Chorioretinal Changes Heralding Metastatic Malignancy

Here we report 2 cases of choroidal disease and subretinal fluid heralding metastatic malignancy. The first case was in a patient with central nervous system Burkitt lymphoma who was positive for human immunodeficiency virus (HIV) and the second was a patient with metastatic non–small cell lung carcinoma.

Report of Cases. Case 1. A 54-year-old man experienced decreased vision in his right eye for 1 week. His medical history was notable for HIV without AIDS with a CD4 count of 714 one month prior to initial examination. He reported recent rhinitis and jaw, back, and hip pain as well as numbness of his face. Visual acuity was 20/40 OD and 20/20 OS. Anterior segment examination was unremarkable. There was no vitreous cell. Fundus examination results were normal OS with areas of subretinal fluid and creamy retinal pigment epithelium lesions OD (Figure 1). Fluorescein angiogram (FA) showed pinpoint subretinal leaks, which coalesced into larger subretinal plaques (Figure 1). Physical examination results, complete blood count findings, tuberculosis skin testing, blood testing for syphilis, and chest x-ray were negative. One week later, the visual acuity was 20/640 and systemic prednisone was started. Two weeks after initial examination, the visual acuity was 20/500 with decreasing subretinal fluid and leakage on FA.

One week later, the patient was admitted for abdominal pain, myalgias, paresthesias, and bilateral cranial nerve VI palsies. CD4 count was 379 with HIV RNA polymerase chain reaction of greater than 100 000. Magnetic resonance imaging revealed abnormal enhancing material in the brain, pachymeninges, and spine. A computed tomographic scan revealed pleural effusion, mediastinal lymph nodes, and a thickened gallbladder. Lumbar puncture revealed a massive lymphocytosis with plasmacytoid variant Burkitt-type cells. Fluorescent in situ hybridization revealed MYC rearrangement of chromosome 8; myc abnormalities are seen in virtually all cases of Burkitt lymphoma. Epstein-Barr nuclear antigen antibodies were detected. The diagnosis of Burkitt lymphoma with central nervous system involvement was made. The patient began receiving highly active antiretroviral therapy and hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone but achieved only partial remission. There was no further ophthalmic follow-up before the patient died of his disease 9 months later. Autopsy was refused.

Case 2. A 78-year-old white woman underwent cataract extraction in her right eye 30 days prior to initial examination. Preoperative visual acuity was 20/70 OD and 20/60 OS, and she was noted to have “subtle retinal pigmentary changes.” Her visual acuity improved only slightly to 20/60 following surgery.

Her medical history was notable for presumed polymyalgia rheumatica diagnosed by her internist, for which she was taking 5 mg of prednisone daily, as well as borderline Mediterranean anemia. She had a smoking history of 10 cigarettes per day. Review of symptoms was otherwise negative for abnormalities.

At the time of the patient’s initial examination by the retina department, her visual acuity was 20/100 OD and 20/125 OS. She was noted to have optic nerve hypoplasia, macular edema, and tortuous, dilated retinal vessels bilaterally (Figure 2). The anterior segment was normal and there was no vitreous cell. Fluorescein angiogram showed bilateral multiple areas of punctate hyperfluorescence with leakage in later frames (Figure 2). B-scan showed bilaterally thickened choroids with high reflectivity. Laboratory testing revealed normal complete blood count and blood chemistry results and an erythrocyte sedimentation rate of 63. Total protein and albumin test results were normal with a minimally elevated α₂-globulin of 1.5 g/dL (normal range, 0.5–1.0 g/dL) and β-globulin of 1.1 g/dL (normal range, 0.5 to 1.0 g/dL). Her prednisone dose was increased to 60 mg per day.

Two weeks later, a right neck mass was noted. Computed tomographic scan showed a heterogenous mass at the right thoracic inlet with paratracheal and mediastinal adenopathy. Fine-needle aspiration results were consistent with non–small cell carcinoma, which stained positive for keratin and negative for S100, HMB-45, carcinoembryonic antigen, and thyroid transcription factor-1. She was referred to a cardiothoracic surgeon and oncologist and diagnosed as having advanced non–small cell lung carcinoma.

Final ophthalmic follow-up revealed a visual acuity of 20/320 OU with decreasing serous retinal detachments and presence of trace panuveitis. Topical and systemic
Figure 1. Case 1 at initial examination. Fundus photographs showing subretinal fluid and creamy lesions in the retinal pigment epithelium in the right eye (A) and a normal left eye (B). Fluorescein angiogram at 16 seconds (C), 54 seconds (D), and 12 minutes (E) showing pinpoint subretinal leaks, which coalesced into larger subretinal plaques.

Figure 2. Case 2 at initial examination. Color photographs notable for optic nerve hyperemia and macular edema with tortuous, dilated retinal vessels in right eye (A) and left eye (B). Fluorescein angiogram at 15 seconds (C) and 55 seconds (D) in the right eye and 15 minutes in the left eye (E) showing punctate subretinal hyperfluorescence, which leaks in later frames.
steroids were tapered. The patient died 4 months after initial examination, and autopsy was refused.

Comment. Retinopathy in patients with HIV presents a wide differential of infectious, inflammatory, and invasive etiologies. Patients with AIDS are at an increased risk of developing a range of lymphoproliferative disorders. Burkitt lymphoma is a high-grade lymphocytic lymphoma, which typically appears in younger patients with higher CD4 counts as compared with other HIV-associated lymphomas and often serves as an AIDS-defining illness.

Lymphoma may manifest in the eye as an extension of central nervous system disease or less frequently as diffuse uveal metastasis. Ophthalmic involvement can masquerade as various retinopathies, retinal vasculitides, or nonremitting uveitis. Burkitt lymphoma frequently invades the orbit and infrequently can extend into the eye. In these cases, the fundus appearance is similar to that of leukemic infiltration.

In our first case, the subretinal fluid with multiple pinpoint areas of leakage on FA gave a clinical appearance similar to that seen in Vogt-Koyanagi-Harada disease. Vogt-Koyanagi-Harada disease is a bilateral idiopathic granulomatous panuveitis with shallow, serous, retinal detachment associated with meningitis, auditory, and dermatologic manifestations. The patient did not fill the criteria for Vogt-Koyanagi-Harada disease because the mandatory bilateral disease was absent. The differential diagnosis included severe idiopathic central serous choriotoretinopathy, acute leukemia, uveal melanocytic proliferation associated with systemic carcinoma, idiopathic uveal effusion syndrome, sympathetic ophthalmia, and benign reactive lymphoid hyperplasia of the uveal tract. Initial workup was inconclusive and the apparent steroid response pointed to an inflammatory origin. To our knowledge, this retinal condition has not been previously described as heralding the onset of Burkitt lymphoma, particularly without direct orbital extension.

Metastatic carcinoma to the choroid typically demonstrates elevated pale white or yellow lesions, which may be associated with serous retinal detachments. Fluorescein angiogram usually shows diffuse leakage from these lesions. The differential diagnosis includes amelanotic nevus, amelanotic malignant melanoma, leukemia, large cell lymphoma, choroidal osteoma, choroidal hemangioma, and choroidal neovascularization. Our second case had serous detachments reminiscent of Vogt-Koyanagi-Harada disease with multiple punctate spots of leakage on FA. Ultimately, systemic evaluation revealed a neck mass, which uncovered the etiology. We were unable to find any previously published reports of metastatic carcinoma with this symptomatology. Gass described a case of acute Vogt-Koyanagi-Harada–like syndrome in a patient with metastatic cutaneous melanoma. We lack pathologic evidence to prove that our cases represent malignant invasion. It is possible that these cases do not represent tumor in the eye, but rather an inflammatory reaction heralding the onset of cancer. They could also represent a paraneoplastic response. There is no such known association with either of these malignancies. In the face of widespread disease with central nervous system involvement, we feel these lesions likely represent tumor invasion.

In summary, we present 2 cases with choroid disease and serous retinal detachments in the setting of systemic malignancy. These cases highlight the variability in clinical symptoms that can occur with systemic disease and particularly in the setting of HIV.

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Financial Disclosure: None reported.