Renal salt wasting syndrome in a patient with COVID-19; a case report and review of the literature

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Abstract

Introduction: Cerebral salt wasting or renal salt wasting (RSW) syndrome, may be more common than syndrome of inappropriate antidiuretic hormone secretion (SIADH); and may even occur in the absence of cerebral disease. We report a case of RSW in a Bangladeshi patient positive for COVID-19 without clinical cerebral disease.

Case Presentation: A 53 years-old Bangladeshi patient presented with history of chest pain and acute MI. On examination, the patient was conscious, alert, vitally stable, chest with fine bilateral basal crepitation and heart with additional S3 sound and abdomen was lax with no organomegaly. There was no lower limbs oedema. His serum creatinine; 68 umol/L, urea; 3.4 mmol/L, K; 4.7 mmol/L, sodium; 135 mmol/L, uric acid; 141 mmol/L and phosphate was 1.3 mmol/L. Echocardiography (ECG) revealed anterior lateral wall STEMI. PCI was done for LAD. ECG revealed ejection fraction (EF) 10-15%. Nasopharyngeal swab for COVID-19 was positive. Serum sodium decreased from 135 to 108 with signs of hypovolemia. Work up for hyponatremia revealed serum osmolality of 237 mOsm/kg, urine NA; 109 mmol/L, urine osmolality; 295 mOsm/kg, urine uric acid; 685 umol/L, and urine phosphate: 6.5 mmol/L. Additionally serum T3, T4, TSH and serum basal cortisol were normal. The patient received normal saline infusion and fludrocortisone and serum sodium increased to 134 mmol/L. Our patient had all the important clinical and laboratory characteristics of RSW in the absence of cerebral disease which include hyponatremia associated with hypovolemia, high urinary sodium excretion, increased fraction excretion of phosphate and persistent hypouricemia with increased fractional excretion of urate after correction of hyponatremia and with normal renal, adrenal and thyroid functions. Furthermore, there was a prompt response to saline replacement and fludrocortisone and steady improvement in serum sodium with negativity and improvement of COVID-19. Our diagnosis was RSW in the absence of cerebral disease and to our knowledge; this is the first case report of RSW in a patient with COVID-19 in the literature.

Conclusion: RSW should be considered in patients with COVID-19 with hyponatremia and absence of cerebral disease. We suggest changing cerebral salt wasting to the more appropriate term RSW.

Keywords: COVID-19, Cerebral salt-wasting syndrome, Renal salt wasting syndrome, Syndrome of inappropriate antidiuretic hormone secretion, SARS-CoV-2

Case Presentation

A 53 years-old Bangladeshi patient presented to Al-Adan hospital casualty, Kuwait on 28/4/2020, with a history of chest pain and acute myocardial infarction. On examination, the patient was conscious, alert, body mass index was 30 kg/m², blood pressure 113/57 mm Hg, pulse 84 b/m, temperature 37.3°C, chest with fine bilateral basal crepitation and heart with additional S3 sound and abdomen was lax with no organomegaly. There was no lower limbs edema. His serum creatinine ≥8 umol/L, urea; 3.4 mmol/L, K; 4.7 mmol/L, sodium; 130 mmol/L, uric acid; 141 mmol/L, ALT; 39 IU/L, AST;
Hyponatremia is the most common electrolyte abnormality that is undergoing dramatic changes in terms of its diagnostic approach and clinical outcomes (13).

In CSW or RSW, abnormalities in the proximal tubule result in excessive sodium losses, which lead to decreased effective circulating volume. This activates baroreceptors, which increase antidiuretic hormone (ADH) secretion. This results in water conservation and a return to an equilibrated state. In contrast, SIADH primarily occurs due to an inappropriate euvoletic rise in ADH secretion (14). In our case the abnormalities most probably in proximal tubule due to increased urinary sodium excretion with increased FEurate, urea and phosphate.

Differentiation of this disorder from the SIADH, a common cause of hyponatremia, can be difficult because both can present with hyponatremia and concentrated urine with natriuresis. However, distinguishing between the two disorders is important because treatment options differ. Attention to the volume status of the patient is important in making the distinction. Failure to distinguish CSW syndrome from SIADH in a patient with hyponatremia who has brain injury could lead to inappropriate therapy with fluid restriction. RSW should be considered a discrete clinical entity and may be more common than perceived (4). It should also be considered in patients without cerebral disease (3,15).

The relationship among serum urate, FEurate, and hyponatremia in CSW syndrome is unclear. FEurate may remain elevated even after correction of hyponatremia in patients with CSW syndrome. This is distinct from SIADH, in which FEurate returns to the reference range once the hyponatremia is corrected (4,15). The physiologic basis for this in CSW syndrome may be related to the receptor-mediated processing of sodium and urate in the proximal tubule, which may be defective in this syndrome. The physiologic basis for hypouricemia in SIADH remains unclear.

The abnormalities in proximal tubular transport may be secondary to a plasma natriuretic factor that reduces proximal and, possibly, distal sodium transport in renal salt-wasting syndrome. It may also inhibit the tubular transport of urate, phosphate, and urea in addition to sodium (16).

The cause of kidney involvement in COVID-19 is likely to be multifactorial, with cardiovascular comorbidity and predisposing factors (such as sepsis, hypovolemia, and nephrotoxins) as important contributors (6).

Cardiorenal syndrome, particularly right ventricular failure secondary to COVID-19 pneumonia, might lead

**Discussion**

Hyponatremia is the most common electrolyte
| Variables                              | 28/4/2020 | 11/5/2020 | 15/5/2020 | 18/5/2020 | 19-20/5/2020 | 21/5/2020 | 23/5/2020 | 24-25/5/2020 | 26/5/2020 | 28/5/2020 | 30/5/2020 |
|----------------------------------------|-----------|-----------|-----------|-----------|--------------|-----------|-----------|--------------|-----------|-----------|-----------|
| Creatinine (umol/L)                    | 68        | 58        | 60        | 58        | 58           | 67        | 61        | 61           | 60        | 70        | 65        |
| S. urea (mmol/L)                       | 3.4       | 1.7       | 3.5       | 3.3       | 3.6          | 2.8       | 3.7       | 4.2          | 6.4       | 5.6       | 5.6       |
| S. K (mmol/L)                          | 135       | 108       | 110/113   | 131       | 124/128      | 129       | 133       | 132          | 131       | 125       | 134       |
| S. osmolality (mosmo/kg)               | 237/240   | 258       | 254/253   | -         | -            | 281       | 273       | -             | 282       |           |           |
| S.CL (mmol/L)                          | 89        | -         | 89        | 85        | 94           | -         | -         | 94.1         | 92        | 88        | 95        |
| S. uric acid (mmol/L)                  | - -       | - -       | 141       | - -       | - -         | - -       | 157       | 148          | -         | 172       |           |
| S.PO4 (mmol/L)                         | - -       | - -       | - -       | - -       | - -         | 1.1       | - -       | 1.3          | 1.2       | -         |           |
| Urine NA (mmol/L)                      | - -       | 88        | 109       | 160       | 146         | 141       | 78/59     | 44           | 46        | 102       |           |
| Urine osmolality (mosmo/kg)            | - -       | 295       | 446       | 446       | 452         | 346/505   | 252       | 321          | 463       |           |           |
| Urine urate (umol/L)                   | - -       | - -       | 685       | - -       | - -         | - -       | 1187      | 1508         | 1543      |           |           |
| Urine K (mmol/L)                       | - -       | 11.6      | - -       | 27.04     | 20.7/42.7   | 27.6      | 42.3      | 45.07        |           |           |           |
| Urine CL (mmol/L)                      | - -       | 104       | - -       | 132       | 66          | 38        | -         | 113          |           |           |           |
| Urine creatinine (mmol/L)              | - -       | 1.93      | - -       | 4.26      | 3.3         | 4.1       | -         | 4            |           |           |           |
| Urine urea (mmol/L)                    | - -       | 49        | 74        | 74        | -           | 200       | -         | 143          |           |           |           |
| Urine P04 (mmol/L)                     | - -       | - -       | 0.3       | 0.3       | 4.1         | 6.5       | -         | 9.2          |           | 5.7       |           |
| FEurate (%)                            | - -       | 14.6      | - -       | - -       | - -         | 14.58     | -         | 14.57        |           |           |           |
| FEPHosphate (%)                        | - -       | - -       | - -       | - -       | - -         | - -       | -         | 13.9         |           |           |           |
| Frusimide/spironolactone               | +         | - -       | - -       | - -       | - -         | - -       | - -       | - -          |           |           |           |
| Normal saline                          | -         | +         | +         | -         | -           | - -       | -         | - -          |           |           |           |
| Fludrocortisone                        | -         | - -       | - -       | +         | -           | - -       | -         | - -          |           |           |           |
| CVP                                    | 6         | 4         | 2         | 4         | 5           | 6         | 3         | 5            | 6         | 7         |           |
| Urine output (mL/h)                    | 40        | 70        | 70        | 70        | 70          | 100       | 100       | 80           | 70        | 80        | 80        |
| CRP                                    | 60        | 53        | 67        | 68        | 60          | -         | 64.85      | 81.2         | 29.2      | 18.4      |           |
| COVID-19                                | -VE       | +VE       |           |           |             |           |           |               |           |           | -VE       |
to kidney congestion and subsequent acute kidney injury (AKI). Similarly, left ventricular dysfunction might lead to low cardiac output, arterial under-filling, and kidney hypoperfusion.

Autopsy data (7), indicates that the endothelium is affected in the lung and in the kidney, where it is probably responsible for proteinuria. Furthermore, virus particles were reported to be present in renal endothelial cells, indicating viremia as a possible cause of endothelial damage in the kidney and a probable contributor to AKI (7).

Additionally, SARS-CoV-2 can directly infect the renal tubular epithelium and podocytes through an angiotensin-converting enzyme 2 (ACE2)-dependent pathway and cause mitochondrial dysfunction, acute tubular necrosis, the formation of protein reabsorption vacuoles, collapsing glomerulopathy, and protein leakage in Bowman’s capsule (8,9).

Another potential mechanism of AKI involves SARS-CoV-2-related immune response dysregulation, as indicated by observed lymphopenia and cytokine release syndrome (cytokine storm) (10,11).

The report of C/RSW occurring in patients without cerebral disease has led to proposal to change CSW to the more appropriate term RSW.

In conclusion, RSW should be considered in patients with COVID-19 with hyponatremia and absence of cerebral disease. We suggest changing CSW to the more appropriate term RSW.

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Authors’ contribution
All authors contributed equally to prepare the manuscript.

Conflicts of interest
The authors declared that they have no conflict of interest.

Ethical considerations
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