A 59-year-old woman presented with acute-onset, bilateral, painless loss of vision, dysarthria, and ataxia. Ophthalmoscopy showed bilateral optic disc edema. A magnetic resonance scan of the head was normal. Chest radiography showed mediastinal adenopathy. Mediastinoscopy and biopsy identified small-cell carcinoma of the lung. An autoantibody to optic nerve and retina was demonstrated in the patient's serum. An electroretinogram was normal. The patient was diagnosed with a paraneoplastic optic neuropathy and paraneoplastic cerebellar syndrome. After treatment for her lung cancer, the patient remains stable from a visual and neurologic standpoint.

**Key Words:** Paraneoplastic optic neuropathy—Autoantibody—Small-cell lung carcinoma.

**CASE REPORT**

A 59-year-old white woman presented with acute, bilateral, painless loss of vision. In January 1996, she had a flare-up of psoriasis treated with etretinate 25 mg per day. She developed severe, right-sided headaches in April 1996, and the etretinate was discontinued after 2 months of therapy. Her headaches resolved. In June 1996, the headaches returned and she was referred to a neurologist by her family physician. Neurologic examination was normal. A magnetic resonance (MR) scan of the head was normal. She subsequently developed lower extremity weakness, difficulty walking, blurred vision bilaterally, and intermittent episodes of binocular diplopia. An ophthalmologist noted bilaterally swollen optic nerves but normal visual acuity. Approximately 3 weeks later, she developed progressive numbness in the right hand, worsening of her lower extremity weakness, and decreased visual acuity.

Her past medical history was significant for Lyme disease in 1991, treated with doxycycline for 21 days, psoriasis, and adult-onset diabetes mellitus. Her past surgical and family histories were noncontributory. Her medications included estrogen and glyburide. She had a 40-pack-year history of cigarette smoking. Her review of systems was significant for a persistent, dry cough. She was referred to the neuro-ophthalmology service on July 9, 1996.

Ophthalmologic examination showed a best corrected visual acuity of 20/30 in the right eye and 20/40 in the left eye. Color vision testing, pupill examination, external examination, and intracocular pressure measurements were normal. Slit-lamp biomicroscopy showed old keratic precipitates in both eyes, but no active cells or flare in the anterior chamber. Visual fields, tested by static technique (Humphrey 24-2), demonstrated severe constriction bilaterally (Fig. 1). Motility examination showed full ductions and versions. She had intermittent, gaze-evoked, horizontal jerk nystagmus. There were mild vitreous cells present bilaterally. There was moderate optic disc edema bilaterally (Fig. 2). The remainder of the macula, vessels, and periphery were within normal
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FIG. 1. Visual fields, tested by static technique (Humphrey 24-2) in July 1996, demonstrate severe field constriction bilaterally. The patient had slurred speech. Cerebellar examination showed significant axial dystaxia, truncal ataxia, and markedly unsteady gait.

Magnetic resonance scan of the head and MR venogram showed nothing abnormal. Lyme titers of both serum and cerebrospinal fluid (CSF) were negative. An electroencephalogram was normal. A chest radiograph revealed mediastinal lymphadenopathy. A computed tomography (CT) scan of the chest confirmed adenopathy of the superior mediastinal, paratracheal, and hilar nodes on the right. No pulmonary mass was seen. Mediastinoscopy and biopsy demonstrated small-cell carcinoma of the lung in the right parasternal lymph nodes. Staging evaluation for cancer showed no other sites of involvement. Bronchial washings showed no malignant cells. Bilateral mammograms were negative for malignancy. Computed tomography scans of the abdomen and pelvis were normal. A bone scan demonstrated no malignancy. Bone marrow aspiration and biopsy showed no evidence of tumor infiltration. Three lumbar punctures (LP) showed negative cytology for malignancy.

The first LP showed 122 white blood cells (93% lymphocytes, 3% monocytes) and 111 mg/dl of protein (normal <50 mg/dl) with a normal opening pressure. Syphilis serology and CSF Venereal Disease Research Laboratory (VDRL) studies were nonreactive. Viral, fungal, and acid-fast bacillus cultures of both CSF and serum were negative. Urine and stool studies showed no evidence of bacterial or fungal infection. Antibodies against DNA were not present. Granular cytoplasmic staining anti-neutrophil cytoplasmic antibodies and perinuclear staining anti-neutrophil cytoplasmic antibodies were negative. The patient received intravenous methylprednisolone 1 g per day for 5 days of therapy with improvement in her visual and neurologic symptoms.

Cancer-associated retinopathy, neuronal nuclear (Hu), Purkinje cell (Yo), and neuronal nuclear (Ri) serum antibody studies were negative. An electroretinogram (ERG) gave normal results. A focal ERG was not performed. Autoantibodies were present that were reactive to a neural protein approximating 60 kDa in a titer of 1:1000 using an enzyme-linked immunosorbent assay and Western blot method. This protein has been demonstrated previously in the optic nerve, retina, cerebellum, and cerebral cortex (30). The patient received six cycles of chemotherapy with cisplatin and VP-16, which she tolerated well. She had pulse intravenous methylprednisolone 1 g/day for 5 days for her visual and cerebellar symptoms.

Ophthalmologic examination in March 1997 showed a visual acuity of 20/20 in the right eye and 20/25 in the left eye. Visual fields, tested by static technique (Humphrey 24-2) demonstrated marked improvement compared with July 1996 (Fig. 3). Indirect ophthalmoscopy showed mild optic atrophy bilaterally. Her dysmetria had improved and her gait was notably steadier. On August 26, 1997, she remained stable with no radiologic evidence of tumor recurrence or metastatic disease, a repeat LP was normal, a repeat MR of the head was unremark-
able, and the ophthalmologic examination was unchanged. A repeat antibody titer to the 60-kDa antigen identified previously remained positive at 1:1000.

DISCUSSION

We believe that this patient had a paraneoplastic optic neuropathy. Optic neuropathy is a rare paraneoplastic syndrome, but has been reported in patients with small-cell carcinoma of the lung (2,11,12,18) and Hodgkin's and non-Hodgkin's lymphoma (14-17). Most reported cases have been bilateral and progressive (2,3,11,12). Many cases involve papilledema at initial presentation (2,3,11,12,14-17). Some patients, such as the one described here, may demonstrate symptomatic improvement after treatment with steroids (2,6,16-18). Subacute cerebellar degeneration is a well-characterized paraneoplastic phenomenon in patients with lung cancer and presents with progressive ataxia (1). The progressive, bilateral optic neuropathy with cerebellar dysfunction in the absence of other infections, infiltrative, or inflammatory etiology in our patient is suggestive of a paraneoplastic optic neuropathy. Carcinomatous meningitis was considered in our patient, but three consecutive CSF studies failed to identify malignant cytology. The clinical course of marked improvement would also argue against carcinomatous meningitis.

Murphy et al. reported a novel autoantibody against CNS antigens in a patient with small-cell lung cancer and CAR. The autoantibody was found to be reactive to antigen not only in the retina, but also in the spinal cord, cerebral cortex, cerebellum, and optic nerve (30). The anti-Hu antibody, which is highly specific for small-cell carcinoma of the lung, has been associated with multiple paraneoplastic syndromes including subacute cerebellar degeneration (19,26,31). Our patient had no retinal features of CAR and negative 23 Kd CAR antibodies, but a focal ERG was not performed. An ERG was normal, but a focal ERG was not performed. Serum anti-Hu antibodies were also negative. However, in our patient's serum antibodies were detected against a 60-kDa antigen common to the optic nerve, retina, and cerebellum. We believe that the pattern of autoantibody reactivity demonstrated by our patient may be the same as that exhibited by the patient reported by Murphy et al. (30).

Malik et al. also reported a case of paraneoplastic optic neuropathy and cerebellar degeneration associated with autoantibody production (18). These two cases, along with that presented here, raise the possibility that there is an autoimmune basis for neuro-ophthalmologic paraneoplastic syndromes and provide incentive for the pursuit of research into the specific role of autoantibody production in paraneoplastic optic neuropathy. Ophthalmologists should be aware of paraneoplastic optic neuropathy as a cause of unexplained bilateral optic disc edema.

Acknowledgement: This work was supported in part by an unrestricted grant to Research to Prevent Blindness, Inc., New York, NY, U.S.A.

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