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CASE REPORT

Teaching case: A man with a progressive gait impairment and visual compromise

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Abstract
Primary progressive multiple sclerosis can present with a wide variety of symptoms. We report a case of a 52-year-old man presenting with visual symptoms and gait impairment in whom a diagnosis of a primary progressive multiple sclerosis was established. Symptomatic treatment with dalfampridine was started but did not result in a considerable improvement. Gait disorders in multiple sclerosis are common and can have a considerable effect over the patient's quality of life. Dalfampridine is the first drug approved for the symptomatic treatment of gait in MS, although only a 40% of patients show an objective response to this medication. Primary progressive multiple sclerosis represents a therapeutic challenge. Currently, there are no disease modifying treatments approved but there are several medications undergoing assessment for this indication. Further research in the underlying pathophysiology of PPMS will help us develope more successful disease-modifying treatments. Meanwhile, a symptomatic approach should be offered in order to improve the patient's quality of life.

1. Case presentation

A 52 year-old right-handed man presented to our Neurology clinic for evaluation of a 15-year history of a progressive paraparesis associated with left sided hypoesthesia, fatigue and erectile dysfunction. The patient also reported blurred vision while exercising and episodes of constipation and urinary retention without incontinence. Past medical history

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was significant for diabetes mellitus and left cataract surgery.

On examination, his blood pressure was 120/80 mmHg, his pulse rate was 70 beats per minute and his respiratory rate was 18 breaths per minute. The neurological examination revealed a left hyporeactive dyscoria consistent with past history of cataract surgery. Ishihara test detected a loss in color vision, scoring 9/16 and 15/16 in the right and left eye, respectively. His visual acuity was 20/30 on the right eye and 20/30 on the left.

Motor examination revealed bilateral lower limb weakness with a strength of 3/5 in the left lower limb and 4/5 in the right. Hyperreflexia was present in his lower limbs. The plantar response was extensor on the left and flexor on the right. Vibration sense was diminished in the lower limbs and joint position sense was reduced at the toes. The gait was spastic and unstable (Video 1).

A complete blood cell count, chemistry panel, and levels of serum electrolytes were within normal limits.

How should this patient be further evaluated?

1. Lumbar puncture (CSF analysis including oligoclonal bands).
2. Contrasted brain and spine magnetic resonance imaging.
3. Serum vitamin B12, metilmalonic acid and copper levels.
4. Anti-Aquaporin 4 antibodies.
5. All of the above*.

What is the most likely diagnosis?

1. Neuromyelitis Optica.
2. Vitamin B12 deficiency.
3. Copper deficiency.
4. Multiple sclerosis*.
5. Sarcoidosis.

2. Case diagnosis

This 52-year-old man presenting with a progressive spastic paraparesis, left sided hypoesthesia, visual and genitourinary symptoms had a contrasted brain and spinal cord magnetic resonance imaging (MRI), which revealed areas of increased T2 signal corresponding to multifocal subcortical white matter lesions. Small lesions compromised the frontal lobes, pons, medulla and right superior cerebellar peduncle (Figure 1). The spinal cord MRI revealed the presence of multiple small hyperintense lesions compromising the cervical and thoracic cord on the T2 weighted images (Figure 2). None of the observed lesions enhanced after the application of contrast.

Erythrocyte sedimentation rate, C reactive protein, thyroid function tests, liver enzymes, blood glucose, vitamin B12 and folic acid levels were all normal. CSF-VDRL and ELISA for HIV were both negative. Serum antibodies, including Anti-aquaporin-4 antibody (anti-NMO), antinuclear antibody (ANA), and Rheumatoid factor (RF) were also negative. Visual evoked potentials revealed a diffuse bilateral and symmetric compromise of the retino-cortical pathway, associated with axonal loss and demyelination.

A lumbar puncture was performed with an opening pressure of 12 cm of water. Cerebrospinal fluid (CSF) analysis showed a protein concentration of 38.13 mg/dL [15–45 mg/dL], glucose of 77 mg/dL, 0 white blood cells per mm^3 and 2 erythrocytes per mm^3. Gram stain, India ink and CSF cultures were all negative while oligoclonal bands were positive.

A diagnosis of primary progressive multiple sclerosis (PPMS) was done.

Which of the following medications could be used for the treatment of walking impairment in this patient?

1. Glatiramer acetate.
2. Baclofen.
3. Dalfampridine*.
4. Tizanidine.
5. Amantadine.

Symptomatic treatment with oral Dalfampridine and Baclofen were given without major improvement of spasticity or gait (Video 2). A program of physical therapy was also started.

3. Case discussion

Primary progressive multiple sclerosis (PPMS) accounts for 10-15% of patients with multiple sclerosis (MS). This clinical pattern is characterized by an insidious onset, where disability gradually progresses with no clear history of relapse or remission (Katz Sand and Lublin, 2013). The course of MS has been recently revised (Lublin et al., 2014) and now the disease activity and progression are incorporated as modifiers of basic MS phenotypes. Thus, a patient with PPMS who presents an acute attack would be considered to have active PPMS instead of a progressive relapsing phenotype of the disease. On the contrary a patient without acute attacks or MRI evidence of activity (i.e. gadolinium-enhancing lesions or new or unequivocally enlarging T2 lesions) would be considered to have a non-active course of the disease.

PPMS typically presents as a progressive myelopathy (Katz Sand and Lublin, 2013). Difficulties with gait, balance, spasticity, weakness, and bladder or bowel compromise are common, while sensory symptoms occur less frequently than in relapsing-remitting MS (RRMS). There is no clear gender predominance and patients with PPMS also tend to be older than those with RRMS, with a mean age of 40 years (Stys et al., 2012).

The most common clinical phenotype of PPMS is spastic paraparesis, which is seen in 83% of cases (Antel et al., 2012); other symptoms include cerebellar dysfunction (8%), hemiplegia (6%), brainstem syndromes (1%), visual loss (1%), and cognitive decline (1%) (Antel et al., 2012). These phenotypes are not mutually exclusive (Antel et al., 2012), as seen in our patient where a spinal cord syndrome is present in association with visual compromise. Visual loss is more frequently seen in association to RRMS. There is a reported prevalence of visual symptoms in PPMS varying from 1% (Antel et al., 2012) to 4% (Rice et al., 2013). Progressive visual failure is thought to be the result of optic neuropathy (Miller and Leary, 2007) and therefore the prevalence of visual symptoms could be higher. A recent