Biomedicine Hub

Novel Insights from Clinical Practice

Biomed Hub 2024;9:62–66
DOI: 10.1159/000538279

Received: November 6, 2023
Accepted: March 4, 2024
Published online: April 18, 2024

Spontaneous Remission of Minimal Change Disease in a Colon Cancer Patient: A Case Report

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Established Facts

- Colorectal cancer is a less common cause of minimal change disease.
- There is still no established treatment for secondary MCD.

Novel Insights

- Spontaneous remission of MCD can be achieved by treating the extraglomerular disease without immunosuppressive therapy.

Keywords
Case report · Nephrotic syndrome · Minimal change disease · Colon cancer · Spontaneous remission

Abstract

Introduction: Minimal change disease (MCD) is most often primary but may occur secondary to other systemic diseases such as malignancy. In secondary MCD, spontaneous remission of nephrotic syndrome after the treatment of related diseases without steroid therapy is rare. ***Case Presentation:*** A 78-year-old man visited the outpatient clinic with foamy urine and generalized edema that had persisted for 2 months. The patient had nephrotic syndrome. Before a kidney biopsy, he underwent several tests to determine the secondary cause of the nephrotic syndrome. The serum CEA was slightly elevated, and colon cancer was detected in the sigmoid colon. MCD was diagnosed from a

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kidney biopsy. He immediately underwent surgery for colon cancer. Complete remission of the MCD was achieved within 2 weeks after surgery. ***Conclusion:*** Here, we report a rare case of a patient with secondary MCD who successfully achieved spontaneous remission after colon cancer surgery.

Introduction

Minimal change disease (MCD) is a major cause of nephrotic syndrome. Although it mainly occurs in children, it accounts for 15.5% of nephrotic syndrome in adults [1, 2]. MCD is most often primary but may occur secondarily to other systemic diseases such as malignancy, drugs, infections, and autoimmune diseases in adults [3]. Although membranous nephropathy is the most common nephrotic syndrome associated with solid organ tumors, it may also occur as paraneoplastic nephropathy associated with solid organ tumors, such as thymoma and renal cell cancer. Colorectal cancer is a less common cause of MCD [4]. Steroids are the first-line treatment for MCD, unless there are contraindications of steroids for patients [5]. We report a rare case of complete remission (CR) without steroid treatment in a patient with MCD concomitantly diagnosed with colon cancer.

Case Presentation

A 78-year-old man visited the outpatient clinic with foamy urine and generalized edema that had persisted for 2 months. He had been taking a selective COX-2 inhibitor nonsteroidal anti-inflammatory drug (NSAID) for left osteoarthritis for several months. He had no history of other drug use, recent infections, allergies, or autoimmune diseases. The patient was admitted for further evaluation. His blood pressure was 149/68 mm Hg, heart rate 72 beats/min, height 161.3 cm, and weight 73.7 kg. The laboratory findings were as follows: white blood cell count 4,950/mm^3, hemoglobin 12.9 g/dL, platelets 351,000/μL, blood urea nitrogen 29.3 mg/dL, creatinine 1.25 mg/dL, ad total protein 4.2 g/dL. C-reactive protein and uric acid levels were normal. The serum albumin was 2.1 g/dL and total cholesterol 315 mg/dL. The 24-h urinary protein excretion was 6.8 g. The spot urine protein/creatinine ratio was 10.1 mg/g Cr and the urinalysis was negative for occult blood. Serum immunoglobulin (Ig)G, IgA, IgM, complement 3 (C3), complement 4 (C4), and rheumatoid factor levels were normal. Anti-phospholipase A2 receptor (anti-PLA2R) IgG, hepatitis B/C, and HIV serology results were all negative. Serum protein electrophoresis revealed no abnormal monoclonal

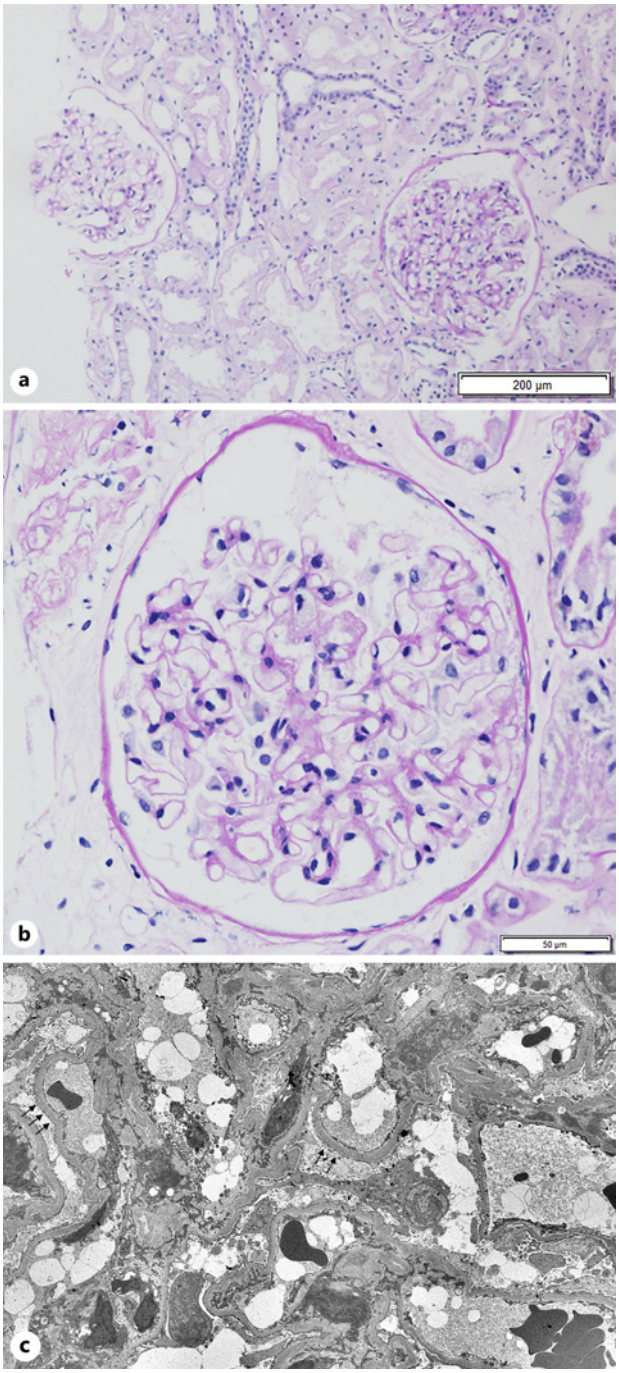

Fig. 1. Histological findings of the renal biopsy specimen. **a** Glomeruli appear normal by light microscopy. The tubule shows slight atrophy, and the interstitium shows mild edema (periodic acid-Schiff (PAS) stain, ×100). **b** PAS stain, × 400. **c** Electron micrograph. One glomerulus is examined. Glomerular basement membrane (GBM) is mild to moderately irregular with diffuse effacement of epithelial foot processes (black arrows). The mesangial matrix is slightly increased. Electron-dense deposits are not found.

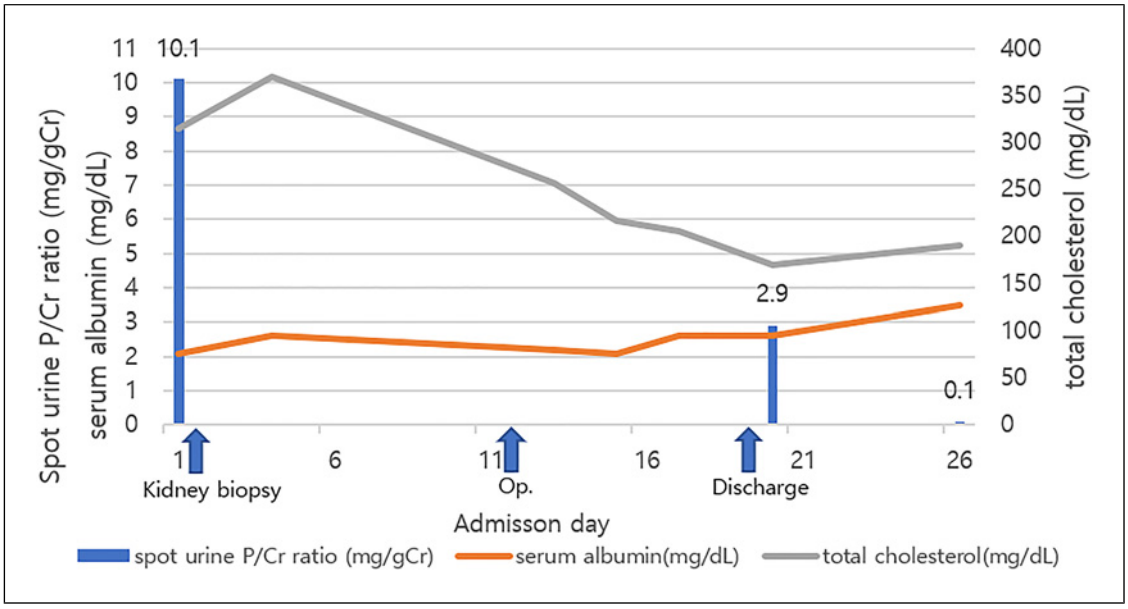

Fig. 2. Clinical course of the patient.

Table 1. Previous cases of patients with MCD associated with colorectal cancer

	Age/ sex	Tumor	Therapy for malignancy		Therapy for MCD	Clinical course
			surgery (type)	chemotherapy	steroid	
Caruana et al. [11]	27/M	Colonic carcinoma	Yes (total colectomy)	No	Yes	CR
Gandini et al. [12]	72/M	Cecum carcinoma	Yes (unknown)	No	No	CR
Taniguchi et al. [7]	55/F	Rectal carcinoma	Yes (low anterior resection, ileocecal resection, partial resection of the urinary bladder)	No	No	CR
Our case	78/M	Colonic carcinoma	Yes (low anterior resection)	No	No	CR

CR, complete remission; MCD, minimal change disease.

spikes. Both kidneys were of normal size, and there were no visible cysts or masses on abdominal computed tomography. Because his generalized edema worsened, furosemide was started before the kidney biopsy, and tests were performed to determine the secondary cause of the nephrotic syndrome. The serum CEA was slightly elevated to 4.13 ng/mL and a 2-cm mass was found in the sigmoid colon at colonoscopy. Thereafter, kidney biopsy was performed. The kidney biopsy sampled 12 glomeruli and no changes were observed by light microscopy or immunofluorescence. On electron microscopy, the glomerular basement membrane was moderate to severely irregular in contour, with diffuse effacement of the epithelial foot processes; no electron-dense deposits were found (shown in Fig. 1a–c). The tumor in the sigmoid colon was identified as an adenocarcinoma on histopathological examination, and 5 days later, the patient was also diagnosed with MCD. His generalized edema was well controlled with furosemide, and there was no evidence of metastasis; therefore, surgery was requested. The patient agreed not to take steroids for the nephrotic syndrome and to be followed to assess his improvement after surgery. On the 12th day of admission,

laparoscopic anterior resection was performed to remove the tumor. On postoperative day 8, the spot urine protein/creatinine ratio fell significantly to 2.9 mg/g Cr from 10.1 mg/g Cr (shown in Fig. 2). His foamy urine and edema improved. The patient stopped taking furosemide and was discharged. The patient visited the outpatient clinic on the 14th postoperative day. The spot urine protein/creatinine ratio was 0.1 mg/mg Cr, and the other laboratory abnormalities had normalized.

Discussion

This is a rare case of MCD related to colon cancer in which CR was achieved rapidly after surgery without steroid treatment. Membranous nephropathy is the most common secondary glomerular disease and is particularly associated with solid tumors [6]. The pathophysiology of the development of malignancies-related MCD remains unknown. One report suggested that it may be related to vascular endothelial growth factor (VEGF) production. That study showed that MCD associated with rectal cancer was significantly related to VEGF levels; when the tumor was removed, the VEGF decreased, and MCD improved. Therefore, it has been proposed that vascular growth factor antagonists be administered to patients with unresectable tumors and high VEGF levels [7]. Some studies have found that proteinuria occurs in patients treated with high-dose VEGF antibodies. Thus, the treatment decision should be made cautiously [4, 8]. Our patient's colon cancer was at an early stage, without metastasis. Since the tumor was resectable, we did not measure the serum VEGF levels.

MCD can cause nephrotic-range proteinuria, despite the absence of abnormal lesions on light microscopy. Electron microscopy can identify effacement changes in the epithelial cell foot processes [9]. Cytokines secreted by infiltrated lymphocytes and macrophages can increase glomerular permeability and are associated with pathological changes in MCD. Solid tumors can induce these glomerular responses. Tumor-induced immunological disturbances involving macrophages and type 2 helper T lymphocytes may occur in MCD [10].

We considered several factors that might have contributed to the spontaneous remission of MCD in this case. First, the colon cancer treatment may induce CR of MCD. In our patient, the proteinuria improved dramatically on the 4th postoperative day, and CR was rapidly achieved by the 14th postoperative day. The median time to remission in adults with primary MCD exceeds 2 months [9]. In secondary MCD that is histologically indistinguishable from primary MCD, if extraglomerular disease treatment induces an improvement in the MCD, a causal relationship is strongly supported [3].

The Kidney Disease: Improving Global Outcomes guidelines also recommend high-dose oral glucocorticoids as the first-line treatment for primary MCD [5]. In general, treatment options for secondary MCD associated with malignancies include immunosuppressive therapies and tumor-related therapies. However, more evidence is needed to determine which therapeutic option is more reasonable. To the best of the authors' knowledge, there have been 3 case reports of spontaneous CR of secondary MCD strongly associated with colorectal cancer [7, 11, 12]. In our case, the patient was older than the others, and the cancer was in an early stage that required only simple surgery (shown in Table 1).

Second, NSAIDs may have been one of the causes of MCD in the present case. NSAIDs are a common cause of nephrotic syndrome [13]. Of the types of NSAIDs, acetic acid and propionic acid derivatives were the most common chemical groups, and selective COX-2 inhibitors had the lowest risk of MCD. In addition, a high risk of nephrotic syndrome was reported in patients taking a conventional NSAID for at least 2 weeks recently, or taking an NSAID for the past 2 months to 2 years [14, 15]. Our patient had been taking a selective COX-2 inhibitor for 8 months before the onset of foamy urine and this was discontinued while he was hospitalized. After the colon cancer surgery, he started retaking the selective COX-2 inhibitor because of worsening knee joint pain. Nevertheless, no recurrence of nephrotic syndrome has occurred to date.

Conclusion

We report a rare patient with secondary MCD who successfully achieved spontaneous remission after colorectal cancer surgery. Evaluation of the secondary causes is necessary for older patients with nephrotic syndrome. Spontaneous remission of MCD can be achieved by treating the extraglomerular disease without immunosuppressive therapy. Therefore, we expect our report to provide useful evidence for treating patients with secondary MCD.

Statement of Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Gyeongsang National University Hospital (approval No.: GNUH

2023-03-016). Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study was not supported by any sponsor or funder.

Author Contributions

Conception and final approval of the version to be published: Se-Ho Chang. Investigation: Seunghye Lee, Hyejin Jeon, and Sehyun Jung. Supervision: Dong Jun Park, Eunjin Bae, and Tae Won Lee. Writing – original draft: Seunghye Lee. Writing – reviewing and editing: Hyun-Jung Kim, Hani Jang, and Seunghye Lee.

Data Availability Statement

All relevant data are within the paper. Further inquiries can be directed to the corresponding author.

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