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

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), infections
and some autoimmune connective tissue disorders (systemic lupus erythematoses,
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 strength in all four limbs.

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 catheter 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
• Th1 – th3 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 dysarthria.

The laboratory studies revealed increased non-specific
inflammatory markers (erythrocyte sedimentation rate – ESR,
C-reactive protein, fibrinogen), thrombocytopenia (90 – 114 x
10⁹/l), borderline serum creatinine (138 – 147 mkmol/l). A lumbar
puncion 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 T₃-T₄ 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 C₅-T₄. A MRT of the
head was also performed, showing altered signal in the thalamus and left middle cerebellar peduncle – 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 interpreted 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 administered 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 strength in the upper limbs.

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 veins and arterioles). The immunofluorescent staining demonstrated deposition of IgM, IgA, C₃ 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, Moschowitz 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 hemodialysis 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 metabolic 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 quadriaparesis 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 neutrophilia 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 enhanced 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 supratentorial 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 specificities – 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 exclude 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, antcardiolipin antibodies, rheumatoid factor – 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, Guillaine-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, cyanocobalamine). After 9 months of therapy the patient regained muscle strength in all four limbs, without any sensory abnormalities.
References


