Ocular complications of heart, lung, and liver transplantation

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Abstract

Aim—To document the nature and frequency of ocular complications in a large group of patients who underwent heart, lung, or liver transplantation.

Methods—A retrospective audit of the medical records of all patients undergoing heart, lung, or combined heart-lung transplantation at St Vincent's Hospital, Sydney, or liver transplantation at Royal Prince Alfred Hospital Sydney, was performed to detect patients with symptomatic ocular complications following transplantation. 19 of 860 patients were identified as having ocular complications. **Results**—Ocular complications occurred in 2% of patients with 65% of these being opportunistic infections. Herpes group viral retinitis (77%) and fungal chorioretinitis (22%) were seen. Other complications included choroidal pseudolymphoma, central retinal vein occlusion, herpes zoster ophthalmicus, herpetic keratitis, dacryocystitis, cyclosporin retinopathy, and rifabutin associated uveitis.

Conclusion—Herpes group viral retinitis was the most common ocular opportunistic infection and occurred most frequently during the second year after transplantation. Delayed diagnosis was associated with poor visual outcome.

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being 87% and 78% respectively. Lung transplantation has been performed since 1990 with 132 transplants being performed. One year and 5 year survival rates are 82% and 58% respectively. Liver transplantation in NSW is performed at the Royal Prince Alfred Hospital, Sydney and since 1986, there have been 303 liver transplants performed. There are at present 205 surviving liver transplant patients with the 1 year and 5 year survival rate being 77% and 71% respectively. The aim of the present study was to determine the ocular complications in this group of patients.

Patients and methods

A retrospective audit of the medical records of all heart and lung transplant recipients from St Vincent's Hospital was performed. A similar retrospective audit of the medical records of all liver transplant recipients from Royal Prince Alfred Hospital was performed. Detailed data regarding each patient's medical condition, indication for transplantation, post transplant medications, and follow up were available from computerised data bases used within each transplant unit. A total of 19 patients were identified who had been referred for evaluation of ocular symptoms. The extent of ophthalmological documentation varied and all available information was used. The ocular infections described in this study were all diagnosed clinically on the basis of the history, physical signs, and clinical course. Invasive diagnostic procedures such as vitreous biopsies were not performed routinely.

The patient data, treatment, and ocular findings are detailed in Tables 1, 2, and 3. Local patients had been seen and followed up by the authors at the ocular immunology clinics of each hospital. Patients from interstate and other countries were contacted directly regarding their ocular status at the time of the study and additional information was obtained from their treating physician and ophthalmologist.

Patients developing cataracts following transplantation were not included in this study as cataract surgery in transplant recipients is similar to cataract surgery in the general population and has an excellent outcome.

Results

Thirteen heart, four lung, and two liver transplant recipients developed symptomatic ocular disease other than cataract following transplantation. A range of opportunistic infections including acute retinal necrosis (ARN), cytomegalovirus (CMV) retinitis, and

Organ transplantation is an established therapeutic modality for the treatment of end stage heart, lung, liver, kidney, pancreas, and bone marrow disease. The use of new selective immunosuppressive drugs particularly cyclosporin A has enabled the long term survival of transplanted organs such as hearts, lungs, and livers where previously rejection was less readily controlled. The development of specialist transplant units has improved medical and surgical care of transplant recipients with resultant low mortality and morbidity rates. Ocular complications associated with organ transplantation have been well documented in patients following renal transplantation¹⁻²; however, few studies of ocular complications following heart, lung, or liver transplantation have been reported.³⁻⁵

Since 1984, there have been 416 heart or combined heart-lung transplants performed at St Vincent's Hospital, Sydney under the National Heart Transplant programme. There are at present 320 surviving heart transplant patients with the 1 year and 5 year survival rate

Table 1 Clinical features of transplant patients

Patient/ age/sex	Diagnosis	Time after transplant (days)	Non-ocular opportunistic diseases	CMV status	
				Donor	Recipient
1/53/M	ARN	400	BCC, herpes simplex 1	Negative	Positive
2/56/M	ARN	892	Candida oesophagitis, BCC	Positive	Positive
3/43/F	ARN	402	Oral candidiasis, oral herpes simplex, thoracic herpes zoster	Positive	Positive
4/51/M	ARN	282	Nil	Negative	Positive
5/52/M	ARN	326	Nil	Positive	Negative
6/36/M	CMV	473	CMV enteritis, CMV marrow disease	Positive	Positive
7/55/M	CMV	151	CMV hepatitis, oral herpes simplex	Positive	Positive
8/50/M	CMV	190	Aspergillus pneumonia	Positive	Positive
9/53/F	Fungal	147	Nil	Positive	Positive
10/57/M	Fungal	255	Oral herpes simplex, CMV gastritis/myocarditis	Negative	Negative
11/36/F	Herpetic keratitis	1210	Nil	Positive	Negative
12/63/M	Herpetic keratitis	1482	Nil	Positive	Positive
13/37/F	PTLD	123	CMV hepatitis	Positive	Positive
14/53/M	HZO	950	Tinea versicolor	Negative	Positive
15/62/M	CRVO	440	BCC/SCC	Positive	Negative
16/62/M	Dacryocystitis	1179	BCC oral herpes simplex, olfactory neuroblastoma	Negative	Positive
17/26/M	RV	213	Tinea versicolor	Positive	Positive
18/54/M	Cyclosporin retinopathy	2272	Nil	Positive	Positive
19/56/F	Rifabutin uveitis	603	MAI thrombophlebitis	Negative	Negative

ARN = acute retinal necrosis; CMV = cytomegalovirus; PTLN = post-transplant lymphoproliferative disorder; HZO = herpes zoster ophthalmicus; CRVO = central retinal vein occlusion; RV = retinal vasculitis; BCC = basal cell carcinoma; SCC = squamous cell carcinoma

fungal endophthalmitis occurred. A variety of other diseases such as retinal vasculitis, cyclosporin retinopathy, central retinal vein occlusion, post-transplant lymphoproliferative disorder (PTLD), herpes zoster ophthalmicus, and dacryocystitis were seen. This represented an overall ocular complication rate of 2%. This is clearly an underestimate of the incidence of ocular complications as only symptomatic eye patients were identified and included in the study.

ARN was a common ocular complication. Two male and one female heart transplant recipients developed ARN. Ages ranged from 43 to 56 years with an average age of 50 years. Bilateral ocular involvement occurred in one patient. The time of onset of ARN following transplantation ranged from 326 to 892 days with a mean of 540 days. Following transplantation, all patients had been managed with a combination immunosuppressive regimen of prednisone, cyclosporin A, and azathioprine. The prednisone dose ranged from 0.13 to 0.19 mg/kg/day with a mean of 0.16 mg/kg/day and cyclosporin dose ranged from 2.2 to 2.5 mg/kg/day with a mean dose of 2.6 mg/kg/day.

The mean azathioprine dose used was 1.5 mg/kg/day (range 1.3–1.7 mg/kg/day). Acute rejection episodes classified as 3a or worse according to the International Society of Heart and Lung Transplantation⁶ were recorded. The mean number of rejection episodes requiring treatment in ARN patients was eight with up to 16 episodes seen in a patient. No patient developed ARN following liver transplantation. Blurred vision was the most common presenting complaint (100%), followed by floaters (60%) and reduced visual field (20%). There was asymptomatic disease in the right eye of the only patient with bilateral involvement. Visual acuity ranged from 6/9 to 6/24 at presentation. The three patients received intravenous aciclovir 10 mg/kg three times per day for 7–14 days followed by oral maintenance therapy for 3 months. They also received prophylactic barrier laser photocoagulation. Each of these patients had a final visual acuity of 6/6 in the affected eye.

CMV retinitis occurred in three patients (one heart, one liver, and one lung recipient). All patients were male with an average age of 45 years. One patient had bilateral ocular

Table 2 Treatment of transplant patients

Patient/ age/sex	Cyclosporin (mg/kg/day)	Azathioprine (mg/kg/day)	Prednisone (mg/kg/day)	Acute rejection episodes	Acute rejection treatment	Vascular risk factors
1/53/M	1.2	1.5	0.15	1	Oral steroids	Cigarettes, cholesterol
2/56/M	2.2	1.7	0.15	7	IV/oral steroids, OKT 3	Diabetes, cigarettes, cholesterol
3/43/F	3.1	1.4	0.19	16	Oral steroids, OKT 3, plasmapheresis, nodal irradiation	Nil
4/51/M	5.2	1.1	0.14	4	IV/oral steroids	Hypertension, cholesterol
5/52/M	2.5	1.3	0.13	1	IV steroids	Cholesterol
6/36/M	3.7	1.7	0.9	3	IV steroids	Diabetes, cigarettes, cholesterol, hypertension
7/55/M	2.7	1	0.3	3	IV/oral steroids	Cholesterol
8/50/M	2.1	1.7	0.2	1	IV steroids	Cigarettes, hypertension, cholesterol
9/53/F	5.5	0.9	0.2	2	IV steroids	Cigarettes
10/57/M	0.7	1.4	0.1	1	IV steroids	Diabetes, hypertension
11/36/F	1.25	1.9	0.5	3	Oral steroids	Nil
12/63/M	3.1	2.2	0.14	2	IV steroids	Cholesterol
13/37/F	1.6	1.6	0.2	2	IV steroids/OKT 3	Diabetes, hypertension, cholesterol
14/53/M	2.5	1.7	0.1	3	IV/oral steroids	Nil
15/62/M	0.8	1.1	0.2	5	IV/oral steroids	Hypertension
16/62/M	3.9	0.8	0.2	4	IV/oral steroids	Hypertension
17/26/M	7	1.5	0.2	4	IV steroids	Cigarettes
18/54/M	7.1	0	0.25	1	IV steroids/ATG	Nil
19/56/F	4.2	2.4	0.2	3	IV/oral steroids	Cholesterol, hypertension

involvement with disease developing 151 days after transplantation. Another patient developed CMV retinitis in his right eye 473 days after transplantation and the third patient developed right CMV retinitis 189 days after transplantation. All recipients had positive serology to CMV and all had received organs from donors with positive serology to CMV. In two cases there was culture proved or biopsy positive extraocular CMV disease in the post-transplant period, with the heart recipient having CMV enteritis and bone marrow involvement and the liver recipient CMV hepatitis. In addition, the patients had multiple risk factors for vascular disease. One patient had a 10 year history of diabetes mellitus with diabetic nephropathy, proliferative diabetic retinopathy, and maculopathy in the CMV affected eye. Each of the patients had been heavy cigarette smokers and two patients had chronic severe hypertension. Patients complained of blurred vision (three patients), floaters (two patients), and reduced peripheral visual field (one patient). Visual acuity was 6/12 in the heart recipient, 6/18 in both eyes of the liver recipient, and 6/5 in the lung recipient. Intravenous ganciclovir was administered to all patients. The diabetic patient developed a vitreous haemorrhage in the affected eye and required a vitrectomy. His final visual acuity was 6/12. Unfortunately the liver transplant recipient died from complications of chronic rejection. His final visual acuity recorded was 6/18 in each eye. The retinitis

in the lung transplant recipient regressed with a final visual acuity of 6/5 being achieved.

In two cases a diagnosis of presumed viral retinitis was made retrospectively. One patient had received ganciclovir therapy while the other received no antiviral therapy. No laser therapy had been used in either patient. Both had presented with retinal detachments associated with areas of peripheral retinal scarring and opacification. One patient ultimately developed rubeosis iridis and neovascular glaucoma. The other patient had successful retinal reattachment surgery. The final visual acuities were no light perception and hand movements. The large areas of peripheral retinal scarring, the development of retinal detachments, and the lack of other ocular signs made presumed viral retinitis a likely diagnosis.

Two patients developed fungal chorioretinitis. Both were heart recipients with an average age of 55 years. Bilateral ocular involvement occurred in one patient. The average time after transplantation was 201 days (range 147–255 days). Non-ocular opportunistic infections consisted of CMV gastritis/myocarditis/pneumonitis in one patient and mucocutaneous herpes simplex in the other. One patient presented with a painful red eye and a visual acuity of 6/18 and had a 30 year history of diabetes mellitus. *Candida albicans* was isolated from a biopsy of a subretinal mass in the involved eye. The patient was not on systemic antifungal therapy before this. Candidaemia had not been documented at any time in this

Table 3 Ocular features of transplant recipients

Patient/ age/sex	Diagnosis	Eye involved	Symptoms	Signs	Investigations	Complications	Treatment	Visual outcome
1/53/M	ARN	L	Blurred vision, floaters	Vitritis, retinitis	Nil	Retinal detachment	Scleral buckle	HM
2/56/M	ARN	R	Blurred vision, floaters	Vitritis, retinitis	Nil	Nil	Aciclovir, barrier laser	6/6, 6/9
3/43/F	ARN	L	Blurred vision	Vitritis, retinitis, papillitis	Nil	Nil	Aciclovir, barrier laser	6/6
4/51/M	ARN	R	Blurred vision	Vitritis, retinitis	FA, histopathology	Vitreous haemorrhage, retinal detachment, neovascular glaucoma	Ganciclovir Molteno implant, enucleation	NLP
5/52/M	ARN	R	Floaters, blurred vision	Vitritis, retinitis	Nil	Nil	Aciclovir, barrier laser	6/6
6/36/M	CMV	R	Floaters, epiphora, constricted field	Vitritis, retinitis, diabetic retinopathy	Nil	Vitreous haemorrhage	Ganciclovir, vitrectomy	6/24
7/52/M	CMV	R	Blurred vision	Vitritis, retinitis	Nil	Macular cyst	Ganciclovir	6/18, 6/12
8/50/M	CMV	R	Blurred vision, floaters	Vitritis, retinitis	Nil	Nil	Ganciclovir	6/6
9/53/F	Fungal	R	Pain, red eye	Vitritis, subretinal mass	Choroidal biopsy	Retinal hole + detachment	Fluconazole	NLP
10/57/M	Fungal	R	Bilateral chemosis	Chemosi, choroidal infiltrates	Nil	Nil	Ketoconazole, itraconazole	6/6, 6/6
11/36/F	Herpetic keratitis	L	Pain, red eye	Dendritic ulcer	Nil	Nil	Topical aciclovir	6/5
12/63/M	Herpetic keratitis	R	Pain, red eye	Dendritic ulcer	Nil	Nil	Topical aciclovir	6/5
13/37/F	PTLD	R	Blurred vision	Choroidal infiltrates	FFA, choroidal biopsy, vitreous biopsy	Nil	Reduced cyclosporin radiotherapy	6/18, CF
14/53/M	HZO	R	Rash	Rash	Nil	Nil	Aciclovir	6/6
15/62/M	CRVO	L	Blurred vision	Retinal haemorrhages	FFA, ophthalmodynamometry	Cystoid macular oedema	Steroids, warfarin, hyperbaric oxygen	6/60
16/62/M	Dacryocystitis	R	Tender mass at lacrimal sac	Painful red lump	Wound culture	Nil	Flucloxacillin	6/6
17/26/M	RV	L	Visual loss	Vitritis, papillitis, retinal oedema, retinal haemorrhages	FFA serology	Nil	Observation	6/6
18/54/M	Cyclosporin retinopathy	R	L scotoma	Bilateral disc swelling	Ct lp ffa	Optic atrophy	Diamox	6/9, 6/6
19/56/F	Rifabutin uveitis	R	Pain, blurred vision	Hypopyon, uveitis	Nil	Nil	Topical corticosteroids	6/6, 6/6

patient. Her lesions resolved on oral fluconazole. Subsequently she developed a retinal detachment and proliferative vitreoretinopathy. Her final visual acuity was no light perception. The other patient presented with blurred vision and bilateral chemosis. Visual acuity was 6/6 in both eyes. Numerous bilateral pale choroidal lesions consistent with fungal choroiditis were seen. At the time of presentation, there were clinical signs consistent with pulmonary aspergillosis. He was treated with ketoconazole and itraconazole with resolution of the choroidal and pulmonary lesions. The chemosis has persisted and investigations revealed no evidence of other disease. The chemosis was attributed to his immunosuppression in the absence of any other identifiable cause.⁴

Choroidal pseudolymphoma, an entity belonging to the spectrum of PTLDs, developed 123 days post-transplantation in a liver transplant patient. The patient was aged 37 years, had positive serology to CMV, and had received a CMV positive donor organ. Following transplantation she developed severe steroid resistant acute rejection necessitating the use of OKT3 and high dose cyclosporin. She developed CMV hepatitis in her donor liver. She developed worsening blurred vision in each eye over a 6 week period. Visual acuity was 6/6 and 6/18 in her right and left eye at the time of referral. Funduscopy revealed numerous discrete white choroidal lesions up to 1 disc diameter in size and a vitreous cellular infiltrate. Fluorescein angiography revealed numerous focal areas of hyperfluorescence and retinal vascular leakage with no macular oedema. Both choroidal and vitreous biopsies were performed. Histological examination revealed numerous large, atypical lymphocytes. There was no evidence of malignancy or of infective organisms on smear or culture. Her ocular lesions settled with reduction of her immunosuppression and local radiotherapy.

One heart patient developed a central retinal vein occlusion in his left eye 440 days post-transplant. He had steroid induced diabetes and a 10 year history of hypertension. He was treated with a regimen of warfarin to achieve an international normalised ratio (INR) of 3–4 for 4 weeks, hyperbaric oxygen and haemodilution with Rheomacrodex. He developed chronic cystoid macular oedema with a visual acuity of 6/60 at last examination.

Another patient developed non-ischaemic retinal vasculitis 213 days after heart transplantation. Extensive investigations revealed no evidence of underlying or associated systemic disease. The retinal vasculitis resolved over 3 weeks without alteration of his treatment.

One lung transplant recipient developed cyclosporin retinopathy 2272 days post-transplantation. He was on high doses of cyclosporin (7.1 mg/kg/day) and presented with a left inferior visual field defect and bilateral disc swelling. Cerebral computed tomograph scan and lumbar puncture were normal. Fluorescein angiography showed minimal retinal ischaemia. He was treated with oral Diamox which led to a reduction in the disc

swelling. The retinopathy and disc swelling slowly resolved without further treatment.

A further lung transplant recipient developed rifabutin associated uveitis while taking rifabutin, clarithromycin, and ciprofloxacin therapy for subcutaneous nodules involving the right forearm caused by *Mycobacterium haemophilum* infection. Each eye developed hypopyon anterior uveitis which resolved without loss of vision following treatment with intensive topical corticosteroids, mydriatics, and cessation of rifabutin.

Three patients developed non-retinal ocular herpetic infections. One patient (heart recipient) developed left herpes zoster ophthalmicus 950 days following transplantation. Two patients (both lung recipients) developed herpetic keratitis at 1210 and 1482 days post-transplantation. These infections resolved with a combination of oral and topical aciclovir therapy.

One patient developed right dacryocystitis 1179 days post-transplantation. *Staphylococcus aureus* was isolated and the infection resolved with appropriate antibiotics.

Discussion

Opportunistic infections were the most common cause of ocular disease in this study with herpes group viruses being the most frequent pathogens, accounting for 56% of ocular complications and 88% of the infections. Both ARN syndrome and CMV retinitis were seen in this study. Progressive outer retinal necrosis (PORN), the other clinically distinct form of herpetic retinitis was not seen in patients in this study. ARN occurred in three patients (55%). This syndrome was first recognised in 1971 by Urayama and co-workers⁷ who described a severe inflammatory syndrome consisting of vasculitis, retinitis, and vitritis which has been reported in both immunocompetent and immunosuppressed individuals.⁸ Herpes simplex 1 and varicella zoster are known to cause this disease. These viruses are neurotrophic and establish latency in the central nervous system.⁹ ARN is thought to be a manifestation of latent virus reactivation. In our study the average time of onset of ARN was more than 1 year following transplantation. This delayed onset of infection following transplantation has not been emphasised previously. There were no differences in the immunosuppressive regimen between the group with ARN and the other transplant recipients. Affected patients were treated with high dose aciclovir which has been shown to promote healing and to reduce the incidence of second eye involvement.¹⁰ Prophylactic laser photocoagulation was also performed to protect against rhegmatogenous retinal detachment which may occur in up to 75% of patients and represents a major cause of visual loss.¹¹ None of our patients developed a retinal detachment.

CMV retinitis was also seen in three patients and most frequently in patients with systemic CMV infection. Two patients also had evidence of clinically significant vascular disease. One patient had a 15 year history of diabetes with proliferative retinopathy and maculopathy. The

other two patients had been heavy smokers and one patient had a long history of severe hypertension. Previous reports have emphasised CMV as the most common opportunistic retinal pathogen in transplant recipients.^{3,4} CMV retinitis is the most common ocular opportunistic infection in HIV patients occurring in up to 40% of patients.¹² This heightened awareness of CMV retinitis and the rarity of other types of herpetic retinitis may result its overdiagnosis as the causative agent in any patient with widespread retinitis. We postulate that CMV retinitis is unlikely to occur unless there is microvasculopathy such as that seen in diabetes, smoking related microvascular disease, or chronic severe hypertension that can disrupt the blood-retinal barrier. Additionally, patients have evidence of systemic CMV infection either clinically or serologically. A similar situation occurs in HIV infection where microvasculopathy is seen in up to 50% of patients¹³ and disrupts the blood-retinal barrier allowing CMV access to the retina where it typically begins in areas of the retina previously damaged by HIV microvasculopathy. CMV retinopathy is most common in HIV infected patient groups with a high incidence of CMV infection.

The diagnosis of viral retinitis is clinical and based on ophthalmoscopic findings some of which are quite similar. Laboratory investigations such as direct fluorescent antibody testing and polymerase chain reaction may be useful in selected patients but their role is yet to be clearly defined.¹⁴ It may therefore be difficult in some patients to differentiate between different forms of herpetic viral retinitis. In our study, two patients developed a presumed viral retinitis where an exact clinical diagnosis could not be made. One patient developed visual symptoms of blurring approximately 3 months before the development of a retinal detachment which were attributed to refractive error. At the time of retinal detachment surgery, a large area of atrophic peripheral retina associated with retinal breaks was documented. The location and clinical features of the atrophic retina and retinal breaks were typical of those seen in patients with viral retinitis. There was no evidence of other ocular disease and no evidence of active systemic CMV infection. The second patient was treated for presumed CMV retinitis with ganciclovir. The retinitis was located peripherally, responded poorly to ganciclovir and a fluorescein angiogram revealed peripheral vasoconstriction with widespread leakage. There was no evidence of other ocular disease and no evidence of active systemic CMV infection. He subsequently developed a retinal detachment and neovascular glaucoma with no light perception. Enucleation of his blind eye was performed and histopathological studies failed to detect the presence of viral particles. Immunofluorescence studies were not performed. The clinical and pathological features were consistent with a diagnosis of viral retinitis but a more specific diagnosis could not be made. We hypothesise that these two patients developed ARN rather than CMV retinopathy and that this was not recognised. By the time of

the detachment surgery, it was not possible to make an accurate diagnosis.

Viral retinitis was much commoner in the heart transplant patients than in the patients who had undergone liver transplantation and this difference reflects the lesser degree of immunosuppression needed for liver transplantation. In all patients who developed viral retinitis the immunosuppressive therapy was reduced by decreasing the dose of corticosteroids by 10–20% and the dose of cyclosporin and azathioprine by 10%. All transplant patients receiving CMV mismatched grafts (donor positive, recipient negative) were given prophylactic anti-CMV therapy consisting of ganciclovir 5 mg/kg three times weekly for 6 weeks post-transplantation and for 2 weeks following acute anti-rejection therapy.

Fungal chorioretinitis was seen in two patients and occurred earlier after transplantation than viral retinitis. One patient presented with advanced disease and had a poor visual outcome despite aggressive treatment. The other patient presented and was diagnosed early, and was treated with appropriate antimicrobial therapy. His lesions resolved without significant visual loss. Transplant recipients are at risk of metastatic fungal intraocular infection as a result of their immunosuppression and because of the large number of invasive vascular procedures performed, such as intravenous catheters and endomyocardial biopsy.^{15–17}

One case of herpes zoster ophthalmicus and two cases of herpetic keratitis were seen. In all cases, these occurred late in the post-transplantation period. This is consistent with our hypothesis that herpetic opportunistic infections relate to the chronicity of immunosuppression rather than its severity.

One patient developed choroidal pseudolymphoma which is a type of PTL and whose spectrum ranges from benign reactive lymphoid hyperplasia to high grade non-Hodgkin's lymphoma of large cell type.¹⁸ The occurrence of these disorders appears to relate to the intensity of immunosuppression. Our patient's course was marked by steroid resistant rejection necessitating the use of OKT3 and high dose cyclosporin. The latency period of 123 days to the onset of disease in this patient is similar to those reported in other studies. The pathogenesis of PTL appears to be an exaggerated proliferation of Epstein-Barr virus infected B cells released from the control of suppressor T cells. Cessation or reduction of immunosuppression leads to the regression of PTL as was seen in our patient.

Another patient developed retinal vasculitis soon after heart transplantation. Although initially severe, the vasculitis resolved without visual sequelae and without change in the patient's immunosuppressive therapy. In the absence of any other cause, it was felt that the vasculitis represented an ocular autoimmune reaction developing from mechanisms analogous to those seen in PTL.

One patient developed bilateral disc swelling and an associated visual field defect while on high dose cyclosporin. No cause for the disc

oedema could be found despite extensive investigations. Minimal change occurred with treatment although the retinopathy resolved with time. It was felt that the clinical features and outcome were consistent with cyclosporin retinopathy even though the patient did not fulfil all the criteria for this diagnosis. Combined use of cyclosporin and radiotherapy is commonly associated with a transient ischaemic vasculopathy characterised by visual field defects, optic disc swelling, and cotton wool spots.¹⁹ This syndrome has also been reported in patients treated with high dose cyclosporin in the absence of radiotherapy.²⁰

A single patient developed signs typical of rifabutin associated uveitis while taking combination therapy including rifabutin and clarithromycin for *Mycobacterium haemophilum* infection.²¹ This syndrome is now well characterised although its pathogenesis remains obscure. It responds to intensive local corticosteroid therapy and reduction of the rifabutin dose.

CRVO occurred in one patient. Numerous risk factors for vein occlusion are potentially present in heart transplant recipients.²² This patient had both diabetes and hypertension which are recognised risk factors for CRVO.

In this study the patients could be divided into two groups. In one group, complications occurred early following transplantation and were related to severe immunosuppression and/or systemic infection. The patients who developed PTLD, retinal vasculitis, and fungal choroiditis are typical of this group. In the second group, ocular complications occurred late following transplantation and were related to the length of immunosuppression. Herpes group viral infections were typically seen in this group of patients. Both ARN and CMV retinopathy were frequent with CMV occurring in patients with systemic CMV infection and a damaged blood-retinal barrier.

As heart, lung, and liver transplantation are performed at relatively few specialised centres, transplant recipients who develop ocular complaints may present to ophthalmologists geographically remote from the transplant unit as occurred in 10 of the 19 patients in this series. The development of visual symptoms in transplant recipients warrants careful ophthalmic assessment as they may result from a variety of opportunistic ocular infections and other ocular diseases. Failure to recognise and treat ocular infection appropriately can result in devastating visual loss. This study shows that herpes group viral retinitis was by far the most common intraocular opportunistic infection in this large group of heart, lung, and liver transplantations. Arriving at the correct diagnosis

was delayed in several patients and required intensive investigation including intraocular biopsies in some. An understanding of the type and frequency of ocular complications associated with transplantation is needed by both transplant units and general ophthalmologists to avoid the devastating visual consequences of inaccurate or delayed diagnosis. Physicians managing transplant recipients who develop ocular complaints should seek urgent ophthalmic assessment. Uncertainty regarding the diagnosis should lead to prompt consultation with the transplant unit and its ophthalmologist.

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