Dear Editor,

Guillain–Barré syndrome (GBS) is an autoimmune, acute-onset polyneuropathy, characterized by ascending paralysis and areflexia. Both intravenous immunoglobulin (IVIg) and therapeutic plasma exchange (TPE) may be used in the treatment of GBS.[1,2]

TPE is indicated in the treatment of neurological, hematologic, dermatological, rheumatological, renal, and metabolic diseases (i.e., thyrotoxicosis) that are resistant to conventional treatments or in which rapid improvement is expected.[3,4]

Because medical treatment of thyrotoxicosis during pregnancy may cause some fetal problems, TPE may be the choice in pregnant patients as a safe, well-tolerated, and effective procedure.[5,6]

Here, we report a pregnant woman presenting with thyrotoxicosis, encephalopathy, ophthalmopathy, and quadriplegia. She was treated with five sessions of therapeutic plasma exchange (TPE) with the diagnosis of thyrotoxicosis and overlapping Bickerstaff encephalitis and Guillain–Barré syndrome. After TPE treatment, her hormone levels returned to normal and there was a prominent improvement in her neurological findings.

A 34-year-old pregnant woman presented with a 3-day history of weakness, fatigue, difficulty in walking, nausea, vomiting, and blurred and double vision. She was on the 14th week of gestation. She had no history of systemic or autoimmune diseases.

Physical examination of the patient showed a body temperature of 38°C, pulse rate of 165 beats/min, blood pressure of 120/60 mmHg, and respiratory rate of 20/min. She had confusion and hypophonic speech. Limitation of conjugate vertical and horizontal gaze was observed. Her muscle strength was bilaterally 4/5 in the deltoid, 3/5 in the quadriceps, and 4/5 in feet dorsiflexor muscles. Deep tendon reflexes (DTR) were absent in four extremities. She complained of pain, especially in the lower limbs.

The laboratory values are shown in Table 1.

Elevated levels of thyroid hormones, tachycardia, and high temperature were attributed to thyroid storm; propylthiouracil (200 mg/day), propranolol (60 mg/day), and methylprednisolone (20 mg/day) were applied. She was referred to the intensive care unit (ICU).

Doppler appearance of the thyroid gland revealed increased vascularity, and ultrasonography showed heterogeneous parenchyma. Anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin (anti-TG), and anti-TSH receptor antibody levels were within normal limits.

As she had acute onset quadriplegia and absence of DTR, lumbar puncture was performed to help the diagnosis of possible GBS or variants of GBS such as overlapping Bickerstaff brainstem encephalitis and GBS (BBE/GBS). There was no albuminocytologic dissociation. Her clinical findings were in deterioration; therefore, on the third day of her admission, TPE was applied for rapid achievement of hormonal and clinical control. Five sessions of TPE were done consecutively (on alternate days). After the second TPE, the patient’s vaginal bleeding started and she had complete abortus after the third TPE. After TPE, thyroid hormone concentrations decreased and clinical improvement started. Her confused state and ophthalmopathy disappeared in a few days. Improvement in muscle strength was slow. Both the clinical features and laboratory findings recovered in a month.

Electroencephalography of the patient, who was in a confused state, showed slowing of waves bilaterally in the frontal regions. Electroneuromyography (ENMG) revealed myopathic findings, especially in lower limb muscles and normal nerve conduction studies in the early period of the disease. Cranial, cervical, dorsal, and lumbar magnetic resonance imaging (MRI) showed no abnormalities. Paraneoplastic antibody panels and vasculitis-specific autoantibodies were

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**Table 1: Laboratory findings of the patient**

| Test       | Value before TPE | Value after TPE | Normal range       |
|------------|------------------|-----------------|--------------------|
| WBC        | 8.17×10⁶/mm³     | 7.76×10⁶/mm³    | 3.7-10.01×10⁶/mm³  |
| Hgb        | 9.23 g/dL        | 8.99 g/dL       | 10.8-14.2 g/dL     |
| Hct        | 27.6%            | 27.3%           | 35-45%             |
| RBC        | 3.15×10¹²/mm³    | 3.12×10¹²/mm³   | 3.6-4.69×10¹²/mm³  |
| Platelet count | 150×10³/mm²    | 212×10³/mm²     | 155-366×10³/mm²    |
| ESR        | 106 mm/1st h     | 20 mm/1st h     | 0-30 mm/1st h      |
| AST        | 26 U/L           | 31 U/L          | 0-32 U/L           |
| ALT        | 43 U/L           | 20 U/L          | 0-32 U/L           |
| GGT        | 47 U/L           | 32 U/L          | 5-36 U/L           |
| CK         | 40 U/L           | 24 U/L          | 0-170 U/L          |
| Albumin    | 5.2 g/dL         | 6.2 g/dL        | 6.4-8.3 g/dL       |
| Calcium    | 8.1 mg/dL        | 9.1 mg/dL       | 8.6-10.2 mg/dL     |
| Free T3    | 14.27 pg/mL      | 2.34 pg/mL      | 2.0-4.4 pg/mL      |
| Free T4    | >7.77 ng/dL      | 1.45 ng/dL      | 0.93-1.7 ng/dL     |
| TSH        | <0.005 µIU/mL    | 0.01 µIU/mL     | 0.27-4.2 µIU/mL    |

WBC: White blood cell; RBC: red blood cell; ESR: erythrocyte sedimentation rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyl transferase; CK: creatine kinase; TSH: thyroid-stimulating hormone; T3: triiodothyronine; T4: thyroxine.
normal. Anti-ganglioside GD1a, GQ1b, and GT1a antibodies were positive.

This case is a very complicated presentation of a variant of GBS with co-existing thyrotoxicosis, myopathy, and pregnancy, which may be a facilitative factor for this multisystemic involvement. This is the first reported case in the literature with overlapping BBE/GBS and thyrotoxicosis. Concomitant occurrence of GBS and Graves’ disease is very rare. Although the exact mechanism of this association is not well-understood, autoimmunity triggered by multiple factors (environmental or genetic) seems to be the leading cause of the occurrence of both diseases. We aimed to emphasize the benefit of TPE in overlapping BBE/GBS with anti-GQ1b positivity and thyrotoxicosis, which were probably co-existing, separate autoimmune events, triggered by a common factor.

Gestational transient thyrotoxicosis was considered in the differential diagnosis of thyrotoxicosis in our patient. However, thyroid storm or life-threatening severe thyrotoxicosis was not expected in gestational transient thyrotoxicosis. As thyroid storm was observed clinically and ultrasonographic examination revealed increased vascularity and heterogeneous parenchyma, our patient was diagnosed as having autoantibody-negative Graves’ disease. Radioactive iodine treatment could not be given due to her pregnancy. TPE might be the treatment option to achieve rapid improvement in Graves’ disease.

In pregnancy, the diagnosis of GBS should be made as soon as possible and should be treated promptly. IVIg or TPE have been of proven benefit, especially in rapidly progressive cases. Our patient had also thyrotoxicosis and there was a need for a fast therapeutic response. We chose TPE instead of IVIg because its beneficial effects could be observed within 2 weeks.

TPE can be safely performed in GBS of pregnancy and leads to improvement in both fetal and maternal survival rates. There exist no distinct safety issues related to TPE in pregnancy compared to TPE in the general population. Only, the clinician should be careful about hypotension, which is described more often during TPE in pregnant cases rather than in non-pregnant cases.

Some authors report that GBS, Miller Fisher syndrome, and Bickerstaff brainstem encephalitis might be within the same disease spectrum. Overlapping signs and symptoms between these diseases and a high titer of anti-GQ1b IgG antibody might suggest a common autoimmune mechanism. Established treatments of GBS might be suggested in these conditions.

Our patient was diagnosed as having overlapping BBE/GBS because she had limb weakness, areflexia, disturbance in consciousness, and ophthalmopathy. She responded well to TPE therapy and recovered in a month. Her recovery implied that the removal of the autoantibody might be effective for patients with anti-GQ1b IgG antibodies. Moreover, muscle weakness in proximal muscles, prominent in lower limbs, myopathic changes in ENMG, and normal creatine kinase (CK) levels might be related to thyroid dysfunction. However, anti-GQ1b IgG positivity, which is a strong marker for variants of GBS, led us to think that overlapping BBE/GBS dominated the multidisciplinary diagnostic approach of our patient rather than probable thyroid myopathy.

In conclusion, TPE may be used in GBS and its variants and also in thyrotoxicosis to achieve rapid clinical improvement. We emphasize the comorbidity of overlapping BBE/GBS and thyrotoxicosis in a pregnant patient and the life-saving, beneficial effect of TPE in such complicated cases. Early performed TPE may be life-saving in severe autoimmune diseases with multisystemic involvement and that are associated with pregnancy.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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Dear Editor,

Two siblings born from consanguineous parents were admitted to our hospital with the complaint of seizures. The seizures were in the form of unresponsiveness attacks that lasted less than 1 min. Before these seizures, the patients described an aura with an unusual bad smell. No ictal motor phenomenon was described.

The first patient was a 37-year-old man. In addition to the seizures, he also had behavioral changes. The patient was no longer afraid of animals that he used to fear. He had irritability and aggressive behaviors, as well as increased libido and hypersexuality. He had sex with multiple partners multiple times despite being married. In his past medical history, he had a putaminal hemorrhage [Figure 1a]. The patient also had hoarseness since early childhood. His neurological examination was normal. On physical examination, he had alopecia. There were multiple papules on the eyelid margins and the malar region (moniliform blepharosis) [Figure 1b]. Cranial magnetic resonance imaging (MRI) showed bilateral, symmetrical calcification of the hippocampus and parahippocampal regions, which had a hypointense appearance on T1 and Fluid-attenuated inversion recovery (FLAIR) sequences [Figure 1c and d]. Cranial MRI features were compatible with Urbach-Wiethe disease. Extracellular matrix protein 1 (ECM-1) gene mutation was shown by genetic testing. Electroencephalography (EEG) did not show any abnormalities.

The second patient was a 23-year-old man. Although he did not have any neuropsychological complaints, he had hoarseness and alopecia. His neurological examination was normal. He also had bilateral, symmetrical calcification of the hippocampus and parahippocampal regions [Figure 2]. The genetic testing showed ECM-1 gene mutation. EEG did not show any abnormalities.

Valproic acid was the preferred drug for the patients. The seizures were controlled with valproic acid therapy. Urbach-Wiethe disease (also known as lipoid proteinosis; hyalinosis cutis et mucosae) is a rare disorder caused by mutations in ECM-1.

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