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CASE REPORT

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Pacemaker implantation for persistent sinus node dysfunction in a patient with COVID-19

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Abstract

A 46-year-old woman was admitted with coronavirus disease-2019 infection. Symptomatic sinus bradycardia occurred, followed by congestive heart failure. Therapeutics such as isoproterenol, theophylline, and cilostazol could not safely improve her symptoms. She underwent pacemaker implantation 53 days after admission. Atrial pacing remained was at 60% after 6 months.

KEYWORDS

bradycardia, COVID-19, pacemaker, sinus node dysfunction

1 | INTRODUCTION

Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), was first reported in December 2019 and quickly spread throughout the world. As of 22 December 2022, more than 650 million confirmed cases of COVID-19 and more than 6.65 million deaths have been reported worldwide by the World Health Organization.[1]

Although COVID-19 clinical manifestations are mainly respiratory, there are well-documented cardiac complications including arrhythmia, heart failure, myocarditis, and thrombosis. In a report from China, 16.7% of hospitalized and 44.4% of ICU patients with COVID-19 had cardiac arrhythmias.[2]

Tachyarrhythmias are common in hospitalized patients with COVID-19, according to an arrhythmia study, but sinus bradycardia is also reported in 4.9%.[3]

To the best of our knowledge, there have been no reports with follow-up data of sinus node dysfunction caused by COVID-19 who underwent pacemaker implantation (PMI). This case report describes clinical characteristics of prolonged sinus node dysfunction caused by COVID-19 refractory to medical therapies.

2 | CASE PRESENTATION

A 46-year-old woman presented to her primary care physician with dyspnea, fever, headache, cough, dysgeusia, and dysosmia. A nasopharyngeal antigen swab test was positive for SARS-CoV-2.

The patient has a history of bronchial asthma without current use of inhalational medication. She had no history of cardiac disease nor arrhythmia. Her average HR was 70 bpm before this infection.

Consequently, she was admitted to our institution for COVID-19 treatment on day 1, 7 days after the onset of her symptoms.

Upon admission, the patient had a blood pressure of 111/70 mmHg, heart rate (HR) of 59 beats/min (bpm), oxygen saturation at 99% (room air), respiratory rate of 18/min, and body temperature of 38.0°C.

A 12-lead electrocardiography (ECG) displayed normal sinus rhythm. Radiographic imaging indicated pneumonia **(**Figure 1**)**.

Blood tests revealed a slight increase in hepatobiliary system enzymes, C-reactive protein (CRP), ferritin, brain natriuretic peptide (BNP), and fibrinogen levels **(Table 1)**.

COVID-19-specific treatment was begun on the day of admission (day 1), with remdesivir (100 mg daily), dexamethasone (6 mg daily), baricitinib (4 mg daily), and heparin calcium (10,000 U, twice a day), according to the Japanese Ministry of Health, Labor, and Welfare guidelines.

On day 4, the patient exhibited symptomatic sinus bradycardia (30–35 bpm), with presyncope, dizziness, and nausea.

A 12-lead ECG showed sinus rhythm bradycardia with isorhythmic atrial ventricular dissociation **(**Figure 2**)**.

Cardiac enzyme and electrolyte levels were normal **(**Table 1**)**.

Drug-induced bradycardia, caused by remdesivir, was suspected. Consequently, remdesivir was discontinued on day 4. A continuous intravenous infusion of isoproterenol (0.006 mcg/kg/min) was prescribed, which increased the patient's HR to 60–70 bpm.

Although, we attempted to wean the patient off isoproterenol on days 8 and 9, we had to resume it as her HR drastically dropped from 60–70 bpm to 40–45 bpm and she started displaying orthopnea. Chest radiography on day 11 revealed congestive heart failure **(**Figure 3**)**. Blood tests revealed worsening in hepatobiliary function and an elevated BNP profile compared to the patient's unremarkable blood profile upon admission **(**Table 1**)**. Transthoracic echocardiography (TTE) showed a dilated inferior vena cava with poor respiratory fluctuation, despite normal left ventricle (LV) dimensions, and preserved LV ejection fraction (60%), without signs of valvular disease. Diuretics were promptly administered on day 11 until day 17, and the patient's heart failure symptoms improved. Intravenous isoproterenol was discontinued and substituted with oral isoproterenol (15 mg four times daily) on day 11. She was discharged on day 20.

Post-discharge, the patient's HR ranged between 40 bpm with presyncope, before taking isoproterenol, and 150 bpm with palpitations after medications.

On day 28, the patient presented to the emergency department again, with palpitations. On assessment, the patient's HR was 118 bpm, while a 12-lead ECG showed sinus tachycardia with frequent premature ventricular contractions.

On day 38, the patient was re-hospitalized for drug adjustment; isoproterenol was replaced with theophylline (200–400 mg twice a day); however, it caused nausea and could not effectively control her symptoms.

On day 43, theophylline was switched to cilostazol (50–100 mg twice a day). Although, the HR went up to 50–60 bpm and nausea disappeared, she developed headaches.

Pharmacologic therapy was discontinued, and the HR decreased to 30 bpm presyncope and malaise. She subsequently underwent dual-chamber pacemaker implantation (PMI) on day 54 **(**Figure 4**)**. Post-PMI, the patient's symptoms improved, and she was discharged on day 61.

The patient's capacity for exercise was significantly reduced at discharge since she was bedridden for 2 months. At 3 weeks post-PMI, she enjoyed cycling around 100 kilometers daily as she did before hospitalization.

The percentage of atrial pacing decreased from 87.1% on day 60 to 61.5% on day 88 and to 58.5% on day 185.

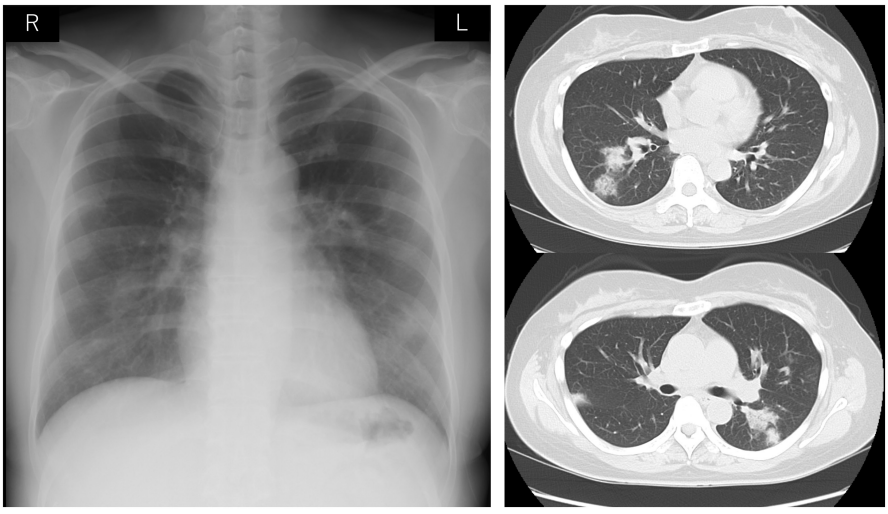

FIGURE 1 Imaging on initial presentation. Chest radiography (left) and computed tomography scan image (right) at presentation showing bilateral ground glass opacities. Chest–thoracic ratio is 49%.

TABLE 1 Blood test results

Blood test	Day 1	Day 4	Day 13	Day 40	Normal values
Hemoglobin, g/dl	15.7[a]	13.6	15.6[a]	14.1	11.6–14.8
White blood cell count, $\times 10^3/\mu l$	4.3	6.3	8.37	5.23	3.3–8.6
Lymphocyte count, $\times 10^3/\mu l$	0.79[b]	2.66	3.98	2.11	0.9–4.0
Platelet count, $\times 10^3/\mu l$	109[b]	142[b]	298	237	158–348
Creatinine, mg/dl	0.65	0.59	0.70	0.63	0.46–0.79
Sodium, mmol/L	140	141	136	141	138–145
Potassium, mmol/L	4.1	3.7	3.9	3.9	3.6–4.8
Aspartate aminotransferase, U/L	73[a]	33[a]	191[a]	22	13–30
Alanine aminotransferase, U/L	80[a]	67[a]	396[a]	30[a]	7–23
Lactate dehydrogenase, U/L	208	264[a]	249[a]	166	124–222
Fibrinogen, mg/dl	528[a]	NA	NA	NA	200–400
D-dimer, μg/ml	<0.5	<0.5	<0.5	<0.5	<1.0
C-reactive protein, mg/dl	1.85[a]	0.34[a]	0.03	0.02	<0.14
Ferritin, ng/ml	163[a]	NA	NA	NA	5–152
Troponin, pg/ml	NA	3.91	NA	<2.50	<14
Creatinine kinase-MB, μg/L	NA	<4	NA	NA	<6.2
Brain natriuretic peptide, pg/ml	36.6[a]	240.1[a]	NA	21.5	<18.4

Abbreviation: NA, not available.

[a]The value is greater than normal.

[b]The value is less than normal.

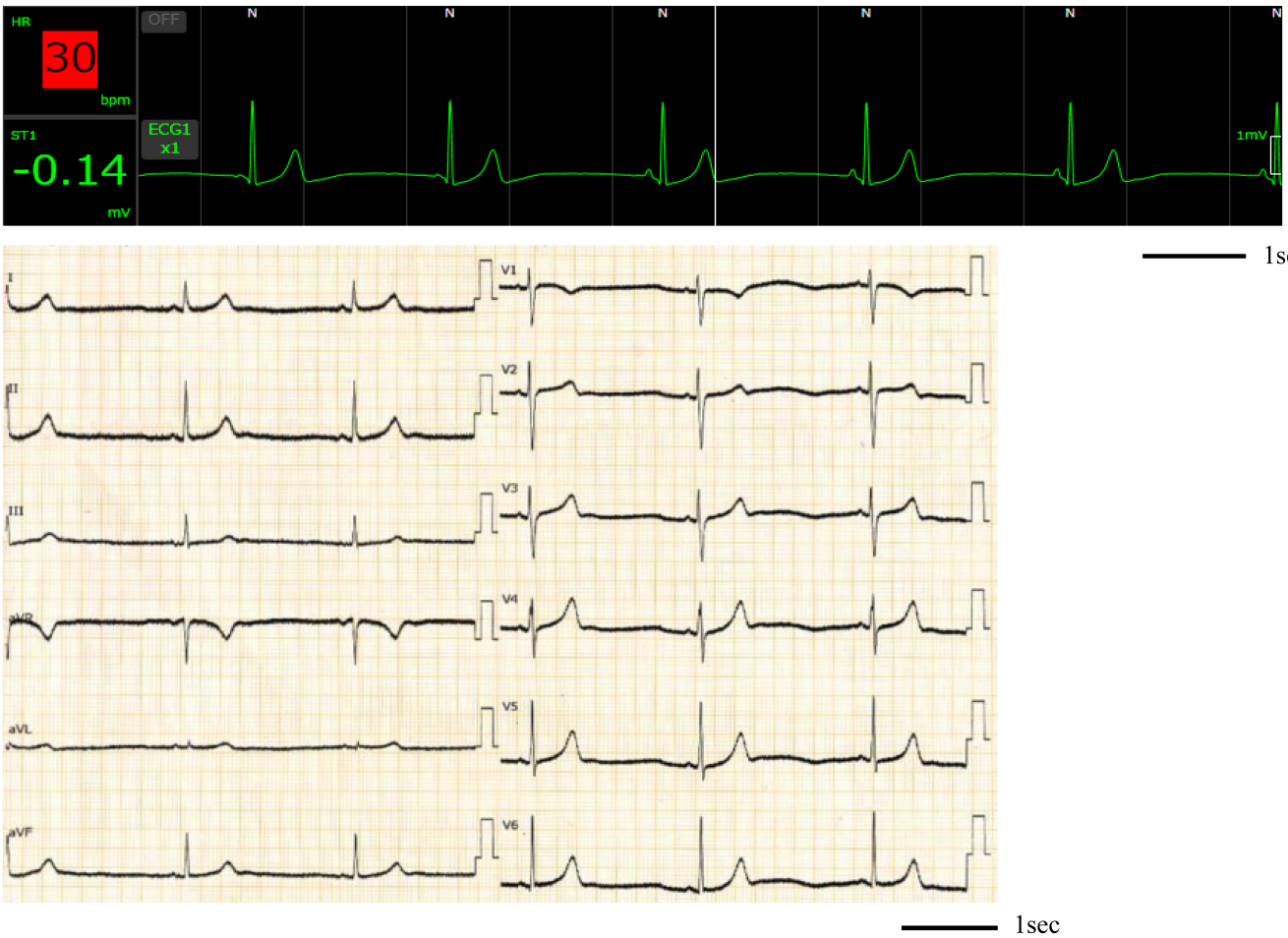

FIGURE 2 Electrocardiography of sinus bradycardia. Electrocardiography continuous monitoring (upper) and 12-lead electrocardiography (lower) showing sinus rhythm bradycardia with isorhythmic atrial ventricular dissociation.

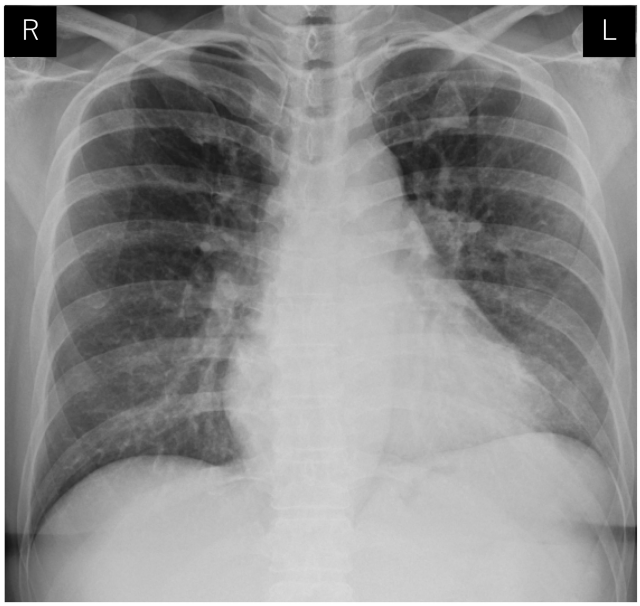

FIGURE 3 Chest radiography of congestive heart failure due to bradycardia. Chest radiography showing cardiomegaly and de novo pulmonary vascular shadow dilation. Chest–thoracic ratio is 55%.

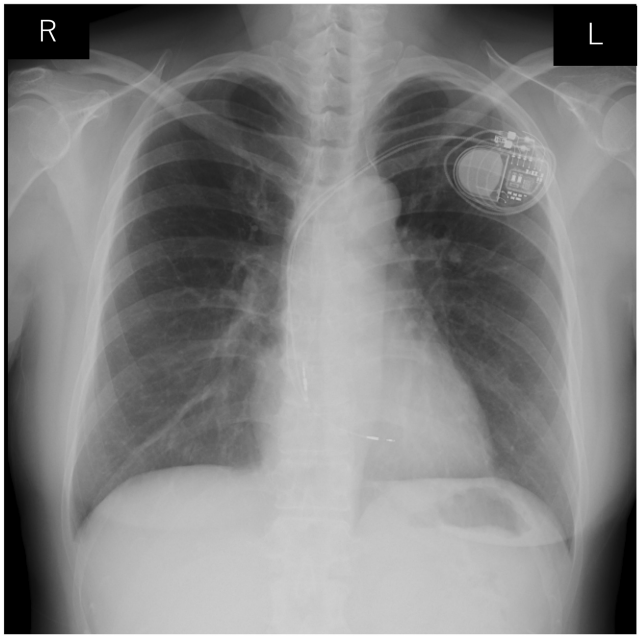

FIGURE 4 Chest radiography after dual-chamber pacemaker implantation.

3 | DISCUSSION

Tachyarrhythmias are common in hospitalized patients with COVID-19, according to an arrhythmia study, but sinus bradycardia is also reported in 4.9%.[3]

Various theories on how COVID-19 causes bradycardia are hypothesized, including direct viral myocardial inflammation, pro-inflammatory cytokines acting on the sinoatrial node, hypoxia, hypotension, angiotensin-converting enzyme 2 (ACE2) receptor downregulation, drug toxicity, and endogenous cathecholamine adrenergic status.[4]

Remdesivir can induce bradycardia more frequently than other drugs used for COVID-19 therapy. This may be due to the fact that the molecular structure of remdesivir is similar to that of adenosine triphosphate (ATP). Bradycardia was documented in 94 out of 2603 cases (3.6%).[5] Remdesivir has a half-life of 0.98 h, confirmed by reports that remdesivir-induced bradycardia improves within a few days after discontinuing its administration.[6] Therefore, remdesivir is unlikely to be the cause of bradycardia lasting more than 6 weeks past its discontinuation.

Recently, a study of two COVID-19 cases with symptomatic bradycardia reported on the improvement of symptoms by oral administration of theophylline (200 mg once a day). In both cases, bradycardia and its symptoms improved a week after starting medication; all symptoms resolved after 5–6 weeks.[7] This demonstrates that sinus bradycardia associated with COVID-19 may be reversible in some patients.

Our investigation found only one other case of sinus node dysfunction caused by COVID-19 who underwent PMI. In this particular case, PMI was performed while the patient was on the ventilator.[8] Unfortunately, follow-up data, such as the percentage of atrial pacing, were unavailable.

An international survey of cardiac electronic device implantation in active COVID-19 cases indicated high complication rates of 13.9% at 30 days and high mortality rates of 9.6% at 6 months.[9] PMI in active COVID-19 patients should be carefully considered.

Pharmacologic therapy available for sick sinus syndrome include theophylline, cilostazol, and isoproterenol. In our patient, oral medication was trialed for more than 6 weeks, but pharmacologic therapy failed to safely control her bradycardia and its accompanying symptoms.

Post-PMI, the bradycardic symptoms of the patient completely disappeared and her capacity for exercise remarkably improved. The percentage of atrial pacing decreased from 87.1% on day 60 to 61.5% on day 88 and 58.5% on day 185. Incidentally, the lower pacing rate was set to 60 bpm since her average heart rate was 70 bpm before COVID-19 infection. The decrease in the percentage of atrial pacing after discharge was attributed to increased amounts of exercise. Conversely, 60% of atrial pacing observed from day 88 through day 185 indicates that sinus node dysfunction, in our case, is probably permanent.

Recent studies reveal evidence of severe deterioration, associated with the cytokine storm, in some patients with COVID-19. Reports suggest a correlation between bradycardia associated with COVID-19 and the severity of COVID-19 illness.[4]

Even though COVID-19 was not particularly severe in our patient, her inflammatory markers (ferritin, CRP, D-dimer, lactate dehydrogenase, and fibrinogen) were barely elevated; she still exhibited persistent symptoms of sinus bradycardia. Bradycardia caused by COVID-19 may have multiple mechanisms. Further research is needed to confirm this finding.

4 | CONCLUSION

We report a rare case of symptomatic, persistent sick sinus syndrome associated with COVID-19 infection. Pacemaker implantation was observed to be more effective than pharmacologic therapy, even after 6 months of follow-up.

AUTHOR CONTRIBUTIONS

Tsuyoshi Ota: Writing – original draft. **Katsunori Okajima:** Writing – review and editing. **Yuichi Nagamatsu:** Writing – review and editing. **Tomoyuki Nakanishi:** Writing – review and editing. **Yasuhiro Kaetsu:** Writing – review and editing. **Takahiro Sawada:** Writing – review and editing. **Takeaki Shirai:** Writing – review and editing. **Rio Shiraki:** Writing – review and editing. **Makoto Kadotani:** Writing – review and editing. **Yoshio Onishi:** Writing – review and editing.

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No financial support was received for this case report.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT.

All data regarding this case has been reported in the manuscript. Please contact the corresponding author if you are interested in any further information.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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