellow-white retinal infiltrates, retinal hemorrhages and retinal vasculitis.

Infections

Cytomegalovirus (CMV) retinitis

CMV retinitis is a potentially sight-threatening infection caused by CMV, a deoxyribonucleic acid (DNA) virus of the herpesviridae family. It can be established as a new infection in seronegative recipients or from reactivation of latent disease. The virus can also be transmitted to the recipient from the transplanted lungs. Serological mismatch between a seropositive donor and a seronegative recipient is the biggest risk factor for CMV infection. Another risk factor is the use of lymphocyte-depleting antibodies, such as Basiliximab, as part of anti-rejection induction therapy. The incidence of CMV infection in lung or heart-lung transplant patients is higher compared to other solid organ transplants (SOTs); 50–75% versus 22–29% after liver and 8–32% after kidney transplantation (2,3).

Patients usually present with floaters or reduced vision with the latter occasionally progressing to painless total loss of vision. Fundoscopy reveals yellow-white retinal infiltrates, retinal hemorrhages and signs of retinal vasculitis (*Figure 1*). The diagnosis can be made on the basis of a detailed history and fundoscopic examination. CMV viral load quantification can be performed using polymerase chain reaction (PCR). Monitoring CMV viral load over time can be more important in predicting disease rather than the absolute viral load.

Prophylaxis with oral valganciclovir is recommended for a minimum of 100 days with consideration for longer periods of up to 6 months (4). Periodic testing for CMV viremia—every 2 weeks for the first six months and monthly from 6 to 12 months—is also part of the protocol. Chmiel *et al.* showed a reduction in the incidence of CMV related disease from 75% (6/8) to 11% (11/96) in patients receiving antiviral prophylaxis with ganciclovir or valganciclovir (5).

Treatment for CMV retinitis varies based on its severity and resistance patterns and consists of induction with intravenous ganciclovir (5 mg/kg) twice a day for 2–3 weeks followed by maintenance therapy. Valganciclovir has emerged as an effective alternative in patients relapsing on ganciclovir therapy due to its higher bioavailability. Antiviral drug resistance can develop with prolonged treatment. Ganciclovir-resistance is due to mutations in the drug target protein kinases UL97 and UL54. Foscarnet is reserved for ganciclovir-resistant cases. Resistance to both oral valganciclovir and systemic and intravitreal foscarnet can be successfully overcome by addition of leflunomide (6). An experimental drug, AIC 246, now called letermovir, which acts on the terminase complex, in conjunction with reduced immunosuppressive therapy was successfully used to treat a multidrug-resistant CMV disease involving the

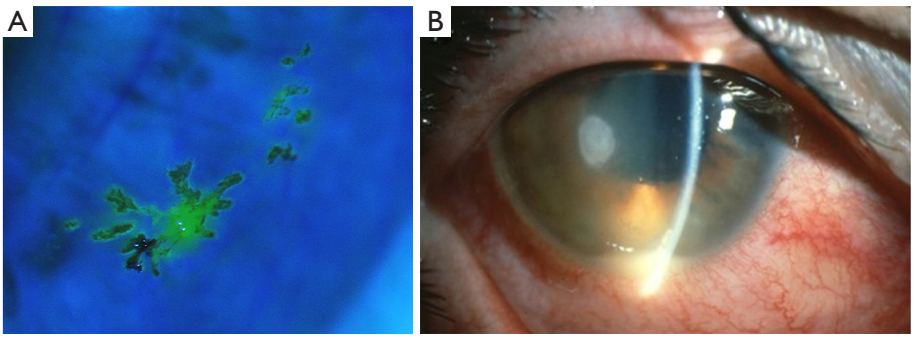

Figure 2 Herpetic keratitis. (A) Herpetic keratitis; typical corneal dendrite as seen on slit-lamp examination aided with fluorescein dye; (B) herpetic keratouveitis with hypopyon, keratic precipitates and corneal edema.

lungs, gastrointestinal tract and retina (7). With a growing number of resistant strains, newer and targeted therapies towards CMV, such as adaptive T-cell therapy are being tested.

Herpetic keratitis

Herpetic keratitis is a viral infection of the cornea caused by the herpes simplex virus (HSV), a DNA virus from the herpesviridae family. It is estimated that around 500,000 people are infected with ocular HSV in the United States (8). After primary infection has been established through the mucous membranes, the virus establishes latency in the trigeminal ganglia. This property of the virus is responsible for recurrent infections, particularly in the immunosuppressed population. Transplant recipients are particularly at risk of reactivation during the first month after surgery. Epithelial keratitis is the most common subtype of the infection. Infection is typically unilateral and presents with redness, watery discharge, irritation, pain, and photophobia (9). Visualization of a typical dendrite is carried out on a slit-lamp examination aided with fluorescein dye (*Figure 2A*). Slit-lamp examination may also reveal corneal edema, keratic precipitates and hypopyon (*Figure 2B*). Atypical corneal lesions described as non-dendritic or geographical ulcers with terminal bulbs and epithelial infiltrations may be seen. In such cases, diagnosis can be made using PCR (10). Infection with other viruses like varicella zoster, adenovirus, enterovirus, amebic or fungal infections can mimic herpetic keratitis.

Treatment of herpetic keratitis involves topical and systemic acyclovir. Mutation in viral thymidine kinase, which is essential for phosphorylation of acyclovir to its active form, is the most common cause of resistance (11). Turner *et al.* reported a case of acyclovir-resistant herpetic keratitis in a patient with cystic fibrosis, post bilateral lung transplantation, who was successfully treated by addition of trifluridine eye drops to oral valacyclovir (12). Intravenous foscarnet is the drug of choice based on other case reports of acyclovir-resistant cases (13,14). Other treatment options include cidofovir, vidarabine, and interferon. Some cases seem to occur after a prolonged period of time, even years, indicating a possible association with duration of immunosuppression as hypothesized by Ng *et al.* (15). Complications of the condition include uveitis, corneal plaques, and acute retinal necrosis (ARN).

Prevention is possibly the best treatment. It is important to test for HSV IgG serostatus of the recipient prior to transplantation. Seropositive patients are at a higher risk of reactivation if they do not receive prophylaxis (16). Many transplant recipients receive CMV prophylaxis in the form of oral valganciclovir, which is also approved for HSV prophylaxis. Patients who are not on CMV prophylaxis should receive acyclovir. Seronegative patients can acquire the infection through asymptomatic intimate contact. Patients should be educated appropriately as the use of protection during sex may help prevent transmission (16).

Herpes zoster ophthalmicus

Herpes zoster ophthalmicus is caused by reactivation of the varicella-zoster virus (VZV). The virus lies dormant in the sensory ganglia after primary infection, usually during childhood. Factors that can trigger reactivation include advanced age, immunosuppression and hematological malignancies such as leukemia and lymphomas. Reduced cell-mediated immunity is thought to play a role as well. In a review of 314 heart transplant recipients, 51 developed

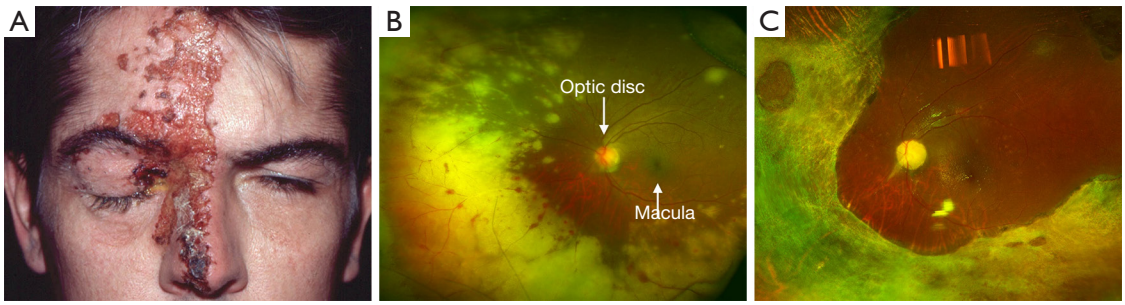

Figure 3 Manifestations of herpes zoster ophthalmicus. (A) Herpes zoster ophthalmicus. Typical unilateral distribution of vesicular lesions along V1 distribution; (B) fundoscopy in a 57-year old lung transplant recipient who presented with left eye pain, redness and blurry vision revealed a swollen optic disc and extensive necrotizing retinitis, worse inferiorly and nasally, clinically consistent with herpes zoster retinitis; (C) two months following therapy with intravitreous Foscarnet and intravenous Acyclovir, there is complete resolution of infiltrates with residual retinal fibrosis and a pale optic disc.

herpes zoster including 14% with eye involvement and 45% with postherpetic neuralgia (17).

The disease presentation is similar among immunocompetent and immunocompromised individuals, while disease duration and severity may be longer and more severe in the latter group. Herpes zoster can involve eyelids, presenting as vesicular lesions, which can become pustular and/or hemorrhagic (*Figure 3A*). They form crusts in 7–10 days at which point the virus is not transmissible. Patients are prone to developing secondary bacterial infections like Staphylococcus aureus. Corneal involvement includes various types of keratitis. The punctate type of keratitis can coalesce to form a pseudodendritic pattern. Differentiation between herpes simplex and zoster is key as herpes simplex lesions can worsen with steroids. Steroids are not recommended in the immunocompromised population as they may cause dissemination of the virus unless there is severe involvement. Conjunctival involvement could also occur in a papillary or follicular pattern. Patients with uveitis may exhibit pain and/or photophobia. Its neurologic sequelae include extraocular muscle palsies, Horner's syndrome, optic neuritis, retrobulbar neuritis and ischemic optic retinopathy. Retinal involvement can occur in the form of retinal vasculitis, ARN, and progressive outer retinal necrosis syndrome. ARN is characterized by necrotizing retinitis and usually panuveitis (*Figure 3B,C*). Postherpetic neuralgia is a common complication which may present as burning or lancinating pain, allodynia, with or without sensory deficits. Herpes zoster ophthalmicus should be considered in transplant patients presenting with changes in visual acuity, headaches, cranial nerve dysfunction and a pustular skin rash.

Management involves initial intravenous acyclovir followed by an oral regimen. Intravitreal drugs may also be required (18). A tricyclic antidepressant amitryptiline, is considered the first line treatment for postherpetic neuralgia (19).

There is insufficient evidence to support long term use of prophylactic antivirals in SOT recipients (18). Prevention with varicella vaccine (live attenuated Oka vaccine) should be given to susceptible patients prior to the transplantation (18).

Rhino-orbital mucormycosis

Rhino-orbital mucormycosis (zygomycosis) is a potentially devastating invasive fungal infection (IFI) caused by fungi belonging to the genera Mucor, Rhizopus, Rhizomucor and Absidia. Incidence of mucormycosis in SOT recipients ranges from 0.4–16% (20). Mucormycosis comprised 2% of all IFIs, as reported in the Transplant-Associated Infection Surveillance Network (TRANSNET) data (21). Renal failure, diabetes mellitus, and prior voriconazole and/or caspofungin use were associated with a higher risk of mucormycosis in SOT recipients (22). Tacrolimus use has been associated with a reduced risk for mucormycosis over cyclosporine (22). Iron overload along with the iron chelator deferoxamine have also been associated with increased risk (23,24).

Infection in humans is established by inhalation of spores and its subsequent proliferation in the nasal sinuses. The fungi invade the blood vessels leading to thrombosis and tissue necrosis. Intraocular spread occurs from invasion of the lamina papyracea. Infection can also spread through the

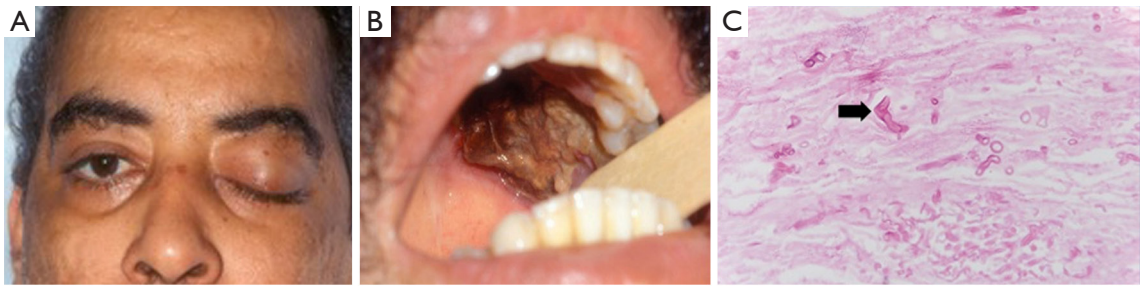

Figure 4 Rhino-orbital mucormycosis. (A) Acute orbital cellulitis of the left eye; (B) note ulcerative palatal lesion with black eschar that provides an important diagnostic clue; (C) histological examination showing presence of wide, aseptate or poorly septated ribbon-like hyphae. Reprinted with permission from (25).

ethmoidal and orbital veins to the cavernous sinus.

Patients can present with bloody nasal discharge, facial pain, fever, headache, decreased visual acuity, orbital edema, proptosis, ophthalmoplegia or diplopia depending on site of involvement (*Figure 4A*). Palatal ulceration due to maxillary spread and cranial nerve involvement can also be seen (*Figure 4B*).

Magnetic resonance imaging (MRI) and computed tomography (CT) of the involved area is useful in assessing the spread of the disease. Negative imaging studies, however, do not rule out infection. Cultures from the sinuses, nasal discharge and blood rarely confirm the diagnosis and may be contaminated with nasal flora. Rapid diagnostic tests like PCR have been used but there are no standardized tests currently recommended. Hadaschik *et al.* reported the detection of *Rhizopus pusillus* using a commercially available panfungal PCR assay (26). The diagnosis requires a high degree of suspicion due to its similarities with other filamentous fungi. Histological examination may demonstrate presence of wide, aseptate or poorly septated ribbon-like hyphae (*Figure 4C*).

Treatment involves an aggressive multidisciplinary approach. Liposomal amphotericin and amphotericin lipid complex are the drugs of choice and should be started empirically in cases with strong clinical suspicion. Surgical debridement of the affected tissue is key. Reduction of immunosuppression should be considered along with correction of ketoacidosis and hyperglycemia. The use of granulocyte colony-stimulating factor (G-CSF) and granulocyte-monocyte colony stimulating factor (GM-CSF) has been advocated in neutropenic patients. Posaconazole has been used for salvage therapy in many cases with good results (27). Despite advances in surgical and medical therapies, morbidity and mortality from the condition remain high. The infection can be fatal if not treated early and aggressively. *Sun et al.* found an overall mortality of 52.3% (46/88) in SOT recipients with rhino-orbital-cerebral mucormycosis. The mortality in patients with CNS disease was 73.5% (36/49) (28).

Pseudallescheria boydii infection

Pseudallescheria boydii or *Scedosporium apiospermum* (Sca) is a ubiquitous, filamentous fungi commonly found in the soil and stagnant or polluted water. They are rare causes of opportunistic infection in the immunocompromised population including SOT recipients. Risk factors include neutropenia and steroid use. Transmission occurs via inhalation through the lungs, paranasal sinuses or traumatic inoculation of the skin. Cimon *et al.* reported that 11/128 (8.6%) sputum samples are positive for Sca in cystic fibrosis patients (29). Disseminated infection can be life-threatening and involve the skin, heart, lung, bone, eye and central nervous system. Presenting symptoms vary depending on the organ involved. Patients may present with fever, intractable headache, lung involvement or neurological complaints like hemiplegia, aphasia, decreased visual acuity and eye pain.

Diagnosis is made by histopathological examination of bronchoalveolar lavage (BAL) culture, sputum, pleural fluid, and radiology. Microscopically, the organism appears as septate hyphae with acute angles of branching. Its resemblance to Aspergillus and Fusarium species in terms of clinical presentation and histopathological examination makes the diagnosis challenging (*Figure 5A,B,C*). Molecular techniques of DNA sequencing and random amplification of polymorphic DNA (RAPD) genotyping is used for species identification. This is particularly important as

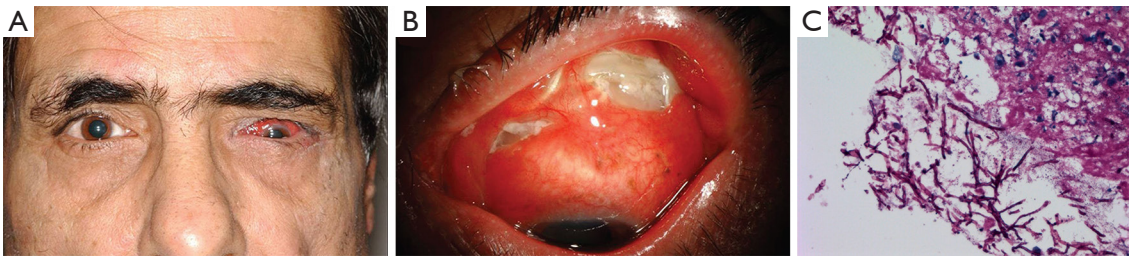

Figure 5 Eye involvement in Pseudallescheria Boydii (A,B) [Reprinted with permission from (30)]. Histological appearance of Pseudallescheria Boydii is similar to that of Aspergillus and Fusarium species: septate hyphae with acute angles of branching (C), periodic acid Schiff stain ×400 magnification. Reprinted with permission from (31).

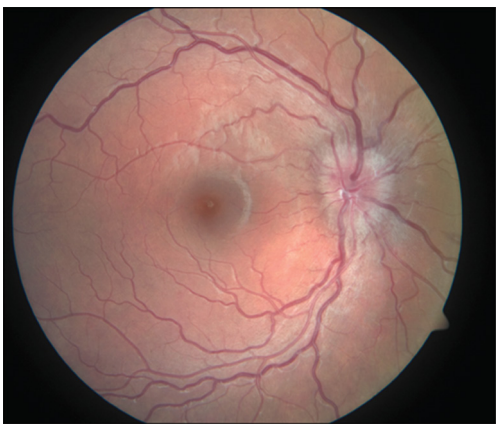

Figure 6 Optic disk edema in cyclosporine (CsA) toxicity. Reprinted with permission from (38).

most infections with Sca are resistant to amphotericin B. Voriconazole is widely considered as the drug of choice (32). Some cases have been treated with the addition of echinocandins and/or terbinafine (33). Surgical debridement of the paranasal sinuses and additional local voriconazole therapy to prevent invasive disease has also been suggested (33). Surgical intervention with debridement and keratoplasty is commonly used alongside medical therapy. Evisceration is needed in many cases. Mortality for disseminated infection in SOT recipients remains extremely high (34).

Non-infectious complications

Non-neoplastic

Cyclosporine-induced ocular toxicity

Cyclosporine (CsA), used as part of the immunosuppressive regimen in lung transplant patients, inhibits transcription of interleukin-2 (IL-2) in T cells, thereby preventing the proliferation of activated T cells. Owing to its narrow therapeutic window and high variability in absorption rates, CsA levels need to be carefully monitored. High cyclosporine levels have shown to cause ocular toxicity. CsA-induced neurotoxicity is also well documented and the occipital white matter seems to be uniquely susceptible (35). CsA-related ocular toxicity can vary from optic disc edema to retinopathy and in some cases cortical blindness (36).

Patients can present with blurry vision or visual field defects months to years after starting therapy. The average latency for development of optic disc edema and retinopathy in BMT recipients is approximately 150 days (37). Fundoscopy is essential for the diagnosis. Cotton wool spots, bilateral optic disc edema, retinal hemorrhages, lipid deposits, retinal edema, macular edema, and ischemic vasculopathy are all possible findings on examination (*Figure 6*). Evaluation of cyclosporine-induced cortical blindness with the help of an MRI has also been reported (39).

Acetazolamide has been reported to successfully treat CsA induced bilateral disc swelling in lung transplant patients (15). Discontinuing or reducing the CsA dose is adequate in most cases with complete resolution in a few weeks (40,41). Patients with cortical blindness show a more immediate response after withdrawal of cyclosporine.

Central retinal vein occlusion (CRVO)

CRVO is the second most common retinal vascular disorder after diabetic retinopathy (42). It can be ischemic or non-ischemic depending on the areas of perfusion. Ischemia can lead to complications like macular edema and neovascularization of the retina. Risk factors include advanced age, hypertension, diabetes and hyperlipidemia (43). Hypercoagulable states such as low plasma Antithrombin III levels, elevated fibrinogen levels, factor V Leiden mutation resulting in active protein C resistance along

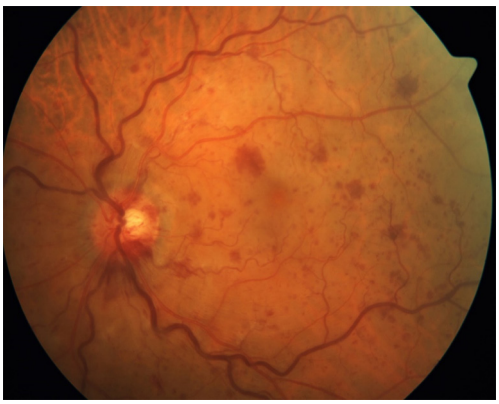

Figure 7 Central retinal vein occlusion. Fundus photograph showing dilation and tortuosity of the retinal veins with intraretinal hemorrhages.

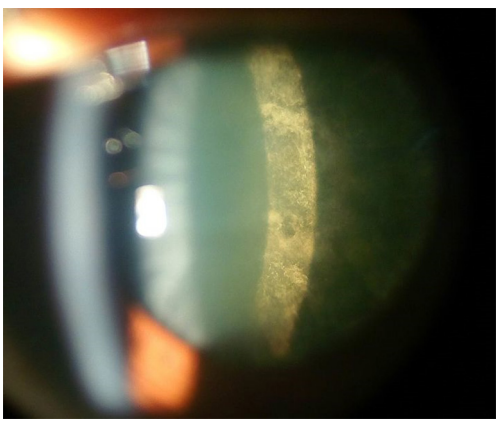

Figure 8 Slit lamp findings in PSC revealing a sheen with granular deposits. Image courtesy: Imrankabihossain; https://commons.wikimedia.org/wiki/File:Posterior_Subcapsular_Cataract.jpg. PSC, posterior subcapsular cataract.

with protein C and S deficits, elevated factor VIII and IX levels have also been described in the literature as risk factors in the general population with limited information regarding the transplant population (44-47). Post-transplant immunosuppressive drugs such as cyclosporine and tacrolimus increase platelet aggregation in response to physiologic agonists and are postulated to increase the risk of CRVO in this subpopulation.

Patients typically present with sudden loss or blurring of vision. Fundoscopy reveals dilation of the retinal veins, tortuosity or intraretinal hemorrhages (*Figure* 7). Macular edema is a common finding at the time of diagnosis. Fundus fluorescein angiography helps to differentiate between ischemic and nonischemic CRVO. In a systematic review by McIntosh *et al.*, the authors reported resolution of symptoms within 15 months in around 30% of nonischemic cases and 73% of ischemic cases of CRVO (48).

Treatment options include the following: intraocular ranibizumab, an antibody against vascular endothelial growth factor antibody (anti-VEGF), is effective for reducing macular edema and improving the vision (49). Intravitreal steroid injections or implants along with laser photocoagulation have also been found to be effective (50-52).

Posterior subcapsular cataract (PSC)

Subcapsular cataracts often develop in the posterior cortical layer of the lens among SOT recipients. They are more common in younger patients compared to the nuclear and cortical cataracts in the general population. In the transplant population, this is a common complication of prolonged steroid use. Black *et al.* was the first to notice the relationship between steroid use and cataract formation in rheumatoid arthritis patients in 1960; 17 (39%) of his 44 patients developing PSC (53). Many different mechanisms have been proposed in the formation of PSC, including oxidative damage, role of the glucocorticoid receptor and defective differentiation due to dysregulation of apoptosis (54). PSC has also been related to the advancing age. These factors lead to the high incidence in the transplant population. Use of even a single dose of intravitreal steroids has been shown to induce cataract (55,56). Both topical, as well as inhaled steroids, have been shown to induce cataract (57,58).

Tarabishy *et al.* reported the finding in 13 (28.3%) out of 46 lung transplant recipients, making it the most common ophthalmologic complication in this population (59). Data from other SOT recipients show a similar trend. Debnath *et al.* reported an incidence of 32.8% among 61 renal transplant patients (60). After 15 years, the incidence plateaued. Multivariate analysis showed age, body mass index (BMI) and cumulative dose of steroids as independent risk factors. Use of cyclosporine has been shown to increase the incidence of steroid-induced cataract (61).

Glare and reduced visual acuity are the most common symptoms. Slit-lamp examination shows a sheen on the posterior cortical layers early on followed by granular and plaque-like opacities (*Figure 8*).

Treatment involves surgical removal and replacement of the lens as in other forms of cataract. In children, withdrawal of steroids early on may occasionally result in resolution of changes (62).

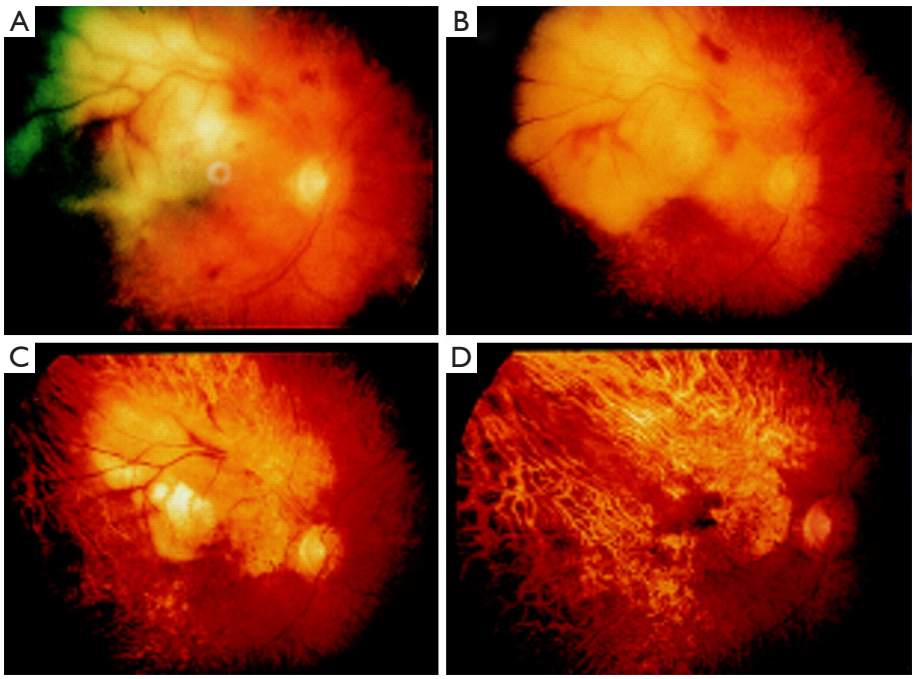

Figure 9 Retinal findings in PTLD: chorioretinal yellow-white lesion extending towards the macula with arterial and venous thrombosis of the superotemporal arcade (A). Progressive healing of the chorioretinal over 6 months (B,C,D). Reprinted with permission from (70). PTLD, post-transplant lymphoproliferative disorder.

Neoplastic

Post-transplant lymphoproliferative disorder (PTLD)

PTLD is a term that encompasses a wide array of disorders due to B lymphocyte proliferation after organ transplantation. It can range from benign lymphoid hyperplasia to highly aggressive lymphomas. Intraocular involvement is a rare manifestation of PTLD. However, central nervous system involvement is common with Penn reporting an incidence of 28% (63).

Epstein-Barr virus (EBV) is thought to be the causative organism. An imbalance between B cell stimulation and anti-EBV response leads to the disease, in most instances. Chronic antigenic stimulation from the allograft, oncogenic potential of EBV and immunosuppression result in B lymphocyte proliferation (64-67). In some cases, there is monoclonal proliferation, which may result in malignancy. The degree of immunosuppression is a major risk factor, with higher levels portending an increased risk (64,68). Use of cyclosporine, in particular, has been found to be associated with many cases of ocular PTLD (69).

Posterior segment of the eye is frequently involved including the retina, vitreous and optic nerve. Tumor cells in the vitreous may mimic uveitis. Uvea may also be affected particularly in patients with systemic lymphoma. Patients present with decreased vision, floaters, photosensitivity or may even be asymptomatic. Bilateral involvement is a common occurrence. On examination, anterior chamber cells, varying degrees of flare, and iris nodules are seen in almost all patients. Posterior chamber involvement in the form of a vitreous haze and retinal involvement may also be seen (*Figure 9A,B,C,D*). The differential diagnosis includes toxoplasmosis, CMV, and bacterial infections. Measurements of EBV antibody titers, nuclear and capsid antigens are used to confirm clinical suspicion. Biopsy of the choroid and vitreous are other diagnostic options.

Treatment for non-clonal PTLD involves a reduction in the dose of the immunosuppression and use of antivirals like acyclovir (65,66). There may be a period of months where there is no improvement and even clinical worsening before improvement. Patients with only lymphoid hyperplasia may not need a reduction in the immunosuppressive dose. Those with true lymphoma (stage III) may not improve even with immunosuppressive dose reduction. They are treated with radiation therapy, chemotherapy, surgery and discontinuation of immunosuppression if possible (65).

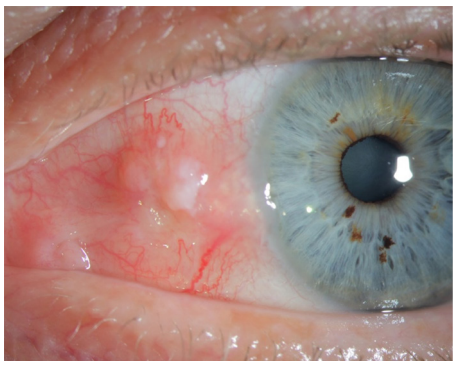

Figure 10 Squamous cell carcinoma of the conjunctiva. Twelve years following liver and renal transplantation, patient developed gelatinous lesion on the nasal bulbar conjunctiva with intrinsic and feeder vessels and surface leukoplakia.

Squamous cell carcinoma (SCC) of the conjunctiva and eyelids

SCC of the eye primarily involves the conjunctiva, cornea and eyelids (*Figure 10*). In HIV patients, the standardized incidence ratio (SIR) which measures excess risk was 12.2 for conjunctival SCC (71). Incidence in the SOT populations has been reported to be 65–250 times more than the general population for cutaneous SCC (72,73). Incidence increases with the duration of immunosuppression (72). Risk factors include ultraviolet (UV) light exposure, human papillomavirus (HPV) infection and prior skin cancers (74-76). Individual drugs increase its risk by different mechanisms. Calcineurin inhibitors act by increasing transforming growth factor B and VEGF (77). Tacrolimus and mycophenolate mofetil compromise the proper response to UV-B induced apoptosis and UV-B induced checkpoint signalling (78). In addition, SCC is much more aggressive in the immunocompromised population, including lung transplant recipients.

Patients with conjunctival SCC usually have a pinkish, fleshy appearing mass close to or involving the limbus. Eyelid involvement is also seen, with lower eyelid involvement more common. Visual acuity remains unchanged in most cases. Aggressive tumors may show extension to the neighboring periocular structures, lymph nodes and even the brain. Biopsy of the suspected tissue is used for diagnostic purposes showing squamous cells.

Treatment includes surgical excision with clear margins whenever possible. Moh's micrographic technique has been used in some cases (76). Invasive tumors require extensive surgical procedures including use of skin flaps, parotidectomy, cheek lift and even exenteration (76,79). Reduction in immunosuppression may be useful, but it must be balanced with the risk of rejection. Additional treatment with topical therapy like interferon eye drops (1 million units/mL) and mitomycin (0.04%) drops has been used (80).

Conclusions

Ophthalmic complications following lung transplantation although rare can be sight-threatening and potentially life-threatening if left unchecked. These conditions require a high degree of suspicion for early diagnosis and treatment. Use of antiviral prophylaxis helps to reduce the incidence of CMV retinitis and herpetic keratitis and hence form an integral part of treatment protocols. Treatment of infectious complications and cyclosporine toxicity may need reduction or discontinuation of immunosuppression. Adjunctive and alternative treatments should be pursued in cases that do not respond adequately. An ophthalmologist should urgently evaluate all patients with ocular symptoms. Although there are guidelines for ocular screening in hematopoietic cell transplants recipients, no such recommendations exist for lung transplant patients (81). There have been conflicting data to incorporate routine ocular screening in SOT including lung transplant recipients (82,83). Future research should look into the utility of scheduled ocular screening at regular intervals with the possibility of incorporating it into existing guidelines.

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Footnote

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