

CHOROIDAL MORPHOLOGY IN A PATIENT WITH HELLP SYNDROME

Ayaka Kasai, MD,* Yukinori Sugano, MD,* Ichiro Maruko, MD,†
Tetsuju Sekiryu, MD*

Purpose: We report here, the morphological characteristics of the retina and choroid in a patient with hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome, who was not aware of her pregnancy before visiting our hospital.

Methods: Case report.

Results: The patient complained of visual disturbances in both eyes for a few days. Extensive serous retinal detachment and hyperreflective foci were observed in both eyes on spectral domain optical coherence tomography (SDOCT). Enhanced depth imaging technique using SDOCT revealed choroidal thickening and unclear choroidal vessel contour. Her blood pressure was 230/168 mmHg. Laboratory data showed hemolysis and liver dysfunction. Obstetrical examination disclosed her pregnancy. She was diagnosed as having HELLP syndrome. Because her general condition improved after prompt Cesarean delivery, the fundus lesions were rapidly resolved with choroidal thinning.

Conclusion: The eyes in a patient with HELLP syndrome showed characteristic choroidal morphology. The choroidal morphology shown with SDOCT might be one of the pathognomonic signs for a diagnosis of HELLP syndrome.

RETINAL CASES & BRIEF REPORTS 10:273–277, 2016

From the *Department of Ophthalmology, Fukushima Medical University School of Medicine, Fukushima City, Japan; and †Department of Ophthalmology, Tokyo Women's Medical University, Tokyo, Japan.

Preeclampsia is a pregnancy complication characterized by high blood pressure, proteinuria after 20 weeks gestation, and signs of damage to another organ system. Uteroplacental and maternal endothelial dysfunction might happen during the course of the disease, such as renal failure, disseminated intravascular coagulation (DIC), pulmonary edema, placental abruption, and hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome. HELLP syndrome is defined by hemolysis, elevated liver enzymes, and a low platelet count.¹ This syndrome might be considered as a severe variant of preeclampsia/

eclampsia² or as a separate disorder with features that overlap preeclampsia/eclampsia.^{3–6} Complaints of visual disturbances occur in 20% to 25% of patients with severe preeclampsia and eclampsia.^{7–9} Serious visual loss has been reported in patients with HELLP syndrome.¹⁰ Optic disc edema, hemorrhages, and cotton wool and Elschnig spots with a fundus finding similar to hypertensive retinopathy have been found with ophthalmoscopy. Fluorescein angiography has revealed a filling delay in the choriocapillaris and abnormal choroidal leakage of dye unassociated with signs of retinal angiospasm.¹¹ Abnormal choroidal circulation in preeclampsia is more obvious with indocyanine green angiography.^{12–14} Although angiography is useful for establishing a diagnosis, the poor general condition of patients with preeclampsia might not allow performance of angiography.

Another noninvasive examination, that is, spectral domain optical coherence tomography (SDOCT), can produce fine retinal images of macular edema and a serous retinal detachment in preeclampsia patients.¹⁵ Recently, an enhanced depth imaging (EDI) technique with SDOCT enables analysis of the choroidal morphology for various macular diseases.¹⁶ We present detailed choroidal morphology in a patient with HELLP syndrome.

None of the authors have any financial/conflicting interests to disclose.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND), which permits downloading and sharing the work provided it is properly cited. The work cannot be changed in any way or used commercially.

Reprint requests: Tetsuju Sekiryu, MD, Department of Ophthalmology, Fukushima Medical University School of Medicine, 1 Hikarigaoka, Fukushima 960-1295, Japan; e-mail: sekiryu@fmu.ac.jp

Case Report

A 41-year-old woman, who was multigravida, was not aware of her pregnancy as of her first visit to the Ophthalmology Department of Fukushima Medical University Hospital. She complained of visual loss in both eyes for a week. A few days before her visit, she saw an internist and complained of a low-grade fever and back pain and was diagnosed as having pyelonephritis. Her best corrected visual acuity (BCVA) was 0.3 (20/67, 59 ETDRS letter scores) in the right eye and 0.4 (20/50, 65 Early Treatment Diabetic Retinopathy Study (ETDRS) letter scores) in the left eye. ETDRS letter scores were calculated according to the formula.¹⁷ She did not notice neck stiffness, headache, tinnitus, and hearing loss. Her ocular pressure was 17 mmHg in the right eye and 15 mmHg in the left eye. Slit-lamp examination showed no abnormalities in either eye. Fundus examination revealed a bilateral papilledema and severe macular edema with retinal hemorrhage and fibrin deposits. We planned to perform angiography to evaluate the permeability of the vessels and the retinal pigment epithelium. We had to abandon the examination because of her poor health condition and high blood pressure, which was 230/168 mmHg.

Spectral domain optical coherence tomography showed bilateral extensive serous retinal detachment with swelling of the sensory retina. The inner retinal layers were separated by multiple cysts. Different irregularities and undulations were detected in the retinal pigment epithelium. The outer plexiform layer delaminated (Figure 1). Hyperreflective dots became evident in the subretinal space, which became remarkable in the resolving stage (Figure 2). Enhanced depth imaging optical coherence tomography showed extreme thickening of the choroid (over 500 μm in both eyes), such that the outer border between the choroid and the sclera was unclear. The lumens of the choroidal vasculature in Sattler and

Hurler layers were barely identifiable. As a result, the choroid showed a “ground glass appearance” (Figure 2).

Ocular manifestation and systemic abnormalities suggested malignant hypertension or Vogt-Koyanagi-Harada (VKH) disease. She was referred to the Department of Internal Medicine and the Obstetrical Department in our hospital.

Her height and body weight was 152 cm and 70 kg, respectively. Her body mass index was 30.3. The patient neurological status was normal. Her urine protein was 4+. Laboratory examination showed elevated liver enzymes and a low platelet count; the hemoglobin concentration was 15.0 g/dL (11.6–14.0 g/dL), hematocrit was 45.0% (34.1–41.7%), and the red blood cell count was $5.11 \times 10^6/\mu\text{L}$ ($3.66\text{--}5.8 \times 10^6/\mu\text{L}$), and the mean corpuscular volume was 88.1 fL (81.8–97.2 fL). The white blood cell count was $10,900/\mu\text{L}$ (normal range 2,800–8,800/ μL), the blood platelet count was $88 \times 10^3/\text{dL}$ ($147\text{--}341 \times 10^3/\text{dL}$), blood urea nitrogen was 18 mg/dL (8–22 mg/dL), serum creatinine was 1.08 mg/dL (0.40–0.70 mg/dL), estimated glomerular filtration rate was 45 mL $\cdot\text{min}^{-1}\cdot\text{L}^{-1}$ (60 mL $\cdot\text{min}^{-1}\cdot\text{L}^{-1}$), aspartate transaminase was 45 U/L (13–33 U/L), alanine aminotransferase was 51 U/L (6–27 U/L), elevated lactate dehydrogenase was 648 U/L (119–229 U/L), alkaline phosphatase was 490 U/L (115–359 U/L), elevated C-reactive protein was 1.91 mg/dL (0.00–0.30 mg/dL), total protein in the blood was 5.4 g/dL (6.7–8.3 g/dL), serum albumin was 2.2 g/dL (3.9–4.9 g/dL), delayed prothrombin time was 148.7% (70.0–125.0%), and activated partial thromboplastin time was 26.3 seconds (23.0–38.0 seconds).

Systemic abnormalities suggested malignant hypertension or HELLP syndrome. They finally discovered her pregnancy and concluded a diagnosis of HELLP syndrome. After initial stabilization, the patient underwent prompt Cesarean delivery, which resulted in the birth of a low-birthweight boy (872 g). Two weeks later, serous detachment

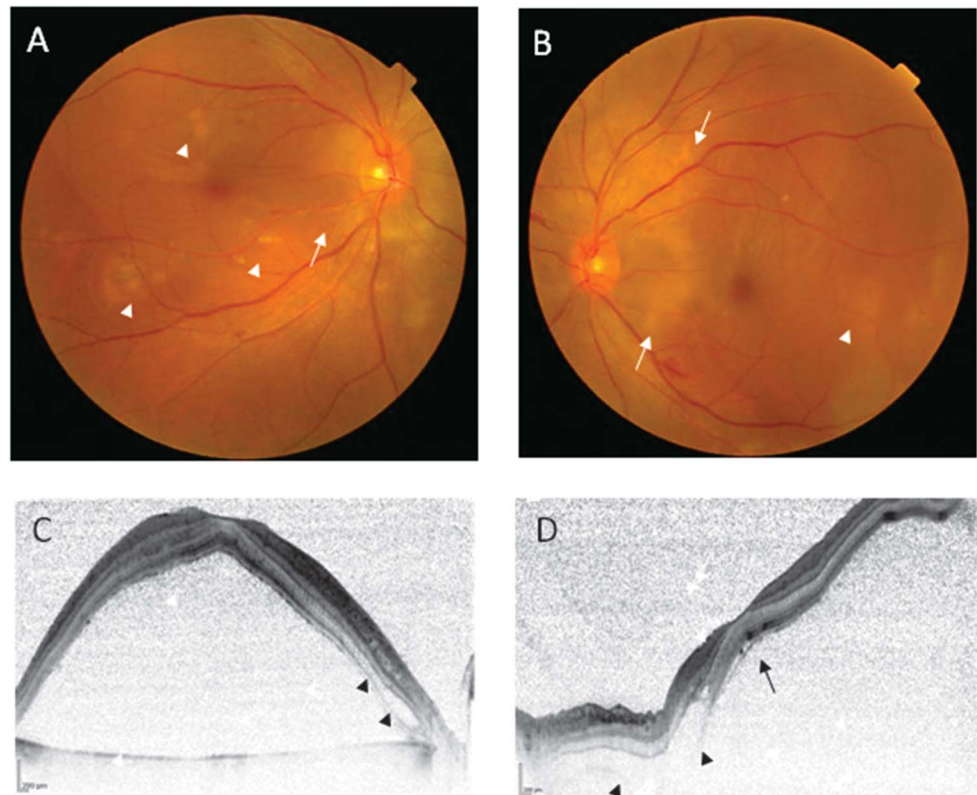


Fig. 1. Fundus photographs of the first medical examination (A and B) Fundus photographs show retinal edema focusing on bilateral optic discs (white arrows). Elschnig spots are scattered in the posterior pole fundus (white arrow heads). Optical coherence tomography showed the presence of a cyst, which continued to the optic disk (C and D). The cyst was in the strongest area of retinal edema around the optic disc. Additionally, OCT showed a structure that was similar to a membrane beyond the retina in the fovea (black arrow).

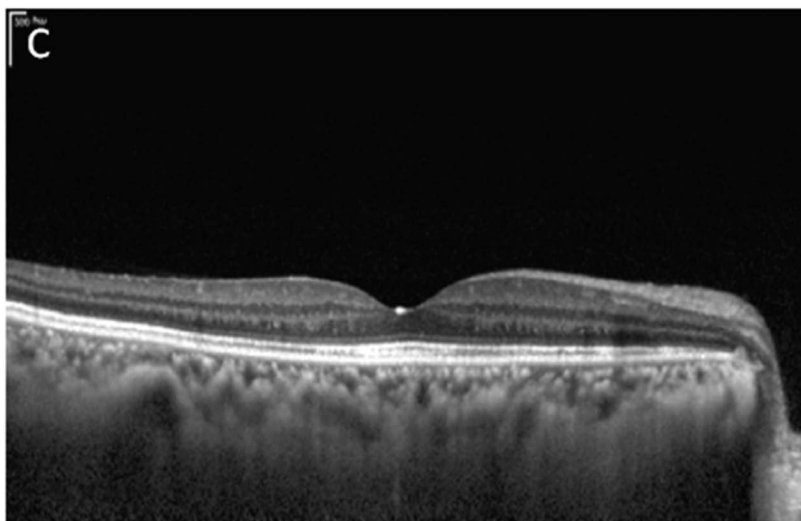
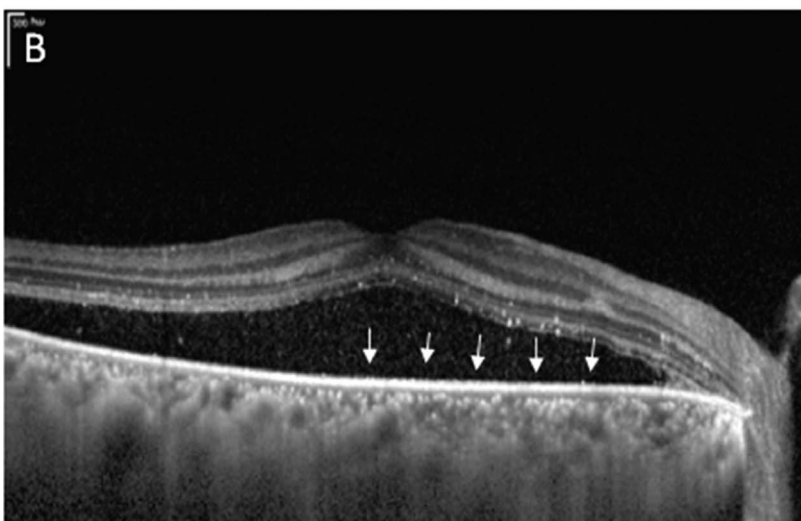
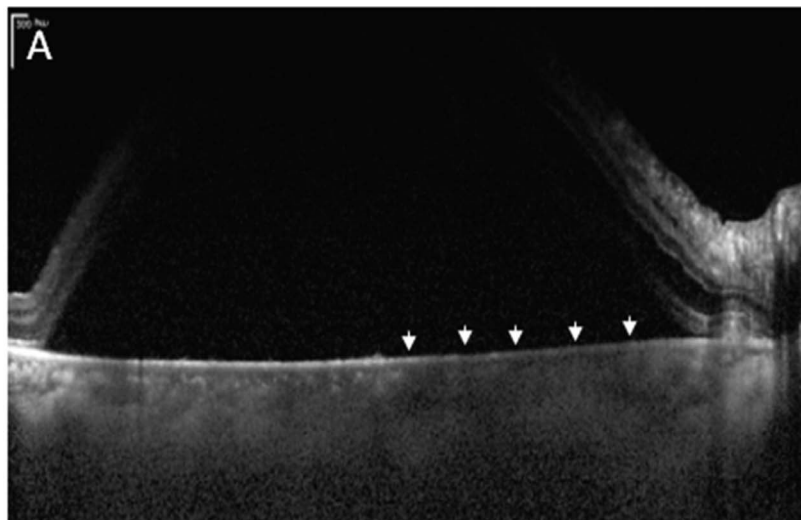


Fig. 2. Changes of OCT findings (A) from the first medical examination. The luminal structure of a choroidal vessel was ambiguous throughout the choroid. It is especially remarkable on the optic disc side in which the retinal edema was strong (arrow heads). **B.** Six days later, the luminal structure of the choriocapillaris and Sattler layer could be recognized (arrows). **C.** Four months later, the luminal structure of Haller layer could be recognized.

associated with hyperreflective irregular dots and intraretinal cysts resolved spontaneously with choroidal thinning. The lumen of the choroidal vessel was clearly delineated with EDIOCT. One month after delivery, blood pressure was decreased to 127/81 mmHg. Her BCVA improved to 1.0 (20/20, 85 ETDRS letter scores) in both eyes. The choroidal thickness, at this point, was restored to the normal range, that is, 271 μm in the right eye and 282 μm in the left eye. On fundus evaluation, the retina appeared flat with some Elschnig spots.

Discussion

We report a patient with HELLP syndrome showing characteristic choroidal morphology. She complained of bilateral visual loss and was not aware of her pregnancy at presentation. Optical coherence tomography showed serous retinal detachment and choroidal thickening. These findings rapidly disappeared after delivery with immediate Caesarian incision.

Four percent to 12% of patients with preeclampsia or eclampsia have HELLP syndrome.^{18–20} Patients might demonstrate one or more aspects of the syndrome; that is, microangiopathic hemolytic changes, elevated liver enzymes, and low platelet levels. Incomplete expression has been reported in 50% of HELLP-syndrome patients.^{20,21} The diagnosis of HELLP syndrome in 15% of patients without underlying preeclampsia is often delayed.^{4,18} Most investigators agree on the general definition of HELLP syndrome. However, they disagree on the precise diagnostic criteria because of the diversity of symptoms and laboratory data at onset.^{3–5} For these reasons, although the laboratory data suggesting hemolysis were not remarkable in our patient, her diagnosis fell into the category of HELLP syndrome.

In female patients, the menstrual cycle²² or pregnancy²³ might influence choroidal thickness. A recent study reported that choroidal thickness was thinner in preeclampsia patients than in normal pregnancies.²⁴ The choroidal characteristics of our patient were different from this report. However, indocyanine-green angiography showed the abnormal choroidal vessel leakage with filling defects and late choroidal vessel staining in the patients with malignant hypertension.²⁵ As the main characteristic of preeclampsia is hypertension during pregnancy, the abnormal choroidal circular changes due to severe hypertension might lead to choroidal thickening. In contrast, hypercoagulability also plays a crucial role in HELLP syndrome. The pathophysiology of HELLP syndrome is assumed to be similar to that of DIC. Microthrombi, through general activation of coagulability, disturb the microcirculation of the choroid, which has been demonstrated by angiography in severe preeclampsia or toxemia.^{11,13,14,26} Exudation from the choroidal vasculature after microinfarction might cause choroidal thickening and subretinal serous detachment. Extravasation into the choroidal stroma causes compres-

sion of the choroidal vessels resulting in a ground glass appearance of the choroid.

Central Serous Chorioretinopathy (CSC) in eclamptic patients or VKH disease should be considered as a differential diagnosis. Pregnancy is considered as a predisposing factor of CSC.²⁷ However, the ground glass appearance of the choroid in the OCT images of our patient was different from that in the case of CSC. The lumen of a choroidal vessel is usually dilated and is clearly delineated in CSC.²⁸ The choroidal and retinal characteristics in the OCT images of our patient seemed quite similar to those in VKH disease.²⁹ VKH disease was ruled out because we could not find any sign of inflammation and the patient did not complain of symptoms related to VKH disease, such as a headache or tinnitus. Considering these facts, choroidal characteristics might be one of the adjunctive findings for making a diagnosis of HELLP syndrome.

However, we should consider the possibilities of the choroidal appearance on OCT in hypertensive chorioretinopathy or HELLP syndrome similar to VKH. In fact, it is not well known about the changes in the choroidal vessels under the severe hypertension. Kishi et al³⁰ reported the pathology of hypertensive chorioretinopathy in monkeys with experimental malignant hypertension. They showed extensive occlusion of choroidal vasculature in the acute stage and recanalization in the chronic stage. The ground glass appearance of the choroid on OCT at an acute phase may indicate the occlusive changes, and the visualization of luminal structure of the choriocapillaris and Sattler layer after 6 days and Haller layer after 4 months may represent the recanalization of the choroidal vessels at chronic phase. However, as this is the first report on the choroidal morphology in HELLP syndrome, to our knowledge, the findings need to be confirmed with the accumulation of case reports in the future.

In conclusion, noninvasive evaluation of the choroidal morphology with OCT might be helpful for establishing a diagnosis of HELLP syndrome.

Key words: choroidal morphology, HELLP syndrome, optical coherence tomography.

References

1. Lamarca B, Brewer J, Wallace K. IL-6-induced pathophysiology during pre-eclampsia: potential therapeutic role for magnesium sulfate? *Int J Interferon Cytokine Mediator Res* 2011;2011:59–64.
2. Greer IA, Cameron AD, Walker JJ. HELLP syndrome: pathologic entity or technical inadequacy? *Am J Obstet Gynecol* 1985;152:113–114.
3. Weinstein L. Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. *Am J Obstet Gynecol* 1982;142:159–167.

4. Sibai BM, Taslimi MM, el-Nazer A, et al. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. *Am J Obstet Gynecol* 1986;155:501–509.
 5. Martin JN Jr, Files JC, Blake PG, et al. Plasma exchange for preeclampsia. I. Postpartum use for persistently severe preeclampsia-eclampsia with HELLP syndrome. *Am J Obstet Gynecol* 1990;162:126–137.
 6. Sibai BM. The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): much ado about nothing? *Am J Obstet Gynecol* 1990;162:311–316.
 7. Amata AO. Blindness associated with severe preeclampsia/eclampsia. *Anesth Analg* 2001;93:1081.
 8. Cunningham FG, Fernandez CO, Hernandez C. Blindness associated with preeclampsia and eclampsia. *Am J Obstet Gynecol* 1995;172:1291–1298.
 9. Rosenow F, Huber M, Scheidt W, Heiss WD. Neurological cause of late postpartum seizures. *Arch Gynecol Obstet* 1991;248:151–155.
 10. Murphy MA, Ayazifar M. Permanent visual deficits secondary to the HELLP syndrome. *J Neuroophthalmol* 2005;25:122–127.
 11. Mabie WC, Ober RR. Fluorescein angiography in toxemia of pregnancy. *Br J Ophthalmol* 1980;64:666–671.
 12. Valluri S, Adelberg DA, Curtis RS, Olk RJ. Diagnostic indocyanine green angiography in preeclampsia. *Am J Ophthalmol* 1996;122:672–677.
 13. Iida T, Hagimura N, Otani T, et al. Choroidal vascular lesions in serous retinal detachment viewed with indocyanine green angiography [in Japanese]. *Nippon Ganka Gakkai Zasshi* 1996;100:817–824.
 14. Iida T, Kishi S. Choroidal vascular abnormalities in preeclampsia. *Arch Ophthalmol* 2002;120:1406–1407.
 15. Pastore MR, De Benedetto U, Gagliardi M, Pierro L. Characteristic SD-OCT findings in preeclampsia. *Ophthalmic Surg Lasers Imaging* 2012;43:S139–S141.
 16. Spaide RF. Enhanced depth imaging optical coherence tomography of retinal pigment epithelial detachment in age-related macular degeneration. *Am J Ophthalmol* 2009;147:644–652.
 17. Gregori NZ, Feuer W, Rosenfeld PJ. Novel method for analyzing snellen visual acuity measurements. *Retina* 2010;30:1046–1050.
 18. Sibai BM, Ramadan MK, Usta I, et al. Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome). *Am J Obstet Gynecol* 1993;169:1000–1006.
 19. MacKenna J, Dover NL, Brame RG. Preeclampsia associated with hemolysis, elevated liver enzymes, and low platelets—an obstetric emergency? *Obstet Gynecol* 1983;62:751–754.
 20. Fish R. The HELLP syndrome: case report and review of the literature. *J Emerg Med* 1993;11:169–174.
 21. Audibert F, Friedman SA, Frangieh AY, Sibai BM. Clinical utility of strict diagnostic criteria for the HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. *Am J Obstet Gynecol* 1996;175:460–464.
 22. Ulas F, Dogan U, Duran B, et al. Choroidal thickness changes during the menstrual cycle. *Curr Eye Res* 2013;38:1172–1181.
 23. Takahashi J, Kado M, Mizumoto K, et al. Choroidal thickness in pregnant women measured by enhanced depth imaging optical coherence tomography. *Jpn J Ophthalmol* 2013;57:435–439.
 24. Sayin N, Kara N, Pirhan D, et al. Subfoveal choroidal thickness in preeclampsia: comparison with normal pregnant and nonpregnant women. *Semin Ophthalmol* 2014;29:11–17.
 25. Spaide RF, Goldbaum M, Wong DW, et al. Serous detachment of the retina. *Retina* 2003;23:820–846.
 26. Schreyer P, Tzadok J, Sherman DJ, et al. Fluorescein angiography in hypertensive pregnancies. *Int J Gynaecol Obstet* 1991;34:127–132.
 27. Haimovici R, Koh S, Gagnon DR, et al; Central Serous Chorioretinopathy Case-Control Study Group. Risk factors for central serous chorioretinopathy: a case-control study. *Ophthalmology* 2004;111:244–249.
 28. Yang L, Jonas JB, Wei W. Choroidal vessel diameter in central serous chorioretinopathy. *Acta Ophthalmol* 2013;91:e358–e362.
 29. Maruko I, Iida T, Sugano Y, et al. Subfoveal choroidal thickness after treatment of Vogt-Koyanagi-Harada disease. *Retina* 2011;31:510–517.
 30. Kishi S, Tso MO, Hayreh SS. Fundus lesions in malignant hypertension. I. A pathologic study of experimental hypertensive choroidopathy. *Arch Ophthalmol* 1985;103:1189–1197.
-