Case Report: Intravenous Sedation For An Office-Based Dental Patient With A Severe Chronic Cough Associated With Post-COVID-19 Syndrome.

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Abstract

The pathologic basis and the successful anesthetic management of an office-based dental patient with a chronic cough, secondary to post-Covid-19 syndrome (PCS), is presented and discussed. Intravenous (IV) sedation for patients with PCS must include a complete assessment of the wide-range of the potential systemic effects of this newly defined disease. In this case, a multi-modal approach was utilized and a symptom-specific antitussive anesthetic was successfully administered which also safely achieved an adequate level of sedation.

INTRODUCTION

Post-COVID-19 syndrome (PCS) or "Long COVID" is an emerging diagnosis. It is manifested by the presence of one or more symptoms such as: chronic fatigue, dyspnea, joint pain, coughing, anosmia, and xerostomia arising after the acute presentation of COVID-19. Other symptoms indicative of gastrointestinal, neurologic, psychiatric, renal and cardiovascular involvement may also occur. (1,2,3)

We report successful office-based intravenous (IV) anesthesia for a dental patient with a severe chronic cough secondary to PCS.

CASE PRESENTATION

The patient was a 52-year-old female who initially had COVID-19 following infection with SARS-CoV-2. She had not been hospitalized and had been conservatively managed, at the time, with oral zinc phosphate. This occurred approximately 10 months prior to her requiring endodontic surgery on tooth #14. The patient also reported that her dental pain initially started with her acute viral infection. Prior to her acquiring COVID-19, the patient had no respiratory diseases. Overall, she had no pre-existing risk factors which would have presumably led to complications arising from COVID-19. Furthermore, her weight was 64 kg, her height was 157.5 cm, and her BMI was 25.8 kg/m2. Her past medical history was otherwise negative whereas her

past surgical history included a recent bronchoscopy, right total knee replacement, and a lumbar diskectomy. Her airway was assessed as a Mallampati 1. She reported an allergy to trimethoprim/sulfamethoxazole which resulted in "throat closing." Furthermore, she was a non-smoker and reported rare alcohol use. Additionally, she denied marijuana and illegal drug use.

However, she suffered from a severe chronic dry cough which occurred several times per minute. Furthermore, she had stated that this cough arose with COVID-19 and that she did not have this condition prior to her symptomatic viral infection from SARS-CoV-2. Moreover, other than coughing she had no other symptoms which are characteristic of PCS. In addition, she appeared to have considerable distress. An appropriate IV sedation regimen, which would also be antitussive, was therefore indicated.

Approximately one month prior to her dental procedure, the patient had undergone a full clinical evaluation of her chronic cough. This included pulmonary function tests (PFTs) and a bronchoscopy with a bronchoalveolar lavage (BAL). The subsequent cytologic examination of her BAL had identified macrophages and epithelial cells from her right middle lobe. These are both consistent with PCS. Moreover, these findings were similar to those from autopsy studies of both humans (4) and primates (5) who had also been infected with SARS-CoV-2. There was no evidence of

any acute active pulmonary infection or neoplasm at the time of her bronchoscopy.

Furthermore, inspection of her PFTs revealed a low forced vital capacity (FVC) of 2.32 liters and some reduction in her forced expiratory volume at 1 second (FEV1) of 2.01 liters. It should be noted that this resulted in an FEV1/FVC ratio which was elevated to an abnormal level of 86%. This is indicative of a restrictive lung pattern and is consistent with low pulmonary compliance. (6) This has been demonstrated in other PCS patients as well. (7) In addition, her PFTs did not demonstrate any evidence of obstruction, air trapping, or gas transfer defects. Moreover, she did not bronchodilate in response to albuterol.

A CT scan of her chest failed to identify any significant anatomic explanation for her chronic cough and showed no gross abnormalities. Her EKG demonstrated normal sinus rhythm with a heart rate of 67 beats per minute (BPM). Non-specific T waves changes were also noted. She had no evidence of jugular venous distention, orthopnea, or ankle edema which would suggest congestive heart failure.

Her coughing was symptomatically managed with gabapentin 600 mg PO TID, benzonatate (Tessalon Perles) 200 mg PO TID, promethazine with codeine (6.25 mg/10 mg)/5 mL PO PRN, and revefenacin (Yupelri) 175 mcg inhaled QD. She was also receiving 81 mg aspirin PO QD. Furthermore, the patient had been treated with numerous opiate-based cough suppressants for months. These included hydromorphone, hydrocodone, and oxycodone. The patient was deemed medically optimized for office-based IV sedation by her pulmonologist.

Dentally, it was noted that the patient had a palatal cusp fracture just above the cemento-enamel junction on tooth #14. Buccal swelling was present with gingival inflammation and a buccal sinus tract was also observed. Her oral radiographic examination revealed signs of osseous destruction which resulted in a radiolucent area within the tooth. This is consistent with other reported dental pathology associated with the Covid-19 pandemic (See: Discussion). The endodontic surgical plan was to perform a root canal and to surgically excise redundant gingival tissue which was growing over the fractured palatal cusp. Additionally, her dental infection had been treated initially with oral tramadol and amoxicillin.

Prior to inducing sedation, her room air oxygen saturation was 97 % with a respiratory rate of approximately 17 breaths

per minute and she had a considerable, very frequent, dry cough. Her breath sounds were clear bilaterally. Although apprehensive and somewhat tachypneic she was hemodynamically stable with an initial blood pressure of 160/90 mmHg and a heart rate of 105 BPM. Furthermore, she was afebrile.

Initially, she was slowly given lidocaine 100 mg. Hydromorphone was then administered in divided doses for a total of 2 mg. Her sedation was subsequently maintained with a propofol infusion of 25 mcg/kg/min with a total dose of 92 mg.

Ketamine was also administered using repetitive intermittent boluses of 20 to 30 mg to maintain adequate sedation. A total dose of 90 mg of ketamine was utilized. During the procedure, all anesthesia-related medications had been administered IV. Full ASA monitoring, including nasal capnography, was utilized.

Her coughing was fully abated for the entire surgery. Throughout the procedure, the patient maintained a respiratory rate of approximately 10-20 breathes per minute and she remained conscious with a moderate level of sedation. Nasal cannula oxygen was also administered at a rate of 2 liters per minute.

Furthermore, she received IV metoclopramide 10 mg, ondansetron 4 mg, and methylprednisolone 40 mg. Atropine 200 mcg was administered for its antisialagogue and vagolytic effects. Note that these medications all have antiemetic properties. (8) Additionally, a pilot study has shown that metoclopramide may also function as an antitussive. (9)

Following the removal of her IV catheter, the patient experienced mild nausea. This was treated with an additional dose of ondansetron 4 mg given intramuscularly and inhaled isopropyl alcohol. (10) She subsequently recovered adequately for discharge. There was no evidence of ketamine-induced dysphoria.

On telephone follow-up, the patient had no post-anesthesia complications and even reported minimal coughing on post-operative day zero and post-operative day one. Her dental pain also had resolved. On post-operative day two the patient's cough returned to its baseline severity. However, she continued to be free from odontalgia.

DISCUSSION

The management of chronic cough, secondary to PCS, has not been established. Of note, her preoperative medication regimen included gabapentin. While this drug is traditionally utilized for its anti-epileptic properties, it has been reported to be beneficial for chronic cough. Its mechanism of action is believed to be related to its central neuromodulatory ability. (11,12) Gabapentin is also utilized for chronic pain syndromes, (13) depression, (14) and mood disorders. (15) Its mechanism of action is believed to be similar for these neurologic and psychiatric conditions. (16) Furthermore, these illnesses can also occur with PCS.

It should be noted that hydromorphone has been utilized as an antitussive for patients with lung cancer and acute bronchitis. (17,18) Intravenous lidocaine (19) and the combination of propofol with ketamine have also been reported to have antitussive properties. (20,21) Ketamine is a known bronchodilator (22,23) which is most likely a function of it being sympathomimetic. (24) Additionally, ketamine has anti-inflammatory properties (25,26) as well as antidepressant properties. Moreover, fentanyl is associated with coughing and was avoided. (28-30)

It has been documented that the COVID-19 pandemic has resulted in an increase in the need for emergency dental services. The Department of Oral Emergency, Peking University, Beijing, China, reported that the proportion of dental and oral infections has increased from 51% before the pandemic to 71.9% with the pandemic. Dental pulpal and periapical lesions (44.7%) have been the main reasons for these emergencies. Moreover, cellulitis from abscessed teeth has also increased. Note that routine dental care was not available in China during the onset of this pandemic. (31)

In addition, a much greater frequency of dental trauma, occurring since the beginning of the COVID-19 pandemic, has also been described by the American Dental Association and in the American lay press. The reported cause is most likely bruxism secondary to anxiety. (32-34) An escalation in the incidence of viral-associated intra-oral (35) and dermatologic soft-tissue lesions (36,37) has also been observed with the both the acute SARS-CoV-2 infection and PCS. (38,39)

Patients with chronic cough have been studied prior to this pandemic. Typically, they are middle-aged females who have COPD or have suffered from a respiratory tract infection. Other causes include an autoimmune or "lupus-like" etiology, gastro-esophageal reflux, prolonged airway or pharyngeal irritation, and laryngeal sensory neuropathy. (40)

The pathological basis of chronic cough and other pulmonary symptoms associated with PCS is currently attributed to fibrotic changes occurring within the lung parenchyma following the acute SARS-CoV-2 infection. (7) Specifically, persistent viremia, inflammatory, and autoimmune-mediated effects may also be involved in the pulmonary and extra-pulmonary aspects of this newly reported chronic disease state. (41,42) Furthermore, COVID-19 and PCS-associated vasculitis, (43) dermatologic (36,39), arthritic, (44,45) and neurologic (46) issues appear to be immune-mediated. This would readily explain the broad range of symptoms from both the acute and chronic disease processes. (47)

Using MRI, chronic myocardial involvement has also been documented in PCS patients. Specifically, myocardial edema, fibrosis, and decreased right ventricle ejection fraction have been identified. (48) Renal, (49) hepatic, and splenic aspects of PCS have also been reported. (50)

CONCLUSIONS

As PCS will undoubtedly increase in its presentation, the use of IV sedation for these dental patients, when indicated, should be considered as a reasonable anesthetic option. A symptom-specific approach will be necessary given the highly variable presentation of PCS. In this case, an "antitussive and anti-inflammatory" sedation regimen proved useful and safe. Furthermore, the anti-inflammatory properties of both methylprednisolone and ketamine may have been beneficial for her brief post-operative reprieve from coughing.

References

1. Carfì A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. JAMA. 2020 Aug 11;324(6):603-5.
2. Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, Walshaw C, Kemp S, Corrado J, Singh R, Collins T. Postdischarge symptoms and rehabilitation needs in survivors of COVID‐19 infection: A cross‐sectional evaluation. J Virol. 2021 Feb;93(2):1013-22.
3. Tenforde MW, Kim SS, Lindsell CJ, Rose EB, Shapiro NI, Files DC, Gibbs KW, Erickson HL, Steingrub JS, Smithline HA, Gong MN. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network—United States, March–June 2020. Morb Mortal Wkly Rep. 2020 Jul 31;69(30):993.
4. Wang C, Xie J, Zhao L, Fei X, Zhang H, Tan Y, Nie X, Zhou L, Liu Z, Ren Y, Yuan L. Alveolar macrophage

dysfunction and cytokine storm in the pathogenesis of two severe COVID-19 patients. EBioMedicine. 2020 Jul 1;57:102833.

5. Fahlberg MD, Blair RV, Doyle-Meyers LA, Midkiff CC, Zenere G, Russell-Lodrigue KE, Monjure CJ, Haupt EH, Penney TP, Lehmicke G, Threeton BM. Cellular events of acute, resolving or progressive COVID-19 in SARS-CoV-2 infected non-human primates. Nat Commun. 2020 Nov 27;11(1):1-4.

6. Schultz K, D'Aquino LC, Soares MR, Gimenez A, Pereira CA. Lung volumes and airway resistance in patients with a possible restrictive pattern on spirometry. J Bras Pneumol. 2016 Oct;42(5):341-7.

7. Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, Vilaró J. Respiratory function in patients post-infection by COVID-19: A systematic review and meta-analysis. Pulmonol. 2020 Nov 25.

8. Kovac AL. Prevention and treatment of postoperative nausea and vomiting. Drugs. 2000 Feb;59(2):213-43.

9. Gupta VK. Metoclopramide aborts cough-induced headache and ameliorates cough–a pilot study. International journal of clinical practice. 2007 Feb;61(2):345-8.

10. Beadle KL, Helbling AR, Love SL, April MD, Hunter CJ. Isopropyl alcohol nasal inhalation for nausea in the emergency department: A randomized controlled trial. Ann Emerg Med. 2016 Jul 1;68(1):1-9.

11. Ryan NM, Birring SS, Gibson PG. Gabapentin for refractory chronic cough: A randomised, double-blind, placebo-controlled trial. Lancet. 2012 Nov 3;380(9853):1583-9.

12. Gibson PG, Vertigan AE. Gabapentin in chronic cough. Pulm Pharmacol Ther. 2015 Dec 1;35:145-8.

13. Wiffen PJ, Derry S, Bell RF, Rice AS, Toelle TR, Phillips T, Moore RA. Gabapentin for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2017(6).

14. Yasmin S, Carpenter LL, Leon Z, Siniscalchi JM, Price LH. Adjunctive gabapentin in treatment-resistant depression: A retrospective chart review. J Affect Disord. 2001 Mar 1;63(1-3):243-7.

15. Harden CL, Lazar LM, Pick LH, Nikolov B, Goldstein MA, Carson D, Ravdin LD, Kocsis JH, Labar DR. A beneficial effect on mood in partial epilepsy patients treated with gabapentin. Epilepsia. 1999 Aug;40(8):1129-34.

16. Türközer HB, Öngür D. A projection for psychiatry in the post-COVID-19 era: Potential trends, challenges, and directions. Mol Psychiatry. 2020 Oct;25(10):2214-9.

17. Molassiotis A, Smith JA, Bennett MI, Blackhall F, Taylor D, Zavery B, Harle A, Booton R, Rankin EM, Lloyd-Williams M, Morice AH. Clinical expert guidelines for the management of cough in lung cancer: Report of a UK task group on cough. Cough. 2010 Dec;6(1):1-8.

18. Knutson D, Braun C. Diagnosis and management of acute bronchitis. Am Fam Physician. 2002 May 15;65(10):2039-2045.

19. Clivio S, Putzu A, Tramèr MR. Intravenous lidocaine for the prevention of cough: Systematic review and meta-analysis of randomized controlled trials. Anesth Analg. 2019 Nov 1;129(5):1249-55.

20. Safavi M, Honarmand A, Khazaei M. The effects of propofol, ketamine and combination of them in prevention of coughing and laryngospasm in patients awakening from general anesthesia: A randomized, placebo-controlled, double blind clinical trial. Adv Biomed Res. 2016;5.

21. Chungsamarnyart Y, Pairart J, Munjupong S. Comparison of the effects of intravenous propofol and propofol with low-dose ketamine on preventing

postextubation cough and laryngospasm among patients awakening from general anaesthesia: A prospective randomised clinical trial. J Perioper Pract. 2020 Apr 17:1-6.

22. Goyal S, Agrawal A. Ketamine in status asthmaticus: A review. Indian J Crit Care Med. 2013 May;17(3):154-161.

23. Petrillo T, Petrillo TM, Fortenberry JD, Linzer JF, Simon HK. Emergency department use of ketamine in pediatric status asthmaticus. J Asthma. 2001 Jan 1;38(8):657-64.

24. Morris C, Perris A, Klein J, Mahoney P. Anaesthesia in haemodynamically compromised emergency patients: Does ketamine represent the best choice of induction agent? Anaesthesia. 2009 May;64(5):532-9.

25. Loix S, De Kock M, Henin P. The anti-inflammatory effects of ketamine: State of the art. Acta Anaesthesiol Belg. 2011 Jan 1;62(1):47-58.

26. Dale O, Somogyi AA, Li Y, Sullivan T, Shavit Y. Does intraoperative ketamine attenuate inflammatory reactivity following surgery? A systematic review and meta-analysis. Anesth Analg. 2012 Oct 1;115(4):934-43.

27. Fond G, Loundou A, Rabu C, Macgregor A, Lançon C, Brittner M, Micoulaud-Franchi JA, Richieri R, Courtet P, Abbar M, Roger M. Ketamine administration in depressive disorders: A systematic review and meta-analysis. Psychopharmacology. 2014 Sep;231(18):3663-76.

28. Meng Q, Chen R, Tang L, Sun T, Zeng Z, Zhang Y, Ding K. Mechanism and management of fentanyl-induced cough. Front Pharmacol. 2020;11:1691.

29. Oshima T, Kasuya Y, Okumura Y, Murakami T, Dohi S. Identification of independent risk factors for fentanyl-induced cough. Canadian Journal of Anesthesia. 2006 Aug;53(8):753-8.

30. El Baissari MC, Taha SK, Siddik-Sayyid SM. Fentanyl-induced cough--pathophysiology and prevention. Middle East J Anaesthesiol. 2014 Jun 1;22(5):449-56.

31. Guo H, Zhou Y, Liu X, Tan J. The impact of the COVID-19 epidemic on the utilization of emergency dental services. J Dent Sci. 2020 Mar 16.

32. Versaci, Mary Beth. HPI poll: Dentists see increase in patients' stress-related oral health conditions. ADA News [Internet]. Published September 28, 2020. Available from: http://www.ada.org.

33. Chen, Tammy. A dentist sees more cracked teeth. What's going on? The New York Times [Internet]. Published Sept. 8, 2020. Updated Sept. 11, 2020. Available from: http://www.nytimes.com.

34. Shannon, Joel. Cracked teeth, gross gums: Dentists see surge of problems, and the pandemic is likely to blame. USA Today [Internet]. Published Sept. 11, 2020. Updated Sept. 14, 2020. Available from: http://www.usatoday.com

35. Sinadinos A, Shelswell J. Oral ulceration and blistering in patients with COVID-19. Evid Based Dent. 2020 Jun;21(2):49.

36. Gottlieb M, Long B. Dermatologic manifestations and complications of COVID-19. Am J Emerg Med. 2020 Sep 1;38(9):1715-21.

37. Seirafianpour F, Sodagar S, Pour Mohammad A, Panahi P, Mozafarpoor S, Almasi S, Goodarzi A. Cutaneous manifestations and considerations in COVID-19 pandemic: A systematic review. Dermatol Ther. 2020 Nov;33(6):e13986.

38. Bezerra TM, Feitosa SG, Carneiro DT, Costa FW, Pires FR, Pereira KM. Oral lesions in COVID-19 infection: Is long-term follow-up important in the affected patients? Oral Dis. 2020;00:1–2.

39. McMahon DE, Gallman AE, Hruza GJ, Rosenbach M, Lipoff JB, Desai SR, French LE, Lim H, Cyster JG, Fox LP,

Fassett MS. Long COVID in the skin: A registry analysis of COVID-19 dermatological duration. Lancet Infect Dis. Available from:
https://doi.org/10.1016/S1473-3099(20)30986-5

40. Simpson CB, Amin MR. Chronic cough: State-of-the-art review. Otolaryngol Head Neck Surg. 2006 Apr;134(4):693-700.

41. Manzo G. COVID-19 as an immune complex hypersensitivity in antigen excess conditions: Theoretical pathogenetic process and suggestions for potential therapeutic interventions. Front Immunol. 2020 Oct 21;11:2665.

42. Chang SE, Feng A, Meng W, Apostolidis SA, Mack E, Artandi M, Barman L, Bennett K, Chakraborty S, Chang I, Cheung P. New-onset IgG autoantibodies in hospitalized patients with COVID-19. medRxiv. 2021 Jan 1. Available from: http://www.medrxiv.org

43. Becker, RC. COVID-19-associated vasculitis and vasculopathy. J Thromb Thrombolysis. 2020;50:499–511.

44. Waller R, Price E, Carty S, Ahmed A, Collins D. Post COVID-19 reactive arthritis. Rheumatol Adv Pract. 2020 Oct; 4(Suppl 1): rkaa052. Available from: http://academic.oup.com/rheumap

45. Schenker HM, Hagen M, Simon D, Schett G, Manger B. Reactive arthritis and cutaneous vasculitis after SARS-CoV-2 infection. Rheumatology. 2021 Jan;60(1):479-80.

46. Paterson RW, Brown RL, Benjamin L, Nortley R, Wiethoff S, Bharucha T, Jayaseelan DL, Kumar G, Raftopoulos RE, Zambreanu L, Vivekanandam V. The emerging spectrum of COVID-19 neurology: Clinical, radiological and laboratory findings. Brain. 2020 Oct;143(10):3104-20.

47. Davido B, Seang S, Tubiana R, de Truchis P. Post–COVID-19 chronic symptoms: A postinfectious entity? Clin Microbiol Infect. 2020 Nov 1;26(11):1448-9.

48. Huang L, Zhao P, Tang D, Zhu T, Han R, Zhan C, Liu W, Zeng H, Tao Q, Xia L. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. JACC Cardiovasc Imaging. 2020 Nov 1;13(11):2330-9.

49. Fisher M, Neugarten J, Bellin E, Yunes M, Stahl L, Johns TS, Abramowitz MK, Levy R, Kumar N, Mokrzycki MH, Coco M. AKI in hospitalized patients with and without COVID-19: A comparison study. J Am Soc Nephrol. 2020 Sep 1;31(9):2145-57.

50. Dennis A, Wamil M, Kapur S, Alberts J, Badley A, Decker GA, Rizza SA, Banerjee R, Banerjee A. Multi-organ impairment in low-risk individuals with long COVID. medRxiv. 2020 Jan 1. Available from: http://www.medrxiv.org

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