Case Report

COVID-19 infection with severe hypocalcaemia and superior mesenteric artery syndrome—a case report

Shomesh Raj Selva Raj[1], Guan Hoe Han[2], Malathi Karupiah[1], Shree Vidhya Nagendram[1], Waye Hann Kang[3]^

[1]Department of Medicine, Hospital Ampang, Ampang, Malaysia; [2]Department of Radiology, Hospital Ampang, Ampang, Malaysia; [3]Department of Medicine, M. Kandiah Faculty of Medicine & Health Sciences, Universiti Tunku Abdul Rahman, Kajang, Malaysia

Contributions: (I) Conception and design: WH Kang; (II) Administrative support: M Karupiah, SV Nagendram; (III) Provision of study materials or patients: M Karupiah, SV Nagendram; (IV) Collection and assembly of data: SR Selva Raj, GH Han; (V) Data analysis and interpretation: SR Selva Raj, GH Han, WH Kang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Waye Hann Kang, MD (UNIMAS), FRCP (Glasgow). Department of Medicine, M. Kandiah Faculty of Medicine & Health Sciences, Universiti Tunku Abdul Rahman, Bandar Sungai Long, 43000 Kajang, Malaysia. Email: kangwh@utar.edu.my.

Background: Coronavirus disease 2019 (COVID-19) infection has been associated with various endocrinopathies. Few literatures have reported cases of transient hypoparathyroidism in acute COVID-19 infections, or even exacerbation of hypocalcaemia in previously known hypoparathyroidism patients. The mechanism of hypocalcaemia in COVID-19 infection remains unclear.

Case Description: Our patient is a young gentleman who was incidentally diagnosed with superior mesenteric artery (SMA) syndrome and symptomatic primary hypoparathyroidism while presenting with an acute COVID-19 infection. He initially presented with high-grade fever, followed by multiple episodes of vomiting and abdominal pain and subsequently hypocalcaemic symptoms such as tonic-clonic seizures and carpopedal spasms. A computed tomographic scan of his abdomen revealed a SMA syndrome while his blood investigation showed a parathyroid hormone (PTH)-dependent hypocalcaemia. His SMA syndrome was a result of severe malnourishment and improved with refeeding, but his primary hypoparathyroidism persisted despite having recovered for 6 months from the initial COVID-19 infection. There was no evidence to suggest a congenital cause of hypoparathyroidism.

Conclusions: To the best of our knowledge this is the first case report that describe this unique case of persistent primary hypoparathyroidism related to COVID-19 infection. Parathyroid gland involvement in a COVID-19 infection is rare but not impossible. Further studies are needed to determine the mechanism and extent of damage of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to the parathyroid glands.

Keywords: Coronavirus disease 2019 (COVID-19); hypoparathyroidism; hypocalcaemia; superior mesenteric artery syndrome (SMA syndrome); case report

Received: 24 July 2023; Accepted: 02 February 2024; Published online: 22 March 2024.

doi: 10.21037/acr-23-106

View this article at: https://dx.doi.org/10.21037/acr-23-106

Introduction

Primary hypoparathyroidism secondary to coronavirus disease 2019 (COVID-19) is an uncommon presentation. Till date there have only been three cases reported in the literature so far (1-3). We report a case of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

^ ORCID: 0000-0003-3209-7196.

positive young gentleman who presented symptomatic hypocalcaemia secondary to primary hypoparathyroidism, which may have complicated his superior mesenteric artery (SMA) syndrome. We present this case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-23-106/rc).

Case presentation

We hereby report a previously well 14-year-old gentleman who presented with hypercalcaemic symptoms, i.e., generalised tonic-clonic seizures, carpopedal spasms, perioral numbness, and bilateral hand numbness. Prior to these symptoms, he has had 4 days of fever with multiple episodes of vomiting and abdominal pain. The patient was from an impoverished family and has not been receiving adequate nutrition for the past few months, resulting in a significant history of weight loss. His younger brother and he are currently living with his divorced father, who has financial difficulty in providing adequate food for them. The patient is still schooling and has average academic achievement with no difficulty in school. Clinically he was dehydrated with a distended abdomen and sluggish bowel sounds. His body weight was merely 32.9 kg (<5th centile in growth chart for boys age 2–20 years) whilst his height was 153 cm (between 10th and 25th centile in growth chart for boys age 2–20 years), hence his body mass index was 14.1 kg/m^2. Otherwise, aside from fever, his vital signs were normal and there were no clinical features suggestive of pseudohypoparathyroidism.

Blood investigations showed severe hypocalcaemia and hyperphosphatemia with an inappropriately lowish serum intact parathyroid hormone (iPTH) levels, suggesting a primary hypoparathyroidism with vitamin D insufficiency (serum 25-hydroxyvitamin D levels were 54.41 nmol/L) (*Table 1*). There was also prolonged corrected QT interval (QTc) interval in the electrocardiography (ECG) whilst his nasopharyngeal SARS-CoV-2 rapid antigen test was positive. His chest X-ray was normal whilst an urgent contrasted computed tomography scan of the abdomen suggested SMA syndrome (*Figures 1A,1B,2*).

He was treated as category 2 COVID-19 infection with severe hypocalcaemia and SMA syndrome. The calcium levels were promptly corrected, and the patient was commenced with total parenteral nutrition since he was unable to tolerate oral feeding. Interestingly, with the correction of his calcium levels, his gastrointestinal symptoms dramatically improved. Eventually, after 40 days hospital stay with medical nutrition therapy, as well as calcium and calcitriol replacement, the patient was able to tolerate orally and hence uneventfully discharged with a body weight of 37.3 kg. During his post-discharge review (day 80 from discharge), a computed tomography scan of his abdomen was repeated, showing improvement in his SMA syndrome (*Figure 3A,3B*) The patient's body weight had increased till 39 kg and still had primary hypoparathyroidism, requiring both oral calcium and calcitriol replacement.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's father for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Highlight box

Key findings

- A young male who was admitted for coronavirus disease 2019 (COVID-19) infection also presented with concurrent symptomatic hypocalcaemia, as well as superior mesenteric artery syndrome from malnourishment. There were no features of chronic hypoparathyroidism in this patient, ruling out congenital causes of hypoparathyroidism and further strengthening the suspicion of COVID-19 as the cause of his permanent primary hypoparathyroidism.

What is known and what is new?

- Acute COVID-19 infections have been associated to various transient or permanent endocrinopathies, with several literature reporting transient hypocalcaemia or acute hypocalcaemic exacerbation in known hypoparathyroidism patients.
- This case report is the first to report persistent hypoparathyroidism as a sequela of a COVID-19 infection.

What is the implication, and what should change now?

- Further studies are required to determine the effects of severe acute respiratory syndrome coronavirus 2 infection on the parathyroid glands and its pathophysiology.

Discussion

SMA syndrome, a rare cause of small bowel obstruction, happens due to a compression of the duodenal segment between SMA and abdominal artery, often by loss of the retroperitoneal mesenteric fat pad that keeps these structures apart. The normal angle between the small

Table 1 Summary of investigations of the patient during his admission, discharge, and post-discharge review

Parameters	Day 1 (admission)	Day 40 (discharge)	Day 80 (review)
Body weight (kg)	32.9	37.3	39.0
Haemoglobin (normal range, 13.5–17.4) (g/dL)	14.5	9.8	11.3
Haematocrit (normal range, 40.1–50.6) (%)	43.5	30.2	34.3
Total white cell (normal range, 4.078–11.37) ($\times 10^9$/L)	8.1	9.4	7.3
Platelet (normal range, 142–350) ($\times 10^9$/L)	179	221	163
Urea (normal range, 3.2–8.2) (mmol/L)	9.6	3.7	1.8
Creatinine (normal range, 49–115) (μmol/L)	103	58	51
Corrected calcium (normal range, 2.08–2.65) (mmol/L)	0.89	2.34	2.24
Magnesium (normal range, 0.66–1.07) (mmol/L)	0.75	0.62	0.73
Phosphate (normal range, 0.78–1.65) (mmol/L)	3.30	2.16	1.91
Alkaline phosphatase (normal range, 46–116) (U/L)	225	151	151
Iron (normal range, 9.0–31.3) (μmol/L)	5.2	–	–
iPTH (normal range, 14.9–56.9) (pg/mL)	14.7	–	5.5
24-hour urine calcium (normal range, 2.5–7.5) (mmol/d)	11.73	–	–
Anti-thyroid peroxidase Ab (normal range, <9) (IU/mL)	0.39	–	–
25-hydroxy-vitamin D (normal range, 50–80) (nmol/L)	54.41	–	–

iPTH, intact parathyroid hormone; Ab, antibody.

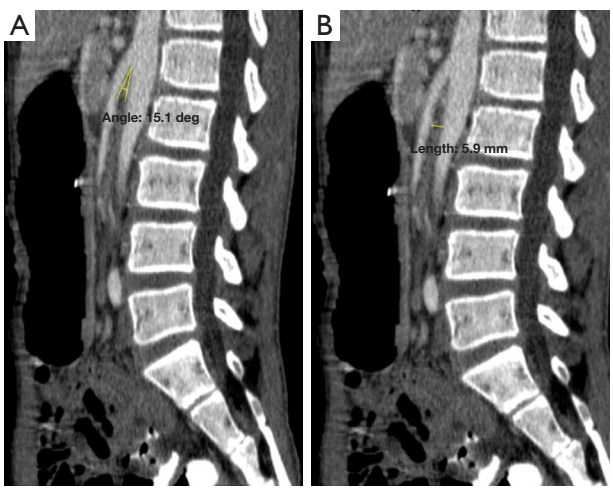

Figure 1 Sagittal view of initial contrast-enhanced computed tomography scan of the abdomen showing: (A) the aortomesenteric angle is 15.1°, while (B) the aortomesenteric distance is 5.9 mm, suggestive of a SMA syndrome. SMA, superior mesenteric artery.

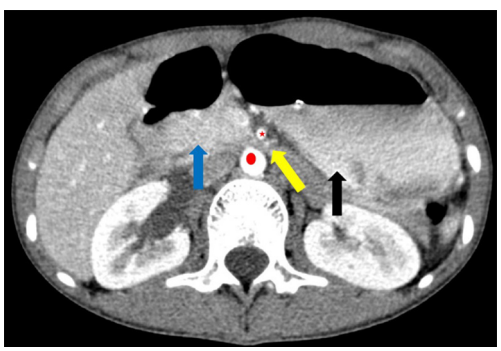

Figure 2 Axial view of the initial contrast-enhanced computed tomography scan of the abdomen showing a compression of the retro-mesenteric 3rd duodenal part (yellow arrow) between the abdominal aorta (red dot) and SMA (red star) with upstream distension of contrast-filled stomach (black arrow) and proximal duodenum (blue arrow). SMA, superior mesenteric artery.

mesenteric artery and the aorta is often between 38° and 65° and any reduction of this angle causes the SMA syndrome (4,5). SMA syndrome often occurs in unwell individuals with extreme weight loss, resulting in the loss of the mesenteric fat pad (6). This syndrome is usually seen in older children and adolescents (7).

Classically, patients with SMA syndrome present with features of bowel obstruction, which are abdominal pain and

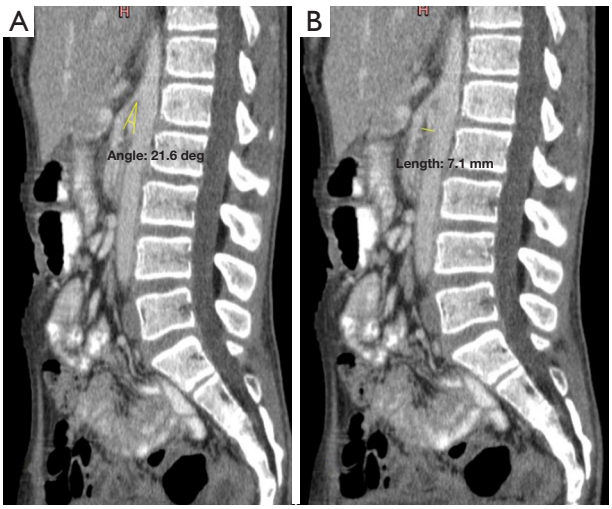

Figure 3 Repeated contrast-enhanced computed tomography scan of the abdomen 80 days post-discharge showing a slight improvement in the degree of compression, with (A) aortomesenteric increasing to 21.6° and (B) aortomesenteric distance of 7.1 mm, suggesting a slight improvement in the degree of compression.

distension, vomiting and obstipation. A plain radiograph often shows evidence of proximal obstruction, whilst a barium study may demonstrate an abrupt narrowing of the third part of the duodenum with obstruction. The aortomesenteric angle can be measured by ultrasonography (4), or by contrast-enhanced computed tomography scan. Often the diagnosis is made when there is a presence of an aortomesenteric angle <22° and the aortomesenteric distance <8–10 mm (7,8).

Treatment options include nutritional support for adequate weight gain and regrowth of the mesenteric fat pad and subsequently improvement in the aortomesenteric angle (9). Symptomatic relief can be opted with postural therapy (prone, knee-chest or left lateral position) or placement of a nasogastric tube, which aids by restoring the aortomesenteric distance, allowing enteral feeding and subsequently weight gain, and eventually relieving the obstruction (5,9). Finally, surgical intervention such as gastrojejunostomy, duodenojejunostomy, or division of the ligament of Treitz can be performed in severe cases with failure of conservative management (8).

We believe that the SMA syndrome in our patient is a result of malnourishment due to his impoverished family as he was severely underweight during admission. His symptoms improved with correction of the hypocalcaemia, as well as weight gain with medical nutrition therapy.

On the other hand, the severe hypocalcaemia as a complication of the COVID-19 infection in our patient might have exacerbated his SMA syndrome. Ca^{2+}-sensing receptors have been discovered in intestinal epithelial cells, and are postulated to play a vital role in modulating intestinal motility (10,11). It is well known that hypercalcaemic states often present with constipation or other gastrointestinal complaints, but due to its critical role in muscle and nerve conduction, there is a possibility that severe hypocalcaemia may present with gastrointestinal symptoms (12).

Hypocalcaemia has been associated with severe COVID-19 infection (13), but the exact mechanism is still unclear. Inflammatory responses during COVID-19 infection may lead to various forms of endocrine tissue damage, including the parathyroid glands (3). The SARS-CoV-2 virus may damage the parathyroid glands by binding to the angiotensin-converting enzyme 2 (ACE2) receptors on acidophilic cells of the glands (3,14). Besides that, a relative hypoparathyroidism may occur due to chronic respiratory alkalosis, a sequela of raised respiratory effort, resulting in resistant PTH receptors to PTH hormones (14). However, this is unlikely in our patient, as the hypocalcaemia and hypoparathyroidism persisted despite him having recovered from the COVID-19 infection with no respiratory complications.

Prior to this, there had been three case reports on SARS-CoV-2 infection induced primary hypoparathyroidism (1-3), as well as several case reports on decompensation of existing primary hypoparathyroidism during COVID-19 infection (*Table 2*).

We believe that our patient only developed acute hypoparathyroidism recently as there were no features of chronic hypoparathyroidism, such as bilateral cataracts or presence of intracerebral calcifications on computed tomography scan of the brain. He also had normal developmental milestones as a child with an average academic performance in school, with no obvious neuropsychiatric abnormalities. There were no other features of autoimmune diseases, but we were unable to completely rule out autoimmune hypoparathyroidism as we could not send for an anti-calcium sensing receptor antibody test. Furthermore, unlike the other cases, our patient may be suffering from permanent hypoparathyroidism as his serum iPTH levels were still severely low, requiring calcium and calcitriol supplementation, despite more than 2 months of recovery from the COVID-19 infection.

We have excluded other causes of primary

Table 2 A comparison of parameters of previous reported cases of hypoparathyroidism secondary to COVID-19 infection

Parameters	Elkattawy *et al*., 2020 (1)	Dianatfar *et al*., 2021 (2)	Georgakopoulou *et al*., 2022 (3)	Current report
Age (years)	46	44	53	14
Sex	M	F	M	M
Presentation	Incidental finding	Tonic-clonic seizure, depressed mood	Incidental finding	Tonic-clonic seizures with carpopedal spasms, perioral numbness, and distal limb tingling
Course of COVID-19 infection	Critical	Severe	Severe	Mild
Onset	Late (2nd month of hospitalization)	Late (40 days after COVID-19 infection)	Early (during presentation of acute COVID-19 infection)	Early (during presentation of acute COVID-19 infection)
iPTH level [normal range] (pg/mL)	8–10 [12–88]	<3 [11–67]	11.7 [12–65]	14.7 [14.9–56.9]
25-OH vitamin D level [normal range] (ng/mL)	7 [30–100]	33.1 [30–100]	38.4 [30–100]	54.41 [30–100]
Magnesium [normal range] (mg/dL)	1.9 [1.8–2.6]	2 [1.8–2.6]	Not mentioned	1.9 [1.8–2.6]
Calcium [normal range] (mg/dL)	9.2 [8.5–11]	6.2 [8.5–11]	6.9 [8.6–10.2]	3.6 [8.6–10.3]
Phosphorus [normal range] (mg/dL)	6.9 [3.4–4.5]	5.7 [2.7–4.5]	4.7 [2.5–4.5]	12.6 [3.4–4.5]
Albumin [normal range] (g/L)	2.9 [3.5–5.5]	3.9 [3.5–5.5]	3.74 [3.5–5.0]	3.12 [3.5–4.5]
Outcome	Recovery	Recovery	Recovery	Requires calcium and calcitriol supplementation

COVID-19, coronavirus disease 2019; M, male; F, female; iPTH, intact parathyroid hormone.

hypoparathyroidism, such as iatrogenic, autoimmune diseases, infiltrative diseases, or any complex genetic defects. Hence, we conclude that our patient may have developed permanent hypoparathyroidism as a sequela of COVID-19 infection. Till date, our patient remains the first patient reported with permanent hypoparathyroidism from a severe COVID-19 infection.

Patient's perspective

The patient and his guardian were surprised when being explained that the underlying acute endocrinal dysfunction might be a sequela of the acute COVID-19 infection. Nonetheless, they were relieved that his condition improved tremendously with proper nutrition and adequate calcium and vitamin D supplementation.

Conclusions

Parathyroid gland involvement in a COVID-19 infection is rare but not impossible. Further studies are needed to determine the mechanism and extent of damage of SARS-CoV-2 to the parathyroid glands.

Acknowledgments

We would like to acknowledge all medical personnel involved in the care of this patient.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-23-106/rc

Peer Review File: Available at https://acr.amegroups.com/article/view/10.21037/acr-23-106/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-23-106/coif). The authors

have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's father for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Elkattawy S, Alyacoub R, Ayad S, et al. A Novel Case of Hypoparathyroidism Secondary to SARS-CoV-2 Infection. Cureus 2020;12:e10097.
2. Dianatfar M, Sanjari M, Dalfardi B. Hypoparathyroidism after COVID-19 pneumonia. Shiraz E-Medical Journal 2021;22:e115832.
3. Georgakopoulou VE, Avramopoulos P, Papalexis P, et al. COVID-19 induced hypoparathyroidism: A case report. Exp Ther Med 2022;23:346.
4. Reece K, Day R, Welch J. Superior Mesenteric Artery Syndrome with Abdominal Compartment Syndrome. Case Rep Emerg Med 2016;2016:7809281.
5. Zaraket V, Deeb L. Wilkie's Syndrome or Superior Mesenteric Artery Syndrome: Fact or Fantasy? Case Rep Gastroenterol 2015;9:194-9.
6. Sahni S, Shiralkar M, Mohamed S, et al. Superior Mesenteric Artery Syndrome: The Dark Side of Weight Loss. Cureus 2017;9:e1859.
7. Gozzo C, Giambelluca D, Cannella R, et al. CT imaging findings of abdominopelvic vascular compression syndromes: what the radiologist needs to know. Insights Imaging 2020;11:48.
8. Merrett ND, Wilson RB, Cosman P, et al. Superior mesenteric artery syndrome: diagnosis and treatment strategies. J Gastrointest Surg 2009;13:287-92.
9. Esmat HA, Najah DM. Superior mesenteric artery syndrome caused by acute weight loss in a 16-year-old polytrauma patient: A rare case report and review of the literature. Ann Med Surg (Lond) 2021;65:102284.
10. Kirchhoff P, Geibel JP. Role of calcium and other trace elements in the gastrointestinal physiology. World J Gastroenterol 2006;12:3229-36.
11. Tang L, Cheng CY, Sun X, et al. The Extracellular Calcium-Sensing Receptor in the Intestine: Evidence for Regulation of Colonic Absorption, Secretion, Motility, and Immunity. Front Physiol 2016;7:245. Erratum in: Front Physiol 2016;7:315.
12. de Boer FJ, van Ieperen I, Boersma HE, et al. Severe hypocalcaemia and hypomagnesemia presenting with severe neurologic and gastro-intestinal symptoms: a case report and review of literature. CJEM 2021;23:401-3.
13. Di Filippo L, Formenti AM, Rovere-Querini P, et al. Hypocalcemia is highly prevalent and predicts hospitalization in patients with COVID-19. Endocrine 2020;68:475-8.
14. Abobaker A, Alzwi A. The effect of COVID-19 on parathyroid glands. J Infect Public Health 2021;14:724-5.

doi: 10.21037/acr-23-106
Cite this article as: Selva Raj SR, Han GH, Karupiah M, Nagendram SV, Kang WH. COVID-19 infection with severe hypocalcaemia and superior mesenteric artery syndrome—a case report. AME Case Rep 2024;8:54.