Guillain-Barre like syndrome associated with risperidone use: A case report

Risperidon ile ilişkili Guillain-Barre benzeri sendrom: Bir olgu sunumu

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SUMMARY

Guillain-Barre Syndrome is an autoimmune response that usually occurs due to infectious or idiopathic causes. Rare case reports have also been shown to be caused by the intake of many substances and drugs. GBS cases results in 10% mortality and 25% respiratory failure. This case report describes the occurrence and termination of GBS-like syndrome following first time risperidone intake at a patient in the psychiatric ward. A 42-years old female patient without any prior psychiatric history admitted to psychiatric ward with paranoid and persecutory delusions, disorganized speech and behaviors related to systematic delusions aiming infidelity of her spouse. Risperidone 4 mg day prescribed for treatment for first time. In seventh day, neuromuscular symptoms started as dizziness, ataxia, muscle weakness and ascending paralysis. Neurological examination and consultation, imaging and lumbar puncture was performed, resulting GBS diagnosis. With the immediate transfer to intense care unit, Risperidone treatment stopped and hIG treatment administered. Patient Recovered without any physical impairment. Current case presents a GBS like syndrome associated with Risperidone treatment. There are several Atypical antipsychotic drug treatment related GBS like case reports but this is the first to be associated with Risperidone in adults. Infection related etiology was excluded by patient history but no specific antibody test or immunological survey was performed for GBS.

Keywords: Antipsychotics, risperidone, Guillain-barre syndrome, neuropsychiatry

ÖZET

Guillain-Barre Sendromu, genellikle enfeksiyöz veya idiyopatik nedenlere bağlı olarak ortaya çıkan bir otoimmün yanıttır. Nadir vaka raporlarının da birçok madde ve ilacın alımından kaynaklandığı gösterilmiştir. GBS vakaları %10 mortalite ve %25 solunum yetmezliği ile seyretmektedir. Bu olgu sunumu, psikiyatri servisinde bir hastada ilk kez risperidon alımını takiben GBS benzeri sendromun ortaya çıkışı, seyri ve sonlanımını bildirmektedir. Daha önce psikiyatrik öyküsü olmayan 42 yaşında kadın hasta, paranoid ve perseküsyon sanrıları, dezorganize konuşma ve eşinin ihanet ettiğine yönelik sistematik sanrılar ve ilişkili davranışlarla psikiyatri polikliniğine başvurmuş ve yatışı yapılmıştır. İlk tedavi için günde 4 mg risperidon düzenlenmiştir. Yedinci günde nöromüsküler semptomlar baş dönmesi, ataksi, kas güçsüzlüğü ve asendan felç olarak başladı. Nörolojik muayene ve konsültasyon, görüntüleme ve lomber ponksiyon yapılarak GBS tanısı konuldu. Yoğun bakım ünitesine acil transfer ile Risperidon tedavisi durduruldu ve hIG tedavisi uygulandı. Hasta herhangi bir fiziksel bozukluk olmadan iyileşti. Mevcut vaka, Risperidon tedavisi ile ilişkili GBS benzeri bir sendrom sunmaktadır. Literatürde GBS benzeri kliniğe yol açan Atipik antipsikotik ilaç tedavisi ile ilgili olgu sunumları bulunmakta, ancak bu yetişkinlerde Risperidon ile ilişkilendirilen tek olgu olarak görünmektedir. Hasta öyküsü ile enfeksiyonla ilişkili etiyoloji dışlanmış olmakla birlikte, GBS için spesifik bir antikor testi veya immünolojik araştırma yapılamaması, sunumun kısıtlılığı olarak belirtilebilir..

Anahtar Kelimeler: Antipsikotikler, risperidon, Guillain-barre sendromu, nöropsikiyatri

(Turkish J Clinical Psychiatry 2022;25:426-429)
DOI:10.5505/kpd.2022.70846

The arrival date of article: 26.01.2022, Acceptance date publication: 20.03.2022

INTRODUCTION

Guillain-Barre syndrome (GBS) is characterized by rapidly evolving ascending weakness, mild sensory loss, and hyporeflexia or areflexia. Acute inflammatory demyelinating polyneuropathy was the first to be recognized over a century ago and is the most common form of GBS (1). About 25% of patients develop respiratory insufficiency and many show signs of autonomic dysfunction. Diagnosis can usually be made on clinical grounds, but lumbar puncture and electrophysiological studies can help to substantiate the diagnosis, Intravenous immunoglobulin and plasma exchange are proven effective treatments (2). Acute symptoms and clinical findings are seen usually after a GI infection, but commonly, GBS is in sporadic subacute progress. GBS is also seen after several drug intakes. There are case reports of GBS following L-dopa/carbidopa intestinal intake, antineoplastic agent treatment of hairy-cell leukemia, arsenic exposure (3–5). Olanzapine, Clozapine, and Aripiprazole were also found in association with Guillain-Barre syndrome-like clinical manifestations (6–9).

An inpatient with atypical psychosis treated with risperidone, experiencing neurological symptoms, followed by diagnosis and progress of GBS will be presented in this case. This report aims to inform about the rare adverse effect of a commonly used atypical antipsychotic and reveal the complexity of a sensory-motor deficiency of a possible neurological phenomenon.

CASE HISTORY

A 42-years old female patient was admitted to the psychiatry outpatient clinic with her family. The main complaint of the patient was irritability, anger, crying regularly, and sleep disturbances. According to her family members, she felt unreasonably angry about everything and she started talking to herself meaninglessly and accused her husband of betraying her against others, and marital infidelity. It was her first admission to a psychiatrist and there was no past similar complaints before. Her medical history and family history showed no relevant illness or disorders. Mental status examination revealed blunt affect, loss of thought pattern, and tangential speech pattern. There were well-organized paranoid–jealousy delusions, but the perception was normal. The symptoms were present almost for four weeks, and for the last ten days, the patient started to take physical measures such as locking doors, blockading rooms, and windows, following her spouse around the house, and fighting without reason.

After admission to the psychiatry ward, complete blood count, blood glucose level, lipid profile, hepatic and renal blood tests, Blood serology for HIV, HCV, and HBV, thyroid function tests, and urinal biochemistry tests were performed and all came back within normal parameters. After the first admission Interview, the diagnosis was atypical psychosis and risperidone 4mg/day p.o. (2mg twice a day) was prescribed, and the routine treatment was supplied with lorazepam 2.5mg night if needed. After two days, paranoid thought and related disorganized behaviors decreased, and speech patterns reformed. During the fifth day of admission, responsive and relatively euthymic mood re-organized, resulting in appropriate social adjustment in the ward. On the seventh day of admission, the patient complained about feeling dizzy when standing, and losing balance when fast walking around. There was no significant neurological deficit in neurological examination (NE), vital signs were within normal perimeters. CBC and blood chemistry were taken and came back normal. These symptoms were associated with alpha-adrenergic properties of risperidone and the dose decreased to 3 mg daily.

On the eighth day of admission, the patient experienced low feet when walking, and fatigue if walked for more than 30-40 steps. The lower extremities showed 4/5 muscle strength and additional paresthesia of bilateral dorsal feet was observed. During the daytime, the first dose of risperidone was skipped considering NE findings. Lorazepam hasn't been given for the last 4 days, and everyday mental status exam showed no psychosis-related symptoms for 3 days. Neurology consultation was performed to be advised about symptoms. Spinal and brain fMRI and diffusion MRI tests were planned and the neurology physician advised to repeat NE every two hours. During following NE,

muscle strength of lower extremities-Cruz and femoral groups- decreased to 3/5, and standing without help became impossible. fMRI showed no pathological findings. The patient exhibited ascending muscle strength loss within 6 hours of diagnostic course, leveling to lower abdominal muscles. The clinical course and findings were re-assessed with a neurologist, and the patient was transferred to the Neurological intense care unit (ICU).

After transfer, all antipsychotic drug prescriptions stopped, and to verify the GBS diagnosis, an LP was performed. The results of the cerebrospinal fluid sample came back showing the increased protein and immunoglobulin count (108 mg/dl), and absence of cellular materials (2 lymphocytes per area), meaning albumin-cytological dissociation, evidencing GBS. The specific antibodies couldn't be detected because of the lack of specific assay kits. During the first day of ICU, the patient experienced dyspnea and respiratory distress, resulting in external respiratory support.

After GBS diagnosis was certain, 5-day consequent human immunoglobulin was administered intravenously (0,4 gr/kg per day), resulting in fast improvement in muscle control and loss of respiratory symptoms. Three days after the fifth H-Ig dose, the patient gained back standing and walking independence and was transferred to the neurology ward, then she was observed for any more neurological symptoms without medication. With no complaints or symptoms, the patient was discharged. She was re-admitted to the outpatient clinic of psychiatry after four weeks and aripiprazole 10 mg p.o. treatment planned. There were no similar clinical neuro-psychiatric symptoms till that time for three months on follow-ups.

DISCUSSION

Guillain-Barre syndrome (GBS) is clinically defined as an acute peripheral neuropathy causing limb weakness that progresses for days or, at the most, up to 4 weeks. GBS occurs throughout the world with a median annual incidence of 1.3 cases per population of 100.000, with men being more frequently affected than women.

GBS most often develops after the upper respiratory tract or GI infections. Pathogens of Campylobacter jejuni, Mycoplasma Pneumoniae, Hemophilus influenza and CMV have been associated with GBS. When the case reports were examined, GBS-like syndrome was reported after the use of Aripiprazole and Olanzapine, after clozapine-associated agranulocytosis resulted in septicemia, after arsenic intoxication, and after the antineoplastic agent used during Leukemia treatment. In one case, A lower bulbar palsy patient with pathogenesis-related GM-1 and GD1b antibodies was detected after aripiprazole use.

Risperidone is a commonly used atypical antipsychotic for the indications of schizophrenia, bipolar affective disorder, autism and childhood irritability with FDA approval. It is also frequently used in dementia-related irritability, psychotic symptoms, and disorders that require anger management. While the drug shows atypical properties when used at low doses, it acts similarly to high doses of conventional antipsychotics. It can be used orally and parenterally, it is preferred due to its long-acting depot form. The most common side effects are EPS-related movement disorders, Hyperprolactinemia and galactorrhea. More rare side effects; neutropenia, agranulocytosis, thrombocytopenia, elevated idiopathic ADH, edema, dermatitis, rhabdomyolysis.

In a seven-year-old case, a case of GBS, which was diagnosed with the clinical and neurophysiological examination, was reported with loss of strength, gait difficulty, loss of balance in the upper extremities after the use of Risperidone. Similarly, complete recovery was achieved by discontinuation of drug intake and five-day human immunoglobulin treatment (10). Our case shares the same temporal intersection between drug intake, clinical manifestation, discontinuation, treatment and recovery. To our knowledge, this is the first case report presenting risperidone-related GBS in an adult patient.

One proposed mechanism for GBS is that an antecedent infection evokes an immune response, which in turn cross-reacts with peripheral nerve components because of the sharing of cross-reactive epitopes. But the main mechanism of drug-

induced GBS is not a well-known phenomenon. In the formation of GBS, the immune system produces both a cellular and humoral response. Atypical antipsychotics presented in this case and other cases may activate antibodies from infections that have previously been occult, perhaps by stimulating the immune system through an unknown mechanism. From another point of view, the immune system may be forming antibodies that cross-react with similar proteoglycans in the cell membrane. Recent studies reveal the immune-boosting effects of atypical antipsychotic drugs. In a review performed on in-vitro experiments showing immune effects of antidepressants and antipsychotics, risperidone is associated with increased proinflammatory cytokines such as IL-1beta and IL-6 levels11. Also, TNF- Alpha takes an important role in GBS pathophysiology. But to our knowledge, there is no clinically relevant proof regarding the effects of risperidone on GBS development.

Guillain barre syndrome mostly develops after gastrointestinal or upper respiratory tract infection. In this patient, the history taken from him and his family was considered safe. In the last three months, no history of infection could explain these symptoms. Infection-specific parameters such as WBC, CRP, and sedimentation were observed in the natural range in blood tests taken at admission and during follow-up. In addition, discontinuation of the possible causative drug and rapid response to treatment also support the cause-effect relationship. But also, no previous infection or specific antibody-related GBS determination was made. Although clinical findings and LP have been performed and treatment has been administered, the most important limitation is that there is no additional examination linking drug intake and GBS clinic with an organic bond except temporal connection.

This case evaluates the possible relationship between a commonly used antipsychotic such as Risperidone and a neuromuscular disorder with GBS-like symptoms. In conclusion, It is necessary to design and carry out more detailed studies on the subject.

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