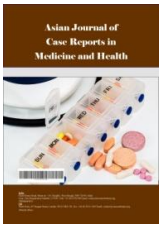

Asian Journal of Case Reports in Medicine and Health

6(2): 24-28, 2021; Article no.AJCRMH.74823

Diabetes Insipidus–Is it a Sequelae of COVID-19 Infection?

Priyanka H. Chhabra[1*], P. K. Verma[1], Binita Jaiswal[1], Vanya Chugh[1] and Harish Sachdeva[1]

[1]Department of Anaesthesiology and Critical Care, VMMC & Safdarjung Hospital, New Delhi – 110029, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author PHC was directly responsible for admission and management of this case in ICU and is the primary author of the case report. Author PKV was the ICU in charge involved in case management and helped in data collection. Author BJ helped in searching the literature, while authors HS and VC were the faculty in ICU involved in supervising the manuscript preparation. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. Hab. Mariusz Cycon, Medical University of Silesia, Poland.
(2) Dr. Avinash Borkar, Late Shri Lakhiram Agrawal Memorial Medical College, India.
(3) Dr. Ayhan Goktepe, Selcuk Universitesi, Turkey.
Reviewers:
(1) Arumugam R. Jayakumar, University of Miami Miller School of Medicine, USA.
(2) Samia Hamouda, Bechir Hamza Children's Hospital of Tunis, University El Manar, Tunisia.
(3) Ermias Sisay Chanie, College of Health Sciences, Debre Tabor University, Ethiopia.
(4) Ashani Ratnayake, Sri Lanka.
Complete Peer review History: http://www.sdiarticle4.com/review-history/74823

Case Study

Received 22 September 2021
Accepted 22 October 2021
Published 08 November 2021

ABSTRACT

Introduction: COVID-19 has diverse clinical presentations. We are now quite familiar with the usual symptoms---fever, cough, breathlessness, anosmia, fatigue. Diabetes insipidus could also be a symptom related to covid-19 or it can be a post covid complication.
Case Report: This is a case of a 40 years old patient who presented to the emergency department with breathlessness and desaturation. He was treated with non-invasive ventilation and steroids. His clinical status improved subsequently and he was discharged after 1 week. After two days of discharge, he developed polyuria, hypernatremia, dehydration and hypotension. We performed a water deprivation test and confirmed a diagnosis of neurogenic diabetes insipidus.
Discussion: Diabetes insipidus is a disorder of water homeostasis characterized by polyuria. It is possible that SARS Cov-2 virus due to its predilection for ACE 2 receptors enters hypothalamus and affects the neuronal secretion of vasopressin.

**Corresponding author: E-mail: priyankahsinghani@gmail.com;*

Conclusion: Diabetes insipidus could be one of the delayed manifestations of the disease.It is possible that SARS-Cov2 virus has a possible endocrinopathic effect.

Keywords: COVID-19; nephrogenic; diabetes; clinical manifestation.

1. INTRODUCTION

Covid-19 pandemic is one of the most devastating event causing immense suffering of the mankind. It has resulted in millions of cases worldwide and still continues to haunt us as we prepare for the third wave of the illness. Most of the patients have respiratory complaints often accompanied byfatigue, diarrhea, anosmia, tinnitis, skin rash, headache, etc to name a few.Recently, several new symptoms have been reported in several case series or case reports.

Diabetes insipidus (DI)is a disease characterised by polyuria and subsequent dehydration. It is usually of two types – central and nephrogenic DI.Diabetes insipidus is characterized by passage of large volumes of dilute urine, often due to deficient secretion of vasopressin by posterior pituitary (Central DI) or due to failure to response of vasopressin (peripheral DI) [1]. It is characterized by polyuria, passage of dilute insipid (tasteless) urine and polydipsia.

2. CASE PRESENTATION

A 40 year- old malepresented to the emergency room with chief complaints of fever, cough and breathlessness for the past two days. His HR was 128 bpm, BP was 110/70 mmHg, Respiratory rate was 42 bpm, spO2 was 79% on room air, respiratory system examination revealed bilateral wheezing. His RTPCR report was positive for SARS Cov-2. Chest x-ray revealed bilateral ground glass opacitiesand CT severity score of 18/22. His Hb was 12.0 g/dl, TLC (total leucocyte count) was 16,000 cells/ mm^3, platelet count was within normal limits.His blood sugar, liver function tests, blood urea and serum creatinine were within normal limits. However, serum procalcitonin was 23.He was than kept on non-invasive ventilation, with a pressure support of 10 mmHg and fiO2 of 1 for 4 days. Simultaneously, he was given methylprednisolone pulse therapy 250 mg twice a day for three days, antibiotics (Tazobactum-Piperacillin, Linezolid and Azithromycin) and a course of remdesivir for five days. He responded well to our management and his oxygen requirement reduced considerably over the next few days.He was than discharged from our ICU after a stay of 12 days. Two days after discharge, he developed polyuria, hypotension and drowsiness. At that time, he tested negative for SARS Cov-2.On re-admission in ICU, his HR was 78 bpm, BP was 92/67 mmHg, RR was 18 bpm, spO2 was 98 % on room air, urine output was 4l on first day. He was givenfluid boluses to match the increased urine output. His TLC was 8,000 cells/mm^3,platelet count, procalcitonin, blood sugar, blood urea, serum cortisol and thyroid profile were within normal limits. NCCT (Head) also did not reveal any abnormality.Neurology consultation was also seeked, no active intervention was advised from their side. His serum sodium was 142 meq/dl, urine sodium was 40meq/l and urine osmolality was 302mosm/kg.Next day after admission, his urine output was 5.5 l. Water deprivation test was performed after deprivation of 8 hrs.His serumsodium increased to 153 meq/dl and urine osmolality increased to 784 mosm/kg, serum vasopressin level was 87 pg/ml(normal range 30-120 pg/ml).MRI Brain was performed, which did not reveal any mass or pituitary haemorrhage.Emperically, he was given Inj Ceftriaxone and his fluid input was increased to match the output.A diagnosis of central diabetes insipidus was made, he was than given desmopressin nasal spray 0.2 mg twice a day on the first day and than as per urine output. He improved symptomatically and serum sodium came down to normal. He was than subsequently discharged after 9 days of ICU stay.

3. DISCUSSION

Majority of patients recover fully from covid-19infection, with only few presenting to the hospitalwithpost covidsequelae [2,3]. After passing through the second wave of this disease, we have encountered varied clinical presentations of the disease. SARS Cov-2 virus can typically involve every organ system and endocrine system is no exception. Diabetes insipidus in our patient could be a sequelae of covid-19 infection.

Diabetes insipidus (DI) is a disorder of water homeostasis characterized by passage of large volumes of dilute urine (hypotonic polyuria) irrespective of body's hydration status [4,5]. It

can be of central or nephrogenic origin. Central DI is primarily due to surgery, trauma, infection or malignancy of brain [6]. We excluded these causes by MRI Brain, which was normal in our patient. Nephrogenic DI is primarily due to failure of response to antidiuretic effect of vasopressin[7].We used waterdeprivation test to distinguish between the two causes [8]. In this test, patient is allowed to be deprived of water overnight (approximately 8 hours). The next morning, desmopressin is administered. This is followed by an assessment of patient's urine osmolality. In central DI, urine osmolality increases by at least >50% from baseline following desmopressin administration whereas urine osmolality does not increase after desmopressin in nephrogenic DI [9].We excluded nephrogenic DI by water deprivation test, after which urine osmolality increased significantly. We also performed serum vasopressin estimation in our patient, which is available in very few centres in India.

Previous studies have also reported similar findings with SARS virus [10]. In a study by Leow et alin 2005 (10)on SARS virus, sixty-one survivors of SARS were followed up for a period of 3 months following disease. They found that 39.3 % of survivors had evidence of HPA axis dysfunction. Authors hypothesized a endocrinopathic effectof SARS virus causing HPA axis dysfunction.

Heidarpour et al [11] reported a case of a 69 year- old Iranian covid patient developing vasopressor resistant hypotension on the fifth day of illness.The authors hypothesizedthat adrenal insufficiency in this patient could be due to HPA axis dysfunction. They also concluded that since pituitary is not protected by blood brain barrier, it is extremely vulnerable to damage by inflammatorycytokines in covid patient [11]. This could possibly explain HPA axis dysfunction in covid 19 patients.

An extensive search of literature revealed only two case reports of patients with covid-19 infection developing DI. In one of the reports, a young male patient presented with covid-19 infection and myocarditis subsequently developed DI after 7 days of admission[12]. The authors concluded that DI in post-covid phase could be due to inflammation mediated reversible hypophysitis or a direct immune mediated damage of the hypothalamus or pituitary [12].In yet another case, a middle aged male patient presented with covid 19 infection. He developed DI on 27 th day of admission and was successfullymanaged with desmopessin nasal spray. The authors concluded that auto immune dysregulation could be responsible for neuroendocrine derangements [13].

In our patient, DI could be due to possible damage to hypothalamus, supraoptic and periventricular nuclei of posterior pituitary during the initial viraemic phase of the disease. SARS Cov-2 virus uses ACE II receptor as an entry point to cells, which is also found in hypothalamus and pituitary [14,15,16]. ACE II receptor acts as not only receptor for entry of virus but it is also deemed as the main receptor of SARS Cov 2 virus [16]. So, it might be possible that after access to human body, the virus may affect endocrine system by causing a reversible hypophysitisor damage of neurons relaying in posterior pituitary [17]. This damage to pituitary may present in the post covid phase as diabetes insipidus. Infact, autopsy studies have also revealed the presence of SARS Cov-2 virus in hypothalamus along with neuronal edema and degeneration [14]. This might be the basis of other neurological manifestations of covid infection like anosmia.

4. CONCLUSION

Diabetes insipidus could be a rare post covid manifestation. It is possible that the virus exerts endocrine effects via posterior pituitary. After going through the second wave of this illness it becomes prudent to know more and more about the various clinical manifestations of this novel disease. Diabetes insipidus is a common clinical presentation of many diseases, hence isolated case report like ours help in knowing about rare manifestations of covid 19 infection.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Priya G, Kalra S, Dasgupta A, Grewal E. Diabetes Insipidus: A Pragmatic Approach to Management. Cureus. 2021;13(1): e12498.
   DOI: 10.7759/cureus.12498. PMID: 33425560; PMCID: PMC7785480.
2. Logue JK, Franko NM, McCulloch DJ, et al. Sequelae in Adults at 6 Months After COVID-19 Infection. JAMA Netw Open. 2021;4(2):e210830.
   DOI:10.1001/jamanetworkopen.2021.0830
3. Nalbandian A, Sehgal K, Gupta A, Madhavan MV, et al Post-acute COVID-19 syndrome. Nat Med. 2021;27(4):601-615.
   DOI: 10.1038/s41591-021-01283-z. Epub 2021 Mar 22. PMID: 33753937
4. Kalra S, Zargar AH, Jain SM, Sethi B, Chowdhury S, Singh AK, Thomas N, Unnikrishnan AG, Thakkar PB, Malve H. Diabetes insipidus: The other diabetes. Indian J EndocrinolMetab. 2016;20(1):9-21.
   DOI: 10.4103/2230-8210.172273. PMID: 26904464; PMCID: PMC4743391.
5. Di Iorgi N, Napoli F, Allegri AE, Olivieri I, Bertelli E, Gallizia A, Rossi A, Maghnie M. Diabetes insipidus--diagnosis and management. Horm Res Paediatr. 2012;77(2):69-84.
   DOI: 10.1159/000336333. Epub 2012 Mar 16. PMID: 22433947.
6. Saifan C, Nasr R, Mehta S, Sharma Acharya P, Perrera I, Faddoul G, Nalluri N, Kesavan M, Azzi Y, El-Sayegh S. Diabetes insipidus: a challenging diagnosis with new drug therapies. ISRN Nephrol. 2013;2013:797620.
   DOI: 10.5402/2013/797620. PMID: 24977135; PMCID: PMC4045430.
7. Moeller HB, Rittig S, Fenton RA. Nephrogenic diabetes insipidus: essential insights into the molecular background and potential therapies for treatment. Endocr Rev. 2013;34(2):278-301.
   DOI: 10.1210/er.2012-1044. Epub 2013 Jan 29. PMID: 23360744; PMCID: PMC3610677.
8. Gubbi S, Hannah-Shmouni F, Koch CA, et al. Diagnostic Testing for Diabetes Insipidus. [Updated 2019 Feb 10]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000. Available: https://www.ncbi.nlm.nih.gov/books/NBK537591/
9. Zerbe RL, Robertson GL. A Comparison of Plasma Vasopressin Measurements with a Standard Indirect Test in the Differential Diagnosis of Polyuria. New England Journal of Medicine, 1981;305(26):1539–1546.
10. Leow MK, Kwek DS, Ng AW, Ong KC, Kaw GJ, Lee LS. Hypocortisolism in survivors of severe acute respiratory syndrome (SARS). ClinEndocrinol (Oxf). 2005;63(2):197-202.
    DOI: 10.1111/j.1365-2265.2005.02325.x. PMID: 16060914; PMCID: PMC7188349.
11. Heidarpour M, Vakhshoori M, Abbasi S, Shafie D, Rezaei N. Adrenal insufficiency in coronavirus disease 2019: a case report. J Med Case Rep. 2020;14(1):134.
    DOI: 10.1186/s13256-020-02461-2. PMID: 32838801; PMCID: PMC7444179.
12. Sheikh AB, Javed N, Sheikh AAE, Upadhyay S, Shekhar R. Diabetes Insipidus and Concomitant Myocarditis: A Late Sequelae of COVID-19 Infection. J Investig Med High Impact Case Rep. 2021;9:2324709621999954.
    DOI: 10.1177/2324709621999954. PMID: 33686899; PMCID: PMC7952841.
13. Rajevac, H, Bachan, M, Khan, Z. Diabetes insipidus as a symptom of Covid-19 infection: case report. Chest. 2020;158:A2576.
    DOI:10.1016/j.chest.2020.09.172
14. Lazartigues E, Qadir MMF, Mauvais-Jarvis F. Endocrine Significance of SARS-CoV-2's Reliance on ACE2. Endocrinology. 2020;161(9):bqaa108.
    DOI: 10.1210/endocr/bqaa108. PMID: 32652001; PMCID: PMC7454499.
15. Pal R, Banerjee M. COVID-19 and the endocrine system: exploring the unexplored. J Endocrinol Invest. 2020;43(7):1027-1031.
    DOI: 10.1007/s40618-020-01276-8. Epub 2020 May 2. PMID: 32361826; PMCID: PMC7195612.
16. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020;181(2):271-280.e8.

DOI: 10.1016/j.cell.2020.02.052. Epub 2020 Mar 5. PMID: 32142651; PMCID: PMC7102627

17. Chiloiro S, Capoluongo ED, Tartaglione T, Giampietro A, Bianchi A, Giustina A, Pontecorvi A, De Marinis L. The Changing Clinical Spectrum of Hypophysitis. Trends EndocrinolMetab. 2019;30(9):590-602. DOI: 10.1016/j.tem.2019.06.004. Epub 2019 Jul 22. PMID: 31345630.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/74823