Case Report

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Hemoptysis Resolution with Rituximab in Behçet's Disease: A Case Report

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Behçet's disease (BD) is a multisystem, progressive, and inflammatory disorder of unknown etiology. Vasculitis is believed to underlie various clinical manifestations of BD and is known to be one of the main causes of death due to BD, in cases of large vessel involvement. The current study is done in order to examine the effects of rituximab on the patient's debilitating clinical manifestations, as a result of not responding to the standard treatment regimens. The present case is a 28-year-old female patient with BD associated vasculitis. She was referred to the respiratory referral center, chiefly complaining of intermittent episodes of massive hemoptysis. She had also recurrent oral and genital ulcers, and difficulty in walking, despite considering the common treatment approaches for BD. Our patient received two courses of rituximab in combination with intravenous methylprednisolone. Over six months follow-up period from the date of treatment initiation with rituximab, symptoms of BD such as recurrent hemoptysis and aphthous ulcers were reduced in both frequency and severity. Lower limb weakness and difficulty in walking were improved as well. To summarize, rituximab appears to be an effective alternative for treatment-resistant vasculitis in BD patients.

Key words: Behçet's disease; Hemoptysis; Refractory cases; Rituximab; Vasculitis

INTRODUCTION

Behçet's disease (BD) is a multisystem, progressive, and inflammatory disorder of unknown etiology (1, 2), mainly seen in distinct geography, extending from the Mediterranean and the Middle East to the Far East countries (3). BD is characterized by a triple-symptom complex of recurrent attacks of oral aphthous and genital ulcers, and ocular lesions; other clinical features include dermatological, cardiovascular, gastrointestinal, and neurological manifestations (4). Vasculitis is believed to underlie various clinical manifestations of BD. The vasculitis of BD affects arteries and veins of all sizes. Large vessel vasculitis in BD patients is associated with an increased rate of mortality. High-risk patient identification, early detection of vasculitis, and rigorous treatment program are essential for optimal patient outcomes (5). The aim of this presentation is to report the effects of rituximab, as a novel treatment approach, in a patient with uncontrolled BD, despite administration of the standard treatment regimen.

CASE SUMMARIES

A 28-year-old female patient was referred to the Masih Daneshvari hospital, chiefly complaining of massive hemoptysis. She reported chest pain and dyspnea following daily activities accompanying with dry cough

and intermittent episodes of hemoptysis firstly developed 3 years ago. Also, she has been suffering from recurrent and painful oral ulcers for several years with genital ulcerations appearing recently. Moreover, dizziness and impaired balance were reported by the patient as well as pain, edema, and progressive weakness in the lower right leg, which resulted in walking difficulties.

The following medications prescribed for probable diagnosis of rheumatoid arthritis, were reported in her previous drug history: prednisolone 5 mg daily, pantoprazole 40 mg twice daily, colchicine 1 mg daily, azathioprine 75 mg daily in two divided doses, bisoprolol 1.25 mg twice daily, domperidone 10 mg three times daily, alprazolam 0.5 mg twice daily and dextromethorphan 15 mg four times daily. Past surgical history included cholecystectomy and appendectomy, 6 and 15 years ago, respectively.

Echocardiographic evaluations showed mitral valve prolapse, mild diastolic dysfunction, tricuspid regurgitation, and pleural effusion while other values were normal, and sinus rhythm was observed. Bronchoscopic findings showed no abnormality. Similarly, there was no pathological significance on CT scan. The patient underwent two sessions of bronchial artery embolization for hemoptysis, without any remarkable symptom improvement. Embolization was performed for several branches of bronchial arteries. The procedure was not carried out for one artery despite identifying an abnormal flow due to the possibility of anterior spinal artery complication. Neurology consultation was performed due to 3 episodes of syncope, and psychosomatic disorder was diagnosed in the patient. Finally, diagnosis of BD was then made. Since then, the patient has received multiple corticosteroid and cyclophosphamide pulse therapies for about 2 years.

Patient's symptoms have shown no improvement despite receiving the therapies as mentioned above ever since she was diagnosed with BD. In order to better manage the patient's chronic condition of vasculitis and control symptoms, particularly hemoptysis, she received two courses of rituximab with one-month interval. In each course, 1 g methylprednisolone was infused intravenously in two consequent days before rituximab administration; the patient received 600 mg rituximab by IV infusion on day three of the treatment session. Due to the patient's history of drug allergy, premedication with acetaminophen, chlorpheniramine, and hydrocortisone was considered.

Follow-up and outcomes

Over six months follow-up period from the date of treatment initiation with rituximab, symptoms of BD such as recurrent hemoptysis and oral and genital aphthous ulcers were reduced in frequency and severity. In addition, lower limb weakness and difficulty in walking were improved significantly.

DISCUSSION

Arterial involvement in BD is uncommon but can lead to dilatations and aneurysms of medium- and large-sized arteries (5, 6). The standard medical approach in BD patients suffering from vascular complications involves administration of high-dose glucocorticoids and the second immunosuppressive agent typically cyclophosphamide (7). However, there is no established treatment protocol available for treatment-refractory cases due to the lack of adequate data on these conditions.

Among autoimmune diseases for which rituximab is indicated, rheumatoid arthritis is the most prevalent condition. Limited studies have been done on the effect of rituximab in Behçet's patients, with most of them exploring the ocular manifestations of the disease (8). Nearly all of these reports suggest successful ocular disease treatment with rituximab, particularly in severe and resistant cases (9-11). Case studies on other manifestations of BD, including neurologic involvement and myelitis, are indicative of lasting disease control with rituximab administration.

To the best of our knowledge, no study has examined the effect of rituximab on BD patient with pulmonary artery vasculitis until now. In our case, cyclophosphamide

administration, along with high-dose corticosteroid therapy, as an initial attempt to control symptoms, did not respond well to treatment. Artery embolization did not provide further satisfactory results either. Therefore treatment with rituximab, as an alternative therapy option for a second immunosuppressive agent in BD patients, was assessed.

Rituximab is a chimeric monoclonal antibody that was first approved by the FDA for lymphoma. The drug specifically targets the CD20 antigen (12, 13). Antibody connection to the receptor provokes initiation of a signal cascade that results in B cell death. Although the precise mechanism of cell death remains obscure, it is thought to be caused by a combination of pathways including antibody-dependent cell-mediated cytotoxicity, complement-mediated lysis, growth inhibition and apoptosis (14, 15). Peripheral B cell depletion is effective in inducing remission of B cell monoclonal proliferation as well as systemic autoimmune diseases. Rituximab is typically given as an intravenous infusion under close medical supervision. The therapy results in rapid, long-lasting depletion of peripheral B cells. Additionally, as B cells act as antigen-presenting cells, their removal influence T cell activation. This is suggestive of rituximab's potential use in addition to T-cell-mediated conditions such as BD (10, 11, 16).

CONCLUSION

Considering the results of this study, rituximab appears to be an effective alternative for the treatment of pulmonary artery involvements in BD patients. Long-term remission of inflammatory exacerbations and symptom recurrences by combination therapy of high-dose methylprednisolone and rituximab may give a promising therapeutic option for treatment-resistant vasculitis cases.

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