The Eye in Bone Marrow Transplantation

VI. Retinal Complications

Nezih M. Coskuncan, MD; Douglas A. Jabs, MD; J. P. Dunn, MD; Julia A. Haller, MD; W. Richard Green, MD; Georgia B. Vogelsang, MD; George W. Santos, MD

Objective: To evaluate the posterior segment ocular complications of patients undergoing bone marrow transplantation (BMT).

Design: Retrospective analysis.

Setting: Academic ophthalmology department at a tertiary care hospital with a BMT unit.

Patients: Patients undergoing BMT were seen by an ophthalmologist for clinical care and enrolled in a long-term follow-up study, during which they were seen 6 and 12 months after the transplantation and annually thereafter.

Results: Of 397 patients undergoing BMT, 51 (12.8%) developed posterior segment complications. Fourteen patients (3.5%) developed hemorrhagic complications with either intraretinal and/or vitreous hemorrhages and 17 patients (4.3%) developed cotton-wool spots in the fundus of both eyes. Eleven patients (2.8%) had bilateral optic disc edema, with eight cases attributed to the toxic effects of cyclosporine and three to other causes. Two patients (0.5%) developed serous retinal detachments. Eight patients (2.0%) developed infectious retinitis and/or endophthalmitis. Fungal infections with Candida or Aspergillus usually occurred within 120 days after BMT, while viral infections with herpes zoster or cytomegalovirus and parasitic infections with Toxoplasma occurred later. Intracocular lymphoma occurred in one patient (0.2%).

Conclusion: Severe, potentially vision-threatening, posterior segment complications following BMT occur due to a variety of causes.

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Bone marrow transplantation (BMT) has become the treatment of choice for severe aplastic anemia, when an appropriate donor exists, and for lymphohematopoietic malignant neoplasms that have relapsed or are likely to relapse. Bone marrow transplantation consists of the ablation of the patient's bone marrow using cytoreductive chemotherapy with or without total-body irradiation (TBI), followed by transplantation of donor bone marrow to reconstitute the patient's hematologic function. Bone marrow transplants may be (1) allogeneic, in which an HLA-matched donor, such as a sibling, is used; (2) syngeneic, in which the donor is a monozygotic twin; or (3) autologous, in which case the patient's own stored and chemotherapeutically purged marrow is transplanted. Complications of BMT include (1) hemorrhage due to aplasia during the early posttransplantation period; (2) infection due to aplasia during the early posttransplantation period and/or immunosuppression to treat graft-vs-host disease (GVHD) during either the early or late posttransplantation period; and (3) GVHD in which the transplanted marrow perceives the host as foreign tissue and mounts a lymphocyte-mediated immunologic attack on the host. Acute GVHD (aGVHD) develops in more than 50% of the successfully engrafted recipients and is fatal or contributory to death in more than 25% of these patients. Chronic GVHD (cGVHD) occurs in 50% of

From The Wilmer Ophthalmological Institute, the Department of Ophthalmology (Drs Coskuncan, Jabs, Dunn, Haller, and Green), and The Johns Hopkins Oncology Center (Drs Vogelsang and Santos), The Johns Hopkins University School of Medicine, Baltimore, Md.
PATIENTS AND METHODS

All patients in this report underwent BMT according to the standard protocols used by the Bone Marrow Transplant Unit of The Johns Hopkins University Oncology Center (Baltimore, Md) during two periods: (1) October 1979 to December 1980; and (2) July 1984 to December 1992. Informed consent was obtained for the transplantation, as well as for all transplantation-related procedures. The preparative, marrow ablative regimens were standardized according to the pretransplantation diagnosis and have been described previously.1-4

In general, for severe aplastic anemia, patients were treated with cyclophosphamide at a dosage of 50 mg/kg intravenously per day for 4 days or 60 mg/kg intravenously per day for 2 days, followed by TBI at 8 Gy with lung shielding for 2 to 4 Gy. For acute nonlymphocytic leukemia, eg, acute myelogenous leukemia, patients were treated with 4 mg/kg of oral busulfan per day for 4 days, followed by 50 mg/kg of intravenous cyclophosphamide per day for 4 days. Patients with acute lymphocytic leukemia, chronic myelogenous leukemia, or lymphoma received 50 mg/kg of intravenous cyclophosphamide per day for 4 days followed by 3 Gy of TBI every day for 4 days, with the lungs shielded for the third dose. Bone marrow infusion was given intravenously through a right atrial catheter.

Patients undergoing BMT were evaluated regularly by members of the BMT team for the presence and severity of GVHD. The results of these evaluations have been reported elsewhere using previously published scoring systems.5-7 Since July 1984, patients undergoing BMT have been evaluated prospectively 6 months and 1 year after transplantation and annually thereafter for up to 5 years by an ophthalmologist for the ophthalmic complications of BMT.

All patients were treated prophylactically to minimize the development of GVHD with either methotrexate, cyclophosphamide, cyclosporine, or a combination of methylprednisolone and either cyclophosphamide or cyclosporine; after 1984, patients were generally treated with cyclosporine. The initial treatment of aGVHD consisted of intravenous methylprednisolone at a dosage of 2.5 mg/kg daily for 4 days followed by a tapering schedule. The subsequent treatment of refractory aGVHD was individualized, but in general, consisted of either high-dose cyclosporine and/or antithymocyte globulin. Chronic GVHD was treated with oral prednisone, at a dosage of 1 mg/kg every other day, and oral azathioprine sodium, at a dosage of 1.5 mg/kg daily, for a minimum of 6 months, followed by a tapering schedule.8 Refractory cGVHD was treated with oral thalidomide.9 The usual cyclosporine dose for GVHD prophylaxis was 5 mg/kg per day intravenously for the 2 days before and the first 3 days after transplantation. The dose of cyclosporine was then slowly tapered to 3.75 mg/kg orally twice daily by day 50, and continued at that dose until discontinuation at day 170. The dose of cyclosporine was altered depending on the clinical course of GVHD or on the development of renal impairment.

In the statistical analysis of risk factor for cotton-wool spots, the relative odds ratios with 95% confidence intervals were determined.

of long-term survivors and is a major cause of posttransplantation morbidity and mortality.8,9

The anterior segment ocular complications of BMT have been well described, including keratoconjunctivitis sicca as a consequence of GVHD,10-12 conjunctival GVHD,13 cataracts,14 and corneal infections.15,16 Posterior segment complications are less frequently described but may be subdivided into the following categories: (1) hemorrhagic;10,11; (2) microvascular retinopathy;17-20; (3) optic disc edema;19,21; (4) infections;22-25; and (5) other complications. We report herein our experience with 397 patients undergoing BMT, of whom 51 (12.8%) developed posterior segment complications.

RESULTS

Three hundred ninety-seven patients underwent ophthalmologic examination. One hundred four patients (26.1%) had acute myelogenous leukemia, 69 (17.3%) had acute lymphocytic leukemia, 32 (8.6%) had aplastic anemia, 113 (28.4%) had chronic myelogenous leukemia, 66 (16.6%) had lymphoma, and 13 (3.2%) had other neoplasms. Two hundred thirty-seven patients were male (60%) and 160 were female (40%). The posterior segment findings were divided into five categories (Table 1).

HEMORRHAGIC COMPLICATIONS

Vitreous and/or intraretinal hemorrhages were observed in 14 patients (3.5%). Four patients (1.0%) had vitreous and preretinal hemorrhages, the remaining 10 (2.5%) had intraretinal hemorrhages. The median time to observing hemorrhagic complications was 51 days after BMT (range -10 to +360 days). Ninety-two percent of the hemorrhagic complications were observed within the first 6 months after transplantation, and 71% were observed within the first 100 days after BMT. The mean platelet count in these patients at the time of examination was 27×10^9/L and the mean hematocrit was 0.27. These hemorrhages cleared after the pancytopenia resolved, without long-term visual sequelae.

COTTON-WOOL SPOTS

Seventeen (4.3%) of the 397 patients developed cotton-wool spots. Two patients developed radiation retinopathy after receiving orbital irradiation, one for neuroblastoma and the other for a plasmacytoma. The time of onset of radiation retinopathy in these two patients ranged from 17 to 19 months (average, 18 months) after transplantation. One patient developed
cotton-wool spots in association with fungemia. The other 14 patients had no other known causes for retinopathy.

The median interval to the development of cotton-wool spots in these 14 patients was 150 days after BMT (range, 19 to 360 days). Seven of these 14 patients had chronic myelogenous leukemia, three had acute lymphocytic leukemia, and four had lymphoma as the underlying disease. No patient with aplastic anemia was seen with cotton-wool spots after BMT. Potential risk factors for the development of cotton-wool spots are listed in Table 2. Chronic GVHD was the only risk factor that was significantly (P<.05) associated with this retinopathy.

**OPTIC DISC EDEMA**

Eleven patients (2.8%) developed bilateral optic disc edema. One patient suffered an intracerebral hemorrhage, one patient had Strepococcus viridans meningitis, and one patient had a central nervous system relapse of leukemia manifested only by bilateral optic disc edema. Optic disc edema in the remaining eight patients was attributed to presumed toxic effects of cyclosporine and was resolved by discontinuing or decreasing the cyclosporine dose. Such cases of optic disc edema occurred an average of 148 days after BMT (range, 32 to 321 days).

**OCULAR INFECTIONS**

Eight patients (2.0%) developed nine posterior segment infections (2.3%). Fungal retinitis and/or endophthalmitis was the most common intraocular infection and occurred in six patients (1.5%). Four patients had Candida endophthalmitis and two had Aspergillus retinitis (Figure 1). Fungal infections generally occurred early after BMT. Five of the six patients developed the fungal infection within the first 120 days after BMT and the median time to fungal endophthalmitis was 57 days after transplantation (range, 22 days to 4½ years). Viral retinitis occurred in two patients (0.5%) and was a late complication in both, occurring 350 and 390 days after BMT. One patient developed cytomegalovirus (CMV) retinitis 270 days after developing Candida endophthalmitis; the course of his disease and response to ganciclovir therapy have been previously reported. A second patient developed presumed varicella zoster virus retinitis after an episode of chickenpox, which responded to acyclovir therapy (case 2). Toxoplastic retinitis occurred in one patient and was also a late complication, occurring 341 days after BMT.

This patient had been initially diagnosed as having CMV retinitis, but his retinitis progressed despite therapy for CMV (Figure 2, top). Diagnostic vitreectomy with endoretinal biopsy revealed Toxoplasma gondii (Figure 2, center). and treatment for Toxoplasma resulted in control of the process (Figure 2, bottom). Vitreous and/or endoretinal biopsy established the diagnosis in two patients with intraocular infections. In the other six, the diagnosis was based on the characteristic clinical picture, positive cultures elsewhere (eg, blood), and the response to appropriate antibiotic therapy.

**OTHER**

One patient with the use of vitreous biopsy was diagnosed as having an intraocular relapse of Burkitt’s lymphoma (case 3, Figure 3). Two patients developed serious retinal detachments associated with subretinal hemorrhages. Both of these patients had a history of mild hypertension and intravascular coagulopathy. In one of

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**Table 1. Posterior Segment Complications of Bone Marrow Transplantation (BMT)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. of Complications*</th>
<th>Frequency, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hemorrhagic complications</td>
<td>14</td>
<td>3.5</td>
</tr>
<tr>
<td>Vitreous hemorrhages</td>
<td>4</td>
<td>1.0</td>
</tr>
<tr>
<td>Intraocular hemorrhages</td>
<td>10</td>
<td>2.5</td>
</tr>
<tr>
<td>2. Cotton-wool spots</td>
<td>17</td>
<td>4.3</td>
</tr>
<tr>
<td>Radiation retinopathy</td>
<td>2</td>
<td>0.50</td>
</tr>
<tr>
<td>&quot;BMT retinopathy&quot;</td>
<td>14</td>
<td>3.5</td>
</tr>
<tr>
<td>Fungal infection</td>
<td>1</td>
<td>0.25</td>
</tr>
<tr>
<td>3. Optic disc edema</td>
<td>11</td>
<td>2.8</td>
</tr>
<tr>
<td>Presumed toxic effects of cyclosporine</td>
<td>8</td>
<td>2.0</td>
</tr>
<tr>
<td>Other causes</td>
<td>3</td>
<td>0.8</td>
</tr>
<tr>
<td>4. Ocular infections</td>
<td>9</td>
<td>2.3</td>
</tr>
<tr>
<td>Fungal retinitis or endophthalmitis</td>
<td>6</td>
<td>1.5</td>
</tr>
<tr>
<td>Toxoplasmic retinitis</td>
<td>1</td>
<td>0.25</td>
</tr>
<tr>
<td>Varicella zoster retinitis</td>
<td>1</td>
<td>0.25</td>
</tr>
<tr>
<td>Cytomegalovirus retinitis</td>
<td>1</td>
<td>0.25</td>
</tr>
<tr>
<td>5. Other causes</td>
<td>3</td>
<td>0.75</td>
</tr>
<tr>
<td>Ocular lymphoma</td>
<td>1</td>
<td>0.25</td>
</tr>
<tr>
<td>Serous retinal detachment</td>
<td>2</td>
<td>0.50</td>
</tr>
</tbody>
</table>

*The number of complications exceeds 51 because three patients had more than one complication.

**Table 2. Risk Factors for Cotton-wool Spots**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute GVHD</td>
<td>2.4</td>
<td>0.73-7.73</td>
</tr>
<tr>
<td>Chronic GVHD</td>
<td>4.7†</td>
<td>1.54-14.32</td>
</tr>
<tr>
<td>Acute or chronic GVHD</td>
<td>2.8</td>
<td>0.76-10.05</td>
</tr>
<tr>
<td>Total body irradiation</td>
<td>2.5</td>
<td>0.78-8.16</td>
</tr>
<tr>
<td>Busulfan</td>
<td>0.5</td>
<td>0.17-1.76</td>
</tr>
<tr>
<td>Cyclosporine A</td>
<td>1.8</td>
<td>0.40-8.38</td>
</tr>
</tbody>
</table>

*GVHD indicates graft-vs-host disease. †P<.05.
these two patients, autopsy revealed serous material separating the photoreceptor outer segment layer from the underlying retinal pigment epithelial layer.

SELECTED CASE REPORTS

Case 1

A 29-year-old white woman was referred in January 1991 for evaluation of blurred vision. She had a history of acute myelogenous leukemia diagnosed in July 1990 and underwent an allogeneic BMT in November 1990. She had recently been diagnosed as having CMV colitis and received ganciclovir treatment that had been discontinued 1 week prior to ophthalmologic consultation due to thrombocytopenia. The patient also had a new right lower lobe pulmonary infiltrate that was interpreted as pulmonary aspergillosis.

Her visual acuity was 20/320 OD and 20/20 OS. Slit-lamp examination results and applanation tension were normal in both eyes. Ophthalmoscopy revealed a large serous retinal detachment extending from the temporal edge of the optic disc to the fovea, with intraretinal hemorrhages in the central part of the lesion. Beneath the neurosensory retinal elevation was an area of white flocculent material (Figure 1, top). The fundus of the left eye was normal. She was treated with 69 mg (1 mg/kg) of amphotericin-B intravenously every day and 1250 mg of flucytosine orally every 12 hours and was scheduled to undergo a diagnostic vitrectomy.

Three days later, the lesion was substantially larger (Figure 1, bottom) and a diagnostic vitrectomy was performed on her right eye. She was given 5 μg of intravitreal amphotericin-B at the end of the vitrectomy. Cultures of the vitreous yielded Aspergillus flavus. Despite treatment with intravenous amphotericin and flucytosine and repeated intravitreal amphotericin injections, the patient developed a progressive exudative retinal detachment with a subretinal mass in the right eye. No further surgery was attempted, and the eye became phthisical.

Case 2

A 43-year-old white man was seen in June 1990 complaining of a 1-week history of blurred vision in his right eye. He had a history of acute myelogenous leukemia and had undergone an allogeneic BMT on June 3, 1989. The course of his disease had been complicated by aGVHD that was successfully treated with corticosteroids. He had a history of presumed cyclosporine-induced optic disc edema that had resolved with discontinuation of cyclosporine therapy.

Six weeks prior to examination, he had an episode of chickenpox that was successfully treated with a 3-week course of intravenous acyclovir.

On examination, his visual acuity was 20/40 OD and 20/25 OS. Slit-lamp examination results and applanation tension were normal in both eyes. Ophthalmoscopy revealed scalloped retinal scars with active edematous borders and a sclerotic white vessel superonasally in the right eye and similar scalloped scars with a new area of retinitis adjacent to the macula in the left eye. Goldmann visual fields showed paracentral and midperipheral scotomas bilaterally and constriction of the peripheral isopters in both eyes. Treatment was given at a dose of 1000 mg every 8 hours for presumed varicella zoster retinitis with a 3-week course of intravenous acyclovir. The retinitis resolved leaving only atrophic retinal scars.

In March 1991, his visual acuity was 10/200 OD and 20/30 OS. There was a dense posterior subcapsular cataract in the right eye and a moderate posterior subcapsular cataract in the left eye. Ophthalmoscopy revealed extensive peripheral chorioretinal scars bilaterally with no active retinitis and mild optic disc pallor in the right eye between September and December 1991. Phacoemulsification with posterior chamber intraocular lens implantation followed by neodymium-YAG laser capsulotomy was performed in both eyes. In November 1992, his vi-
sual acuity was 20/30 OD and 20/20–2 OS. Ophthalmoscopy revealed no active retinitis.

Case 3

A 36-year old white man was referred on June 4, 1992, with a 2-week history of blurred vision in the left eye. He had a history of an indolent stage IIIA lymphoma diagnosed in May 1984 that was treated with total nodal irradiation and chemotherapy. He suffered a relapse in 1988, was successfully treated with chemotherapy, and experienced remission until February 1992, when a bone marrow biopsy showed Burkitt’s lymphoma. He was treated with chemotherapy, including seven intrathecal methotrexate injections for central nervous system relapse. He was then referred to The Johns Hopkins Hospital for autologous bone marrow transplantation. On admission, he was found to have a new-onset right Bell’s palsy. Magnetic resonance imaging of the brain and a lumbar puncture were normal. The Bell’s palsy was thought to be due to previous vincristine therapy. He had already undergone bone marrow harvesting and had started receiving cytoxic therapy with busulfan, cytoxan, and etoposide prior to transplantation.

Visual acuity was 20/25 OD and 20/200 OS. Ophthalmologic examination of the right eye was normal. The left eye had 2+ anterior vitreous cells and haze, and a large white lesion was noted over the optic nerve (Figure 3, top). A diagnostic vitrectomy was performed. Cultures for bacteria, fungi, and viruses were negative. Cytologic examination of the specimen showed atypical lymphocytes and nuclear atypia in large lymphocytes diagnostic of intraocular lymphoma (Figure 3, center). Because cytotoxic chemotherapy had already been started, an autologous BMT was performed on June 11, 1992.

On July 14, 1992, his visual acuity had improved to 20/30 OD and the retinal infiltration around the optic nerve had resolved (Figure 3, bottom). Because of the history of central nervous system involvement by Burkitt’s lymphoma, a repeated lumbar puncture was performed on July 15, 1992. Cytologic study revealed malignant lymphocytes. He was treated with intrathecal cytarabine and methotrexate. Outpatient cranial irradiation was planned; however, the patient died in August 1992.

While the anterior segment complications of BMT have been well described, the posterior segment complications have been less frequently reported. In our series of patients undergoing BMT, 12.8% developed posterior segment complications. These complications could be divided into the following four categories: (1) hemorrhagic complications in the period immediately following BMT due to induced aplasia; (2) cotton-wool spots; (3) optic disc edema; (4) infectious complications; and (5) other miscellaneous complications.

Hemorrhagic complications occurred in the early postoperative period and were presumably related to the bone marrow aplasia that occurs at that time. The patients undergoing BMT were given vigorous transfusion support of both red blood cells and platelets with the goal of keep-
ing the hematocrit above 0.30 and the platelet count above $20 \times 10^9/L$. Studies in patients with leukemia have shown that thrombocytopenia is the most important factor in the development of hemorrhages associated with leukemia.\textsuperscript{31} Short-term vision loss due to vitreous and/or preretinal hemorrhages was uncommon, occurring in only 1% of the series, and did not result in long-term visual sequelae.

Cotton-wool spots developed in 17 patients. In two patients, the cotton-wool spots were believed to be due to radiation retinopathy. The neurosensory retina is more resistant to radiation damage than the retinal vascular endothelium and pericytes. The occlusive microangiopathy becomes clinically significant 6 or more months after exposure.\textsuperscript{17} Brown et al\textsuperscript{32} determined that the mean time of onset of radiation retinopathy after irradiation was 18 months. In our series, two patients developed radiation retinopathy after orbital irradiation at 17 and 19 months after BMT. Fourteen patients developed retinopathy with cotton-wool spots without orbital irradiation or other evident causes. Evaluation of risk factors for the development of cotton-wool spots showed that only cGVHD was significantly associated with the development of retinopathy. However, due to the small number of patients with “BMT retinopathy,” the statistical power of our study is limited. Lopez et al\textsuperscript{17} reported a series of five patients who developed retinopathy after BMT for acute leukemia. One of the five patients developed proliferative retinopathy with a subhyaloid hemorrhage. The preparative regimen used in their patients differed from the one used in our patients; specifically, the patients reported by Lopez et al\textsuperscript{17} were treated with high-dose cytarabine hydrochloride and 12 Gy of TBI, while conversely, our patients were prepared with either busulfan and cyclophosphamide or cyclophosphamide and TBI. Bernauer et al\textsuperscript{19} reported microvasculopathy in 10% of 127 patients undergoing BMT. Retinopathy was attributed to therapy with cyclosporine and TBI. As in our series, retinopathy was not seen in patients with aplastic anemia but was seen in patients with leukemia and other pretransplantation diagnoses. These authors attributed the microvasculopathy to a combination of cyclosporine and TBI. Cyclosporine by itself, and TBI by itself did not induce cotton-wool spots. Stuckenschneider and Meiler\textsuperscript{13} reported that four (5.5%) of 72 patients developed an occlusive microvascular retinopathy following BMT. All patients in this series also had malignancies prior to transplantation. The pathogenesis of cotton-wool spots is probably multifactorial. The use of chemotherapy and/or cyclosporine lowers the threshold for radiation retinopathy induced by TBI.\textsuperscript{15,14} However, not all patients who developed cotton-wool spots in our series had a history of TBI, suggesting that it is not a necessary prerequisite for the development of BMT retinopathy, and no single risk factor fully accounted for the development of cotton-wool spots in our series.

Cyclosporine has become widely used in the field of transplantation and has been implicated in a variety of neurotoxic effects, including seizures, encephalopathy, cerebellar and spinal cord syndromes, dysarthria, tremor, coma, cortical blindness, increased intracranial pressure, increased cerebral spinal fluid protein, and papilledema.\textsuperscript{21,15} Eleven (2.8%) of 397 patients developed optic disc edema, of whom eight (2.0%) were thought to
have presumed cyclosporine-related toxic effects. Optic disc edema due to cyclosporine may present a direct toxic effect of the drug, an idiosyncratic response, papilledema due to increased intracranial pressure, or some combination of these mechanisms.34

Infectious complications of BMT are a major therapeutic problem and account for the majority of deaths in transplant recipients.9,36 The immediate posttransplantation period prior to engraftment is characterized by severe marrow aplasia that results from high-dose chemotherapy and TBI. Because of the life-threatening nature of infections in patients undergoing BMT, they are treated aggressively with antibiotics at the first sign of fever, and persistent or recurrent fevers are treated according to standardized protocols. This aggressive approach has markedly decreased the problem of bacterial infections. Fungal disease remains a problem despite the use of antifungal agents as part of the antibiotic protocols for persistent or recurrent fever. No cases of bacterial retinitis or endophthalmitis were encountered in our series, while six patients developed fungal retinitis and/or endophthalmitis. Candida endophthalmitis was the most frequently encountered complication, with Aspergillus encountered in the two additional cases. Five of the six fungal infections occurred within the first 120 days after BMT, with only one occurring later in the setting of a systemic fungal infection.

Bone marrow transplant recipients also have a severe but transient combined immunodeficiency involving both T and B lymphocytes. Patients with aGVHD and cGVHD have delayed recovery or persistent abnormalities of immunity. In addition, GVHD is treated with immunosuppressants that further increase the risk of infection.

The prophylactic use of acyclovir for patients undergoing BMT has largely eliminated mucocutaneous herpetic infections during the immediate posttransplantation period. However, late cases of herpes zoster infection, often disseminated, may occur in association with the immunosuppressive therapy required for cGVHD. We encountered one case of herpes zoster retinitis after a disseminated varicella zoster infection that occurred 370 days after the transplantation. The clinical features were identical to those seen in the acute retinal necrosis syndrome,33 and the disease responded well to intravenous acyclovir therapy.

Systemic CMV infection, particularly CMV pneumonitis, remains a significant problem in patients undergoing BMT.38 Despite the occurrence of CMV pneumonitis, CMV retinitis is uncommon and occurred in only one patient in our series. This finding contrasts with CMV infections in patients with acquired immunodeficiency syndrome, which occurs in an estimated 20% of patients.39 The one patient in our series who developed CMV retinitis was human immunodeficiency virus–antibody negative,28 but his immune function remain suppressed as a consequence of cGVHD.

Toxoplasmic retinochoroiditis also developed as a late ocular complication in a single patient with GVHD who required persistent immunosuppression. The clinical picture was atypical, and the correct diagnosis was made only after endoretnal biopsy. With appropriate antibiotic therapy, the lesion healed. This lesion appeared to represent acquired ocular disease, since no evidence of an old toxoplasmic scar was present prior to ophthalmologic examination. Of interest, two patients with old toxoplasmic scars that presented prior to transplantation underwent BMT without reactivation of disease. Previous reports of toxoplasmonic infection in patients undergoing BMT have emphasized the association with cerebral dissemination.40 In our patient, cerebral dissemination appeared to be present as evidenced by computed tomography.

Cases of anterior segment masquerade syndrome in which anterior chamber paracentesis and iris biopsy allowed definitive diagnosis of leukemic relapse have been reported.41 Our experience with infectious and tumor-related ocular complications emphasizes the need for similarly aggressive vitreoretinal diagnostic procedures in selected patients. In case 3, the clinical picture was suggestive of a fungal endophthalmitis, but a diagnosis of intraocular lymphoma was made using vitreous biopsy.

Posterior chorioretinopathy and retinal detachment have been reported after renal transplantation and heart-lung transplantation by Gass et al.42 The presumed mechanism was intravascular coagulation with damage to the pigment epithelium and subsequent serous retinal detachment. Two of our cases developed a serous retinal detachment in association with a disseminated intravascular coagulopathy. The presumed pathogenic mechanism is choroidal vascular occlusion, pigment epithelial damage, and transudation of fluid beneath the retina, resulting in serous retinal detachment.

Vitreoretinal complications of BMT may result from the effects of high-dose chemoradiotherapy and TBI, infections, GVHD or its prophylaxis or treatment, and recurrent malignancies. Familiarity with the potential ocular complications is important in the successful treatment of these patients.

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Reprint requests to The Wilmer Ophthalmological Institute, 550 N Broadway, Suite 700, Baltimore, MD 21205 (Dr Jabs).

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