Respiratory Medicine Case Reports 31 (2020) 101290

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: http://www.elsevier.com/locate/rmcr

Case report

COVID-19 presented with syndrome of inappropriate ADH secretion (SIADH): A case report from Bangladesh

Md Reaz Uddin Chowdhury [a,*], Kazi Shanzida Akter [b], Mohammad Moksedul Moula [c], Muhammad Anwarul Kabir [a], Sahedul Islam Bhuiyan [d], Bimal Chandra Das [e]

[a] Abdul Malek Ukil Medical College, Noakhali, Bangladesh
[b] Dedicated COVID-19 Hospital, Trauma Center, Feni, Bangladesh
[c] Medinova Specialized Hospital, Feni, Bangladesh
[d] Brahmanbaria Medical College, Brahmanbaria, Bangladesh
[e] Abdul Malek Ukil Medical College, Noakhali, Bangladesh

ARTICLE INFO

Keywords:
Unconsciousness
Hyponatremia
SIADH
COVID-19
Severe pneumonia

ABSTRACT

Backgound: Novel corona virus(SARS-CoV-2) which emerged from Wuhan, China, has spread to whole worlds very rapidly causing enormous health effect and death. Current publications worldwide showed that COVID-19 is a disease involving multiple system of the body with many unusual presentations. So physicians face the challenges to manage it in the hospital.

Case report: The syndrome of inappropriate secretion of anti diuretic hormone (SIADH) is one of the most common causes of hyponatremia accounts for approximately one-third of all cases. In the diagnosis of SIADH it is important to ascertain the euvolemic state of extra cellular fluid volume, both clinically and laboratory measurement. Several infections associated with SIADH have been reported. Howover, Coronavirus disease 2019 (COVID-19) associated with SIADH were only few cases reported. We are presenting a case of 70 year old female admitted with unconsciousness later diagnosed as severe hyponatremia along with COVID-19 complicated with severe pneumonia.

1. Introduction

Hyponatremia is most common electrolyte disorder in clinical practice [1]. Wide spectrum of aetiologies associated with hyponatremia is always a challenge in early diagnosis and treating this serious abnormality. Hyponatremia is associated with an increased risk of overall mortality in all patients [1]. SIADH is characterized by euvolemic hyponatremia, low plasma osmolality, elevated natriuresis, hypouricemia and lack of evidence of other hypouraemic diseases [2]. The most common pathological conditions such as sub-arachnoid haemorrhage, stroke, tumours, drugs and pulmonary disorders including pneumonia [3]. Besides infectious disease, several inflammatory conditions also influenced SIADH. In these situations, interleukin-6(IL-6), released by monocytes and macrophages, plays a pathogenic role in inducing the non-osmotic release of vasopressin [4].

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), transmitted often from human to human by droplet and contact routes [5]. The disease usually manifests as upper or lower respiratory system illness in majority of clinical presentation [6]. We describe a case of 70 year aged woman with SIADH associated COVID-19 with severe pneumonia. Our aim of this work to share how the patient present, steps of diagnosis and to improve patient management during this pandemic period.

2. Case presentation

A 70 year old woman non-diabetic with past medical history of hypertension on antihypertensive(amlodipine 5mg/telmisartan 80mg) presented to the emergency department on 24 June 2020 with one(1) day history of high grade fever, shortness of breath and unconsciousness for 4 hours. She has no history of diarrhoea, vomiting, chest pain, rhinorrhea, headache, blurring of vision, anosmia, dehydration or any history of bronchial asthma, chronic obstructive pulmonary disease (COPD), heart failure or any history of trauma, she didn't take any

Abbreviations: COVID-19, Corona virus disease2019; SIADH, Syndrome of inappropriate anti diuretic hormone secretion.

* Corresponding author.
E-mail addresses: drkazishanzida@gmail.com (M.R. Uddin Chowdhury), drbimalcmc28@gmail.com (B.C. Das).

https://doi.org/10.1016/j.rmcr.2020.101290
Received 11 July 2020; Accepted 9 November 2020
Available online 12 November 2020

antipsychotic rather took only an antihypertensive combination. But she complained of severe fatigue for last 5 days. She developed fever for 1 days which was high grade continued, highest recorded temperature was 104® f relieved by taking antipyretic paracetamol orally and per rectal. On the admission day at morning her son told that she developed drowsiness followed by unconscious, then she was taken to emergency department of Medinova specialized hospital, Feni, Bangladesh. On admission she was unconscious with GCS score 5, Temperature was 103® f, Heart rate was 100/min, Respiratory rate 26/min with oxygen saturation 89% on room air immediately put on supplemental oxygen with simple face mask, Blood pressure was 160/85 mm of Hg. Other general examinations were normal, physical examinations revealed bilateral coarse crepitations in both lungs, Cardiac apex in normal position, 1st and 2nd heart sound normal without any added sound, Jugular venous pressure(JVP) not raised, no leg edema or any organomegaly, she was put on urethral catheterisation and found normal urine output and also put on nasogastric feeding tube for feeding.

Emergency blood/serum send for laboratory investigations and were found(see Table 1) serum sodium of 114mEq/L(normal range 135–145 mEq/L), potassium was 3.6mEq/L(3.5–5.5mEq/L), Other laboratory investigation showed Hemoglobin (Hb%) was 11.1 gm/dl (normal range 11.0–16.0 gm/dl), Erythrocyte sedimentation rate(ESR) (westergren) was 54mm in 1st hour, total white blood cell count(WBC) was 6900/cmm (normal range 4000–11000/cmm), differential count of neutrophils was 74% (normal range 40–75%), lymphocytes was 11%(normal range 20–50%), eosinophils was 0%(normal range 2–9%), platelet count was 177,000/cmm (normal range 150.000–400,000/cmm), random blood sugar was 5.5mmol/L (normal up to 7.8mmol/L), serum creatinine was 1.3mg/dl (normal range 0.5–1.2mg/dl), SGPT was 16 U/L (normal up to 32U/L),C reactive protein(CRP) was 65mg/l(normal range<7mg/l), serum ferritin was 317ng/ml(normal 20–250ng/ml in female), troponin I was <0.1ng/ml (normal <0.1ng/ml), serum thyroid stimulating hormone (TSH) was 1.65μIU/ml (normal range 0.3–5.05 μIU/ml. Chest X-ray showing extensive bilateral pulmonary infiltration mostly in the periphery of the both lungs(see Fig. 1)., Electrocardiogram (ECG) and Computed tomography of brain(CT brain) was un remarkable. Further workup revealed low normal blood urea which was 11.6mg/dl(normal range 10–50mg/dl), low serum uric acid 2.4mg/dl (normal range 2.4–5.7mg/dl in female), urine osmolality of 353mOsm/kg(reference value 60–1400 mOsm/kg), low plasma osmolality which was 219 mOsm/kg(reference value 275–295) (275–295, urinary sodium was 34 mEq/L(around 20 mEq/L), random serum cortisol at 8 a.m. was 14mcg/dl(normal ranges:10-20mcg/dl), ACTH stimulation test was not done. As COVID-19 cases increased in Feni, Bangladesh, we sent a nasopharyngeal swab for RT-PCR for corona which came positive. After all workup she was diagnosed as having COVID-19 with severe pneumonia with SIADH.

Table 1
Base line investigations after admission.

Investigations	Findings with normal Reference range
Hemoglobin (Hb)	11.1 gm/dl(11.0–16 gm/dl)
Erythrocyte sedimentation rate(ESR)	45mm in 1st hour(0–10mm/1st hour)
Total White Blood Cell Count	6900/cmm(4000–11000/cmm)
Neutrophils (Differentials)	74%(40–75%)
Lymphocytes (Differentials)	16%(20–50%)
Platelet count	177,000/cmm(150,000–400,000/cmm)
Random Blood Sugar	5.5mmol/l(<7.8mmol/l)
Sodium(Na^+)	114mmol/l(135–145mmol/l)
Potassium(K^+)	3.6mmol/l(3.5–5.5mmol/l)
Blood urea	11.6mg/dl(10–50mg/dl)
Serum uric acid	2.4mg/dl(2.4–5.7mg/dl)
C reactive protein(CRP)	65mg/l(<7mg/l)
Serum ferritin	317ng/ml(10-125ng/ml)
Serum creatinine	1.3mg/dl(0.5-1.2mg/dl)
Alanine aminotransferase(ALT)	16U/L(10-65U/L)
Serum thyroid stimulating hormone(TSH)	1.65μIU/ml(0.3–5.05μIU)
Plasma osmolality	219mOsm/kg(275–295mOsm/kg)
Urine osmolality	353mOsm/kg(60–1400mOsm/kg)
Urinary sodium concentration	58mEq/L(40-220mEq/L)
Random Serum Cortisol at 8 a.m.	14mcg/dl(10-20-mcg/dl)
Computed tomography of Brain(CT Brain)	Normal
NT-proBNP	1419Pg/ml(<300Pg/ml)
D-dimer	0.82mg/l(<0.5mg/l)
Serum Lactate dehydrogenase(LDH)	973U/L(200–400U/L)

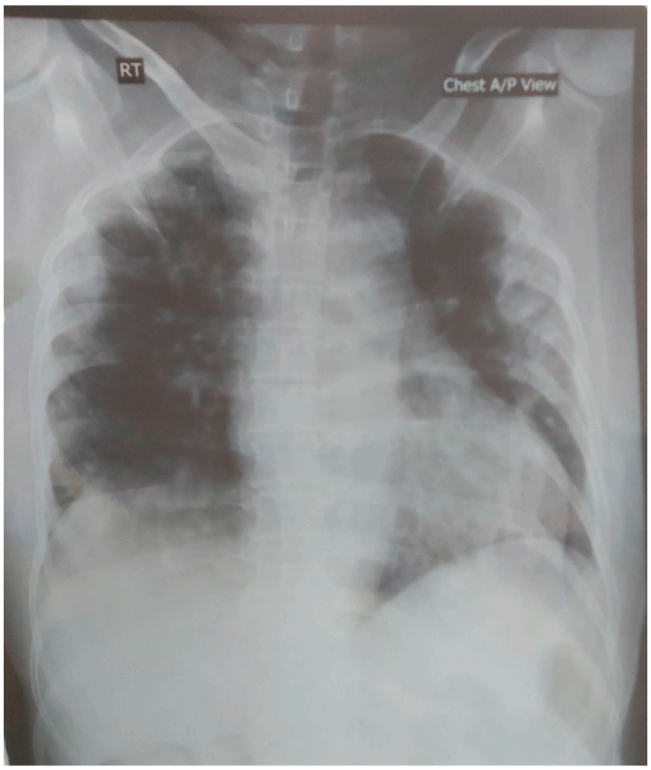

Fig. 1. Chest X-ray posterior-anterior view on admission(24 June, 2020) showing bilateral extensive pulmonary infiltration mostly in the periphery of both lungs.

The treatment was started after getting initial investigation with slow hypertonic 3% sodium chloride solution, after 6 hours of infusion there was remarkable improvement in her consciousness. Nasogastric fluid restriction initiated. She was oriented, responded verbally but drowsy. Sodium levels were monitored in the next 96 hours and fluctuated between 120 and 130 mEq/L. She was on supplemental oxygen 10–12 L/min through a non-rebreather mask and maintained saturation of oxygen above 94% from the day of admission to next 7days. She was started intravenous antibiotic meropenem 1 gm 8 hourly for 10days, thromboprophylaxis with enoxaparin40mg subcutaneous 12 hourly for 7days, antiviral oral favipirapir 1600mg loading on day 1, followed by 600mg twice daily for next 9 days according to national guideline of Bangladesh along with intravenous methylprednisolone 250mg daily for 5 days and oral clarithromycin500 twice daily for 14 days. After 15 days she was withdrawn from nasogastric feeding, started on oral feeding and gradually improving with less oxygen supplymentation. Follow up investigation report(see Table 2) and Chest X ray posterior anterior view showing(see Fig. 2) still bilateral infiltration that is radiological improvement lagged behind the clinical improvement.

3. Discussions

Many causes of hyponatremia in SIADH patients have been documented such as tumours, stroke, Central nervous system trauma, porphyria, psychosis, drugs and pulmonary disorders including

Table 2
Follow up investigations.

Investigations	Findings with normal Reference range
Hemoglobin (Hb)	10.3 gm/dl(13-16 gm/dl)
Erythrocyte Sedimentation Rate(ESR)	80mm in 1st hour(0–10mm in 1st hour)
Neutrophils(Differentials)	87% (40–75%)
Lymphocytes(Differentials)	6% (20–50%)
Sodium(Na^+)	128mmol/l(135–145mmol/l)
Potasium (K^+)	3.8mmol/l(3.5–5.5mmol/l)
Alanine aminotranferase (ALT)	20U/L(Upto 32U/L)
Serum Lactate dehydrogenase (LDH)	364U/L(200–400U/L)
C reactive protein(CRP)	29mg/L(<8mg/L)
Serum Creatinine	0.9mg/dl(0.6–1.2mg/dl)

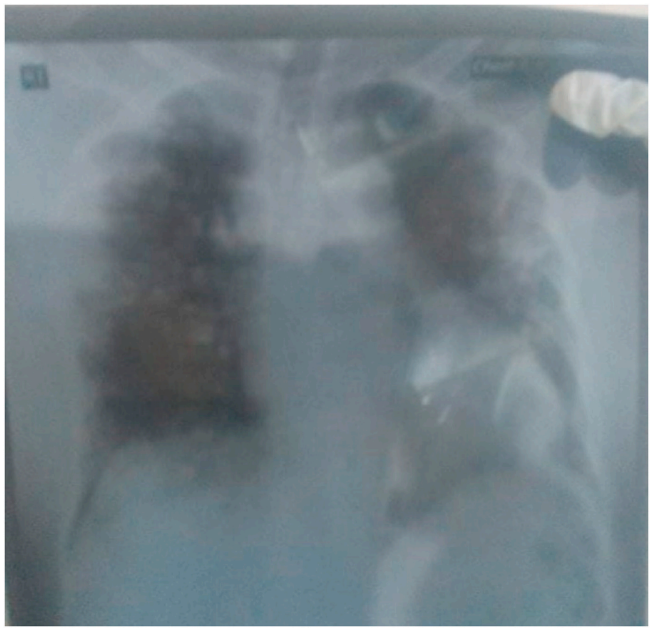

Fig. 2. Follow up X ray (9 July 2020) Chest P/A view still showing bilateral pulmonary infiltration.

tuberculosis, obstructive lung disease [2]. Diagnostic criteria for SIADH comprises low plasma sodium concentration(typically<130mmol/l), low plasma osmolarity (<275mOsml/kg), urine osmolarity not minimally low(typically>100 mOsm/kg), urine sodium concentration not minimally low(>30mmol/l),low-normal plasma urea, serum creatinine, uric acid, clinical euvolemia, absence of adrenal, thyroid, pituitary and renal insufficiency, no recent use of diuretic and appropriate clinical context [7]. Our patient was diagnosed as SIADH based on diagnostic criteria though pituitary functions was not done and she have no symptoms suggestive of adrenal and pituitary disease. Our patient was not taking any drug of inducing hyponatremia and the patient was compliant to antihypertensive drugs (amlodipine 5mg/telmisartan 80mg combination) for 3years without any change or addition of new drug.

The emergence of SARS-CoV-2 around the world and resulting the disease COVID-19 led to high number of cases with severe pneumonia [8]. Hyponatremia is frequently associated with atypical pneumonia. One of the underlying mechanisms is inappropriate ADH secretion [9].

A case series of COVID-19 with SIADH published recently, described two patients who presented with respiratory symptoms, were diagnosed with COVID-19, and found to have SIADH [10]. Howover, in all mentioned cases fever was a common feature and there was evident of pneumonia (abnormal chest X-ray having pulmonary infiltrates) but not present with unconsciousness. In our case patient presented with fever, unconsciousness and respiratory distress. She was found acute hyponatremia excluding other causes of hyponatremia and diagnosed as SIADH with presence of other laboratory findings. So we suggest that SARS-CoV −2 infection is one of the infective causes of SIADH but still high-quality data are urgently needed to get an impression of the potentially manifold faces of COVID-19 and its multidimensional complications.

4. Conclusions

The mechanism of SIADH in COVID -19 pneumonia is not well established. But presence of SIADH could be a clue for diagnosing COVID-19. Emotional, physical or psychological stresses and pain associated with infections such as COVID-19 may result in development of SIADH. So we suggest additional large scale studies require to correlate the incidence and pathogenesis of SIADH in COVID-19. This will advance our knowledge about the mechanism of SIADH in COVID-19 patients and specific recommendation for treatment may be required for management of hyponatremia in these cases.

Consent

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

Declaration of competing interest

The authors have no conflict of interest relevant to this case.

Acknowledgements

The authors would like to thank Medinova specialized hospital, Feni, Bangladesh, SARS-CoV-2 managing director Mr Humayun kabir, Chairman of the hospital Mr Abdul Quddus Sumon, medical assistant team,nursing team and all other stuffs that are fighting against this pandemic disease.

References

[1] G. Corona, C. Giuliani, G. Parenti, et al., Moderate hyponatremia is associated with increased risk of mortality: evidence from a meta-analysis, PloS One 9 (2013), e80451.
[2] G. Decaux, W. Musch, Clinical laboratory evaluation of the syndrome of inappropriate secretion of antidiuretic hormone, Clin. J. Am. Soc. Nephrol. 3 (4) (2008) 1175–1184, https://doi.org/10.2215/CJN.04431997 [Pubmed][CrossRef][Google Scholar].
[3] M. Cuesta, C.J. Thompson, The syndrome of inappropriate antidiuresis, Best Pract. Res. Clin. Endocrinol. Metabol. 30 (2016) 175–187 [CAS][Google Scholar].
[4] J.K. Hodax, S.R. Bialo, A. Yalcindag, SIADH in systemic JIA resolving after treatment with an IL-6 inhibitor, Am Acad Pediatr. 141 (2018), e20164174.
[5] C. Bulut, Y. Kato, Epidemiology of COVID-19, Turk. J. Med. Sci. 50 (SI-1) (2020) 563–570, https://doi.org/10.3906/sag-2004-172. Published 2020 Apr 21. [PMC free article][PubMed][CrossRef][Google Scholar].
[6] D.G. Ahn, H.J. Shin, M.H. Kim, Current status of epidemiology. diagnosis, therapeutics, and vaccines for novel coronavirus disease 2019(COVID-19), J. Microbiol. Biotechnol. 30 (3) (2020) 313–324, https://doi.org/10.4041/jmb.2003.03011 ([PubMed][CrossRef][Google Scholar]).
[7] G. Spasovski, R. Vanholder, B. Alloio, et al., Clinical practice guideline on diagnosis and treatment of hyponatremia, Eur. J. Endocrinol. 170 (3) (2014) G1–G47, https://doi.org/10.1530/EJE-13-1020.
[8] P. Kakodkar, N. Kaka, M.N. Baig, A comprehensive literature review on the clinical presentation and management of the pandemic coronavirus disease 2019(COVID-19), Cureus 12 (4) (2020), https://doi.org/10.7759/cureus.7560. Published 2020 Apr 6. [PMC free article][PubMed][CrossRef][Google Scholar].
[9] A. Dhawan, A. Narang, S. Singhi, Hyponatremia and inappropriate ADH syndrome in pneumonia, Ann. Trop. Paediatr. 12 (4) (1992) 455–462, https://doi.org/10.1080/02724936.1992.11747614 [PubMed][CrossRef][Google Scholar].
[10] R. Svenja, N. Norbert, r. Chantal, et al., The syndrome of inappropriate antidiuresis in COVID-19 pneumonia: report of two cases, Cli K J. .sfaa080 (2020 May 17), https://doi.org/10.1039/ckj/sfaa080.