An Unusual Association of Demyelinating Disease, Chronic Kidney Disease and Heart Failure

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Abstract

Multiple sclerosis (MS) and its variant, neuromyelitis optica (NMO) are autoimmune diseases of the central nervous system that typically cause progressively disabling symptoms involving the entire nervous system. These diseases have rarely been associated with de novo heart failure and only in the setting of bladder dysfunction have they been linked to renal failure. The medications used to treat them can have significant adverse effects on kidney and cardiovascular system. We present a case of a patient with concomitant cervical demyelinating disease and heart failure who was also found to be suffering from chronic kidney disease of unclear etiology.

Keywords Multiple sclerosis; Kidney disease; Heart failure; Demyelinating disease; Diabetes insipidus; Acquaporin

Introduction

Multiple sclerosis (MS) [1] and its variant, neuromyelitis optica (NMO) are autoimmune diseases of the central nervous system that typically cause progressively disabling symptoms involving the entire nervous system. These diseases have rarely been associated with de novo heart failure and only in the setting of bladder dysfunction have they been linked to renal failure. The medications used to treat them can have significant adverse effects on kidney and cardiovascular system [2]. We present a case of a patient with concomitant cervical demyelinating disease and heart failure who was also found to be suffering from chronic kidney disease of unclear etiology.

Case

A 31 year old -Yemeni male presented to the ED with gradually worsening shortness of breath. He was diagnosed with Multiple Sclerosis (MS) 1.5 months prior to admission and started on Interferon-beta 1a and Fingolimod. There was no other significant past medical or surgical history. The family history was significant for a brother who died of unknown renal disease in his 40s but never required dialysis. Social history was significant for 6 pack-year smoking history, no alcohol or illicit drugs. Medication review was negative for NSAIDS, antibiotics or herbal medication use. Approximately 1.5 months prior to admission, he noted a sudden sensation in his legs feeling extremely “heavy,” and when he stood up, he was unable to keep his balance. Associated with this, patient had incontinence of urine and a sensation of "wiggling" in his arms, neck, and legs (possible consistent with fasciculations). He had no visual loss and no weakness of the arms. Pt was seen in a hospital in Yemen and referred to a specialist in Jordan where he had a MRI of the brain, cervical, and lumbar spine which showed multiple T2 lesions in deep white matter, medulla, and cervical spine. Lumbar spine was unremarkable. He was then given diagnosis of multiple sclerosis. The MRI incidentally revealed a fracture/posterior displacement of odontoid bone, which was read as not causing stenosis. There were no enhancing lesions. He underwent LP as well, which showed 2260 RBC, 2 WBC, 34 protein, 51 glucose and negative oligoclonal bands. Serological workup had shown elevated ESR and CRP (25 and 14) so rheumatologic workup was done, showing only borderline SSA (negative anti-phospholipid, ANCA, lupus). Pt was treated with 5 days of cortisone IV and discharged. Since then, gait has improved minimally however it continues to be impaired, and he walks with a cane. Patient was discharged with Rebif (Interferon beta-1b) and fingolimod.

The admission clinical exam was significant for a blood pressure of 168/110 mm Hg, heart rate of 120bpm, crackles bilaterally on lung exam and bilateral lower extremities edema. Neurological exam was significant for diffusely increased spastic tone in both lower extremities and wide based waddling gait with minimal knee flexion, requiring a cane for ambulation.

Diagnostic Work Up

Significant labs: BUN/Creat- 40/2.71 mg/dl, normal sodium, potassium, bicarbonate and chloride, PTH-121 mg/dl, Phosphorus-4.2 mg/dl, Calcium-7.9 mg/dl, Albumin-2.6 mg/dl,Hb-12.8 gm/dl, normal WBCs and Platelets. Urinalysis: No RBC and ~ 2-3 gm proteinuria. Serology: Negative ANA, ANCA, Hepatitis serology, HIV. Complements, ESR, Rheumatoid factor, UPEP and SPEP were normal. Chest x-ray: Mild pulmonary edema, CT head without contrast: Normal, MRI head with and without contrast from Jordan 1.5 months prior to admission: Multiple small white matter hyper intense lesion in the cerebral white matter (some juxtacortical but not periventricular) and increased signal at the ventral medulla; MRI C-spine with longitudinally extensive cord hyper intensity and post displacement of dens. There were no lesions in the MRI of the lumbar spine. Renal Ultrasound: Atrophic right kidney 4.8 cm and a small left kidney 8.2 cm. Trans Thoracic Echocardiogram: Severe diffuse left ventricular hypokinesis with severely reduced contractility (EF-30%) and LVH, Nuclear stress test: Diffuse hypo kinesis and mild LV dysfunction.
Management

On initial presentation the immediate cause of kidney failure was not clear. Differential diagnosis included primary kidney disease, kidney disease secondary to heart failure (Cardiorenal syndrome) or systemic inflammatory disease affecting heart, kidney and nervous system at the same time. The small size of the kidneys on ultrasound and proteinuria on urinalysis was supportive of either primary kidney disease or systemic inflammatory disease. Patient was given Lasix to achieve euvolemia. Lisinopril and Carvedilol were started for BP control and titrated up with a target of <130/80. Urine Protein to Creatinine ratio (UPC) came down to ~1.5 gm but renal function kept worsening with peak creatinine of 3.4 mg/dl after 3 months of follow up. Patient also had a follow up echocardiogram showing normal ejection fraction which essentially excluded the diagnosis of kidney failure secondary to heart failure. Follow up MRI after 3 month showed persistent cervical spine lesion however brain lesions were improving. Patient still has gait abnormality.

Discussion

Kidney injury is Multiple Sclerosis and demyelinating spinal disease is uncommon. Acute kidney injury is more often described than chronic kidney disease in this group of patients. The most common cause of kidney injury is post-renal due to bladder dysfunction leading to recurrent UTI and renal stones [3]. Glomerulonephritis is relatively uncommon in MS patients. Treatment of MS with Interferon beta-1b can lead to thrombotic microangiopathy, membranoproliferative GN and FSGS-tip variant [4-7]. Apart from kidney injury a demyelinating lesion in the hypothalamus can lead to central Diabetes Insipidus. MS patients are prone to get constipation, visual disturbances due to optic neuritis and motor dysfunction which makes hemodialysis preferable to recurrent UTI and renal stones [3]. Glomerulonephritis is relatively uncommon in MS patients. Treatment of MS with Interferon beta-1b can lead to thrombotic microangiopathy, membranoproliferative GN and FSGS-tip variant [4-7]. Apart from kidney injury a demyelinating lesion in the hypothalamus can lead to central Diabetes Insipidus. MS patients are prone to get constipation, visual disturbances due to optic neuritis and motor dysfunction which makes hemodialysis preferable over peritoneal dialysis. Data for kidney transplant in MS patients is very limited. This case is a unique presentation of a young man who presents with MS, sudden onset of systolic heart failure and kidney failure. Once a patient has kidney disease the focus of the management is to diagnose and treat the cause of kidney disease. Many times the cause is not identifiable which shifts the focus of management in slowing the progression of kidney failure and treating complications of kidney failure. Our patient had less than normal-sized kidneys suggestive of advanced disease with significant scarring. One would be tempted to perform a renal biopsy to find out the cause of renal failure but the chance of getting viable glomeruli and interstitium are very minimal with small sized kidney as compared to the risk of a kidney biopsy. We did not find any treatable cause of renal failure in this patient. Our goal then became to minimize urinary protein excretion as much as we can and control BP in order to slow down progression of kidney disease. This was achieved by adding Lisinopril which is an Angiotensin Converting Enzyme Inhibitor (ACEI). It works by decreasing the intraglomerular pressure by dilating efferent arterioles and thereby decreases perfusion pressure and proteinuria. It also decreases BP and prevents left ventricular remodeling. It is uncertain if this is a rare presentation of one disease, such as multiple sclerosis, with an autoimmune component affecting the heart and kidney, which has been described, or the result of the medication given for his MS with an unforeseen renal complication. A highly specific autoantibody directed against the water channel protein aquaporin-4 is present in the sera of 60–70% of patients who have a clinical diagnosis of NMO. Aquaporin-4 is localized to the foot processes of astrocytes in close apposition to endothelial surfaces [9]. There is a diverse yet characteristic distribution of aquaporins in the human body with specific roles in each organ [10]. AQPI is found in the blood vessels, kidney proximal tubules, eye, and ear. AQP2 is expressed in the kidney collecting ducts, where it shuttles between the intracellular storage sites and the plasma membrane under the control of antidiuretic hormone (ADH). Mutations of AQP2 result in diabetes insipidus. AQP3 is present in the kidney collecting ducts, epidermis, urinary, respiratory, and digestive tracts. AQP3 in organs other than the kidney may be involved in the supply of water to them. AQP4 is present in the brain astrocytes, eye, skeletal muscle, stomach parietal cells, and kidney collecting ducts. AQP5 is in the secretory cells such as salivary, lacrimal, and sweat glands. AQP5 is also expressed in the eye and ear. AQP6 is localized intracellular vesicles in the kidney collecting duct cells. AQP7 is expressed in the adipoocytes, testis, and kidney. AQP8 is expressed in the kidney, testis, and liver. AQP9 is present in the liver and leukocytes. AQP10 is expressed in the intestine. One possible explanation for our patient clinical presentation is antibody directed against different aquaporin channels leading to central nervous system findings and kidney failure. It is very difficult to extrapolate it from one case report. We need further research studies in this area to understand the possible disease process.

References