Progressive Visual Loss: An Unusual Presentation Of Multiple Sclerosis

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Abstract

Progressive visual loss as a presenting feature of multiple sclerosis (MS) is unusual. We report three cases who presented with progressive visual loss and in whom MS was diagnosed after other causes of progressive visual loss had been excluded. Two of the three had clinical evidence of neurological involvement outside the visual pathways. All had lesions consistent with MS outside the visual pathways on magnetic resonance imaging. Oligoclonal IgG bands were detected in the cerebrospinal fluid but not in the serum of two of the three patients. We conclude that MS should be considered in the differential diagnosis of progressive visual loss; however, other more common causes of visual loss must first be excluded, and there must be positive evidence to support a diagnosis of MS.

Keywords: progressive visual loss; multiple sclerosis; optic neuritis

Introduction

Visual impairment is common in multiple sclerosis (MS), and typical, remitting, unilateral optic neuritis frequently marks the onset of the disease. However, presentation with progressive visual loss is unusual in MS. Other causes of progressive visual loss must be considered in these patients, and MS cannot be confidently diagnosed until evidence of neurological involvement elsewhere in the central nervous system is found. We wish to report our experience with three cases who presented with progressive visual loss and in whom a diagnosis of MS was made.

Case histories

Case one: AB

This female was referred to us in 1992 at the age of 64 years with a history of progressive visual loss over the preceding 10 years. She had also noted some diplopia over the preceding 6 months but she denied other neurological symptoms. There was no family history of visual loss, neurological disease or autoimmune diseases. Examination revealed a reduction in visual acuity (VA) to 6/18 (with a pinhole) in each eye, impaired colour vision (1 out of 17 Ishihara colour plates correct in the right eye and 2 out of 17 in the left), peripheral restriction of the visual fields bilaterally, bilateral optic atrophy but no other fundal abnormalities, normal intraocular pressures, bilateral partial internuclear ophthalmoplegia, mild bilateral weakness of hip flexion, bilateral extensor plantar responses, bilateral heel-knee-shin ataxia, impaired joint position sense in the toes bilaterally, difficulty walking heel-to-toe and cognitive impairment.

A computerised tomographic (CT) brain scan showed generalised atrophy with moderate dilatation of the ventricular system and bilaterally symmetrical periventricular low density regions. Magnetic resonance imaging (MR/) showed extensive pathology, typical of MS, with high signal on T2-weighted images in the cerebral white matter and also in the cerebellar hemispheres bilaterally. An autoantibody screen was negative. Lumbar puncture (LP) yielded clear cerebrospinal fluid (CSF) with 3 x 10^6/1 leukocytes, 1800 x 10^6/1 erythrocytes, glucose 3.4 mmol/1 and protein 780 mg/1, and on electrophoresis oligoclonal IgG bands were
detected in the CSF but not in the serum. Visual evoked responses (VERs) revealed prolonged P100 latencies in both eyes (167 ms on the right, 168 ms on the left).

A diagnosis of laboratory supported definite MS was made, using the criteria of Poser et al,\(^1\) on the basis of the progressive visual loss with signs of lesions outside the visual pathways on clinical examination, oligoclonal bands in the CSF and MRI abnormalities consistent with MS. No treatment was given at the time, and since then she has had no acute episodes of neurological deterioration requiring treatment. There has, however, been further deterioration in her vision with time. At review in December 1994 her VA was 6/60 with glasses in both eyes, but her other neurological deficits remained essentially unchanged. Mitochondrial DNA analysis for the common mutations seen in Leber's hereditary optic neuropathy (LHON) (at nucleotide positions 11778, 4160, 3460, 15257 and 14484) was negative.

Case two: LC
A 50 year old male was referred in September 1994 with a history that 2 years previously he had been treated for painless loss of vision in the right eye which had evolved over several weeks. He had received oral prednisone but residual visual impairment was severe with VA in the right eye reduced to counting fingers (CF). An LP was done at the time and revealed 10 x 10\(^6\)/l leukocytes, 21 x 10\(^6\)/l erythrocytes, glucose 3.8 mmol/l and protein 740 mg/l, but results of CSF electrophoresis were not available. During the 3 months prior to referral to us he experienced a progressive loss of vision in the left eye, again without any discomfort or other symptoms. This time he had noted that his colour vision seemed to be affected. He gave a past history of gastritis and suffered from mild psoriasis. He smoked 20 cigarettes per day and consumed approximately 60 g alcohol per day. His mother had suffered from hyperthyroidism but there was no family history of MS or other autoimmune disorders, other neurological disorders or visual problems.

Initial examination revealed VA reduced to counting fingers on the right and 6/60 on the left, a right central scotoma and restriction of the left visual field especially inferiorly, bilateral pallor of the optic discs but no other fundal abnormalities, and normal intraocular pressures. There were no other neurological abnormalities.

An autoantibody screen and DNA tests for LHON were negative. An MRI revealed areas of increased signal intensity on T2-weighted images in the right middle cerebellar peduncle and adjacent to the trigone of the left lateral ventricle. An LP yielded clear CSF with 5 x 10\(^6\)/l leukocytes, < 1 x 10\(^6\)/l erythrocytes, glucose 3.5 mmol/l and protein 500 mg/l, and on electrophoresis oligoclonal IgG bands were detected in the CSF but not in the serum. VERs revealed prolonged P100 latencies in both eyes (147 ms on both sides). A diagnosis of laboratory supported definite MS was made on the basis of two episodes of visual loss affecting a different eye on each occasion, with oligoclonal IgG bands in the CSF and MRI abnormalities, typical of MS, outside the visual pathways. He received a 5 day course of intravenous methylprednisolone 500 mg daily in the hope of arresting his visual loss and facilitating recovery. At follow up there has been no significant improvement in his vision and to date he has developed no other signs or symptoms of neurological dysfunction.

Case three: GM
A 38 year old woman was referred to us in May 1994 with a 2 year history of progressive visual loss initially affecting the right eye and subsequently, though to a lesser extent, the left eye. She had been investigated in March 1993 and an MRI brain scan had demonstrated an area of increased signal on T2-weighted images at the junction of the right optic nerve and chiasm, with enhancement on TI-weighted images after intravenous gadolinium. A small pituitary microadenoma was also detected on MRI. Lumbar puncture yielded clear CSF with 10 x 10\(^6\)/l leukocytes, 201 x 10\(^6\)/l erythrocytes, glucose 3.1 mmol/l and protein 410 mg/l, but no oligoclonal IgG bands in the CSF on electrophoresis. An autoantibody screen revealed an increased titre of antinuclear antibody (ANA) of 1/160 with a speckled pattern, negative antidualle- stranded-DNA, and a positive SS-A antibody. Her visual loss was attributed to optic neuritis and a course of oral corticosteroids produced no improvement. She received bromocriptine for 2 months for the pituitary microadenoma but this was ceased when it caused vomiting.

Over the 12 months preceding referral to us in May 1994, the patient had also experienced recurrent episodes of pain or tingling affecting the right side of her face and the right arm and leg lasting up to several hours. These had increased in frequency during this period such that they occurred on most days. She also reported urgency of micturition since September 1993 but had no other neurological symptoms. She reported no symptoms to suggest a connective tissue disorder and specifically no symptoms of Sjögren's syndrome. There was no family history of MS, other autoimmune diseases or other neurological disorders.

Examination in May 1994 revealed VA reduced to the perception of hand movements on the right and to 6/9 on the left. The fields were constricted in the left eye, especially on the temporal side. There was bilateral optic atrophy but no other fundal abnormalities, and a right afferent pupillary defect. The other cranial nerves were intact. Tone, power and coordination in the limbs were normal, as were the deep tendon reflexes, but the
plantar responses were equivocal bilaterally. Sensory testing was normal as was gait, and Romberg's test was negative. An autoantibody screen again revealed an elevated ANA titre of 1/640 with a speckled pattern, negative anti-double stranded DNA, positive SS-A and a slightly elevated anticardiolipin antibody level (19 GPL units, reference range < 18 GPL units). DNA tests for LHON were negative. An MRI scan of the pituitary fossa and optic nerves in May 1994 showed significant reduction in the size of the adenoma and no abnormality in the optic nerves and chiasm. MRI of the brain in August 1994 revealed several small hyperintense lesions on T2-weighted images in the cerebral white matter. An LP yielded clear CSF with 1 x 10^6/1 leukocytes, < 1 x 10^5/1 erythrocytes, glucose 3.0 mmol/l and protein 265 mg/l, and no oligoelonal IgG bands in the CSF on electrophoresis. VERs revealed a prolonged P100 latency (131 ms) on the left but on the right the waveforms were markedly abnormal and a P100 value was not able to be determined.

A diagnosis of clinically definite MS was made on the basis of: (i) impairment of vision sequentially in tile two eyes (ii) recurrent sensory disturbance in the right face, arm and leg; (iii) urgency of micturition; (iv) CSF pleocytosis; and outside the visual pathways. There has been no progression in her symptoms since that time.

Discussion

Progressive visual loss is a rare presenting feature of MS, and reports in the literature are few. Ormerod and McDonald\(^7\) reported 5 cases of progressive visual failure in patients in whom MS was subsequently diagnosed after other potential causes had been excluded. They could not identify any clinical features which helped differentiate these cases from those in whom the cause was not MS. They concluded that progressive visual loss should only be attributed to MS if other causes have been carefully excluded and if accepted criteria for a diagnosis of MS\(^1\) have been fulfilled. They did not define what they considered to be progressive visual failure. We have included patients who suffered a progressive loss of vision over at least a 3 month period in one or both eyes with major residual visual impairment in at least one eye. Each of their patients would satisfy this definition.

Other causes of progressive visual loss which must be considered in these patients, and excluded with appropriate investigations, include compression of the optic nerve or chiasm by tumour, familial causes such as Leber's hereditary optic neuropathy, toxins, infections and connective tissue disorders.

Leber's hereditary optic neuropathy (LHON) typically causes severe progressive visual loss, although remission may occur in some cases.\(^3\)\(^,\)\(^5\) It is more common in males and the majority of cases are associated with mutations in the mitochondrial genome. There are reports of an MS-like syndrome occurring in persons, mostly females, with LHON in whom mitochondrial DNA mutations have been detected.\(^6\)\(^,\)\(^8\) MRI abnormalities similar to those seen in MS have been reported in these patients. We have performed DNA analysis in each of the patients in our series without detecting any of the common mitochondrial genomic mutations seen in LHON.

Connective tissue diseases (CTD) may cause clinical syndromes closely resembling MS.\(^9\)\(^,\)\(^11\) A variety of CTD, including systemic lupus erythematosus\(^12\) and primary Sjögren's syndrome\(^10\) may exhibit optic neuropathy, although it is unusual for this to be the initial manifestation. Kupersmith et al\(^13\) reported 14 patients who presented with progressive or recurrent optic neuropathy in whom laboratory evidence of CTD in the form of circulating autoantibodies or markers of inflammation was found. Visual loss was the initial complaint of all these patients and none had overt clinical signs of CTD at presentation. They suggested that the presence of these abnormalities differentiated this group of patients, in whom they diagnosed 'autoimmune optic neuropathy', from patients with optic neuropathy due to primary demyelinating disease. Their patients rarely recovered vision spontaneously and were often left with severe visual impairment despite conventional corticosteroid therapy. They found that high dose corticosteroid therapy improved the vision in many of these patients but that a significant proportion required continuing immunosuppressive therapy, with other corticosteroids or cytotoxic agents, to maintain vision.

As there is an increased incidence of circulating nonorgan specific antibodies (as seen in CTD) and organ specific antibodies in patients with MS,\(^14\)\(^,\)\(^17\) we consider that cases of optic neuropathy with circulating nonorgan specific antibodies may be due to MS provided that there is no other clinical evidence of a CTD and that there are other features to support a diagnosis of MS. Our third case illustrates this point. Increased levels of circulating autoantibodies (ANA, SS-A and anticardiolipin antibodies) were detected; however, she had no clinical evidence of CTD, and had other clinical features consistent with MS. We believe that the presence of circulating autoantibodies in this patient reflects an underlying predisposition to autoimmunity and not a diagnosis of primary Sjögren's syndrome or other CTD, although we cannot exclude the possible development of a CTD at a later date.

In conclusion, multiple sclerosis may uncommonly present with progressive visual loss and must be considered in the differential diagnosis in this setting. However, other more common causes of visual loss, especially compression of the optic nerve by tumour, must first be excluded and there must be positive evidence to support a diagnosis of MS.
References


