Macrolide Treatment for Primary Immune Thrombocytopenia

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To the Editor,

Macrolides have both immunomodulatory and antibacterial effects. We have already reported 8 cases of primary immune thrombocytopenia (ITP) that showed increased platelet counts (PC) following long-term use of erythromycin (EM) or clarithromycin (CAM) treatment.[1-3] In our previous reports, the fact that PC increased following macrolide treatment suggested immunomodulatory effects of macrolides. Herein we describe 7 patients whose PC had remained stable with prednisolone (PSL) monotherapy or no therapy, treated with short-term use of macrolides for a common cold.

Case 1, a 66 year-old woman who was Helicobacter pylori (HP)-positive patient, had received unsuccessfully eradication therapy (omeprazole, amoxicillin and CAM) for HP-positive ITP at 61 years old. And PC had remained at the level of 20×10^9/L. Concretely, 1 month before catching a cold, her PC were 22×10^9/L. After catching a cold, she was treated with EM at 600 mg/day for 2 weeks. Just before receiving this therapy, her PC were 25×10^9/L with PSL at 5 mg/day. After 2 weeks and about 4 weeks, PC indicated 25×10^9/L and 24×10^9/L, respectively.

Case 2, a 69 year-old woman who was HP-positive patient, had not experienced eradication therapy for HP-positive ITP. 3 months before catching a cold, her PC were 90×10^9/L. After catching a cold, she was treated with CAM at 400 mg/day for 1 week. Just before receiving this therapy, her PC were 84×10^9/L with no therapy. After 2 weeks and about 4 weeks, PC indicated 137×10^9/L and 87×10^9/L, respectively.

Case 3, a 24 year-old woman who was HP-negative patient, caught a cold. 1 month before catching a cold, her PC were 96×10^9/L. She was treated with CAM at 400 mg/day for 2 weeks. Just before receiving this therapy, her PC were 86×10^9/L with PSL at 5 mg/day. After 2 weeks and about 4 weeks, PC indicated 153×10^9/L and 102×10^9/L, respectively.

Case 4, a 75 year-old woman who was HP-negative patient, caught a cold. 1 month before catching a cold, her PC were 41×10^9/L. She was treated with EM at 600 mg/day for 1 week. Just before receiving this therapy, her PC were 43×10^9/L with no therapy. After 1 week and about 4 weeks, PC indicated 97×10^9/L and 41×10^9/L, respectively.

Case 5, an 84 year-old man who was HP-negative patient, caught a cold. 1 month before catching a cold, his PC were 90×10^9/L. He was treated with CAM at 400 mg/day for 2 weeks. Just before receiving this therapy, his PC were 96×10^9/L with PSL at 3 mg/day. After 2 weeks and about 4 weeks, PC indicated 158×10^9/L and 102×10^9/L, respectively.

Case 6, an 88 year-old woman who was HP-negative patient, caught a cold. 3 months before catching a cold, her PC were 36×10^9/L. She was treated with CAM at 400 mg/day for 1 week. Just before receiving this therapy, her PC were 44×10^9/L with no therapy. After 2 weeks and about 4 weeks, PC indicated 184×10^9/L and 32×10^9/L, respectively.

Case 7, a 68 year-old woman who was HP-negative patient, caught a cold. 1 month before catching a cold, her PC were 92×10^9/L.

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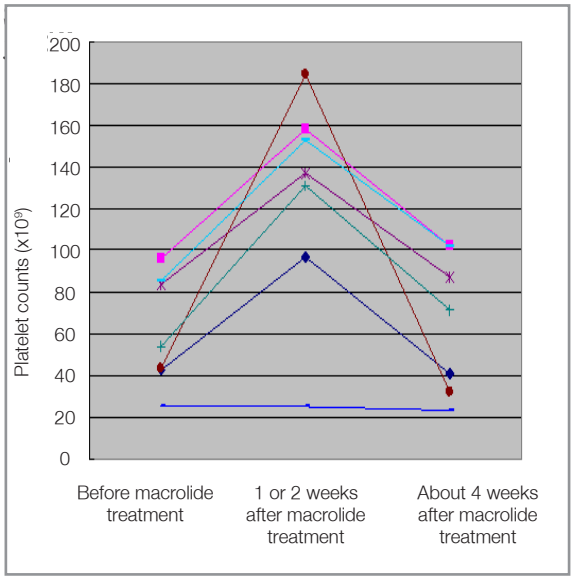

Figure 1. Changes in platelet counts following erythromycin (EM) or clarithromycin (CAM) treatment.

She was treated with EM at 600 mg/day for 1 week. Just before receiving this therapy, her PC were 54×109/L with no therapy. After 2 weeks and about 4 weeks, PC indicated 131×10^9/L and 72×10^9/L, respectively.

In 6 out of 7 patients treated with macrolides, PC increased after 1 or 2 weeks and decreased after about 4 weeks (Figure 1). And only in 1 patient, namely Case 1, PC did not increase and remained at the level of 20×10^9/L (Figure 1). In Case 4, 5, and 6, PC were higher just before taking macrolides than 1 or 3 months before catching a cold. Therefore, PC were thought not to be affected by a cold. As a result, it was suggested that macrolides really increased PC. However, in Case 2, 3, and 7, PC were lower just before taking macrolides than 1 or 3 months before catching a cold. Lower PC just before macrolide treatment and recovered PC 1 or 2 weeks after macrolide treatment might be associated with infection. Recovered PC in Case 2, 3 and 7, might be due to reaction after infection and/or effects of macrolides. After all, at least, in 3 cases, that is, Case 4, 5, and 6, macrolide treatment was thought to be effective, but temporary. Recent studies have suggested that ITP patients infected with HP can be successfully treated with above-mentioned eradication therapy. It is reported that eradication is only achieved in 15% of patients with CAM (1,000 mg/day) monotherapy. So the increased PC in Case 2 might be due to a reduction in the quantity of HP and/or a bacteriostatic effect of CAM,[4] including immunomodulatory effects of macrolides. Because macrolides have steroid-sparing effects via their influence on corticosteroid metabolism, not only immunomodulatory effects but also steroid-sparing effects might increase the PC in Case 3 and 5. Based on these results, ITP patients may benefit from short-term use of macrolides, when they undergo a simple operation such as a tooth extraction or their PC decrease after infection. But repeated short-term or long-term use of macrolides may promote the growth of drug-resistant bacteria, so these macrolides treatment for ITP should not be considered recommended therapies. Otsu et al. reported the effectiveness of a new macrolide which has immunomodulatory effects and no antibacterial effects.[5] So ITP patients will be able to benefit from this new macrolide treatment without the incidence of drug-resistant bacteria in the future.

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