



## Reversible Acute Renal Failure in a Elderly Patient with Minimal Change Disease: A Case Report

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### Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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### Case Report

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### ABSTRACT

**Introduction:** Minimal change disease is a histopathological lesion of the kidneys most commonly associated with nephrotic syndrome. Three pathophysiological mechanisms have been proposed to explain this syndrome: Nephrosarcoma (severe edema of the kidney), presence of acute tubular necrosis and decreased of glomerular filtration rate.

**Presentation of Case:** We present a 69years old patient with minimal change disease presented with severe renal dysfunction, dyspnoea, oedema of the lower extremities and weight gain of 10kg the month prior to admission. Renal function did not improve despite excess fluid removal with hemodialysis. Renal biopsy did not show significant interstitial Oedema but showed signs of tubular damage and mild atherosclerosis. Renal function returned with remission of proteinuria following administration of corticosteroid therapy.

**Conclusion:** Our case does not support the nephrosarcoma hypothesis but the presence of acute tubular necrosis and decreased of glomerular filtration rate theories cannot be excluded.

**Keywords:** Acute renal failure; hemodialysis; interstitial Oedema; minimal change disease; nephrotic syndrome.

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## 1. INTRODUCTION

Minimal change disease (MCD) is the most common cause of nephrotic syndrome (NS) in children, accounting for 70 to 90% of cases in this population and 10% to 25% of cases of nephrotic syndrome in adults. [1-4] Adults with MCD present with acute renal failure (ARF) in 20-25% of cases [2]. However, the correlation of ARF with older age, male sex, presence of hypertension, severe proteinuria, lower serum albumin and atherosclerosis on renal biopsy have been noted by Jennette JC et al.[5].

Histopathology changes on renal biopsy is acute tubular necrosis (ATN) in at least 60% of cases and glomerular filtration rate (GFR) is reduced concurrently with NS in approximately 30% of children and adults. Absolute and effective blood volume and renal plasma flow are relatively well preserved. However, severe reductions in GFR in some patients with MCD NS may result from an interaction between acute ischemic tissue injury and preexisting intrinsic renal abnormalities [6]. ARF develops early at the onset of first episode of NS, and recovers spontaneously or concurrently with steroid treatment. However, in a small number of cases, it may be severe enough to cause rapid decline in renal function accompanied by oliguria or anuria that is resistant to diuretic therapy thus necessitating renal replacement therapy, or may progress to end stage renal disease [2]. We report a case of reversible severe ARF requiring hemodialysis secondary to MCD.

## 2. PRESENTATION OF CASE

A 69 years old Caucasian male with a past history of dilated cardiomyopathy on treatment with carvedilol, ramipril, spironolactone and furosemide, presented in the emergency department with uremic symptomatology. He was dyspnoeic, hypertensive, with severe peripheral oedemas consequence of a weight gain in excess of 10kg the last month and severe decreased of 24-hour urine in the week prior to admission. The patient reported no preceding history of arthralgias, myalgias, fever, skin rash, nasal symptoms, haemoptysis, haematuria, dysuria or nephrotoxic drug intake.

### 2.1 Laboratory Analyses Showed

Metabolic acidosis (pH 7.23, and bicarbonate 16mEq/liter), anemia, hyponatremia, hypoalbuminemia and blood urea nitrogen

=352mg/dl, serum creatinine (SCr) 5.7mg/dl with signs of glomerular involvement. At presentation, his urinalysis had a specific gravity of 1020, pH 6.5, 4+ proteinuria, 3+ blood, 2–3 white blood cells and 25–30 red blood cells. The clinical and laboratory findings on admission necessitated the immediate start of dialysis treatment (Table 1). A 24-hour urine proteins showed 30g/liter (V=0.5liter) and clearance creatinine (ClCr)=12ml/min using the Cockcroft-Gault equation. Immunoglobulin (Ig) IgG, IgA, IgM, Complement (C) 3 and C4 were within normal limits. Antinuclear factor, rheumatoid factor, cryoglobulin, cytoplasmic-antineutrophil cytoplasmic antibody (C-ANCA), perinuclear - antineutrophil cytoplasmic antibody (P-ANCA), hepatitis B and C were negative.

**Table 1. Characteristics of patient at presentation**

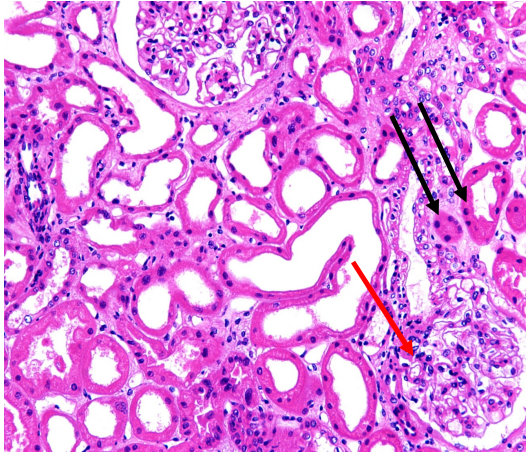
Characteristics	Value	Normal values
HGb	10.5	14-18g/dl
Leukocyte	6.70	3.8-10.5K/ $\mu$ L
Serum creatinine	5.7	0.7-1.3mg/dl
BUN	352	18-50mg/dl
Serum sodium	127	136-142mEq/l
Serum potassium	5.2	3.5-5mEq/l
Serum calcium	7.9	8.4-10.2mg/dl
Serum phosphorous	5.9	2.7-4.5mg/dl
Total protein	4.9	6.4-8.3 g/dl
Albumin	2.9	3.5-5 g/dl
Total cholesterol	287	<200 mg/dl
Triglycerides	254	<150 mg/dl
24-hour urine proteins(g/24h)	30 (V=0.5liter)	0.01-0.15g/24h
Clearance creatinine	12	80-120ml/min
Blood gas analysis		
pH	7.23	7.35-7.45
PaCO <sub>2</sub>	30	35-45ml/min
PaO <sub>2</sub>	89	80-100 mmHg
Sat O <sub>2</sub>	95	%
HCO <sub>3</sub>	16	24 $\pm$ 2 mEq/liter

HGb: Hemoglobin, BUN: Blood Urea Nitrogen, V: volume in liter

Kidney sonography revealed normal size of both kidneys with normal cortical echogenicity and without any evidence of urine obstruction. On admission and during hospitalization of the patient, an echocardiography exam revealed a ventricular ejection fraction=50% and the patient was in a stable state regarding his cardiac function.

A renal biopsy was performed on 7<sup>th</sup> day. The specimen contained a total of 33 glomeruli, 4 of which were globally sclerotic. Light microscopy revealed very mild increase of mesangial matrix, without compromise of the capillary lumina, as

shown in Fig. 1. There was a mild interstitial infiltration by mononuclear cells and interstitial fibrosis without interstitial oedema. The tubules were dilated with flattening and denudation of the epithelium, while some of which contained necrotic cast. Arteries and arterioles showed mild sclerosis of intima. Immunofluorescence was negative for IgE, IgM, IgA, C3, C1q, and Light chains kappa and lambda.



**Fig. 1. Renal histopathology (Hematoxylin & eosin X 200 magnification): The glomeruli appear enlarged by light microscopy (red arrow). Tubules show lesions of acute tubular necrosis (black arrows)**

High-dose intravenous furosemide (180mg/day) was basically ineffective. In view of MCD with ARF, the patient was treated with prednisone (initial dose 1mg/kg/day). He was managed with 10 sessions of HD and required a net negative 15liters of ultrafiltration before he was clinically estimated to have achieved dry weight. The proteinuria and renal function both improved after 4 weeks of prednisone therapy. After 30 days of hospitalization SCr were reduced to 1.5mg/dl and a 24-hour urine proteins=1.44g/liter (V=2.5liters) and the patient was discharged. Two weeks after discharge, SCr levels were 1,3mg/dl and the 24-hour urine proteins=0.83g/liter (V=2.4liters). A month later SCr levels were 1.1mg/dl, the 24-hour urine proteins was 0.250g/liter (V=2liters) and CICr~90ml/min. After attaining remission, prednisone was tapered by 10mg/week until reaching 5mg/day, this dose was continued for a mean 10-12months and the patient did not have relapse during follow-up, and particularly when steroid was tapered. The clinical data

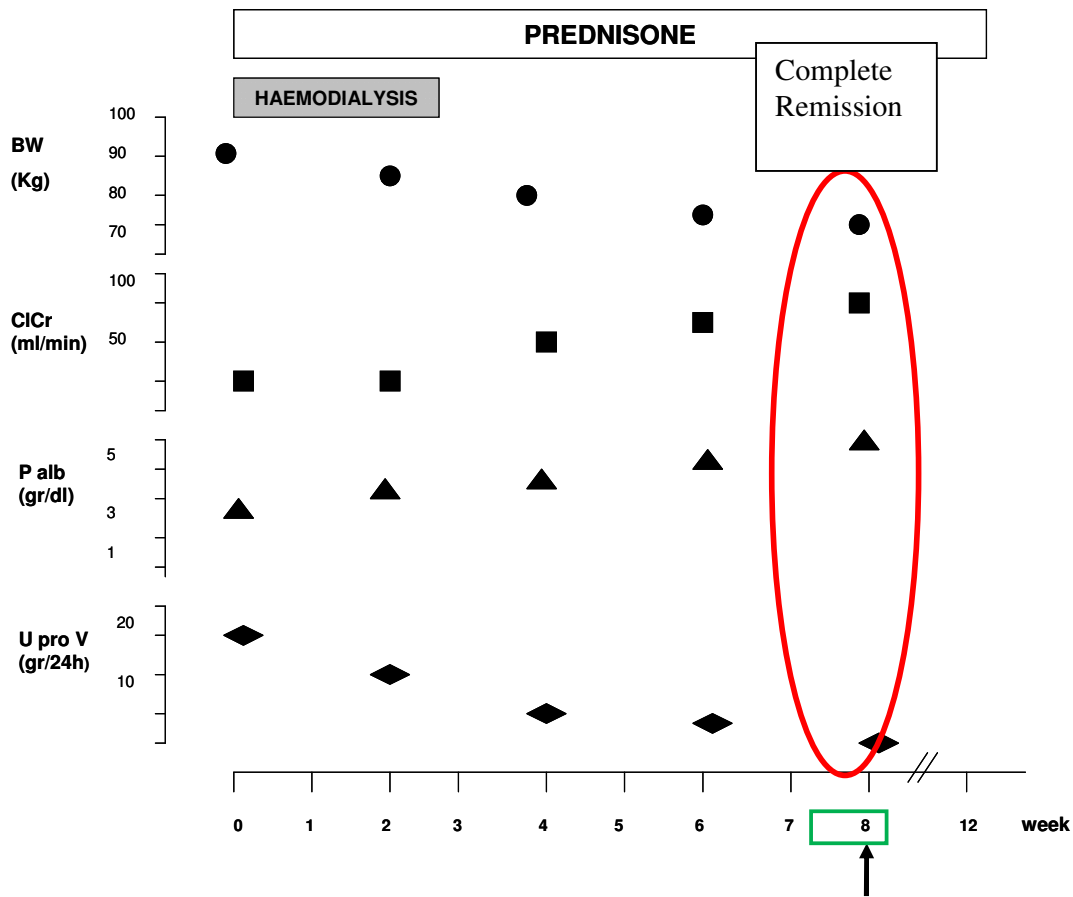
measurements over the entire period are summarized in Fig. 2.

### 3. DISCUSSION

The pathogenesis of MCD is unclear and several mechanisms have been implicated. Three possible mechanisms have been suggested to explain the reduction of GFR: a severe reduction of glomerular permeability [5], the presence of ATN or an increased intrarenal pressure related with interstitial oedema [7]. The last theory, concerns patients with MCD and ARF, is based on the observation that in some patients the ARF can be resolved by the removal of the excess fluid. According to this theory, the accumulation of high protein fluid in the interstitium can occur as a result of ultrafiltration of proteinaceous fluid from the mesangial side of the glomerular capillary and can induce severe interstitial oedema. It must be noted that not all patients presented with MCD and ARF, have evidence of interstitial *Oedema*.

Cameron M et al. [8] reported a case where a patient with MCD complicated by acute renal failure who had no evidence of interstitial oedema on biopsy and whose ARF did not improve with removal of 16 liters of extracellular fluid. The eventual resolution of ARF was temporally concomitant with remission of proteinuria in response to corticosteroids. The authors suggested that the podocytes may play a regulatory role in determining capillary hydraulic pressure, filtration wall distension as well as glomerular basement membrane expansion and thus ultrafiltration [9]. Loss of the charge selective barrier lowers the ultrafiltration and therefore MCD with acute renal failure, it could be explained by this pathophysiologic mechanism.

Rusillo et al. [10] reported another case of patient with glomerulosclerosis who developed ARF but the renal function did not change despite *Oedema* removal with hemodialysis. Renal biopsy did not show signs of tubular damage, obstruction by proteins or interstitial oedema. The authors suggested that acute renal was caused by reduction of GFR. Tinawi et al. [11] presented a case of MCD and ATN. On the renal biopsy was revealed tubular necrosis as well as moderate interstitial *Oedema*. In this case, any of the three theories cannot be excluded.



**Fig. 2. Summary of clinical course. ●BW = body weight; ◆UproV = 24h protein excretion; ■ClCr = creatinine clearance; ▲Palb = plasma albumin**

In the existing literature, approximately one third of children and adult patients with MCD NS show a relevant reduction in renal function during the acute phase of the disease. In general, the dysfunction is completely reversible when patients go into remission. In a minority of patients, especially in adults, GFR is severely reduced and oliguria resistant to diuretic treatment develops so that renal replacement therapy becomes necessary, as it was in our case [12].

The cardinal feature of MCD in children is the abrupt onset of proteinuria with the development of the NS. Whereas hematuria, hypertension, and renal insufficiency are unusual in children, these features can be seen in adult-onset MCD. In a cohort by Waldman et al, hypertension was present in 42.9% and hematuria was seen in 28.9%. Similar findings have been reported in other series of adults with MCD. The mean GFR was also diminished at presentation. However,

this may reflect the age of our patient, other confounding medical problems, and intravascular volume depletion associated with hypoalbuminemia. Our patient had some of these features.

Steroids form the cornerstone of first-line therapy in MCD. In general, adults with MCD will require longer duration of steroid treatment and are not considered steroid resistant until after 4mo of therapy. However, it is interesting to note that three adult Asian studies reported more prompt and favorable responses to steroids (between 80 and 90% response within 8wk). Our patient achieved a complete remission after eight weeks of therapy.

The absent of interstitial *Oedema* cannot be considered a key factor in the pathogenesis of ARF as suggested by Lowenstein et al [7]. The scanty presence of proteinaceous casts and their role in renal dysfunction by a mechanism of

tubular obstruction who advocated by some authors, is questionable. The main findings of tubular lesions observed in our case are reminiscent of those described in biopsy specimens taken from patients with ARF due to renal ischemia and have been reported in other series of ARF in NS [6]. In our case, the patient with MCD and acute renal failure presented with heavy proteinuria and had no evidence of renal interstitial oedema. Histopathology findings showed acute tubular necrosis, interstitial fibrosis and mild arteriosclerosis. Since removal of excess fluid did not reverse the acute renal failure, our case is not accountable by the nephrosarcoma hypothesis. Nevertheless, since biopsy showed lesions of acute tubular necrosis, the theory of reduced glomerular filtration rate due to tubular necrosis cannot be excluded.

Certainly an additional mechanism like decreasing renal blood flow by worsening of cardiac function could be explain the appearance of acute renal failure but our patient was in a stable state regarding his cardiac function.

According to the data from the literature, ARF associated with idiopathic NS is in most cases a reversible condition [6]. Despite the severity of clinical features of our patient, we can confirm that renal function recovery even after a dialysis treatment period and this functional recovery paralleled with the improvement of protein excretion induced by steroid therapy [12].

#### 4. CONCLUSION

In conclusion, it appears that MCD with acute renal failure is a complex disease with many different pathophysiological manifestations and further investigation is needed in order to discover the mechanisms that cause the reduction of glomerular filtration. Finally, our case does not support the nephrosarcoma hypothesis but the presence of acute tubular necrosis and decreased of glomerular filtration rate theories.

#### CONSENT

Written informed consent was obtained from the patient for publication of this Case report.

#### ETHICAL APPROVAL

Ethics approval was obtained from the Research and Ethical Committee of the General Hospital of Piraeus. Informed written consent was obtained

from the patient. Confidentiality and privacy has ensured by not mention the name of subject, and only the investigators have access to the data.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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