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Case Report
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A Patient with Ankylosing Spondylitis, Parkinson's Disease and Seminoma Testis - Three Different Diagnoses or One Disease with Multiple Faces

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Abstract

Introduction: Ankylosing Spondylitis (AS), Parkinson Disease (PD) and Seminoma testis are three different diseases with their own characteristics. The contemporary treatment with biological disease-modifying antirheumatic drugs (bDMARDs) of AS, sometimes can trigger neoplastic processes. Whether there is a relationship between AS and Parkinson disease, or the latter is triggered by biological treatment of AS, similarly to causing cancers, is not well known.

Case Presentation: We report a case of 43 years old man with proven Ankylosing spondylitis, later presented with Parkinson disease and seminoma testis. The patient was diagnosed 6 years ago with AS according to modified New York criteria. Prior to hospitalization he was treated with NSAIDs, parenteral corticosteroids and myorelaxants without any results. One year later he started a therapy with Adalimumab with very good effect lasting one year, thereafter – with Golimumab, because of decreasing of Adalimumab efficacy and disease flare. Around three months after Golimumab therapy, he became stiffed, with slow movements and tremor. The patient was diagnosed as having Parkinson disease and the biologic was stopped as a suspicious for the neurological disorder. One year later he was diagnosed with seminoma and had surgical treatment. When admitted to the Rheumatology department he had a flare of AS with increased inflammatory response, sacroiliitis 3rd degree on X-ray (Figure 1) and extremely stiffness and back pain.

Conclusion: Ankylosing Spondylitis is an autoimmune inflammatory joint disease, disabling when not treated adequately. Sometimes it is complicated by itself or by the treatment especially biologics. It is well known that biologics can cause neoplastic processes in the time of treatment, but whether they can lead to drug-induced Parkinson disease, or no not, is not elucidated.

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Introduction

Ankylosing Spondylitis (AS) is an autoimmune inflammatory disease of the spine, sometimes alongside other peripheral joints involved. Most commonly there is association with HLA-B27 antigen. Treatment may improve symptoms and prevent worsening. This may include medication, exercise, and surgery. Medications used include Non-Steroidal Antirheumatic Drugs (NSAIDs), steroids (local intra-articular injections), conventional DMARDs (cDMARDs) such as sulfasalazine, and biologic agents (bDMARDs), which can stop progression.

Parkinson's disease is a progressive nervous system disorder that affects movement. Symptoms start gradually, with a barely noticeable tremor in just one hand. The disorder also commonly causes stiffness and slowing of movement.

Seminoma (also known as pure seminoma or classical seminoma) is a germ cell tumor of the testicle or, more rarely, the mediastinum or other extra gonadal locations. It is a malignant neoplasm and is one of the most treatable and curable cancers, with a survival rate above 95% if discovered in early stages. Testicular seminoma originates in the germinal epithelium of the seminiferous tubules. Treatment usually requires removal of one testicle. However, fertility usually isn't affected. All other sexual functions will remain intact.

Case Presentation

We report a case of 43 years old man with proven Ankylosing spondylitis according to modified New York Criteria for Ankylosing Spondylitis. The diagnosis was made 6 years ago with bilateral sacroiliitis, relapsing inflammation of the eye, HLA-B27 positivity. He was treated with NSAIDs,

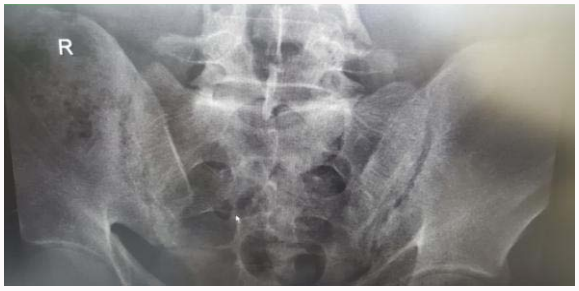

Figure 1: X-ray of Ankylosing spondylitis sacroiliac joints.

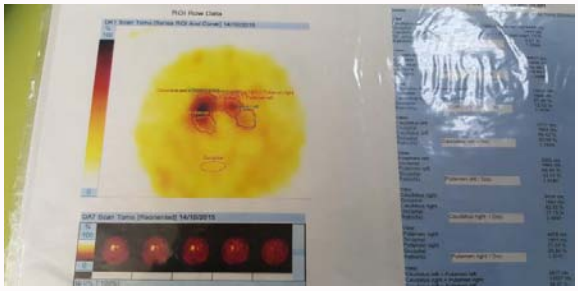

Figure 2: DAT scan.

parenteral corticosteroids and myorelaxants without any results. One year later he started a therapy with Adalimumab with very good effect lasting one year, there after – with Golimumab, because of absence of Adalimumab efficacy and disease flare. Three months after initiation with Golimumab therapy, he was diagnosed with Parkinsonian syndrome. The neurologist supposed Drug-induced Parkinsonism (DIP) and decided to stop the biologic agent. In spite of that his tremor, rigidity and difficulty walking persisted even after stopping the biologic agent. DAT scan (Figure 2) was performed and there were changes typical for idiopathic Parkinson disease; DATs are presynaptic proteins in the membrane on terminals of dopaminergic neurons. These transporters control dopaminergic transmission by spatial and temporal buffering, rendering the molecule an imaging target in diseases affecting the dopaminergic Nigrostriatal pathway. SPECT and PET are available using several DAT ligands. DAT uptake in the striatum is significantly decreased in patients with Parkinson Disease (PD), even during the early stages, because the motor symptoms of PD do not appear until 60% to 80% of dopaminergic neurons degenerate. In addition, drugs causing Parkinsonism have negligible affinity to DAT. DAT scans may show symmetric uptake of the radiotracer in the bilateral striatum in patients with pure DIP, even if they have significant parkinsonism. PD can be diagnosed in DIP whose DAT uptake decreases asymmetrically in the striatum [1,2].

About one year later, he was diagnosed with seminoma and had surgical treatment and following radiotherapy. TNF-blockers increase the risk of cancer, so the seminoma may be a result of adalimumab and golimumab therapy. The Rheumatology Committee decided not to continue TNF-α blockers.

One year after radiotherapy the patient was hospitalized in our Rheumatology department, with clinical activity of as; increased inflammatory response, X-ray with 3rd degree sacroiliitis, severe back pain during the night and morning stiffness more than 2 hrs. Because of very high inflammation activity /ESR and CRP/ we decided to start biological treatment with secukinumab/IL-17A blocker, different from TNF-α blockers, presumably because there is no evidence of risk for tumors and there is no evidence of worsening neurologic diseases such as Parkinson disease. Two years after the cessation of TNF blockers and on the background of Levo-DOPA intake his symptoms of Parkinson disease was less severe. So we are more likely to accept Parkinson disease despite the early age of onset.

Discussion

Relationship of movement and other neurodegenerative disorders in patients with different rheumatic diseases remains uncertain. Inflammatory arthropathies encompass more than 20 different diseases with distinct clinical patterns and etiopathogenic mechanisms. There is similar heterogeneity which is associated with movement disorders. For example, Parkinson's disease is well recognized when presenting with tremor, rigidity, bradykinesia, and postural instability/gait difficulty [3,4]. In contrast, there is a wider spectrum of Atypical Parkinsonian syndromes (to be distinguished from Parkinson's disease). These refer to a wide variety of syndromes, which are differentiated from Parkinson's disease based on distinguishing symptoms, examination findings, and neuropathological features [3,5]. Although frequently presenting with bradykinesia and rigidity (i.e, termed as an akinetic-rigid syndrome) these atypical Parkinsonian syndromes characteristically lead to an earlier and more expansive pattern of injury compared to Parkinson's disease. Such syndromes may cause ataxia, dysautonomia, alien-limb phenomenon, and visual hallucinations [3,6]. These atypical Parkinsonian syndromes may be misdiagnosed and misclassified as Parkinson's disease, and may respond poorly and/or in an unsustained manner to levodopa (L-dopa) therapy [3,7].

We discussed whether our patient with ankylosing spondylitis suffers from coincidental idiopathic Parkinson disease or it is associated with the biologic treatment. DAT scan showed decreased tracer uptake asymmetrically in the striatum and probably this is Parkinson disease and not drug-induced Parkinsonism.

On the other hand there is some evidence in the literature that biologic agents may cause DIP. There were reports of Amyotrophic Lateral Sclerosis (ALS) in 4 patients with RA who were not on TNF-inhibitor therapy [3,8,9] and 3 patients (1 with ankylosing spondylitis and 2 with RA) with ALS developing in the context of TNF-inhibitor therapy [3,8,10,11]. The presence of anti-neuronal antibodies against the P/Q-type calcium channel may also provide a biomarker that a disorder which is presumptively regarded as non inflammatory may be underscored by immune-mediated mechanisms. This concerns a patient with psoriatic arthritis who was diagnosed as having the neurodegenerative disorder of ALS in the context of being treated with TNF-inhibitor therapy. This finding is intriguing given the proclivity of TNF-inhibitors to induce autoantibodies [3,12-15]. The spectrum of neurological disorders which may be attributable to TNF-inhibitors is broadening [3,12,14].

Another report describes 2 patients with Rheumatoid Arthritis (RA) presenting with Parkinsonism [3,16,17]. Neither of these patients presented with findings consistent with idiopathic Parkinson's disease. In 1 of these patients, features inconsistent with idiopathic Parkinson's disease included early-onset of upper-motor neuron findings [3,16,17]. The other RA patient developed rapidly progressive Parkinsonism over a 12- month course of TNF inhibitor therapy (infliximab), culminating with inability to ambulate, severe

bulbar dysfunction, and dyspnea [3,16,17] Given that infliximab otherwise induced remission of her RA, it was suggested that the rapidity of Parkinsonism might be mediated by infliximab.

Conclusion

In summary, we describe a patient with ankylosing spondylitis and neurodegenerative syndrome, which was classified as Parkinson's disease. Although DAT scan (Figure 2) showed changes typical for idiopathic Parkinson disease, it can be assumed that our patient may have other neurodegenerative disorder or atypical Parkinsonian syndrome, due to immune-mediated vasculopathy of CNS in context of inflammatory joint disease, or as a result of biological treatment. Further studies are necessary to characterize the clinical spectrum and mechanisms of movement and other neurodegenerative disorders in rheumatic diseases.

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