American Journal of Medical Case Reports, 2014, Vol. 2, No. 11, 237-239
Available online at http://pubs.sciepub.com/ajmcr/2/11/3

DOI:10.12691/ajmcr-2-11-3

A Transient Proteinuria: An Unusual Complication of Hypothyroidism

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Received October 16, 2014; Revised October 26, 2014; Accepted October 29, 2014

Abstract Background: Although the effect of thyroid hormones is very important on renal function and glomerular filtration rate, it is often overlooked. Hypothyroidism is sometimes accompanied by a decrease in the glomerular filtration rate and hyponatremia. Observation: A33-year-old man was admitted in intensive care unit for an inaugural diabetic ketoacidosis in December 2012. He has been diagnosed as hypothyroidism case since 2005. He had a replacement therapy that he had given up in 2011. On The physical examination he exhibited a general fatigue with fever and sweats. He suffered from myalgia and proximal muscle weakness, edema of renal type and a few crackles. The biology showed ketoacidosis, progressive acute renal failure of deterioration associated with important rhabdomyolysis and proteinuria of 5.7 g/24 h. Normal eye fundus was able to rule out diabetic nephropathy. In addition to the treatment of ketoacidosis, lung disease and the fluid overload, hormone replacement therapy was reinstituted. The evolution was marked bythe disappearance of edema, fever, rhabdomyolysis and proteinuria. Discussion: The rhabdomyolysis, secondary to hypothyroidism, is atthe origin of renal failure. In this case, proteinuria is exceptional. Themajor part of the renal manifestations during thyroid dysfunctions isreversible with hormone therapy. Conclusion: Transient proteinuria isexceptional in hypothyroidism. It is another face of kidney involvementin thyroid disorders.

Keywords: *hypothyroidism, proteinuria, kidney*

Cite This Article: R. Hajji, F. Derbali, K. Mnafgui, S. Zribi, M. Elleuch, N. Kammoun, and Z. Jallali, "A Transient Proteinuria: An Unusual Complication of Hypothyroidism." *American Journal of Medical Case Reports*, vol. 2, no. 11 (2014): 237-239. doi: 10.12691/ajmcr-2-11-3.

1. Background

Dysfunctional thyroid hormone metabolism has been proved to play a crucial role in renal failure [1].

Thyroid dysfunction affects renal development and physiology by affecting the cardiovascular system and the renal blood flow or by disturbing glomerular filtration and the structure of the kidney [2].

Although the major potentials of thyroid hormones (TH), their roles are overlooked. In fact, they are essential for an adequate growth and development of the kidney. Conversely, the kidney is not only an organ for metabolism and elimination of TH, but also a targetorgan ofsome of the TH actions. Thyroid dysfunction could induce remarkable changes inglomerular and tubular functions and electrolytes and water homeostasis objective by decrease in glomerular filtration, hyponatremia, and an alteration of the abilityfor water excretion [3].

In this respect, we describe one case of reversible renal impairment secondary to hypothyroidism. We suggest that patients with renal impairment of unknown cause have thyroid function tests undertaken as part of routine investigation.

2. Observation

A 33-year-old man was admitted in intensive care unit for diabetes revealed by ketoacidosis in December 2012.

He is unemployed. He is not smoker neither alcohol consumer even occasionally. He didn't report any other addiction attitude.

He had hypothyroidism since 2005. He had a hormonal replacement therapy that he had given up in 2011 without any medical advice. Since this date, he hadn't taken any medication.

Since several months, he presented an important polyuria, polydipsia and weight loss in spite of a remarkable polyphagia that he had initially neglected. The patient family had taken him in the emergency department because they noticed that he presented a big asthenia and his behavioral state was deteriorating.

On the physical examination, he was exhausted, feverish and covered by sweats. Severe dehydration was noticed. He suffered from myalgia and proximal muscle weakness, edema of renal type. The pulmonary auscultation showed crackles at both lung bases.

The biology exhibited ketoacidosis, progressive acute renal failure (creatinine initially at 187 µmol/ L reached up 782 µmol/L and urea passed respectively from 7.24 mmol/L to 32.5mmol/L). An important rhabdomyolysis was observed and accompanied with significant increases in the activities of creatine phosphokinase (3300 UI/ L) and lactate dehydrogenase (434 UI/L).

A proteinuria was noted in several times with rates between 4. 3 g/ 24 hand 5.7 g/24 h. Normal eye fundus was able to rule out diabetic nephropathy. However, the blood and urine electrolytes were normal. The chest X-ray revealed signs of moderate acute pulmonary edema.

In the intensive care unit, the patient underwent hemodialysis session because of the acute pulmonary edema due the kidney failure. He had received insulin treatment, adequate hydration and hormone replacement therapy was reinstituted.

The evolution was marked by the progressive disappearance of edema, fever, rhabdomyolysis and proteinuria. All the features were normalized 16 days after treatment instauration. Since this date, the patient was followed up with stable diabetes and hypothyroidism.

3. Discussion

The interactions between kidney and thyroid functions have been demonstrated for several years [1]. In fact, thyroid dysfunction causes remarkable damages in glomerular and tubular functions [3].

Thyroid hormones may directly affect the kidney functions and reversely kidney dysfunction may also contribute to thyroid disorders. The renal manifestations of thyroid disorders are based on hemodynamic alterations or/and to direct effects of thyroid hormones. The renin-angiotensin-aldosterone system (RAAS) plays a crucial role in the cross-talk between the thyroid and the kidney[4].

Else, in hypothyroidism, several mechanisms interact to reduce the renal blood flow (RBF). In fact, the RBF is reduced by decreased cardiac output (negative chronotropic and inotropic effects)[5], increased peripheral vascular resistance and intrarenal vasoconstriction [6,7], and reduced renal response to vasodilators [8]and significantly decreased renal vasodilators such as vascular endothelial growth factor (VEGF) and insulin like growth factor-1 (IGF-1) [9].

Indeed, VEGF, by stimulating endothelial nitric oxide synthase activity, enhances to the relaxation of the renal vasculature [10,11,12,13].

On the other hand, IGF-1 is known to increase renal plasma flow and glomerular filtration rate (GFR) in humans [14,15].

In addition, hypothyroidism was marked by histological changes in the glomerular structure: glomerular basement membrane thickening and mesangial matrix expansion, which may also involve in reduced RBF [16].

In more than 55% of adults with hypothyroidism, the GFR is reversibly reduced by about 40% [17].

Many mechanisms can explain this GFR decrease [18, 19, 20, 21]:Reduced sensitivity to β-adrenergic stimulus and decreased renin release, [22] associated with decreased angiotensin II and defective RAAS activity, contribute to GFR reduction [23].

In addition, hypothyroidism can contribute to renal parenchymal growth retardation which limits glomerular surface area for filtration [16].

Proximal tubular absorption of sodium, chloride, and water is decreased [24].

Moreover, a decrease of the renal basolateral chloride channel expression is noted. This contributes to the reduction of chloride reabsorption and the increment in the delivery the distal chloride, which stimulates the macula densa mediated tubuloglomerular feedback and so reduces the RAAS activity. Consequently, the GFR diminishes.

The decrease of the tubular transport capacity was remarked. We note also the reduction of the Na/K ATPase activity first in the proximal tubules then in almost all segments of the nephron [25].

The Na – H exchanger (NHE) activity is also reduced in hypothyroidism [26].

Thus, there is a remarkable decrement in sodium and bicarbonate reabsorption. As a result of impaired urinary acidification, an increase in sodium and bicarbonate leakage in urine is noted.

The reduction of the tubular reabsorption activity also deals inability to maintain the medullary hypertonicity. As it is the principal element contributing in the urinary concentration, the loss of medullary hypertonicity, in hypothyroidism, causes an important dysfunction in urinary concentrating ability of the kidney [27].

However, hypothyroidism increases reversibly the collecting ducts sensitivity for vasopressin (antidiuretic hormone or ADH), thus increases free water reabsorption. The increased fluid retention, on the other hand, cannot induce maximal ADH suppression [28,29]

Persistent ADH activity and free water retention is due to the resistance of pituitary response to increased fluid retention.

Decreased HT deals to low cardiac output which stimulates the carotid baroreceptors and results in the non-osmotic ADH secretion increase [18,30].

In some patients, the inappropriate ADH secretion could be suspected as the urine sodium is not as low as would be expected with reduced cardiac output. In hypothyroidism, hyponatremia is the result of the decrease of the GFR, the reduction of sodium reabsorption and relative increase of ADH secretion and renal ADH hypersensitivity mediated impaired free water clearance [17,31].

Hyponatremia is twice as common among hypothyroid patients with raised serum creatinine as among those with normal serum creatinine. Our patient didn't have hyponatremia although of severe hypothyroidism.

This disorder can be even life threatening in some cases [32].

Hypothyroidism can deal to reversible elevation in serum creatinine due to not only the GFR decrease but also possible myopathy and rhabdomyolysis. Our observation displays clearly this reality: the renal failure was due to both rhabdomyolysis and decreased TH and it was improved when muscle enzymes (creatine phosphokinase and lactate dehydrogenase) were normalized and hormone treatment was initiated. But other rhabdomyolysis causes as alcohol or illicit drug use, side effects of some medications (statins, corticosteroids...), severe heatstroke, traumatism, seizure, infection and electrolytes disorders (hypokalemia, hyponatremia, hypernatremia,..)… shouldn't

be forgotten [33]. In our case report, all these were ruled out.

Serum Cystatin C, used as biomarker of kidney function, is strongly affected by thyroid diseases. A decrease in serum cystatin C levels is observed in hypothyroidism due to reduced production, consequent to reduced cellular metabolism. Therefore, it should be avoided in thyroid disorders. The recommended kidney function test in hypothyroidism is a creatinine-based GFR estimation (24-hour creatinine clearance, calculated GFR by Cockroft-Gault or the CKD-EPI equation) [34].

All these changes are reversible by TH supplementation. Hypothyroidism also results in increased glomerular capillary permeability to proteins [19]. The consequent proteinuria often precedes the reduction in GFR in this disease [20].

The major part of the renal manifestations during thyroid disorders is reversible with hormone therapy. In our case, all features of kidney dysfunctions were corrected in 16 days of treatment [2].

4. Conclusion

Transient proteinuria is exceptional in hypothyroidism. It is another face of kidney involvement in thyroid disorders. Its pathophysiology is very complex. A detailed knowledge of all these interactions is important for both the nephrologists and endocrinologists for optimal management of the patient. The most common feature is its reversibility after hormone treatment started at time.

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