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Kidney biopsy reveals metastatic adenocarcinoma of the appendix simulating nephrotic syndrome

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Abstract. **Membranous glomerulonephritis (MGN) is among the most common causes of nephrotic syndrome in adults. The malignancy in presumed tumor-induced MGN has usually been diagnosed at the time the proteinuria is discovered.**

Here we report a 57-year-old male patient with a history of refractory pyuria and nephrotic syndrome. The kidney biopsy confirmed the diagnosis of not only MGN, but also metastasis of appendix adenocarcinoma. To our knowledge this is the first case report diagnosed as a metastatic malignancy from a kidney biopsy which no other imaging techniques were able to display.

Key Words:
Nephrotic syndrome, Membranous glomerulonephritis, Appendix adenocarcinoma, Kidney biopsy.

Introduction

Nephrotic syndrome is specifically defined by the presence of heavy proteinuria (protein excretion greater than 3.5 g/24 hours) and membranous glomerulonephritis (MGN) is among the most common cause of nephrotic syndrome in adults. It is characterized by basement membrane thickening with little or no cellular proliferation or infiltration, and the presence of electron dense deposits across the glomerular basement membrane. MGN is most often a primary (idiopathic) disorder in adults and many cases of idiopathic MGN may be due to autoantibodies directed against the phospholipase A2 receptor found on podocytes. Secondary causes include hepatitis B antigenemia, autoimmune diseases, thyroiditis, carcinoma, and the use of certain drugs such as gold, penicillamine, and nonsteroidal antiinflammatory drugs. The malignancy in presumed tumor-induced MGN has usually been diagnosed or is clinically apparent at the time the proteinuria is discovered[1-3].

Case report

A 57-year-old male patient with a six months history of pyuria refractory to antimicrobial therapy was referred to Nephrology Department. The patient's major complains were severe nausea and foamy urine. Laboratory tests showed the progressive loss of renal function; his serum creatinine level was 3.5 mg/dL which was reported to be 1.2 mg/dL six weeks earlier, and proteinuria was 3.8 g/24 hours. The patient did not have any history of hypertension or diabetes mellitus; however, he underwent a right hemicolectomy and received chemotherapy due to appendix adenocarcinoma two years before his admission to our department, and his medical records revealed that he was in full remission since last year. Aside from pale skin, the previous operation scar and 2 (+) pretibial edema; his physical findings were completely stable. The ultrasound showed no organomegaly, mass or lymphadenopathy in the abdomen and both kidneys were in normal size (102x56x32 and 105x58x31 right and left kidneys respectively) and shape; however there was grade 1 increase in echogenity of bilateral renal parenchymas. An ultrasound guided kidney biopsy was performed to rule out the etiology of nephrotic syndrome leading to rapidly progressive renal failure.

Pathology report

Immunofluorescence examination:

- Fluorescent sent for review 1 cm in length trucut biopsy of the kidney seen in section, nine out of fifteen glomeruli were globally sclerotic.
- Microscopic examination of stained slides for the fluorescein-labeled anti IgA, IgG, IgM, C3, C1q, fibrinogen in the glomeruli ("+ + + +" out);
- IgM (+) membranous, focal segmental, irregular, coarse granular;

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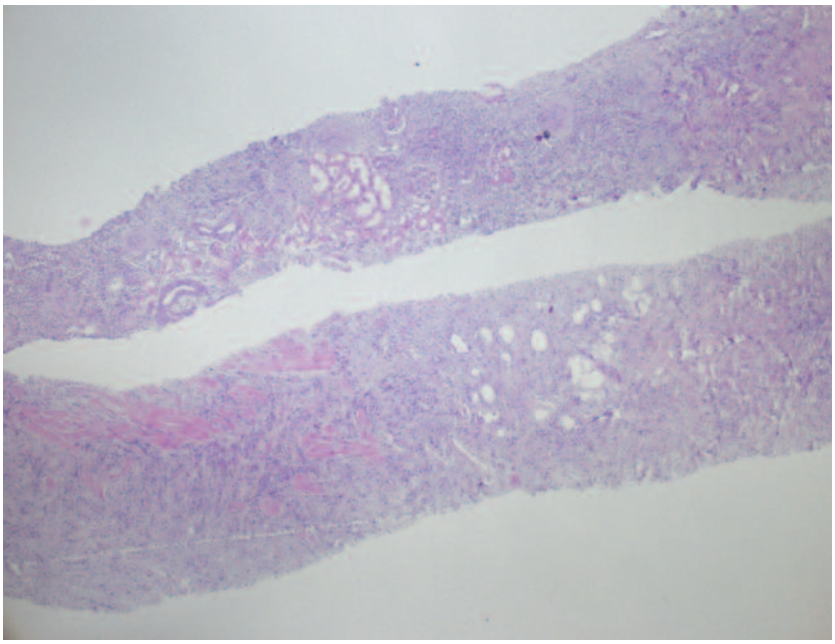

Figure 1. The light microscopic appearance of membranous nephropathy in which the capillary loops are thickened and prominent, but the cellularity is not expected to be increased; however, in this specimen hypercellularity in the interstitial area is significant. H&E, 4X.

- C3 (++) membranous, diffuse, fine granular;
- IgG (++ to +++) membranous, diffuse, coarse granular;
- IgA (-) C1q (-) Fibrinogen (-) Immunohistochemical examination:
- Material: Paraffin blocks.
- Technique: Ventana Benchmark XT – Controls: Standard positive and negative Primary antibodies (s):
- CK7 [Biocare Medical (OV-TL 12/30)]: Negative
- CK20 [Biocare Medical (ks20.8)]: Positive
- CEA-p [Biocare Medical (n/a)]: Positive
- CDX2 [Leica (amt28)]: Positive
- RCC [DAKO (SPM314)]: Negative Diagnosis:
- Kidney, right; tru-cut biopsy:

1. Membranous glomerulonephritis
2. Morphological and immunohistochemical findings support the metastasis of a poorly differentiated adenocarcinoma of appendix (Figures 1-4).

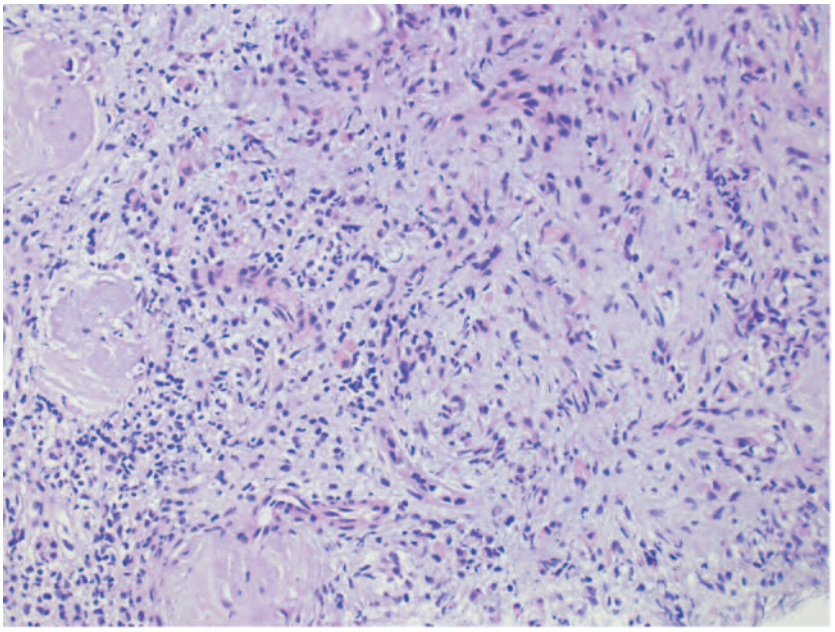

Figure 2. At higher magnification, the neoplastic glands of adenocarcinoma have crowded nuclei with hyperchromatism and pleomorphism. H&E, 20X.

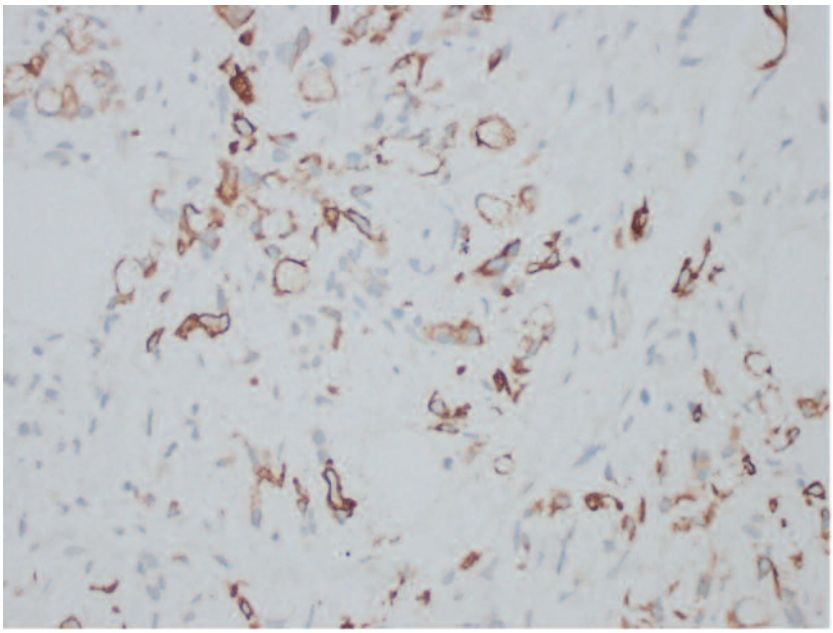

Figure 3. CK7-/CK20+ phenotype is highly specific and sensitive marker of colorectal origin. CK20, 40X.

Clinical follow-up

As soon as the histopathological diagnosis came out, it was decided to treat the malignancy rather than nephrotic syndrome which probably occurred as tumor-induced MGN. The patient was referred to Medical Oncology Department and he was started a chemotherapy regimen including oxiplatin and corticosteroids immediately. The nephrotic range proteinuria and creatinine level decreased back to normal limits at the end of the first month; however, it took three more months for pyuria to disappear completely.

Discussion

Malignancy is responsible for approximately 5-10% of cases of MGN, with the higher risk occurring in patients older than 50 years. On the

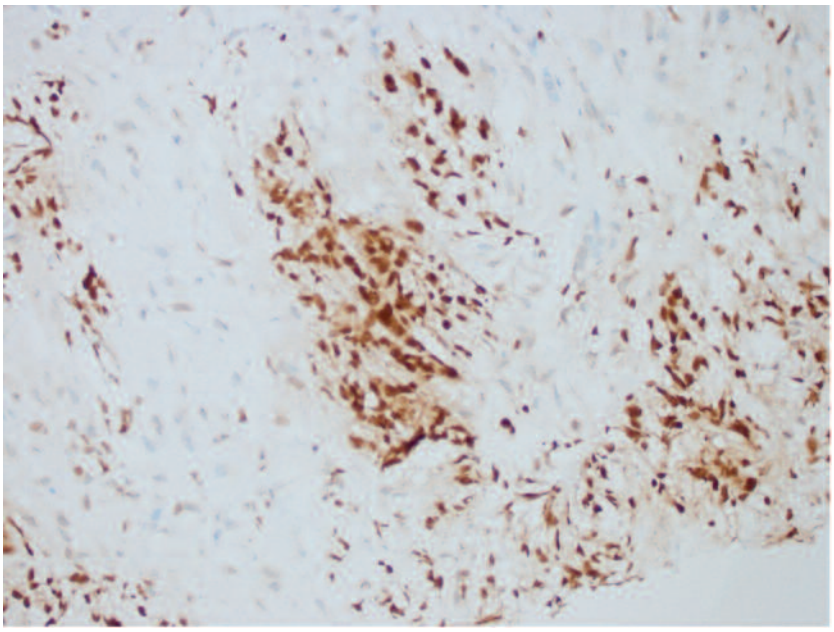

Figure 4. The antibody CDX2 expression should be a useful adjunct for the diagnosis of intestinal adenocarcinomas, particularly when better established markers such as CK7 and CK20 yield equivocal results. CDX2, 20X.

other hand, postmortem biopsies reveal that 12% of patients diagnosed with malignancy have kidney metastasis, possibly due to hematogenic route[4-7]. Among solid tumors, lung cancer is the most common malignancy associated with kidney metastasis. However, colorectal cancers are known to have a low kidney metastasis rate; only a few cases have been reported in literature regarding lesions localized either in the lumen or appear as parenchymal mass[8-10].

The evaluation of the presented case is interesting in two perspectives.

The first one is; it is a routine work-up of ruling out tumor-induced MGN for patients over fifty-years-old, but nevertheless the patients are investigated for clues of a primary malignancy such as mass lesions in lungs, breast, gastrointestinal system, etc., after the kidney biopsy diagnosis has been described as MGN. To our knowledge this is the first case report diagnosed as a metastatic adenocarcinoma of the appendix from a kidney biopsy.

The second interesting feature is the culture negative resistant pyuria, probably due to infiltration of appendix adenocarcinoma into the kidney and bladder wall. It is important to keep in mind that although very rare, tumors of both the gastrointestinal and female reproductive system may mimic refractory urinary tract infections.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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