Treatment of Ormond Disease and Idiopathic Membranous Glomerulonephritis Using Rituximab

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Treatment of retroperitoneal fibrosis usually involves corticosteroids with or without other immunomodulating medications or tamoxifen. Rituximab, a monoclonal antibody that specifically targets CD20 on the surface of B cells, is effective in achieving complete remission of proteinuria in patients with idiopathic membranous nephropathy. We describe a case of a 45-year-old man with idiopathic membranous glomerulonephritis and proteinuria and simultaneously with idiopathic retroperitoneal fibrosis (with a large number of CD20 cells in the histologic image). The patient did not tolerate the treatment with cyclophosphamide, and as rescue therapy, administration of rituximab was indicated with excellent effect. We recorded prompt reduction of proteinuria and significant reduction of retroperitoneal fibrosis. Rituximab is effective in the treatment of idiopathic retroperitoneal fibrosis with positivity of CD20 cells, as well as in the treatment of idiopathic membranous glomerulonephritis.

Keywords. rituximab, idiopathic retroperitoneal fibrosis, idiopathic membranous nephropathy

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Case Report

INTRODUCTION

Retroperitoneal fibrosis is an uncommon condition with estimated incidence of 1.38 cases per 100000 people and most cases are idiopathic.[1] This disorder involves chronic inflammation and fibroblast proliferation, with excessive extracellular matrix deposition.[2] Complications such as acute kidney failure secondary to periureteral involvement require prompt surgical intervention.[1] Treatment usually involves corticosteroids with or without other immunomodulating medications.[2] Steroids can be very valuable but probably play no role when there is minimum inflammation within the fibrosis, and it seems that many patients are often kept on a too high dose for too long, with all expected side-effects. Where steroids fail to control the retroperitoneal fibrosis, we tried to employ new biological disease-modifying agents, including rituximab.[3,4]

CASE REPORT

We present the case of a 45-year-old man with idiopathic membranous glomerulonephritis (histologically confirmed in January 2011; confirmed also by electron microscopy) that was treated by standard method by pulses of corticosteroids in combination with cyclophosphamide. Further, the patient was treated with prednisone in combination with cyclosporine A with excellent effect. In March 2015, the patient was hospitalized due to renal colic. The computed tomography examination identified hypodense mass in the retroperitoneum (Figure 1), and by histology, we confirmed presence of idiopathic retroperitoneal fibrosis (Figure 2). Histology of retroperitoneal fibrosis identified numerous deposits of CD20+ cells. CD34, CD117, CD3 +, CD138 + plasma cells, and CD246 were negative (Figure 3).

In view of the present hydronephrosis in the left

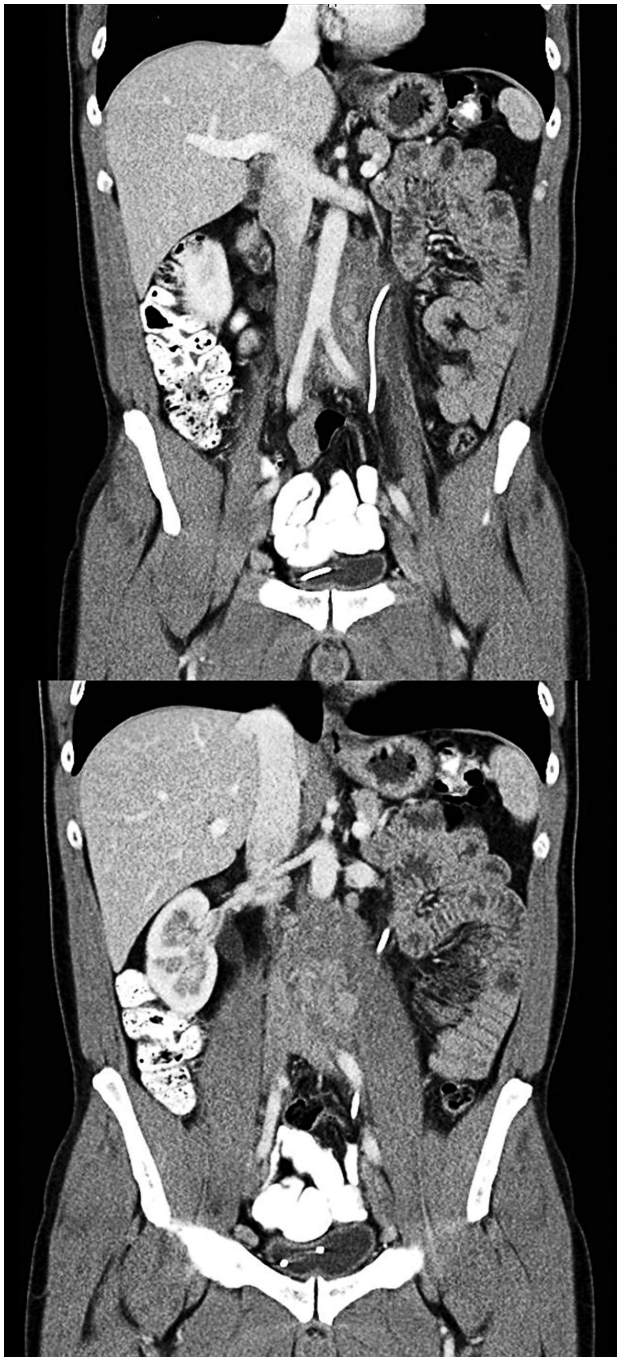

Figure 1. Computed tomography examination at the time of diagnostics of Ormond disease. Left, Kidney with a stent. Right, Kidney with dilated ureter.

kidney, it was necessary to insert a stent into the left ureter. In June 2015, we recorded relapse of grave nephrotic syndrome (excretion of albumins > 30 g/24 hours, decreased level of albumin in serum to 12 g/L, and clinically present anasarca). Biopsy of the kidney revealed present relapse of the membranous glomerulonephritis. We excluded

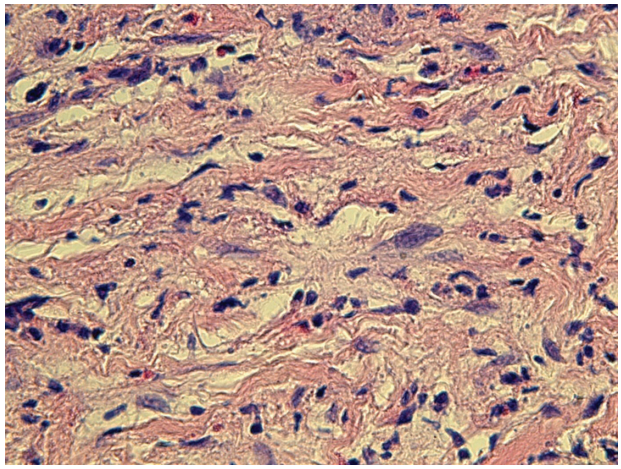

Figure 2. Fibrosis and fibroblasts (hematoxylin-eosin, × 480).

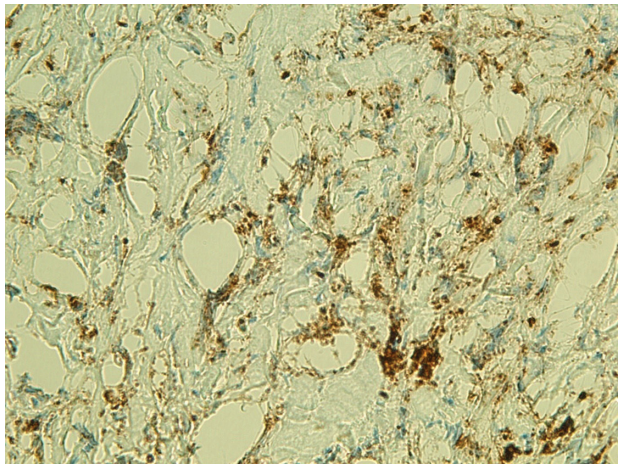

Figure 3. CD20+ cell in fibrosis.

infectious diseases or malignity, the antineutrophil cytoplasmatic antibodies, antinuclear antibodies, antismooth muscle antibodies, and antifibroblast antibodies were negative.

We started pulse treatment by corticosteroids plus cyclophosphamide. In view of presence of large number of CD20 cells in retroperitoneal fibrosis, we indicated as rescue therapy administration of rituximab at the dose of 375 mg/sqm in weekly intervals, 4 times. Already after the 2nd dose of rituximab, the value of proteinuria decreased from the original 33 g/24 hours to 11 g/24 hours, and after the end of the treatment, proteinuria was 0.3 g/24 hours (the values of creatinine, albumin, and proteinuria are show in Figure 4). After termination of the treatment with rituximab, we continue the therapy with prednisone with gradual decrease of the dose from 60 mg/d to 20 mg/d, and the treatment was extended by adding the

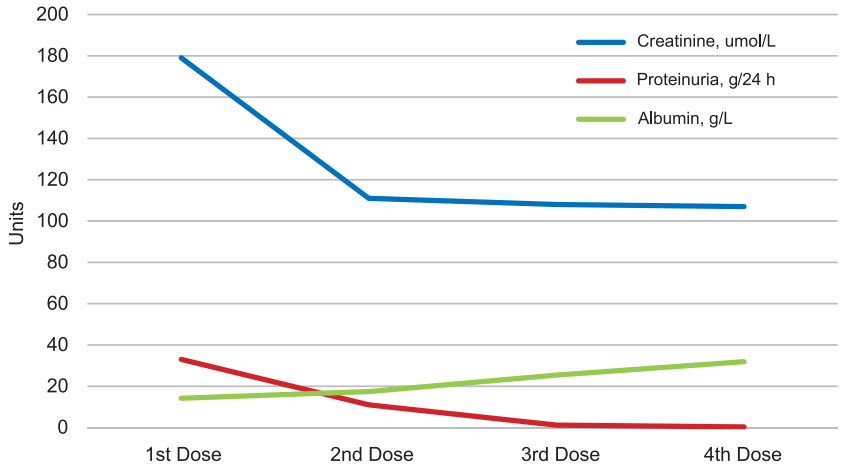

Figure 4. The values of creatinine, albumin, and proteinuria during treatment with rituximab.

mycophenolic acid (180 mg in the morning and in the evening). After the end of the treatment, we performed computed tomography examination, which discovered significant regression of the retroperitoneal mass (Figure 5), with the possibility to extract the stent from the left ureter. At this moment, the patient is in excellent condition, he works and performs sport activities.

DISCUSSION

In the past several years, case reports and small series have documented successful nonsurgical management with various immunosuppressive agents.[5-7] The literature describes several cases of treatment of retroperitoneal fibrosis by rituximab within the immunoglobulin G4 (IgG4)-related disease. Patients with IgG4-related disease typically have elevated serum concentrations of IgG4 and share histopathologic features that are similar across affected organs.[8] Although many patients with IgG4-related disease have lesions in several organs, either synchronously or metachronously, and the pathological features of each organ differ, consensus has been reached on 2 diagnostic criteria for the IgG4-related disease: (1) serum IgG4 concentration greater than 135 mg/dL, and (2) more than 40 % of IgG+ plasma cells being IgG4+ and more than 10 cells per high-power field of biopsy sample.[9] A typical histologic finding in case of patients with retroperitoneal fibrosis within the IgG4-related disease is fibrosis, intense inflammatory cell infiltration with plasma cells, venulitis, and

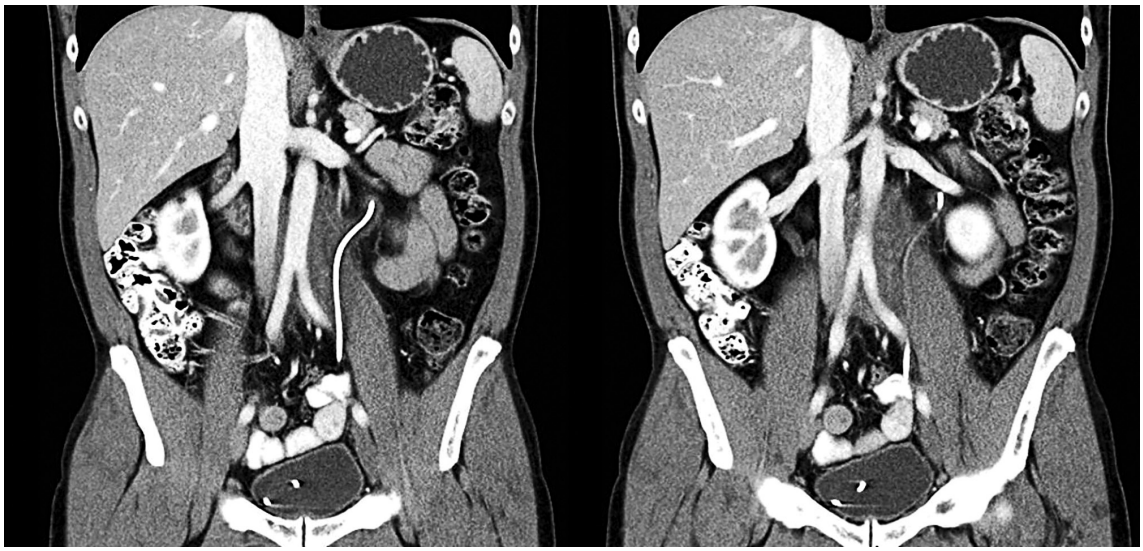

Figure 5. Computed tomography examination after treatment with rituximab.

obliterative arteritis.[10] In the case of our patient, these diagnostic criteria were not fulfilled, and therefore, the diseases is not categorized as IgG4-related disease. In general, treatment of idiopathic retroperitoneal fibrosis is still empiric, because there is only 1 randomized controlled trial reported. Patients often need long-term therapy because this disease may have a chronic relapsing course.[11]

Immunosuppressive treatment of patients with idiopathic membranous nephropathy is heavily debated. The controversy is mainly related to the toxicity of the therapy and the variable natural course of the disease—spontaneous remission occurs in 40% to 50% of patients. The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Glomerulonephritis provides guidance for the treatment of idiopathic membranous nephropathy. The guideline suggests that immunosuppressive therapy should be restricted to patients with nephrotic syndrome and persistent proteinuria, deteriorating kidney function or severe symptoms. Better risk prediction is needed to identify patients who will benefit from immunosuppressive agents.[12] Rituximab has been studied in many well-designed small pilot studies, and the response to the agent correlates with a reduction in antibodies to the M-type phospholipase A2 receptor.[13-16]

In our described case, we elected rescue treatment by rituximab of the Ormond disease due to the high number of CD20 cells in the histologic image from retroperitoneal fibrosis. Rituximab was elected also for treatment of idiopathic membranous glomerulonephritis.

In conclusion, a randomized controlled trial is needed to confirm the encouraging results of rituximab in treatment of idiopathic membranous glomerulonephritis, but the findings indicate high probability that rituximab has beneficial actions on the disease process.[17]

CONFLICT OF INTEREST

None declared.

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