Case Report

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A Clinical Case of A Patient with Moschkovitz Syndrome and Leukocytoclastic Vasculitis in the Childhood and Demyelinating Polyradiculoneuropathy Presenting with Transverse Myelitis in the Elderly

Desislava Kalinova
Alexander Kopchev
and Rasho Rashkov

Medical University, Sofia, Bulgaria

Corresponding author:
Desislava Kalinova

desi.kalinova@abv.bg

Medical University, Sofia, Bulgaria.

Abstract

Transverse myelitis is one of the causes of acute transverse myelopathy, as three main categories are described in the differential diagnosis of transverse myelitis - demyelination (multiple sclerosis, neuromyelitis optica), nfections and some autoimmune connective tissue disorders (systemic lupus erythematodes, vasculitis). We present a clinical case of a 33-year old patient with acute inflammatory demyelinating polyradiculoneuropathy (Guillaine-Barre syndrome) presenting with Landry's acute flaccid (ascending) paralysis and transverse myelitis in the elderly and medical history for Moschkovitz syndrome (thrombotic thrombocytopenic purpura, TTP syndrome) and leukocytoclastic vasculitis when he was 12 years old. The patient was treated with corticosteroids, intravenous immunoglobulin and symptomatic treatment, as after 9 months of therapy the patient regained muscle strenght in all four limbs.

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Clinical case

A 33 year old man was admitted to the Emergency Department (ED) in the summer of 2014 with complaints of fever (up to 38-38.5°C), dysuria and urine retention. An urethral catether was placed with resolution of the retention and the patient was referred to an urological unit. The diagnosis of prostatitis was established and it was started an antibiotic course. Three days later, the patient reported unstable gait, numbness and weakness in the distal parts of the upper and lower limbs. The weakness in the extremities had an ascendent, progressive course, as the condition progressed to quadriparesis in just 24 hours. The patients was admitted to the Department of Neurology because of the neurological nature of the symptoms.

The primary neurological examination showed:

- Moderate to severe central paraparesis of the lower limbs and latent central paresis of the upper limbs
- Th_3 – th_4 sensory level
- Pelvic reservoir dysfunction, manifested as urine retention
- Three days later additional neurological symptoms appeared – bilateral peripheral lesions of nn. Faciales, more pronounced in the left, lesion of the left n. Abducens
- Transient dysphagia and dysartria.

The laboratory studies revealed increased non-specific inflammatory markers (erythrocyte sedimation rate – ESR, C-reactive protein, fibrinogen), thrombocytopenia (90 – 114 x 10^9/l), borderline serum creatinine (138 – 147 mkmol/l). A lumbal punction was performed and the cerebrospinal fluid (CSF) was examined. It showed increased total protein 1.55 g/l (reference level 0.15-0.45 g/l), normal cell count, normal glucose level. The CSF electrophoresis was notable for high γ-fraction without mono- or oligoclonal bands. The microbiological studies of the former were negative for enterovirus, West Nile virus, Tick-borne encephalitis, Human immunodeficiency virus 1, 2 (HIV-1; HIV-2), Herpex simplex virus 1 and 2, Varicella zoster virus. Cytomegalovirus. Nasal, throat, urine and hemocultures were also negative.

A magnetic-resonance tomography (MRT) of the cervicothoracic spine showed altered signal along the T_1-T_4 segment. At the same level, edema in the white and gray matter of the myelon was noted **(Figure 1)**. After contrast application, a disruption of the blood-brain barrier was observed at level C_5-T_4. A MRT of the

head was also performed, showing altered signal in the thalamus and left middle cerebellar peduncule – changes associated with increased fluid content **(Figure 2)**. There was no blood-brain barrier disruption after contrast administration.

The changes in the spinal cord and the brain were interpretated as inflammatory demyelinating condition – acute disseminated encephalomyelitis/transversal myelitis – active phase.

The electroneuromyography (ENMG) study demonstrated polyneuropathy – demyelinating type with secondary axonal damage of the sensory and motor nerves. The findings were consistent with acute inflammatory polyneuropathy.

The differential diagnosis included the following:

1. Acute inflammatory demyelinating polyradiculoneuropathy, Guillaine-Barre syndrome, presenting with Landry's acute flaccid (ascending) paralysis and transverse myelitis.

2. Miller-Fisher syndrome, characterized by external ophtalmoplegia, ataxia and areflexia.

3. Acute disseminated encephalitis and transversal myelitis during the course of a viral infection.

It was started corticosteroid, Methylprednisolone was administrated at a dose of 1 mg/kg intravenous application, as in the next three days it was carried out pulse therapy with Methylprednisolone 1000 mg i.v.; intravenous immunoglobulin in a dose 800 mg/kg, symptomatic treatment - Mannitol, Nivalin, Milgamma N; antibiotics; unfractionated heparin; antihypertensive medications. The neurologic abnormalities ameliorated as a result of the applied treatment – resolution of the cranial nerve lesions, concentrated the sensory disturbances in the distal parts of the limbs and improvement of the muscle strenght in the upper limbs.

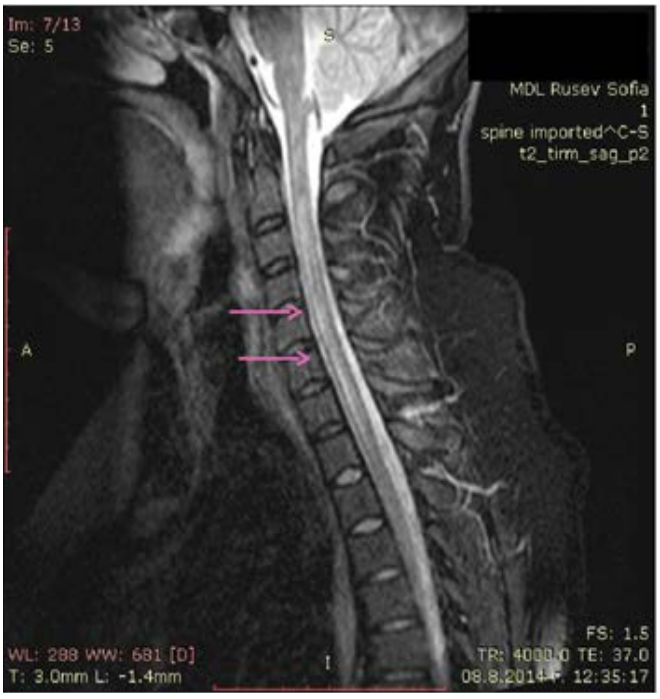

Figure 1 A madnetic-responance tomography (MRT) of the Cervicothoracic spine showed altered signal along the T_1-T_4 segment, edema in the white and gray matter of the myleon was noted, T2_tirm_sag_p2.

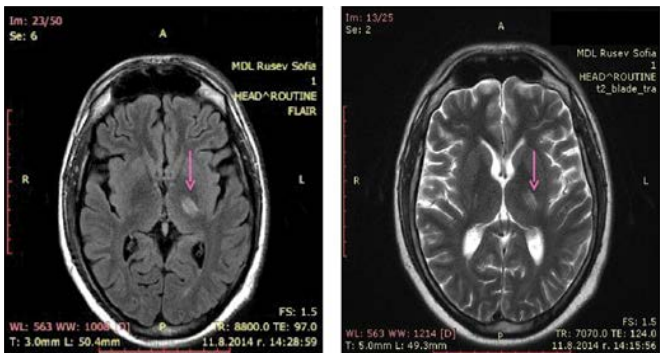

Figure 2 A MRT of the head showed altered signal in the thalamus and left middle cerebellar peduncule-changes associated with increased fluid content (FLAIR, T2_ blade_tra).

The patient's medical history is notable for an adverse reaction to HBV (hepatitis B) vaccination when he was 12 years old. Back then he developed fever, urticaria on the trunk and the limbs, palpable purpura on the lower legs, myalgias and hepatosplenomegaly. This episode was followed by acute renal failure, widespread suffusions, generalized grand-mal type seizures. The skin biopsy of the lower leg revealed leukocytoclastic vasculitis (perivascular and mural infiltrates consisting of mononuclear and neutrophil leukocytes, erythrocyte extravasates, involving the superficial veules and arterioles). The immunofluorescent staining demonstrated deposition of IgM, IgA, C_4 and fibrinogen in the vessel wall. A kidney biopsy was also performed with histological picture of thrombotic microangiopathy. The patient was diagnosed with thrombotic thrombocytopenic purpura (TTP syndrome, Moschcowitz syndrome). Thrombotic thrombocytopenic purpura (TTP) is a rare blood disorder characterized by clotting in small blood vessels of the body (thromboses). In its full-blown form, the disease consists of the pentad of [1,2]:

- Microangiopathic hemolytic anemia
- Thrombocytopenic purpura
- Neurologic abnormalities include hemiplegia, paresthesias, visual disturbance, aphasia and seizures
- Fever
- Renal disease, presenting with acute renal failure.

In the congenital form of TTP, mutations in the gene encoding the protease ADAMTS13 have been described. ADAMTS13 is a protease that is responsible for the breakdown of the ultralarge von Willebrand factor (vWF) multimers. In the more common sporadic form, antibodies against ADAMTS13 can be isolated in most patients [2]. The increase in circulating multimers of vWF increase platelet adhesion to areas of endothelial injury, particularly at arteriole-capillary junctions [2,3].

The patient was treated with corticosteroids, plasmapheresis and hemodyalisis for total of 18 months. The kidney function

improved and the dose of the corticosteroid was tapered to discontinuation. During his teenage years he developed metaboloic syndrome – hypertension, obesity, hyperuricemia, impaired glucose tolerance.

One month after the latest symptoms onset the patient was admitted to our rheumatology clinic. The physical examination showed systolic murmur at the heart apex, propagating to the posterior axillar line, diastolic murmur with punctum maximum at the aortic valve, propagating to the carotic arteries, bilateral knee arthritis. The neurological status revealed quadriparesis to paraplegia for the lower limbs – peripheral type, knee and Achilles areflexia, tactile hypesthesia in the upper limbs – distal type. The routine lab studies were notable for high ESR (45 mm), C-reactive protein (40 g/l), leukocytosis with neutrophillia on background corticosteroid therapy, high BUN (15 g/l), low grade proteinuria up to 0.6 g/l. The serum creatinine was normal (67 mkmol/l).

Given the proven vasculitis in the childhood. a connective tissue disease was included in the differential:

1. Polyarteritis nodosa
2. Systemic lupus erythematosus with involvement of the CNS presenting as transversal myelitis and disseminated encephalitis.

Polyarteritis nodosa is systemic necrotizing vasculitis predominantly affecting the middle-sized muscular arteries [4]. Given this definition we performed a CT angiography of the abdomen and pelvis with no signs of stenoses, thromboses or aneurysms of the abdominal aorta and its branches. Albeit rarely, PAN could affect the cerebral arteries with resulting ischemia, haemorrhage and epileptic seizures [4]. Contrast enchanced MRI of the brain was also performed with no evidence for aneurysms, stenoses or thromboses of the blood vessels. The only finding was a gliotic focus of vascular origin, located supratentorially in the subcortical brain tissue of the left frontal area. An EKG showed Q-wave in leads II, III, avF – finding that has been persisting from the childhood. We assumed that the patient may have had coronaritis due to Moschkowitz syndrome so we performed echocardiography that revealed pericardial effusion, septoapical hypokinesia, anterior mitral leaflet prolapse with resulting mitral regurgitation 2nd grade.; aortic regurgitation - 1st grade. A CT coronarography didn't find any significant stenoses. A muscular band of left anterior descending artery was noted. Given the absence of any changes of the arterial walls, polyarteritis nodosa was excluded as possible diagnosis.

It's possible that transversal myelitis is neurological manifestation of systemic lupus erythematosus [5-8]. This hypothesis is supported by the presence of arthritis, thrombocytopenia, low-grade proteinuria, pericardial effusion. ANA immunofluorescence test was done with further typisation of different antibody specifities – anti-RNP/Sm, Sm, Ro, La, Ro-52, Scl-70, PM/Scl, anti-Jo-1, anti-Cent. B, anti-PCNA, anti-nucleosomes, anti-histones, anti-Rib. P – all negative. The complement levels were normal – C3: 1.85 g/l; C4: 0.35 g/l. The serum level of immunoglobulines A, G and M were also normal. A lupus band test was performed – negative. The absence of specific SLE antibodies, anti-platelets antibodies and the uncertainty about the origin of the kidney damage made us exlude this diagnosis. The kidney changes may be a result of the TTP and could explain the low grade proteinuria, the ultrasound findings of a diffuse parenchymal process.

We tested the patient for presence of the following antibodies – anti-proteinase 3, anti-myeloperoxidase, anti-b2-glycoprotein I, anti-prothrombine, anti-annexin V-IgG, anti-annexin V igM, anticardiolipin antibodies, rheumatoid factror – IgM, IgA, IgG – all were negative. The Guillaine-Barre specific antibodies (anti-GM1, GM2, GM3, GM4, GD1b, GD2, GD3, GT1a, GT1b, Gq1b) were also negative.

A repeat lumbar punction revealed slightly increased protein – 0.65 g/l (0.15-0.45 g/l), normocytosis.

Based on the clinical manifestations and the disease course, the ENMG and MRI data we concluded that the patient has acute demyelinating polyradiculopathy, Gullaine-Barre syndrome presenting with ascending paralysis type Landry and transversal myelitis. We continued corticosteroid therapy with gradual tapering until reaching a maintenance dose of 8 mg/methylprednisolone per day. We also administered Nivalin (galantamine), Milgamma N (benfotiamine, pyridoxine, cyancobalamine). After 9 months of therapy the patient regained muscle strength in all four limbs, without any sensory abnormalities.

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