(VBM) study detected a bilateral gray matter increase in the pulvinar of patients with idiopathic RLS treated with medications affecting the dopamine system, in comparison with control subjects. However, a subsequent study on unmedicated patients did not confirm this finding, which suggests that these changes might have been induced by the treatment [5]. A positron emission tomography study using [11C] FLB 457 supported the involvement of the dopamine system in both striatal and extrastriatal (medial thalamus and the anterior cingulate cortex) brain regions in the pathophysiology of RLS [4]. Metabolic changes in the medial thalamus (notably increased glutamatergic activity) were found in RLS patients using proton magnetic resonance spectroscopy (Ku et al., 2014). In the pons, lesion affecting the tegmentum can interrupt the reticulospinal tract commencing at the reticular formation, and the red nucleus, which are involved in the generation of RLS [2]. The spontaneous healing and the very short time between the stroke and the complete disappearance of the RLS in our case is also in favor of a causal link between the stroke and the apparent healing.

This original observation confirms the role of the thalamus and the tegmentum in the neural network involved in the restless legs syndrome and suggests their participation in the genesis of symptoms.

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Conflict of interest

None of the authors have potential conflicts of interest to be disclosed.

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Coexistence of multiple sclerosis and ankylosing spondylitis: Report of four cases from Russia and review of the literature

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ABSTRACT

Multiple sclerosis is a chronic demyelinating disorder of the central nervous system. There are many cases of multiple sclerosis – like syndrome and demyelinating disorders in systemic lupus erythematosus, Sjogren disease, Behcet disease and other autoimmune conditions. Coexistence of ankylosing spondylitis and multiple sclerosis usually is rare but in this article we report 4 Russian patients with concomitant multiple sclerosis and ankylosing spondylitis diseases. None of these patients received anti-tumor necrosis factor alpha therapy prior to diagnosis of multiple sclerosis. Pathogenesis, diagnostic and treatment challenges are discussed.

1. Introduction

There is still an open debate whether demyelinating lesions in systemic autoimmune diseases are a consequences or coexistence of multiple sclerosis (MS) in the same patient. Coexistence of multiple sclerosis and ankylosing spondylitis (AS, an inflammatory rheumatic disease predominantly of the axial skeleton) is rare. Usually demyelinating lesions in ankylosing spondylitis were described after monoclonal antibodies treatment (for example, rituximab, adalimumab, etc.) but in our article we have presented four Russian patients naïve to anti-tumor necrosis factor (anti-TNF) treatment which met Revised McDonald Criteria for MS [1] and Modified New York and The Assessment of Spondiloarthritis International Society (ASAS) Criteria for AS [2].

We describe cases of 3 men and 1 woman admitted to Bujanov Hospital in 2015 for diagnostic procedures and treatment. In contrast to previously reported cases our patients did not received anti-TNF alpha therapy Diagnosis and adequate treatment of these patients are still challenging.

Abbreviations: ANA, antinuclear antibodies; AS, ankylosing spondylitis; ASAS Criteria, The Assessment of Spondiloarthritis International Society Criteria; ASDAS Score, The Ankylosing Spondylitis Disease Activity Score; CE, contrast enhancement; CSF, cerebrospinal fluid; EDSS, expanded disability status scale; MP, methylprednisolone; MS, multiple sclerosis; NSAIDs, non-steroidal anti-inflammatory drugs; OGBs, oligoclonal bands; TNF, tumor necrosis factor.

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2. Case presentation

2.1. Case 1

A 32-year-old man was diagnosed withAS since 2013 after left sacroiliitis and HLA B27 positive lab test. He has a family history of AS (his sister has AS too). He was treated only with non-steroidal anti-inflammatory drugs (NSAIDs).

First neurological symptoms were developed in 2013 when a numbness and weakness in both legs, Lermitt'sign were presented. Brain MRI (2013) revealed multiple periventricular, juxtacortical and infratentorial demyelinating foci without contrast enhancement (CE). Spinal cord MRI revealed demyelinating T1-Gd negative lesions at Th1-Th2, C3-C4 levels. Visual evoked potentials were normal. Patient was diagnosed with CNS demyelinating disorder due to AS by neurologist at another MS Center and symptoms became better after Methylprednisolone pulse therapy (MP 1000 mg IV for 5 days). In 2014 and 2015 new brain lesions without CE were presented on MRI and patient had second attack with leg weakness but symptoms resolved in two weeks without treatment.

In November 2015 the patient was admitted to our hospital for work-up: thyroid function, routine hematological and biochemical laboratory tests were normal. CRP, rheumatoid factor, antinuclear antibodies (ANA), anti-double strain DNA antibodies, ANCA, ANSA, ssA, ssB, antiphospholipid antibodies, anti-aquaporin-4 antibodies were negative. No cerebrospinal fluid (CSF) cytosis or protein elevation, negative oligoclonal bands (OGBs) were revealed. On admission only mild pyramidal signs, head tremor and urinal incontinence were presented with expanded disability status scale (EDSS) 2.0. Recent brain and cervical spinal cord MRI shows multiple demyelinating foci (Fig. 1). In spite of the negative OGBs this patient was diagnosed with MS based on the revised McDonald criteria and treatment with Glatiramer Acetate, 20 mg s.c. was started. During one year of the treatment he did not have any relapses or new lesions on MRI.

2.2. Case 2

At the end of 2015 a 45-year-old man with a known history of demyelinating disorder since 2012 (first clinical attack with vertigo and nausea) and AS since 2013 (first attack with pain and edema of joints and peripheral arthritis) was admitted to our hospital for diagnostic procedure and lumbar puncture. Neurological examination revealed mild ataxia and pyramidal signs, EDSS1.5. The patient was treated with unusual drug combination: methotrexate 10 mg per day, leflunomide 20 mg per day, and NSAIDs. He had never been treated with anti-TNFα therapy. During this treatment he was stable for MS but AS form changed from peripheral to axial involvement. CSF examination revealed 3 leukocytes/mm^3, slightly protein elevation and Type 2 OGBs (olygoclonal bands only in CSF). Lab tests for ANA, ANCA, anticardiolipin and ENA antibodies screening were negative. CRP was 51.9 mg/dl. Brain MRI displayed typical MS lesions in FLAIR and T2WI without CE, cervical spinal cord MRI was without MS typical lesions. MS was diagnosed in this patient, sulfasalazine was added to therapy and leflunomide 20 mg per day was continued as a prodrug of teriflunomide. During 1 year patient was stable for neurological status. During one year of follow-up his neurological status was stable.

2.3. Case 3

A 48-years old man was diagnosed with AS 10 years ago and has high the Ankylosing Spondylitis Disease Activity Score (ASDAS) activity 5.1, spondylitis, sacroiliitis and bamboo sign at radiography.

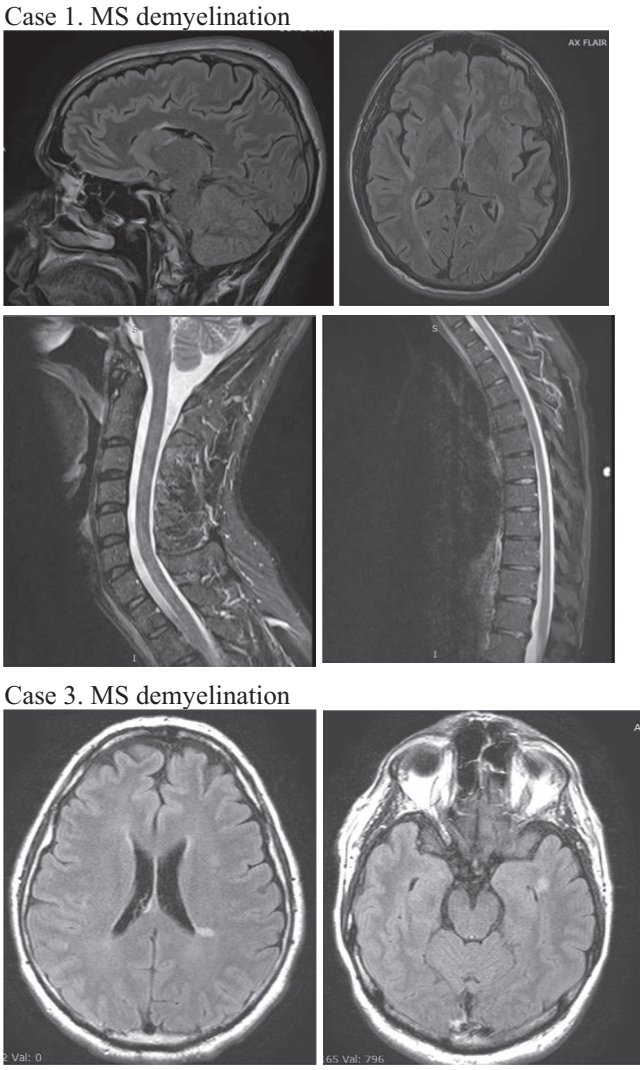

Fig. 1. Brain and spinal MRI of MS-AS patients in case 1 and case 3.

He was treated only with NSAIDS and MP. In 2015 left sided mild hemiparesis and urinal problem were developed. Brain MRI revealed cavernosus angioma in left thalamus and periventricular, subcortical, white matter demyelinating lesions with one infratentorial demyelinating lesion in the pons. Demyelinating lesion at Th7 level was found at spinal cord MRI without CE. He was treated with MP pulse therapy 1000 mg per day for 3 days with positive effect.

After a year prominent left-sided weakness was developed again and patient was admitted to our hospital for treatment and MS verification. In neurological status he had moderate left-sided hemiparesis with higher pyramidal reflexes and Babinski sign, left-sided hemihypesthesia, mild intention and dysmetry in finger-to-noise test, heel-shin test, discoordination at Romberg test and urinaryretention with EDSS 4.0.

Lumbar puncture was not performed due to technical problem. Immunological examinations for ANA, ANCA, anticardiolipin and ENA antibodies were negative. CRP, erythrocyte sedimentation ration and rheumatoid factor were normal. Brain MRI with CE was performed and displayed multiple demyelinating lesions (Fig. 1). Patient was diagnosed with MS and treated with MP 1000 mg per day for 4 days with positive effect.

Patient was consulted by rheumatologist and all indications for anti-TNF therapy were revealed but due to MS NSAIDs and sulfasalazine therapy was recommended.