Quarantine-induced Stress Cardiomyopathy (Takotsubo Syndrome) during the COVID-19 Pandemic

Gassan Moady MD MPH\textsuperscript{1,2} and Shaul Atar MD\textsuperscript{1,2}

\textsuperscript{1}Department of Cardiology, Galilee Medical Center; Nahariya, Israel
\textsuperscript{2}Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel

ABSTRACT

**Background:** Takotsubo syndrome (TTS) is a non-ischemic cardiomyopathy characterized by an acute reversible left ventricular dysfunction with typical apical ballooning, usually with subsequent complete spontaneous recovery. TTS may be triggered by several physical and emotional stressors. The name Covidusubo was recently adopted to describe this emerging entity. TTS during quarantine may be a reasonable outcome of the overwhelming stress and fear of this pandemic. However, according to the current literature, conflicting results have been reported regarding the incidence of this syndrome during the first wave of the pandemic, and further studies are needed. High index of suspicion is needed to identify patients during the next waves of the pandemic, particularly given the need for minimizing imaging modalities and contact with the patients.

**Objectives:** To describe two cases of TTS triggered by quarantine during the coronavirus disease-2019 (COVID-19) pandemic.

**Methods:** Two patients (age 81 years and 70 years) were admitted to our medical center with severe chest pain with normal blood pressure and heart rate.

**Results:** TTS should always be in the differential diagnosis of patients presenting with chest pain suspected to be from coronary origin. Based on the typical clinical, echocardiographic, and angiographic findings, we assumed TTS.

**Conclusions:** The only prominent stressor in the two cases in this article was the stress accompanying quarantine.

**KEY WORDS:** coronavirus disease-2019 (COVID-19), echocardiography, stress, quarantine, Takotsubo syndrome (TTS)

Coronavirus disease-2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which was first described in December 2019 in Wuhan, Hubei, China, and widely spread to become a global pandemic with ongoing medical and economic implications. In an effort to limit the transmission of this pandemic, quarantine and self-isolation have been adopted in several countries. Quarantine used for the prevention of disease spread may be associated with mental stress.

Takotsubo cardiomyopathy (TTS) is characterized by acute reversible left ventricular dysfunction with typical apical wall motion abnormality (apical ballooning) without evidence for epicardial obstructive coronary artery disease. It may be triggered by several physical and emotional stressors. The name Covidusubo was recently adopted to describe this emerging entity. TTS during quarantine may be a reasonable outcome of the overwhelming stress and fear of this pandemic. However, according to the current literature, conflicting results have been reported regarding the incidence of this syndrome during the first wave of the pandemic, and further studies are needed. High index of suspicion is needed to identify patients during the next waves of the pandemic, particularly given the need for minimizing imaging modalities and contact with the patients.

**PATIENTS AND METHODS**

**PATIENT 1**

An 81-year-old female admitted to the intensive cardiac care unit (ICCU) with chest pain, which began 2 days prior to her admission. Her past medical history was significant for well-controlled hyperlipidemia and hypothyroidism. The patient did not report any previous cough, dyspnea, or fever. She stated being in a very stressful period during a quarantine in the previous 3 weeks with no contact with her family members.

On admission, her blood pressure was 100/60 mmHg and her heart rate was 100 beats per minute (bpm). Her physical examination was remarkable for apical systolic heart murmur with no signs of heart failure. Blood count and kidney function tests were within normal limits. Troponin I level was high at 3000 ng/L and B-type natriuretic peptide N-terminal pro B-type natriuretic peptide (NT-pro BNP) was 11400 pg/ml. Real-time PCR for COVID-19 from nasal swab was negative. The electrocardiogram showed normal sinus rhythm with diffuse ST segment elevation, most prominent in the anterior leads with no reciprocal changes [Figure 1A]. Echocardiography showed a moderately reduced global systolic left ventricular function with typical pattern of apical ballooning and left ventricular outflow obstruction [Figure1B].
A 70-old-female with hypothyroidism and remote history of acute myeloid leukemia that was successfully treated with bone marrow transplantation was admitted with severe chest pain, which started a few hours before her presentation. The patient was in quarantine during the previous 2 weeks with no social interactions, and stated having many fears from the disease. Blood pressure was 170/80 mmHg and heart rate 95 bpm, and her physical examination was within normal limits. Elevated troponin level at 6000 ng/l and NT-pro BNP at 12100 pg/ml was noticed. The echocardiogram showed reduced apical contraction with estimated ejection fraction of 42% and hyperkinetic basal segments of the left ventricle. To rule out acute myocardial infarction, an urgent coronary angiography was conducted, which demonstrated revealed normal arteries.

**RESULTS**

Basic characteristics and the clinical course of the two patients are provided in Table 1.

**PATIENT 1**

We proceeded with emergent coronary angiography that was performed via the right radial artery and revealed normal coronary arteries. Basal hypercontractility and apical ballooning were obvious during left ventriculography [Figure 1C]. Based on these findings, a diagnosis of TTS triggered by stress during quarantine period was assumed. The patient required supplemental oxygen and diuretic therapy due to lung congestion. Her condition improved, and 2 days later she was started on beta blockers and discharged 3 days later after near-normalization.
of cardiac function. One month later, complete normalization of the echocardiographic parameters was observed [Figure 1D] and the patient was symptom-free. She was advised for further psychological support during the outbreak.

**PATIENT 2**
The patient was treated with beta blockers and angiotensin-converting enzyme and was discharged after 5 days with complete recovery of cardiac function. We assumed TTS based on the typical clinical, echocardiographic, and angiographic findings.

In addition to its pulmonary complications, the current COVID-19 outbreak has several extra-pulmonary manifestations, including those of the cardiovascular system [1-3]. Quarantine used to limit disease spread across the country is associated with negative psychological effects [4,5]. People in quarantine report high prevalence of depression, stress, insomnia, and anxiety brought on by long durations of quarantine, fear of infection, frustration, and inadequate supplies [6]. Two factors contribute to the development of TTS in

### Table 1. Demographic, clinical, laboratory, and echocardiographic data of two patients with Takotsubo syndrome triggered by quarantine-induced stress

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference range</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>81</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td>Hyperlipidemia, hypothyroidism</td>
<td>Hypothyroidism, remote history of acute myeloid leukemia</td>
<td></td>
</tr>
<tr>
<td>Chronic medications</td>
<td>Etiloxin</td>
<td>Etiloxin, statin</td>
<td></td>
</tr>
<tr>
<td>Duration of quarantine</td>
<td>3 weeks</td>
<td>2 weeks</td>
<td></td>
</tr>
<tr>
<td>Presenting symptoms</td>
<td>Chest pain radiating to neck</td>
<td>Chest pain radiating to left shoulder with dyspnea</td>
<td></td>
</tr>
<tr>
<td>Physical examination</td>
<td>BP 100/60 mm Hg, HR 100 beats/min</td>
<td>BP 170/80 mm Hg, HR 95 beats/min</td>
<td></td>
</tr>
<tr>
<td>Transthoracic echocardiographic findings on admission</td>
<td>Moderately reduced left ventricular systolic function (EF 38%), moderate to severe mitral regurgitation due to dynamic subaortic obstruction, apical ballooning.</td>
<td>Mildly reduced left ventricular systolic function (EF 42%) with apical ballooning and hyperkinetic basal segments.</td>
<td></td>
</tr>
<tr>
<td>ECG</td>
<td>NSR with anterior ST segment elevation.</td>
<td>NSR with anterior ST segment elevation,</td>
<td></td>
</tr>
</tbody>
</table>

**Values at admission**

| Creatinine (mg/dl)               | 0.57-1.11 | 1.19     | 0.97    |
| Troponin (ng/l)                  | < 20      | 3000     | 6000    |
| NT pro BNP (pg/ml)               | < 125     | 11400    | 12100   |
| Coronary angiography             | Patent coronaries | Patent coronaries | |
| Treatment during hospitalization  | Beta blockers and ACE inhibitors | Beta blockers and ACE inhibitors | |
| Complications                    | Dynamic LVOT obstruction | Right groin hematoma after catheterization | |
| Length of stay                   | 3 days    | 5 days   |         |
| Transthoracic echocardiographic findings on discharge | EF 44% with mild apical hypokinesia without LVOT obstruction | Normal cardiac anatomy and function | |

ACE = angiotensin-converting enzyme, BNP = blood pressure, HR = heart rate, EF = ejection fraction, ECG = electrocardiogram, NSR = normal sinus rhythm, NT pro BNP N = B-type natriuretic peptide N-terminal pro B-type natriuretic peptide, LVOT = left ventricular outflow tract
CONCLUSIONS
Quarantine used to prevent the current COVID-19 spread may trigger several stress-induced diseases including TTS. High index of suspicion for this syndrome is required among elderly patients with chest pain.

Correspondence
Dr. G. Mousy
Dept. of Cardiology, Galilee Medical Center, Nahariya 22100, Israel
Phone: (972-4) 910-7273, (972-4) 910-7438
Fax: (972-4) 910-7279
Email: gassan_mousy1@hotmail.com

References

What a strange man is I
You fill him with bread, wine, fish, and radishes, and out come sighs, laughter, and dreams.
Nikos Kazantzakis (1883-1957), Greek poet and novelist