Tuberculosis Meningoencephalomyelitis in Good’s Syndrome: a Case Report

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HIGHLIGHTS

• Good’s syndrome is a rare and highly suspicious disease in patients with thymoma.
• Immunological tests should be performed to confirm the diagnosis.
• This can prevent a delayed diagnosis and allow the timely initiation of treatment.
ABSTRACT

Good’s syndrome is a rare disease characterized by thymoma associated with combined B- and T-cell immunodeficiency in adults. Due to the lack of early onset of symptoms, it is difficult to diagnose this disorder. A 44-year-old man diagnosed with thymic carcinoma was admitted to the hospital with quadriplegia for 6 months. Brain abscess and meningoencephalitis were identified in the magnetic resonance imaging (MRI) of the brain. Antibiotics, steroid, and intravenous immunoglobulin treatment were provided for 3 months. Follow-up MRI showed progression to C7-level. The radiologic findings were consistent with tuberculosis infection and thus, the patient was treated with anti-tuberculosis medication. MRI of the brain and spine showed an improved state of meningoencephalomyelitis. In a laboratory study, there were decreased levels of peripheral B-cell and CD4 T-cell and decreased CD4:CD8 ratio; therefore, it confirmed that cellular immunity deteriorated. In addition to clinical findings, we were able to diagnose the patient with Good’s syndrome. Good’s syndrome is a highly suspicious disease in patients with thymoma who have recurrent unusual infections. Immunologic tests should be performed for diagnosis in which it can prevent delayed diagnosis and allow timely treatment.

Keywords: Tuberculosis Meningitis; Thymoma; Myasthenia Gravis; Immunologic Deficiency Syndromes; Rehabilitation

INTRODUCTION

Thymoma is a rare cancer, but it is the most common type of tumors in the entire mediastinum, accounting for approximately 30% of mediastinal masses [1]. Thymic carcinoma, like thymoma, is a very rare cancer of the thymus but more aggressive in its behavior. The 5-year survival rate is 30%–50%, with poor prognosis [2]. Among patients with thymoma, less than 5% of patients are diagnosed with Good’s syndrome—initially discovered in 1955—have been associated with low or absent B-cells, hypogammaglobulinemia, and a deficiency of cell-mediated immunity [3]. Typical laboratory findings are characterized by hypogammaglobulinemia, decreased peripheral B cells, cluster of differentiation 4 (CD4) lymphopenia, and a reversal of CD4/CD8 ratio on immunologic tests [1]. Patients present with recurrent infections, diarrhea, and lymphadenopathy.
Tuberculosis meningitis (TBM) is the most severe form of tuberculosis (TB) with a mortality rate of 15%–68% and over 50% of the survivors are left with neurological sequelae [4]. Early diagnosis and initiation of effective treatment of TBM is one of the most important prognostic factors that reduces mortality and long-term disability [4]. Unfortunately, because of similar clinical features to meningoencephalitis, which includes headache, fever, vomiting, changes in mental status and focal neurologic features, early diagnosis of TBM is difficult. Furthermore, the data on neurocognitive and functional impairment of TBM are limited [5]. These can lead to a paucity of appropriate treatment [5].

Only a few cases of Good’s syndrome have been reported previously. Among them, there have been no case reports of Good’s syndrome associated with central nervous system tuberculosis. Here we present the case report of rehabilitation treatment of tuberculosis meningoencephalomyelitis in patient diagnosed with Good’s syndrome.

**CASE REPORT**

A 44-year-old male had been hospitalized at the secondary training hospital in August 2016 with fever, general weakness, poor oral intake and dyspnea. He was diagnosed with pneumonia and received conservative management including antibiotics such as piperacillin and tazobactam. He was previously diagnosed with thymoma and myasthenia gravis. There were recurrence and pleural metastasis of thymoma three times in 2004, 2006, and 2014. In April of 2016, he was diagnosed with Pneumocystis jiroveci pneumonia (PCP) and visual loss in his left eye due to viral retinitis.

In October 2016, he exhibited headache, nystagmus, progressive quadriplegia for 6 months, neuropathic pain below cervical level, and mild dysarthria without cognitive impairment. In the neurological examination, the patient’s score on the Korean version of the Mini-Mental State Examination was 30 points. On the manual muscle test (MMT) of the Medical Research Council (MRC), the patient was classified as grade 3 on both upper and lower extremities [6]. In the brain and cervical spine magnetic resonance imaging (MRI) showed brain abscess at the cervicomedullary junction, and basal meningeal enhancement (Fig. 1A-C). The antibiotics were changed from piperacillin and tazobactam to ceftriaxone and vancomycin because a central nervous system (CNS) infection was suspected. The patient also received intravenous immunoglobulin (IVIG) therapy for 400 mg once every 5 days, 500 mg twice a day for 2 days. However, one month later, steroid pulse therapy was administered based on disease progression; the meningoencephalitis had progressed to the cervical spinal cord (Fig. 1D).

His neuropathic pain worsened according to the Numeric Rating Score (NRS) from 3 to 7 and his MMT grade deteriorated from grade 3 to 2 on both sides. His functional levels were totally dependent, so he required maximal assistance for sitting due to progression of motor weakness and lack of muscle endurance.

The cerebrospinal fluid (CSF) study showed a low glucose (38 mg/dL), a high protein (294.7 mg/dL), a high adenosine deaminase level (5.8 IU/L), a negative spinal acid-fast bacilli (AFB) smear, and a negative mycobacterial culture. Additionally, the MRI evidence of basal meningeal enhancement, an infarction in the left basal ganglia, and periventricular white matter was strongly suggestive of tuberculosis meningitis (Fig. 1B). After 6 months (initial two-month period of intensive therapy with four drugs and followed by a prolonged continuation therapy with three drugs except pyrazinamide due to adverse effect) of
anti-tuberculous medication (ioniazid 300 mg daily, rifampin 600 mg daily, ethambutol 1,200 mg daily, and pyrazinamide 500 mg daily) with adjunctive glucocorticoid therapy (dexamethasone and oral prednisolone), the follow-up brain and cervical spine MRI showed improvement (Fig. 2A and B).

The patient had undergone rehabilitation treatment for 8 weeks. The treatments included range of motion exercises and stretching exercises for the prevention of contracture, strengthening exercises and activities of daily living (ADL) training for functional improvement, tilt table standing for the prevention of orthostatic hypotension, management of coccyx pressure ulcer (3 × 4 × 1 cm sized, stage 3), and neuropathic pain control. Although, the patient’s functional levels and MMT grade showed no definite improvement, the severity of neuropathic pain was improved from the NRS seven to five and the coccyx pressure ulcer was improved to 2 × 1 cm size of stage 2 as compared with the time before the anti-tuberculous therapy and rehabilitation treatment. Although we could not perform videofluoroscopic swallow study due to coccyx pressure ulcer, the patient showed intermittent liquid aspiration symptom. Under the clinical
suspicion of dysphagia, dysphagia rehabilitation treatment such as thermal stimulation, neck strap muscle strengthening exercises were conducted and patient education was given. The patient continued his general diet. He showed no clinical symptom aggravation and complications such as aspiration pneumonia.

The anti-tuberculous medication was maintained due to a sustained positive result of the interferon gamma test and the recommended period according to literature. The immunological tests revealed a decreased peripheral B cell level (0.8%, normal range 6.22% to 22.7%), a decreased CD4 T cell level (17.7%, normal range 28.4% to 56.4%), and a decreased CD4:CD8 ratio (0.45). Therefore, it was confirmed that cellular immunity was deteriorated according to immunological tests and with the clinical findings, we were able to diagnose the patient with Good’s syndrome. Informed consent documentation was signed by the patient.

**DISCUSSION**

Good’s syndrome is a very rare disease, and its typical findings include combined B and T cell immunodeficiency. The laboratory findings are characterized by hypogammaglobulinemia, low or absent B cells, defects in the cell-mediated immunity (especially in the peripheral B cells), CD4 lymphopenia, and a reversal of the CD4:CD8 ratio [1,3]. The CD4:CD8 ratio is usually greater than one in immunocompetent individuals [8]. In this case, the patient’s past medical history showed the recurrence of unusual infections, such as viral retinitis, chronic otitis media, TBM, and recurrent pneumonia (including PCP), despite his young age. Therefore, we conducted the immunological testing under the suspicion of an immunodeficiency status. The immunological examination revealed peripheral B cell depletion, CD4+ lymphopenia, and a reversal of the CD4:CD8 ratio. Thus, we were able to diagnose thymoma with immunodeficiency, or Good’s syndrome.

TBM is a relatively rare disease that accounts for approximately 1% of all TB cases. The mortality rate of TBM is 15%–68% and over 50% of the survivors are left with long term disability [4]. The diagnosis of TBM can be difficult because the clinical symptoms of TBM are broad and
current laboratory diagnostic tests lack sensitivity. However, an early diagnosis is vital since prognosis depends mainly on the severity of the patients' symptoms after antibiotics are first administered and the timing of when the therapy is initiated [4,7]. In countries with a high incidence of TB, the possibility of TBM should be considered in all patients presenting with meningoitis. Furthermore, empiric anti-tuberculous therapy should be started immediately in patients with meningitis and CSF findings of elevated protein levels, low glucose levels, and lymphocytic pleocytosis, if there is evidence of TB elsewhere [8].

Although the CSF examination of the AFB smears and cultures was negative, the other CSF study results showed a low glucose concentration (38 mg/dL, normal range 40 to 80 mg/dL), elevated protein level (294.7 mg/dL, normal range 15 to 45 mg/dL), and elevated adenosine deaminase level (5.8 IU/L, reference range > 5 IU/L) [9]. Additionally, the MRI evidence of basal meningeal enhancement, an infarction in the left basal ganglia, and periventricular white matter was also strongly suggestive of tuberculosis meningitis (Fig. 1B) [10]. Therefore, anti-tuberculous therapy was initiated based on a strong clinical suspicion. After 6 months of continuous medication, follow-up MRI of the brain and cervical spine scans showed improvement in the abscess and meningoencephalitis involving the brainstem and cerebellum (Fig. 2A and B). The treatment regimen is based upon the antituberculosis medication used for pulmonary TB: a 2-month initiation phase with four drugs and a continuation phase with 2 drugs (isoniazid and rifampicin) for 7 to 10 months [11]. Adjunctive corticosteroids for 6 to 8 weeks are known as reducing the mortality from TBM [12,13]. In this case, anti-tuberculous therapy with adjunctive corticosteroids was administered for a sufficient dose and duration, and rehabilitation treatment was also performed together. Although the patient’s severity of neuropathic pain and the stage of coccyx pressure ulcer were improved compared with the time before the anti-tuberculous therapy and rehabilitation treatment, it was not enough to improve functional impairment because of delayed diagnosis and treatment. The patient had already advanced illness with severe quadriplegia when the therapy was initiated. However, rehabilitation therapy in patients with an advanced illness is important for improving health-related quality of life by maintaining the general condition and reducing complications such as pain, pressure ulcer, joint contracture, and disuse atrophy of skeletal muscle fibers.

In this case report, the patient was finally diagnosed with TBM and underlying good’s syndrome. There were no case reports of Good’s syndrome with TBM. Through this case report, we expect early diagnosis and achievement of a timely treatment in patients with similar symptoms and progress. If the initiation of appropriate treatment was performed at a time when the patient’s neurologic deficits were not severe, the prognosis of the patient could have been different. In general, it is known that a thymectomy and steroid therapy do not return a state of immunodeficiency to normal [1]. Up until now, immunoglobulins (Ig) replacement has been proven to be effective in treating patients with Good’s syndrome. Ig therapy has been shown to prevent infection, reduce the hospitalization period, and reduce antibiotic use [14]. However, there is no established treatment to reverse the immune deficiency. Therefore, a timely diagnosis of Good’s syndrome through clinical suspicion is important to reduce the long-term complications and mortality in these patients. In addition, adequate therapy, such as proper antibiotics and IVIG infusions may be essential for the treatment of Good’s syndrome patients.

In conclusion, one should be highly suspicious of Good’s syndrome in patients with thymoma who have recurrent, persistent, and unusual infections. Immunological tests for
the serum Ig and cellular immunity functions should be performed to confirm the diagnosis. This can prevent a delayed diagnosis and allow the timely initiation of treatment.

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