CASE REPORT

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Postinfectious Guillain-Barre syndrome in a patient with methimazole-induced agranulocytosis

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Both Graves disease and Guillain-Barre syndrome (GBS) are autoimmune disorders caused by impaired self-tolerance mechanisms and triggered by interactions between genetic and environmental factors. GBS in patients who suffer from other autoimmune diseases is rarely reported, and the development of postinfectious GBS in a patient with Graves disease has not been previously reported in the literature. Herein, we report a patient with Graves disease who developed postinfectious GBS during a course of methimazole-induced agranulocytosis.

Keywords: Agranulocytosis; Graves disease; Guillain-Barre syndrome

INTRODUCTION

Graves disease is a prevalent autoimmune disease that affects approximately 0.5% of the population and is the most common cause (50% to 80%) of hyperthyroidism [1]. Antithyroid drugs have been used as standard therapy for Graves disease and interfere with thyroid hormone synthesis [1]. These drugs, however, have various side effects, including rash, joint pain, hepatic inflammation, and agranulocytosis [1]. Use of thionamides, either propylthiouracil or methimazole, causes agranulocytosis in 0.1% to 0.3% of treated patients [1].

Guillain-Barre syndrome (GBS) is an acute paralytic illness that affects children and adults of all ages. The incidence of the disease worldwide is 0.6 to 4 cases per 100,000 [2]. About two-thirds of cases have been associated with infection occurring 1 to 13 weeks prior to symptom onset, particularly respiratory infection and gastroenteritis [3].

We describe a 57-year-old female patient with Graves disease who suffered from methimazole-induced agranulocytosis and postinfectious GBS.

CASE REPORT

A 57-year-old female presented with fever, abdominal pain, and diarrhea for 3 days. She had been diagnosed

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with Graves disease 25 years prior and was taking methimazole, the dose of which had been increased from 5 to 20 mg twice a day, as of 10 weeks prior. When the patient visited a primary care hospital, her laboratory findings revealed leukopenia and anemia with a white blood cell (WBC) count of 570/mL, absolute neutrophil count of 10/mL, hemoglobin of 9.4 g/dL, and platelet count of 161,000/mL. The physician diagnosed her with methimazole-induced agranulocytosis and stopped methimazole.

During the neutropenic period, the patient developed fever and cough. The pathogen of infection was not confirmed, and she took empirical antibiotics for pneumonia. Clinical features were not improved, and the physician considered fungal pneumonia based on the findings of chest computed tomography. Ten days after onset of respiratory symptoms, she suddenly presented with symmetric weakness of the lower extremities, which progressed to the upper extremities. A nerve conduction study (NCS) showed axonal-type motor polyneuropathy. Intravenous immunoglobulin (IVIg) was started for probable GBS, and she was referred to our hospital for further management.

When the patient first came to our emergency room, a neurologic examination showed quadriplegia, flaccid dysarthria, and aflexia, all of which were worse than 5 days before. The findings of spinal tap were 218.9 mg/dL protein and 10/mL WBC in the cerebral spinal fluid, known as albuminocytologic dissociation, which supported GBS. She was treated with IVIg (0.4 g/kg/day) for 5 days. The patient showed maximum weakness during the first 2 weeks after admission to the intensive care unit, but artificial ventilation was not needed. Neurologic examination and follow-up NCS improved a month after the onset of weakness (Fig. 1).

As methimazole treatment was discontinued, thyrotoxicosis was aggravated. The patient faced an impending thyrotoxic crisis with free thyroxine of 6.59 ng/dL (reference range, 0.89 to 1.8), thyroid-stimulating hormone (TSH) of 0.01 mIU/mL (reference range, 0.35 to 5.5), and TSH receptor antibody of 107 IU/L (reference range, 0.1 to 1.0). Lugol's solution and lithium were prescribed to reduce thyroid hormone production and secretion. A total thyroidectomy was performed three weeks later (Fig. 2).

The patient had been admitted for 40 days and received physical rehabilitation. With gradual neurologic improvement, she could ambulate using a wheelchair when discharged. After discharge, she maintained rehabilitation therapy for 6 months. The patient could walk without orthotics; however, she felt fatigue after a long distance walk.

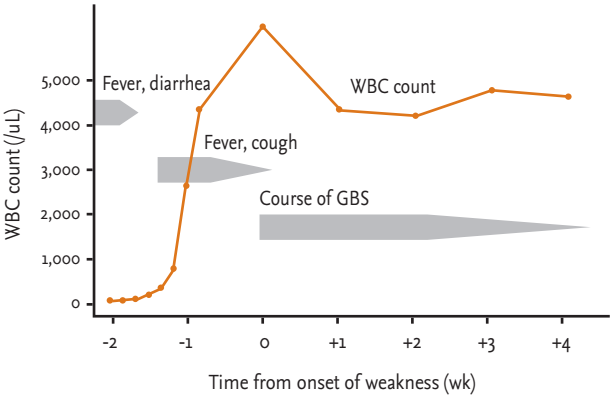

Figure 1. Relation between infections and clinical course of Guillain-Barre syndrome (GBS). WBC, white blood cell.

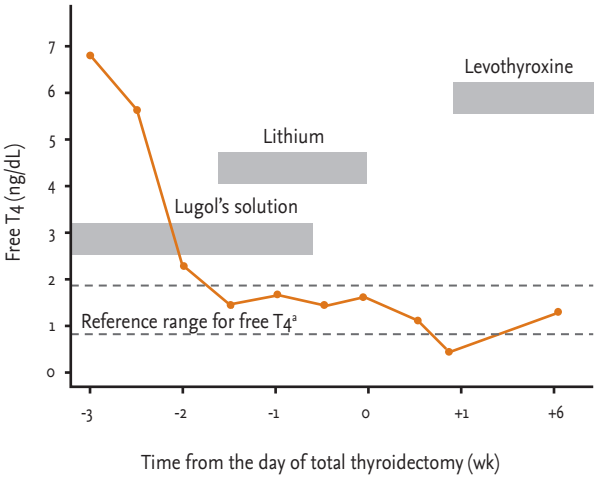

Figure 2. Changes in thyroid function during the clinical course. [a]Reference range for free T4 is 0.89 to 1.8 ng/dL.

DISCUSSION

GBS is an acute flaccid paralysis syndrome characterized by ascending weakness and sensory loss, usually provoked by antecedent infection, vaccination, and/or surgery [2]. About two-thirds of patients have symp-

toms of an infection in the 6 weeks prior to the onset of GBS [2]. In most studies, the predominant preceding infection originated in the upper respiratory tract or gastrointestinal tract [2,3]. Although the pathogen of infection is not often identified, the most frequently reported agents are *Campylobacter jejuni*, Epstein Barr virus, cytomegalovirus, and *Mycoplasma pneumoniae* [2,3]. Among these, *C. jejuni* is the most common cause of infection, reported in 30% to 40% of cases [3,4].

Molecular mimicry seems to be related to GBS development after infection, through the synthesis of autoantibodies against gangliosides of nerves [4]. Autoimmune reactions are found only in a small proportion of all exposed individuals, depending on host factors [4]. Host factors, including genetic polymorphisms, might influence the severity of GBS; however, neither human leukocyte antigen class II alleles nor single nucleotide polymorphisms have shown a consistent association with GBS [5,6].

Paralysis in GBS reaches its nadir within 4 weeks, usually within 2 weeks [2,4]. Then, patients experience a plateau phase, which varies from days to several weeks or even months [4]. The clinical outcome is usually favorable with a spontaneous and complete recovery, although 10% to 20% of patients show residual motor deficits [2]. Even 3 to 5 years after onset of GBS, about one-third of patients have to change their lifestyle due to residual disabilities [7].

Patients with GBS require multidisciplinary treatment to prevent lethal complications. Careful monitoring and control of vital signs are essential, and infections have to be prevented. Immunotherapy, including plasmapheresis and IVIg, is the mainstay of treatment for GBS. Van der Meche and Schmitz [8] showed that treatment with IVIg was at least as effective as plasmapheresis in acute GBS. Currently, the American Academy of Neurology practice guidelines recommend that either plasmapheresis or IVIg be applied for the treatment of immobile patients with GBS [9].

Our patient had symptoms of gastroenteritis before hospitalization and developed respiratory symptoms after admission. Two infectious events, which are considered precipitating factors for GBS, occurred within 3 weeks before the onset of weakness, and no pathogen was indentified. We presume that methimazole-associated agranulocytosis induced an opportunistic infection, which may have evoked GBS. The patient showed maximum weakness during the first 2 weeks, and neurologic signs improved after 4 weeks. Even after her recovery for over a year, she still felt fatigue with daily activities.

Our patient's history included serial presentation with Graves disease and GBS. To our knowledge, there is no other case report of postinfectious GBS in a patient with Graves disease. Further investigation into similar cases could reveal the relationship of these autoimmune diseases.

Conflict of interest

No potential conflict of interest relevant to this article is reported.

REFERENCES

1. Brent GA. Clinical practice: Graves' disease. N Engl J Med 2008;358:2594-2605.
2. Vucic S, Kiernan MC, Cornblath DR. Guillain-Barré syndrome: an update. J Clin Neurosci 2009;16:733-741.
3. Guillain-Barre Syndrome Study Group. Guillain-Barré syndrome: an Italian multicentre case-control study: Guillain-Barré Syndrome Study Group. Neurol Sci 2000;21:229-234.
4. van Doorn PA, Ruts L, Jacobs BC. Clinical features, pathogenesis, and treatment of Guillain-Barré syndrome. Lancet Neurol 2008;7:939-950.
5. Geleijns K, Schreuder GM, Jacobs BC, et al. HLA class II alleles are not a general susceptibility factor in Guillain-Barré syndrome. Neurology 2005;64:44-49.
6. Geleijns K, Jacobs BC, Van Rijs W, Tio-Gillen AP, Laman JD, van Doorn PA. Functional polymorphisms in LPS receptors CD14 and TLR4 are not associated with disease susceptibility or Campylobacter jejuni infection in Guillain-Barré patients. J Neuroimmunol 2004;150:132-138.
7. Bersano A, Carpo M, Allaria S, Franciotta D, Citterio A, Nobile-Orazio E. Long term disability and social status change after Guillain-Barré syndrome. J Neurol 2006;253:214-218.
8. van der Meche FG, Schmitz PI. A randomized trial comparing intravenous immune globulin and plasma

http://dx.doi.org/10.3904/kjim.2013.28.6.724

exchange in Guillain-Barré syndrome: Dutch Guillain-Barré Study Group. N Engl J Med 1992;326:1123-1129.
9. Hughes RA, Wijdicks EF, Barohn R, et al. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2003;61:736-740.