Case Report

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Successful treatment of primary immune thrombocytopenia accompanied by diabetes mellitus treated using clarithromycin followed by prednisolone

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Summary **Macrolides have immunomodulatory effects including anti-inflammatory effects as well as antibacterial activity. In consideration of these immunomodulatory effects, we report a patient with primary immune thrombocytopenia (ITP) treated using clarithromycin (CAM), a macrolide, followed by prednisolone (PSL). A 78-year-old man with thrombocytopenia was admitted to our hospital for further examination. Initial laboratory data showed reduced platelet counts (1.7×10^4/μL). Finally, we diagnosed the patient as having primary ITP. Because the patient was suffering from diabetes mellitus (DM), he was treated with CAM as an alternative to PSL. The platelet count increased to 6.1×10^4/μL. The CAM treatment was terminated owing to gradual nausea and palpitation. During the CAM treatment, the DM was under control. We reinitiated treatment for ITP. The patient was successfully treated using PSL without severe hyperglycemia. This case shows that CAM treatment may represent a useful option for ITP patients who cannot receive PSL due to DM.**

Keywords: Immune thrombocytopenia, clarithromycin, prednisolone

1. Introduction

Macrolides such as clarithromycin (CAM) and erythromycin (EM), have not only antibacterial activity but also immunomodulatory effects including anti-inflammatory effects. In consideration of their immunomodulatory effects, we have previously reported several cases of immune thrombocytopenia (ITP) successfully treated using CAM or EM (*1-4*). We report herein a case of primary ITP accompanied by diabetes mellitus (DM) treated using CAM followed by prednisolone (PSL).

2. Case Report

A 78-year-old man with thrombocytopenia was admitted to our hospital for further examination. Physical examination revealed neither articular swelling nor skin rash suggestive of collagen diseases. His laboratory results included the following: white blood cell counts 5,480/μL (basophils 0.3%, eosinophils 4.2%, neutrophils 69.2%, lymphocytes 19.3%, monocytes 7.0%), hemoglobin (Hb) 10.0 g/dL, platelet count 1.7×10^4/μL, C-reactive protein 0.25 mg/dL, immunoglobulin (Ig) G 1,707 mg/dL, IgM 79 mg/dL, IgA 189 mg/dL, fasting blood sugar 150 mg/dL, and hemoglobin A_{1C} 6.5% (normal range, 4.6-6.2%). Neither antinuclear antibody nor rheumatoid factor was detected. The patient was negative for *Helicobacter pyroli* (HP) stool antigen using the enzyme-linked immunosorbent assay and for *HP* IgG antibodies. A bone marrow aspiration smear revealed normal bone marrow with a nucleated cell count of 90,000/μL and a megakaryocyte count of 55/μL without dysplasia or hemophagocytosis. No abnormal findings suggestive of infection were found in the systemic survey, including the chest roentgenogram and urinalysis. Based on these findings, we diagnosed the patient as having primary ITP. The patient was suffering from DM; therefore, in consideration of its immunomodulatory effects, we initially prescribed CAM (800 mg/day) as an alternative to PSL, after

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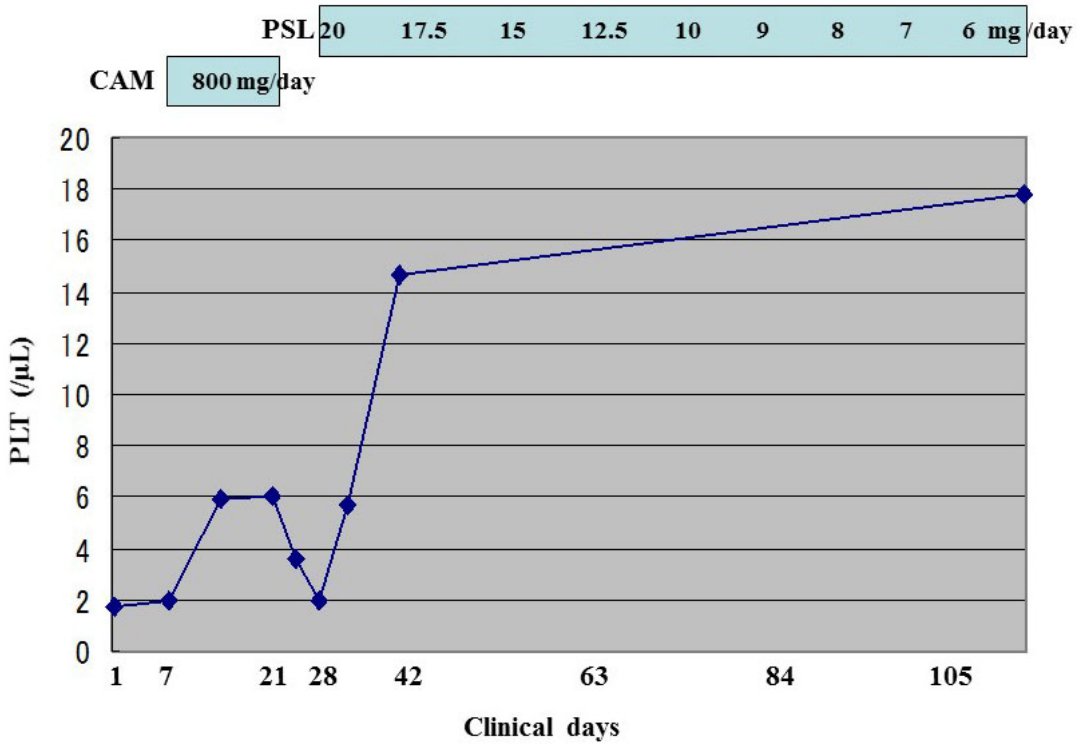

Figure 1. Laboratory data and prescribed agents on clinical days. CAM: clarithromycin, PSL: prednisolone, PLT: platelet

obtaining his informed consent. The clinical course is shown in Figure 1. Two weeks after CAM treatment, the platelet count increased from 2.0 to 6.1 × 10^4/μL. The CAM treatment was terminated owing to gradual nausea and palpitation that are probably adverse reactions of CAM. As a result, the platelet count decreased to 2.0 × 10^4/μL. During the CAM treatment, the DM was under control. We reinitiated treatment for ITP. This time the patient was administered PSL (20 mg/day). After 2 weeks, the platelet count increased to 14.7 × 10^4/μL, and he tolerated a gradual PSL tapering. By the end of the observation period, the platelet count increased to 17.8 × 10^4/μL on PSL (6 mg/day). During the treatment, the blood sugar was almost controlled and the patient presented no severe hyperglycemia episodes.

3. Discussion

Primary ITP is an acquired immune disorder characterized by an isolated thrombocytopenia due to pathogenic anti-platelet autoantibodies, T cell-mediated platelet destruction, and impaired megakaryocyte function. On the contrary, secondary ITP is triggered by inherited or acquired predisposing diseases such as chronic infections, including *HP* and human immunodeficiency virus, or autoimmune diseases such as systemic lupus erythematosus or rheumatoid arthritis (*5*). Recent studies have suggested that *HP*-positive ITP patients can be successfully treated by eradication of the pathogen (proton pump inhibitor, amoxicillin, and CAM) (*6,7*). On the contrary, in primary ITP, first-line treatments include corticosteroids. We have previously reported several cases of primary and secondary ITP such as *HP*-positive ITP showing increased platelet counts following macrolides treatment (*1-4*). In those cases, we speculated that the ITP improved by the immunomodulatory effects of the macrolides or their anti-bacterial activity. In addition to the anti-bacterial activity, macrolides have immunomodulatory effects including anti-inflammatory activities and are used for diseases such as diffuse panbronchiolitis, organizing pneumonia, and rheumatoid arthritis (*8*). The macrolides have effects on neutrophil function (decreased oxidant production, apoptosis) and on the production of cytokines involved in the inflammation cascade (decreased production of IL-1, IL-6, IL-8, and TNF and increased production of IL-10 and, possibly, IL-4) (*9*). EM and its derivatives inhibit T lymphocyte proliferation and induce T lymphocyte apoptosis (*10*). EM has been shown to potentiate the function of regulatory T cells in a rat model (*11*). In the present case, considering our previous experience, we thought that CAM treatment would be effective for our primary ITP patient. Although the CAM had to be stopped due to nausea and palpitation, the DM was controlled during CAM treatment. Consequently, the patient was safely and successfully treated using PSL without severe hyperglycemia. Since older patients have a tendency to suffer from chronic diseases that are exacerbated by the use of corticosteroids, such as DM, osteoporosis, and hypertension, macrolides treatment may represent a

useful option for treating ITP in them. According to the present case, CAM treatment demonstrated the actual benefit to the ITP patient accompanied by DM.

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