



## Case Vignette: OSA and Renal Disease

### Presenting Complaints

A 60-year-old African American man presented to his primary care physician with the main complaint of foamy urine and swelling of hands and face for a week.

### Past History

Around four years ago, at another clinic, proteinuria had been identified. Hypertension and hyperlipidemia had been diagnosed in the previous year. The patient had no history of diabetes or other glomerular diseases.

### Physical Exam

- BP- 148/91 mmHg
- Weight- 68.0 kg (BMI- 27.4 kg/m<sup>2</sup>)
- Pulse rate 73 beats/min
- Body temperature 36.4°C
- Tonsils were not enlarged

### Testing

- **Blood examination** showed a blood urea nitrogen 3.89 mmol/L (10.9 mg/dL), serum creatinine 88.4 μmol/L (1.00 mg/dL), uric acid 39.2 μmol/L (6.6 mg/dL), serum albumin 43 g/L (4.3 g/dL), total cholesterol 4.87 mmol/L (188 mg/dL), immunoglobulin (Ig) G 13.49 g/L (1349 mg/dL), IgA 4.35 g/L (435 mg/dL) and IgM 0.83 g/L (83 mg/dL).
- **Urine examination** revealed proteinuria (protein and creatinine ratio) 0.67 g/g Cr. The urinary red blood cells were at 3 per high power field.
- Autoimmune serological findings and tumor markers such as CEA and CA19-9 were within normal ranges.
- A renal biopsy was not performed because the patient refused it.

His physician added candesartan (2 mg/day), an angiotensin II receptor antagonist to decrease BP and proteinuria. He was asked to follow up in 3 months.

At his F/U appointment, the BP had decreased to within the normal range (120–130/80–85), but proteinuria had increased to 1.5 g/g Cr. In addition, he complained of repetitive apnea during sleep which his wife had noticed and pointed out to him.



# Obstructive Sleep Apnea Awareness

His physician administered the Epworth Sleepiness Scale (ESS).

*The ESS subjectively assesses excessive daytime sleepiness by asking patients to rate their chance of dozing off from 0 (would never doze) to 3 (high chance of dozing) for 8 commonly encountered scenarios, with a total maximal score of 24.*

Would never doze	Slight chance of dozing	Moderate chance of dozing	High chance of dozing	
<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	Sitting and reading
<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	Watching TV
<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	Sitting inactive in a public place (e.g. cinema or in a meeting)
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Being in a car for an hour as a passenger (without a break)
<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	Lying down to rest in the afternoon (when possible)
<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Sitting and chatting to someone
<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	Sitting quietly after lunch (not having had alcohol)
<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	In a car when you stop in traffic for a few minutes
<input type="button" value="Calculate Score"/>				
Your Score				
10				

**Figure 1. Results of Epworth Sleepiness Score**

The ESS score generated was 10/24 (Figure 1). ESS scores of 6-10 represents a “Higher Normal Daytime Sleepiness ‘. [[About the ESS](#)]



# Obstructive Sleep Apnea Awareness

## Test results:

The ESS score generated was 10/24 (Figure 1). ESS scores of 6-10 represents a “Higher Normal Daytime Sleepiness ‘.[\[About the ESS\]](#)”

He was referred to a sleep physician for further evaluation. The patient underwent nocturnal polysomnography for a detailed examination that revealed severe OSA [*total apnea–hypopnea index (AHI) 78.3 events per h, obstructive AHI 77.6 events per h, average oxygen saturation (SaO<sub>2</sub>) 94.0%, minimum SaO<sub>2</sub> 65.0% and cumulative time percentage of total sleep time when SaO<sub>2</sub> was <90% (SaO<sub>2</sub> <90%) 20.7%*].

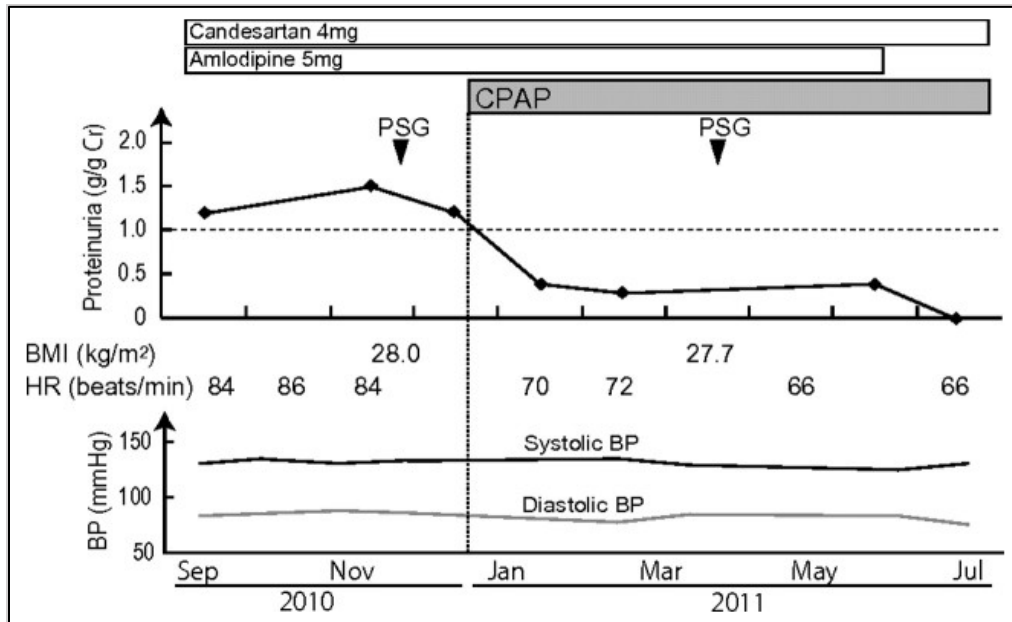
## Discussion of Treatment Plan

After obtaining informed consent, CPAP treatment using a nasal mask was initiated. The setting of the device was auto-titration mode (pressure 4.0–20.0 cm H<sub>2</sub>O), and the patient was instructed to use it overnight. He was asked to follow up after 3 months.

## Outcome of Case

At 3 months after CPAP initiation, CPAP usage days and daily hours were 96.4% and 5.3 h, respectively which indicated a good compliance of CPAP (average usage 5.3 h/day). The efficacy data from a F/U PSG exhibited a clear improvement of OSA: total AHI, 6.1 events per h; average SaO<sub>2</sub>, 96.0%; minimum SaO<sub>2</sub>, 93.0% and SaO<sub>2</sub> <90%, 0%. Notably, total elimination of saturated oxygen levels <90% indicated the disappearance of severe hypoxia during sleep.

Along with the reduction of apnea and hypopnea events, proteinuria also clearly decreased. (Figure 2)



**Figure 2. Changes of proteinuria, BMI, HR and BP before and after CPAP initiation**

(SOURCE: Masuda T, Honma S, Sasaki N, Hanawa-Yazawa S, Iwazu Y, Kusano E, Asano Y. Effect of continuous positive airway pressure on proteinuria in obstructive sleep apnea. *Clin Kidney J.* 2012 Jun;5(3):257-60. doi: 10.1093/ckj/sfs046. Epub 2012 May 3.)

Six months after CPAP initiation, the low level of proteinuria ( $\leq 0.3$  g/g Cr) had continued. In addition, average proteinuria for 6 months after CPAP was markedly lower (0.3 g/g Cr) than before CPAP treatment (1.2 g/g Cr). (Figure 2)

## Teaching Points

This case report demonstrates a remarkable reduction in proteinuria after CPAP treatment in a severe OSA patient without any changes of medication or body weight. Convincing mechanisms of the beneficial effects of CPAP on proteinuria are (i) the betterment of renal hypoxia, (ii) the improvement of sympathetic nerve activation (SNA) and (iii) the decrease of nocturnal BP.

- i. The betterment of renal hypoxia by CPAP has been reported to play a critical role in the decrease of proteinuria. The renal medulla is poorly oxygenated under normal conditions because blood flow to the renal medulla is lower than that of the cortex. Therefore, a hypoxic condition can readily affect the renal medulla and lead to tubular injury. Furthermore, along with the progression of hypoxia, the injured area could spread to the superficial cortex, which includes glomeruli. In this case, the remarkable improvement of



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- hypoxia by CPAP, which is evident in PSG data, might decrease proteinuria through the amelioration of glomerular damage.
- ii. The improvement of SNA by CPAP might also decrease proteinuria. Nocturnal apnea and hypopnea due to OSA causes systemic SNA, and CPAP treatment attenuates OSA-induced SNA. Clearly, both HR and pulse rate rise index, possible markers for SNA, decreased after CPAP treatment. (Figure 2)
  - iii. Furthermore, the decrease of nocturnal BP might have a beneficial effect on proteinuria. OSA plays an important role in nocturnal hypertension, which could cause increased proteinuria. In the above case, home BP in the morning showed mild reductions after CPAP initiation.

Given that OSA and CKD share common comorbidities, it should not be surprising that both conditions commonly coexist. Obstructive sleep apnea-related intermittent hypoxia produces a range of harmful systemic effects including oxidative stress, inflammation, and sympathetic activation that collectively worsen the progression of renal disease. OSA has also been linked to glomerular hyperfiltration leading to proteinuria. Other renal consequences of OSA include nocturnal polyuria and natriuresis. While epidemiological studies indicate a causal relationship between OSA and CKD, additional studies are needed to investigate the clinical outcomes of aggressive treatment of OSA on renal dysfunction.

**This report illustrates that patients with undiagnosed OSA may demonstrate renal signs such as proteinuria. While there may be need of more clarity on a causative connection between OSA and CKD, eliminating OSA improves the prognosis of CKD patients. Therefore clinical vigilance for sleep apnea is paramount when attending to CKD patients with significant**

*Adapted from: Masuda T, Honma S, Sasaki N, Hanawa-Yazawa S, Iwazu Y, Kusano E, Asano Y. [Effect of continuous positive airway pressure on proteinuria in obstructive sleep apnea](#). Clin Kidney J. 2012 Jun;5(3):257-60. doi: 10.1093/ckj/sfs046. Epub 2012 May 3.*

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**proteinuria.**



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## Additional Reading

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