Epstein-Barr virus–positive diffuse large B-cell lymphoma of the elderly. A, A diffuse lymphoid infiltrate with necrosis can be seen at low power (hematoxylin-eosin). B, At higher power, the infiltrate comprises large and pleomorphic tumor cells, including Hodgkin-like cells and Reed-Sternberg-like giant cells, with a background of smaller reactive inflammatory cells (hematoxylin-eosin). The tumor cells express B-cell markers CD20 (C) and Pax-5 (D), while CD30 (E) and latent membrane protein 1 (F) are also positive.

Figure 2. Histological examination findings from the eyelid of a patient with Epstein-Barr virus–positive diffuse large B-cell lymphoma of the elderly. A, A diffuse lymphoid infiltrate with necrosis can be seen at low power (hematoxylin-eosin). B, At higher power, the infiltrate comprises large and pleomorphic tumor cells, including Hodgkin-like cells and Reed-Sternberg-like giant cells, with a background of smaller reactive inflammatory cells (hematoxylin-eosin). The tumor cells express B-cell markers CD20 (C) and Pax-5 (D), while CD30 (E) and latent membrane protein 1 (F) are also positive.

eptoposide. She achieved near complete remission after 4 months of chemotherapy. During the subsequent 4 months, there has been no evidence of local recurrence.

Comment. Epstein-Barr virus–associated B-cell lymphomas have been mainly reported in immunosuppressed patients such as those with human immunodeficiency virus infection, organ transplantation, or methotrexate therapy for rheumatoid arthritis. Epstein-Barr virus–positive DLBCL of the elderly is defined as a lymphoproliferative disorder arising in patients without predisposing immunodeficiency, including human immunodeficiency virus and human T-cell lymphoma virus 1 infection, a history of chemotherapy or radiotherapy, and autoimmune disease, and is thought to result from immunological deterioration associated with aging. According to the World Health Organization classification, EBV-positive DLBCL of the elderly is a rare DLBCL that accounts for 8% to 10% of DLBCL among patients without predisposing immunodeficiency in Asian countries. Interestingly, EBV-positive DLBCL of the elderly frequently involves extranodal sites. Most patients with extranodal disease also have nodal disease. In fact, 70% of patients have extranodal disease affecting sites such as the skin, lung, tonsils, or stomach, while 30% of patients have lymph node involvement alone. However, no case of ocular involvement, which is an extranodal site, has been reported. To our knowledge, our case is the first report of EBV-positive DLBCL of the elderly involving the eyelid and orbit.

Epstein-Barr virus–positive DLBCL of the elderly with ocular involvement is totally distinct, both clinically and pathologically, from extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue, an indolent tumor that is the most common form of lymphoma in the orbital region. Although relatively uncommon, EBV-positive DLBCL of the elderly should be considered in the differential diagnosis of ocular lymphoma since it needs to be treated appropriately as a highly aggressive lymphoma.

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Severe Retinal Vascular Infarction After Photodynamic Therapy With Verteporfin Using the Standard Protocol

Photodynamic therapy (PDT) with verteporfin has been widely used for the treatment of choroidal neovascularization associated with age-related macular degeneration, with both the efficacy and safety of PDT considered to be at tolerable levels. Herein, we describe a patient who experienced severe retinal vascular infarction exactly corresponding to the irradiated spot following PDT using the standard protocol.

Report of a Case. A 60-year-old man was referred because of decreased vision in the right eye. He had a history of diabetes mellitus, systemic hypertension, arteriosclerosis obliterans, and renal failure requiring dialysis. The right
Eye had undergone focal laser photocoagulation in the macula due to uncertain reasons 20 years before the initial visit. Initially, the right eye had subretinal fluid accumulation and hemorrhages in the macula with a visual acuity of 20/200. Moreover, both eyes had retinal microaneurysms and punctate hemorrhages consistent with diabetic retinopathy. Indocyanine green angiography revealed peculiar vascular change in the macula, namely, polypoidal choroidal vasculopathy. In the right eye, we performed the first session of PDT according to the standard protocol. Verteporfin (Visudyne; Novartis AG, Basel, Switzerland) (6 mg/m² of body surface area) was infused intravenously over 10 minutes. Fifteen minutes after the start of infusion, a 689-nm laser light (Carl Zeiss, Dublin, California) delivered 50 J/cm² at an intensity of 600 mW/cm² for 83 seconds covering the dye leakage on fluorescein angiography (the greatest linear dimension of the entire choroidal neovascularization lesion was 2492 μm; the spot size was 3500 μm). Postoperatively, the right eye showed immediate resolution of exudation with no complications. Two years later, the patient noticed vision loss in his right eye attributable to the relapse of exudative change in the macula, and visual acuity was 20/100 (Figure 1). We performed the second session of PDT in the right eye with the same protocol as the first session (the greatest linear dimension of the entire choroidal neovascularization lesion was 4427 μm; the spot size was 5500 μm). A Volk QuadrAspheric contact lens (Volk Optical, Inc, Mentor, Ohio) was used, giving 1.97× magnification of the laser spot at the retina. One week later, he noted sudden visual deterioration from 1 day following treatment, and visual acuity decreased to 20/400. Biomicroscopic examination revealed a well-demarcated, circular, whitish lesion exactly corresponding to the PDT spot (Figure 2). Fluorescein angiography showed complete occlusions of all retinal arterioles, venules, and capillaries within the treated area. Optical coherence tomography revealed hyperreflective thickening of the involved retina. We performed extensive blood testing; however, no particular findings except hyperglycemia were detected. Three months later, the whitish circular retinal le-
sion in the macula was indistinct and the exudative change had resolved. However, the irradiated area was not perfused on fluorescein and indocyanine green angiography. The retina was markedly thin with no subretinal fluid in the optical coherence tomographic image, and visual acuity was 20/200.

Comment. We demonstrated multiple retinal vascular occlusions corresponding to the irradiated area following PDT using the standard protocol. Photodynamic therapy reportedly temporarily affects the normal choroidal vasculature and rarely causes severe infarction of the choroidal vessels. However, to our knowledge there have been no reported cases with such a severe retinal vascular complication by means of the standard protocol. In a phase 1 and 2 study of PDT, the regimen using a double verteporfin dose (12 mg/m²) and a triple light dose (150 J/cm²) with the light application 30 minutes after initiation of infusion induced similar retinal occlusions of both branch retinal arterioles and venules in 1 patient. In our case, it was impossible to identify the reason for the retinal vaso-occlusive event from the medical history and blood testing. However, we should be aware that under certain conditions, serious infarction of retinal vessels can develop following PDT using the standard protocol.

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COMMENTS AND OPINIONS

Diabetic Macular Edema Following Panretinal Photocoagulation

We read with great interest the study by Brucker et al1 describing the effects of single-sitting vs 4-sitting panretinal photocoagulation on macular edema in subjects with severe nonproliferative or early proliferative diabetic retinopathy. The results appear appealing; however, the following aspects need clarification.

Some patients without optical coherence tomographic (OCT) measurements were described by Brucker et al1 to have completed the scheduled follow-up. For example, the study flowchart shows that 74 patients in the 1-sitting group and 58 in the 4-sitting group completed the week 34 visit; however, 72 and 55 patients had OCT measurement in each group, respectively. Wouldn’t the study flowchart be more informative if it described the number of persons who completed the primary outcome measurement (i.e., OCT central subfield thickness) rather than completed visits?

The first major eligibility criterion was reported to be early proliferative diabetic retinopathy or severe nonproliferative or early proliferative diabetic retinopathy. The results appear appealing; however, the following aspects need clarification.

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The first major eligibility criterion was reported to be early proliferative diabetic retinopathy or severe nonproliferative or early proliferative diabetic retinopathy. However, based on the first table, 14 patients with mild to moderate nonproliferative diabetic retinopathy were included in the study. It seems that the classification of diabetic retinopathy in the first table was reported according to the review of the reading center; however, the value of the reading center opinion was not clearly reported. Why were fundus photographs sent to the reading center if they were not used to confirm inclusion criteria or measure the effectiveness of clinical outcome?

Brucker et al1 sent 567 OCT follow-up scans to the reading center “Methods”. However, 555 OCT measurements were reported in the “Results” (Table 2), so what happened for the remaining 12 scans?

Were uncontrolled hypertension and the glitazone group of antidiabetic drugs considered in the analysis, since both are known to be independently associated with diabetic macular edema?2-4

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Falavarjani et al are correct that 5 of the 132 subjects who had a week 34 visit did not have a gradeable OCT scan.1 Eligibility was based on the investigator’s assessment; however, the reading center assessment of the level of retinopathy severity was used to evaluate the comparability of the 2 treatment groups to provide standardization across sites and eliminate bias because the reading center was not aware of treatment group. The number of visits was 567, and the number of visits with OCT measurements was 555; Falavarjani et al are correct that this was not stated properly in the “Methods” section. Unsatisfactory medical status, including blood pressure and glycemic control, was an exclusion criterion. We do not have information to evaluate glitazone effects but there would be no reason to expect an imbalance between treatment groups. None of these issues appear to have relevance to the interpretation of the study results. We wish to thank Falavarjani et al for their comments.

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