

## CASE REPORT

# Nephrotic syndrome after treatment of Crohn's disease with mesalamine: Case report and literature review

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## ABSTRACT

Inflammatory bowel disease and its various treatments may affect the kidney in several ways. Recently, case reports have been published documenting the development of nephrotic syndrome after the treatment for inflammatory bowel disease with 5-aminosalicylic acid derivatives. We report a 50-year-old patient who was diagnosed with Crohn's disease and was treated with mesalamine. The patient subsequently developed nephrotic syndrome and a renal biopsy showed minimal change disease. He was treated with losartan and rosuvastatin and showed improvement in his renal function and serum cholesterol level. This is the first reported case in Crohn's disease although there have been six previous case reports of nephrotic syndrome following salicylic acid derivatives for ulcerative colitis.

**Key words:** Aminosalicilic acid, Crohn's disease, inflammatory bowel disease, mesalamine, minimal change disease, nephrotic syndrome

## INTRODUCTION

Mesalamine, sulphasalazine, and 5-aminosalicylate derivatives have subsequently been developed, approved, and are routinely incorporated into the clinical care of patients with inflammatory bowel disease. Serious toxicities have been reported with these agents but have primarily been limited to be neurologic and gastrointestinal. Nephrotoxicity, especially interstitial nephritis, has been also demonstrated after administration of these agents. Both mesalamine and sulfasalazine are excreted into the urine, which may carry their side effects to the kidneys. Here, we report the first case of nephrotic syndrome occurring in a patient with Crohn's disease receiving mesalamine.

## CASE REPORT

A 50-year-old Moroccan man, with a 2-year history of Crohn's disease and without extraintestinal manifestations, presented with a sudden onset of increasing bilateral swelling in lower extremities and an increase in urine

frequency for 2 weeks. His urinalysis revealed a proteinuria of 3+.

For Crohn's disease, the patient was initiated on sulfasalazine, then changed to a better tolerated 5-aminosalicylate, mesalamine, within 2 months of making the diagnosis; he noted a marked improvement of his symptoms. While on this regimen, he developed the swelling and the increase in urination.

Physical examination showed severe edema in both lower extremities and a blood pressure of 113/62 mm Hg. Further laboratory investigation showed significant hypoproteinemia and hypoalbuminemia with total protein level of 3.3 g/dL and albumin level of 1.2 g/dL, and hypercholesterolemia with serum cholesterol level of 263 mg/dL; the urine protein-to-creatinine ratio was 7.04; his BUN was 12 mg/dL and serum creatinine was 0.8 mg/dL, which are all compatible with nephrotic syndrome. Renal ultrasonography and Doppler disclosed no abnormalities. Renal biopsy showed a normal appearance of glomeruli on

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light microscopy and a presence of effacement of podocyte foot processes on electron microscopy; a diagnosis of nephrotic syndrome, minimal change subtype, was made. Congo red and thioflavin T stains for amyloid were negative. Mesalamine treatment was withdrawn and the patient was started on losartan, furosemide, and rosuvastatin. His symptoms and laboratory studies showed marked improvements; within 2 months after stopping mesalamine treatment, his urine protein-to-creatinine ratio decreased to 2.2, serum albumin level increased to 2.5 g/dL, and serum cholesterol level became 212 mg/dL.

## DISCUSSION AND LITERATURE REVIEW

Six earlier cases of nephrotic syndrome after treatment with 5-aminosalicylate derivatives have been reported in the literature, all in patients with ulcerative colitis<sup>[1-6]</sup> [Table 1]. We believe this is the first description of nephrotic syndrome following the treatment for Crohn's disease secondary to mesalamine intake. One recent case report described the development of nephrotic syndrome in a patient with Crohn's disease following a treatment with certolizumab rather than a 5-aminosalicylate derivative.<sup>[7]</sup>

Among these six case reports, two cases were treated with sulfasalazine before the development of nephrotic syndrome<sup>[1,2]</sup> and three cases were on mesalamine,<sup>[3,4,6]</sup> one patient treated with both sulfasalazine and mesalamine.<sup>[2]</sup> Five patients developed minimal change disease, where only one patient developed focal segmental glomerulosclerosis.<sup>[2]</sup> All the patients, including ours, did have a classical presentation of nephrotic syndrome, presented with sudden onset edema in the ankle, sacrum, or periorbital regions with compatible laboratory values. They all had normal kidney function and normal blood pressure.

We treated our patient with losartan to improve his renal function and with rosuvastatin to control his elevated cholesterol levels; we did not introduce steroids as the patient had responded well. Steroids are considered first-line treatment for nephrotic syndrome, either type. In addition, upon cessation of 5-aminosalicylate, the renal function improved as in the entire cases reported. It is unknown how 5-aminosalicylates produce minimal change nephropathy, but the pathogenesis could be related to reversible podocyte toxicity.<sup>[1]</sup>

## CONCLUSION

In conclusion, we described a patient who developed nephrotic syndrome, minimal change type, following the use of mesalamine for Crohn's disease. This is the

Case report	Age of patient	Gender	Type of IBD	Treatment of IBD	Duration of using 5-ASA before NS (in months)	Type of NS developed	Treatment of NS*	Outcome
Novis 1988	61	Female	Ulcerative colitis	Mesalamine	5	Minimal changes	Steroid†	Improved
Barbour 1990	28	Male	Ulcerative colitis	Sulphasalazine	18	Minimal changes	Steroid†	Improved
Fornaciari 1997	44	Male	Ulcerative colitis	Mesalamine	84	Minimal changes	Steroid†	Improved
Skhiri 1998	59	Female	Ulcerative colitis	Mesalamine	9	Minimal changes	Steroid†	Improved
Fof 2003	33	Male	Ulcerative colitis	Sulphasalazine and mesalamine	12	Focal segmental glomerulosclerosis	Steroid† and ramipril	Improved
Molnar 2010	50	Male	Ulcerative colitis	Sulphasalazine	12	Minimal changes	Steroid†	Improved

\*In addition to these treatments, stopping or reducing 5-ASA and/or chemotherapy if treated it with before the development of nephrotic syndrome took place. †Steroids derivatives used are prednisone and prednisolone with a dose of 1 mg/kg/day. In one case, the patient was treated with prednisolone 1 g/day IV for 3 days, then converted to 0.6 mg/kg/day PO

first reported case in Crohn's disease although there have been six previous case reports of nephrotic syndrome following salicylic acid derivatives for ulcerative colitis. We recommend routine monitoring of renal function and proteinuria during 5-aminosalicylate therapy, and physicians need to be aware of the potential for nephrotic syndrome with these agents.

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