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Guillain-Barre Syndrome following Cushing's Syndrome in a Pregnant Woman: A Case Report

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Abstract

Guillain-Barre syndrome is a neurological disorder that begins with weakness of the limbs and can cause respiratory and cardiac involvement. The subject of this report is a 30-year-old woman who was diagnosed with Cushing's syndrome following recurrent bone fractures and receiving treatment for the Cushing's syndrome. The patient was referred to a hospital during pregnancy because of generalized pain and weakness in the extremities. Abdominal ultrasound showed a mass in the left adrenal gland and so surgery was performed to remove the mass.

However, the patient's symptoms did not improve after surgery. The patient was asked to consult a neurologist who made a diagnosis of Guillain-Barre syndrome after cerebrospinal fluid was examined. Patient was discharged with personal consent. Four months later, the baby was born with a normal Apgar score, and the general condition of mother and child were evaluated as good. This case demonstrates a rare coincidence of Cushing's disease and Guillain-Barre syndrome. Due to the increase in corticosteroids due to Cushing's syndrome, it is expected that symptoms of Guillain-Barre syndrome would not occur. This case could indicate that there are several mechanisms for development of Guillain-Barre syndrome and that animal models can be helpful in this context.

Key Words: Cushing's syndrome, Guillain-Barre syndrome, Pregnant woman.

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1- INTRODUCTION

Guillain-Barre syndrome is a polyradiculoneuropathy that affects the function of the sensory and motor systems and can spread to the central nervous system as well. Symptoms can range from weakness in limbs and cranial nerves to weakening of the respiratory system, and death (1). The prognosis of the disease depends on the degree of respiratory and cardiovascular involvement. Mortality rates in severe cases range from 12 to 42 percent (2). Studies show that between 25% and 30% of patients with a history of hospitalization due to this syndrome experience prolonged disability (3).

The etiology and pathogenesis of inflammatory demyelinating polyneuropathy, also termed Guillain-Barre demyelination, are unknown. Many causes, including viral infections, malignancies, and pregnancy have been proposed as possible initiators of the disease (4, 5). Evidence supports the hypothesis that this disease is at least partially caused by autoimmune mechanisms (6). Given the possibility that the disease is caused by a defective immune response against the peripheral nervous system, it is treated with corticosteroids and immunosuppressants, although their efficacy has not been established (7).

Since corticosteroids are used to treat Guillain-Barre syndrome, considering the association of Cushing's syndrome with increased corticosteroids levels in the body, the simultaneous presence of Cushing's and Guillain-Barre syndromes in one patient seems to be contradictory. In this study, we report the case of a patient who developed Guillain-Barre syndrome following Cushing's syndrome during pregnancy.

2- CASE REPORTS

A 30-year-old married woman referred to Imam Reza Hospital (Mashhad, Iran) complaining of bone pain. The gestational age at the first examination was approximately 16 weeks. About a year prior, the patient had suffered a fracture in one her right toes and further examinations had revealed osteoporosis. Due to complaints of bone pain, the patient underwent bone scan and MRI imaging 6 months later, and multiple micro-fractures were observed in ribs, pelvis, and a left toe. The patient was then referred to an endocrinologist who suggested the possibility of Cushing's syndrome.

Three months later, the patient referred to the hospital with abdominal pain. Since she was suspected of having kidney stones, ultrasound imaging was prescribed which revealed pregnancy. The endocrinologist recommended further tests to verify Cushing's syndrome after parturition. However, the patient experienced generalized bone pain one month prior to the visit. The patient's pain had gradually worsened, to the degree that she had not been able to sit down, stand up for the prior 20 days. The patient's pain was more concentrated in the shoulder girdle and legs. She was admitted to Imam Reza Hospital in Mashhad and was hospitalized. Ultrasonography revealed a distinct hypoechoic and heterogeneous 32*26-mm non-calcified mass between the spleen and left kidney, compatible with the position of adrenal gland. Also, 24-hour urine analysis showed elevated epinephrine and metanephrine (**Table.1**).

Table-1: Tests performed during initial examinations.

Test	Value
ESR (mm/h)	27
24-hour creatinine (mg/dl)	945
ACTH (pg/ml)	<5
Vit D (ng/ml)	59
PTH (pg/ml)	24
8 A.M. cortisol (ng/ml)	22.5
Metanephrine (µg/24 h)	42
Norepinephrine (µg/24 h)	251.3
DHEA	255

ESR: Erythrocyte sedimentation rate; ACTH: Adrenocorticotropic hormone; PTH: Parathyroid hormone; DHEA: Dehydroepinadrosterone.

No lesions were seen on parathyroid ultrasound. The patient was transferred to the intensive care unit because of respiratory distress and retrosternal pain. In simple chest radiographs, a prominent aortic arch, a prominent hilum of the lung, and pulmonary opacity in the inferior zone on both sides of the lung were observed. The radiograph also showed increased cardiothoracic ratio and several circular opacity foci adjacent to the hilum of the left lung (**Figure.1**). A lung disease specialist recommended perfusion and color Doppler scans to rule out embolism, both of which returned normal results. The patient had also reported high blood pressure since about 2 months prior and had been treated with 1000 mg methyldopa every 8 hours and 2.5 mg amlodipine daily. The patient had a history of glaucoma and had undergone surgery for strabismus (in 2015), and infertility (twice). During examination, abdominal distention, abdominal striae, moon face appearance, and limb edema were noted. The muscular force was 5/5 in the all extremities. The patient was sent to Quaem Hospital in Mashhad for adrenalectomy. Surgery at Ghaem Hospital was canceled due to disagreement with the neurosurgeon and cervical MRI was performed. On MRI images, lordosis had reduced in the neck, and vertebrae and the spinal canal were healthy. Two days later, the patient finally underwent left adrenalectomy. After surgery, the patient was treated with potassium due to severe hypokalemia. Due to a decline in muscular force of the patient, particularly in lower limbs, neurologic consultation was sought, which suggested the possibility of neuropathy due to a systemic disease or Guillain-Barre syndrome. Lumbar puncture was performed, favoring the Guillain-Barre diagnosis. The patient also had elevated liver enzymes, so 24-hour urine collection was requested due to high blood pressure. The patient was administrated IVIG to treat Guillain-Barre syndrome and was then discharged. At the time of discharge, she was not able to walk or perform activities. About 4 months after discharge, the patient referred to a hospital in Zahedan, Iran, due to the onset of uterine contractions. The patient underwent Cesarean section because of limitation in position and the neonate was born with a good Apgar score.

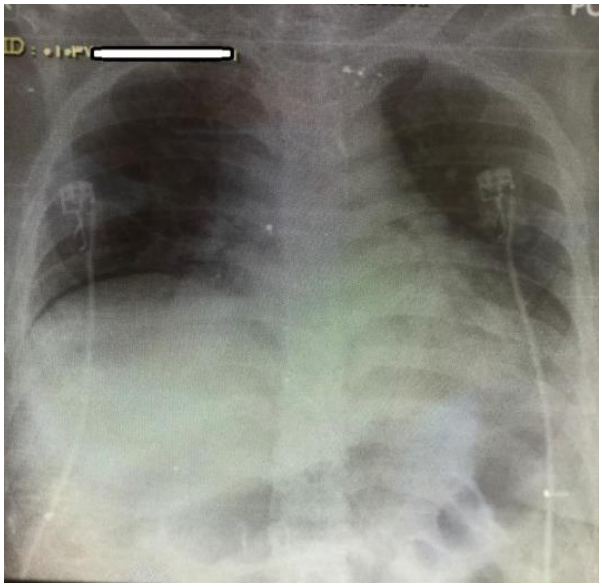

Fig.1: Posteroanterior chest radiograph of the patient.

3- DISCUSSION

What we have reviewed in this case report is a patient who had Cushing's syndrome and developed Guillain-Barre syndrome during pregnancy. The co-occurrence of Guillain-Barre and Cushing syndromes is extremely rare when high levels of endogenous or exogenous steroids are present. In a 1959 study, two cases of concurrent Cushing's syndrome and Guillain-Barre syndrome were reported from Lahey Clinic and one case was reported from Mayo Clinic (8). In all three cases, Cushing's disease preceded the neurological disease and the two syndromes were simultaneously present for several months. Guillain-Barre syndrome was a consequence of respiratory infections in all cases. Symptoms were severe in all cases, with severe neurological and sensory deficits and clear respiratory problems. The diagnosis of Cushing's syndrome was well established and adrenal hyperplasia was pathologically confirmed. Two cases had postoperative neurological abnormalities for several months during which the patients were on cortisone therapy. The third patient died three months after the operation due to an unknown condition. In our study, the patient was a pregnant woman with Cushing's syndrome who developed weakness in limbs after six months, and received a definitive Guillain-Barre diagnosis based on examination of cerebrospinal fluid. In our patient, no symptoms of respiratory infection were observed and virological tests were not performed due to limitations. Guillain-Barre syndrome may have started due to a subclinical viral infection in the patient, but pregnancy can also trigger the disease. Similar to the three previous reports, our patient developed neurological symptoms shortly after adrenalectomy to treat Cushing's disease. A study by Bessler and colleagues reported the emergence of Guillain-Barre syndrome in a patient treated with high doses of corticosteroid for rheumatoid arthritis. The patient received 100 mg of corticosteroids daily for 3 years before the onset of symptoms. As the neurological disease progressed, the patient's corticosteroids dose increased to 300 mg daily, and gradually decreased to 100 mg daily with the gradual improvement of neurologic manifestations. Another case of Guillain-Barre in the presence of high doses of exogenous corticosteroids involves treatment of

erythema multiforme with corticosteroids. Erythema multiforme subsided with the onset of neurological symptoms. The patient later died of respiratory complications (8). In another case study from 1986, Steiner et al. examined the occurrence of Guillain-Barre syndrome in three patients following corticosteroid administration (9). The three patients were suffering from inflammatory demyelinating polyneuropathy based on the diagnostic criteria of Guillain-Barre syndrome. Diagnosis was confirmed based on clinical symptoms, high levels of protein in cerebrospinal fluid, and electrodiagnostic studies. Overall, the disease appeared when the treatment dose of corticosteroids was reduced. The link between corticosteroid treatment and the emergence of Guillain-Barre syndrome can be coincidental. Corticosteroids may also have an effect on regulation of the immune system, which in turn may damage peripheral nerves. There is evidence that demyelination occurs in the presence of inflammatory cells, especially lymphocytes and macrophages since the disease is confined to white blood cells in the peripheral nervous system where the inflammatory processes occur (10).

The temporal sequence of events is such that the inflammatory response occurs before myelin destruction (11). In animal models, experimental allergic neuritis caused by sensitization with peripheral nerve extract mostly led to cellular injury due to cellular immunity (12). Lymphocytes obtained from animals through this method were also capable of destroying myelin in the culture medium (13). It was also possible to transmit experimental allergic neuritis to another animal using lymphocytes taken from affected animals (14). Although the reported sequence of events is associated with inflammatory demyelinating polyneuropathy and may act as the initiator of the pathologic mechanism in the immune system, it appears that specific conditions are needed to enable the disease to progress, such as a genetic predisposition, a specific age, surgery, malignancy, or immunodeficiency (15). The occurrence of inflammatory demyelinating polyneuropathy has been reported frequently in tandem with various immunologic diseases, indicating several factors contribute to the disease (16, 17). Although corticosteroids are considered as immunosuppressant agents, different doses of these drugs can have different effects. For example, in myasthenia gravis, low doses of corticosteroids can exacerbate the disease while high doses are proven helpful. In addition, low doses of azathioprine and hydrocortisone are known to exacerbate, rather than reduce, the symptoms of myasthenia gravis (18). Similarly, patients with lupus may experience a severe recurrence when the dose of the steroid is lowered (19). A controlled study compared the effects of prednisolone and placebo in Guillain-Barre patients, and only reported recurrence in patients treated with steroids (20).

In the laboratory, corticosteroids may facilitate the activity of rat lymphocytes instead of reducing their effect (21). Cyclosporine (another immunosuppressive drug) has a selective suppressive effect on suppressor T cells, such that it suppresses these cells when used at a specific dose and with a specific timing (22). Our patient might have been affected by similar phenomena, being under treatment with corticosteroids while her immune system was stimulated. A selective suppression of suppressor T cells may have stimulatory effects on the development of inflammatory demyelinating polyneuropathy. Different mechanisms seem to cause Guillain-Barre disease in the human body. The administration or increase of corticosteroids in the body, such as that occurring in Cushing's disease, can impair immune regulation, which

could cause flare-ups of Guillain-Barre disease in some patients. This hypothesis should be tested in animal models.

4- CONCLUSION

This case demonstrates a rare coincidence of Cushing's disease and Guillain-Barre syndrome. Due to the increase in corticosteroids due to Cushing's syndrome, it is expected that symptoms of Guillain-Barre syndrome would not occur. This case could indicate that there are several mechanisms for development of Guillain-Barre syndrome and that animal models can be helpful in this context.

5- CONFLICT OF INTEREST: None.

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