

Adalimumab therapy in hepatitis B virus-negative polyarteritis nodosa

A case report

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Abstract

Introduction: Polyarteritis nodosa (PAN) is a difficult-to-treat rheumatology disorder, and biologic agents have been used in such patients with a treatment failure or the disease relapse.

Case presentation: We report a 42-year-old male Han Chinese who received adalimumab (ADA) alone during his vasculitis relapse, manifesting with weight loss, ankle arthritis, testicular inflammation and new-onset hypertension. Under the ADA 40 mg biweekly subcutaneous injection, there were the disappearance of clinical activity and no disease flares with a follow-up period of 26 months.

Conclusion: The clinical observation in this patient suggests a potential efficacy of ADA therapy in controlling the disease activity of PAN.

Abbreviations: ADA = adalimumab, ANCA = antineutrophil cytoplasmic antibody, BVAS = Birmingham Vasculitis Activity Score, FFS = five-factor score, IFX = infliximab, mAb = monoclonal antibody, PAN = polyarteritis nodosa, PSV = primary systemic vasculitis.

Keywords: adalimumab, five-factor score, polyarteritis nodosa, TNF mAb

1. Introduction

Polyarteritis nodosa (PAN) is a rare form of primary systemic vasculitis (PSV) predominantly targeting medium- or small-sized arteries and not associated with anti-neutrophil cytoplasmic antibody (ANCA).^[1,2] Although the natural untreated course of this disease is rapidly progressive with a fatal outcome, the introduction of corticosteroids has brought about an improved survival.^[2] Based on a five-factor score (FFS) developed by the French Vasculitis Study Group as a prognostic tool, current therapeutic approach in PAN considers corticosteroids alone in those without FFS and the addition of cyclophosphamide in the presence of critical organ involvement including renal, gastrointestinal and cardiac manifestations.^[2,3] Biologic agents are prescribed in PSV with a treatment failure or the disease relapse.^[2,4,5] In the PAN pathogenesis, activated endothelial cells,

resulting from the TNF stimulation, can perpetuate and potentiate the inflammatory milieu through the production of pro-inflammatory cytokines.^[2,6] Herein, we reported a PAN patient who received adalimumab (ADA), a TNF monoclonal antibody (mAb), during his vasculitis relapse, resulting in the disappearance of clinical activity and no disease flares with a follow-up period of 26 months.

2. Case presentation

A 42-year-old male Han Chinese visited the dermatological clinic of National Cheng Kung University Hospital with a 6-month history of purpuric reticulate erythema and nodules over the lower extremities in August 2012. Biopsy of a nodule revealed dense infiltrates consisting of abundant neutrophils and lymphocytes around the subcutaneous small artery with neutrophilic fibrin-platelet thrombus in the lumen (Fig. 1), consistent with the histopathological findings of PAN. Weight loss, diffuse myalgia, ankle arthralgia, and testicular pain were also noted, and he was referred to the rheumatological clinic. On physical examinations, he had swollen ankle joints and enlarged right testis with induration. Laboratory profiles showed elevated ESR and CRP values, unremarkable hemogram data, normal creatinine levels, and no significant abnormalities on urinalysis. Autoantibodies were not identified, including ANCA, antinuclear antibody, lupus anticoagulant and rheumatoid factor. Hepatitis B and C viral markers were absent. There were no abnormal findings on chest x-ray, electrocardiogram, abdominal and cardiac echography. High-dose corticosteroids (1 mg/kg/day prednisolone) were prescribed under the diagnosis of PAN, fulfilling the 2012 updated Chapel Hill consensus definitions.^[1] In the clinical remission, prednisolone dosages were tapered down and replaced by azathioprine (2 mg/kg/day). Nevertheless, he had a relapsing event with recurrent weight loss, right ankle swelling and right testicular pain as well as new-onset hypertension controlled by

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The Ethics Committee of National Cheng Kung University Hospital approved this study, and informed consent was obtained from the patient for publication of this case report and accompanying image.

The authors have no conflicts of interest to disclose.

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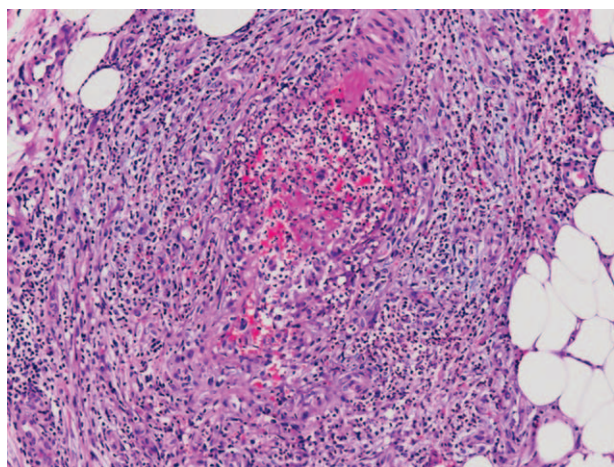


Figure 1. A subcutaneous small artery in a biopsied nodular lesion on the left leg. The vessel wall and adventitia are infiltrated by abundant neutrophils and lymphocytes with neutrophilic fibrin-platelet thrombus in the lumen (hematoxylin and eosin, $\times 200$).

amlodipine (5 mg/day) during the follow-up. There were no proteinuria or hematuria, normal creatinine levels and negative findings on renal angiography. Since the patient had no preference for corticosteroids due to associated side effects in the previous usage, ADA 40 mg biweekly subcutaneous injection was prescribed without other immunosuppressive agents from October 2014 to December 2016, 26 months in total, resulting in the absence of ankle swelling and testicular pain. There were no disease flares and infection complication during the treatment period.

A recurrent episode occurred soon after the discontinuation of ADA (owing to financial limitations) with the onset of bilateral ankle swelling and nodular lesions at left leg, followed by severe aching pain without motor deficit over right leg and foot, confirmed to be peroneal and tibial neuropathy by the nerve conduction examination. High-dose corticosteroids were prescribed again with improvement of arthritis and skin lesions. Currently, his prednisolone dosages are gradually decreased with the addition of weekly methotrexate up to 25 mg. Indeed, cyclophosphamide usage can be considered for his PAN-associated neuropathy during the subsequent follow-up.^[7]

3. Discussion

Owing to the absence of visceral involvement at the disease onset, high-dose corticosteroids were prescribed as the first-line therapy in this patient. Anti-TNF mAb was used as an alternative therapeutics alone in his relapsing episode with a Birmingham Vasculitis Activity Score (BVAS) up to 9,^[8] leading to the disappearance of clinical manifestations and no disease flares in a 26-month follow-up course. However, upon discontinuing its usage, there were recurrent disease activities with ankle arthritis, skin lesions and peripheral neuropathy (BVAS 13). Collectively, despite the clinical observation in 1 patient, it suggests a potential effect of ADA therapy in controlling the disease activity of PAN.

In spite of no fully validated efficacy of TNF blockades on the PAN therapy, such an agent was chosen in the reported case due to lack of autoantibodies and no hepatitis B virus infection. Interestingly, significantly decreased BVAS is observed in a pediatric series with 8 cases on the infliximab (IFX) therapy.^[4] For the adult-onset patients, successful experience has been reported from one

with etanercept injection and 4 receiving IFX infusion including 2 with gastrointestinal or renal involvement.^[9–13] Indeed, the potential of TNF antagonists can be further realized with large-scale randomized trials to ascertain therapeutic regimens and clinical benefits in PAN, a difficult-to-treat rheumatology disorder.

4. Conclusions

PAN is a difficult-to-treat rheumatology disorder, and biologic agents have been used in such cases with a treatment failure or the disease relapse. We report a male patient who received ADA therapy alone during his vasculitis relapse, resulting in the disappearance of clinical activity and no disease flares with a follow-up period of 26 months.

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Author contributions

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