Case Report

An uncommon combination: a case report of herpes simplex virus encephalitis induced takotsubo cardiomyopathy

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Background: Takotsubo cardiomyopathy, also known as stress-induced cardiomyopathy or broken-heart syndrome, is a non-ischemic cardiomyopathy that presents as a transient regional systolic dysfunction of the left ventricle with minimal increase in troponins. The pathogenesis of takotsubo cardiomyopathy is not well understood. Some possible theories include increased catecholamines causing sympathetic overdrive, microvascular dysfunction, coronary spasm, or inflammation. The association of herpes simplex virus (HSV) encephalitis with takotsubo cardiomyopathy has rarely been reported with only two cases being described in literature.

Case Description: We present a patient that came in with altered mental status who was found to have herpes simplex virus 1 (HSV-1) encephalitis. During his hospital stay, the patient had developed shortness of breath on hospital day 3. The patient's troponin was found to be mildly elevated and echocardiogram revealed takotsubo cardiomyopathy with left ventricle ejection fraction (LVEF) of 20% and severe hypokinesis of all left ventricle segments except the basal segments. His echocardiogram nine months prior revealed a LVEF 60–65%. He was treated with intravenous (IV) acyclovir and repeat echocardiogram three weeks following hospitalization revealed resolution of his takotsubo cardiomyopathy.

Conclusions: Physicians should keep HSV encephalitis induced takotsubo cardiomyopathy in their differential diagnosis when patients present with HSV encephalitis along with shortness of breath and pulmonary vascular congestion on imaging.

Keywords: Herpes simplex virus (HSV); encephalitis; takotsubo; case report

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Introduction

Takotsubo cardiomyopathy is a non-ischemic cardiomyopathy that presents as a transient regional systolic dysfunction of the left ventricle that is similar to a myocardial infarction, however it presents with the absence of coronary artery disease and minimal increase in troponins (1-3). Herpes simplex virus (HSV) encephalitis is the most common sporadic encephalitis in the world (4). We report a case of a patient who was found to have HSV-1 encephalitis that was subsequently found to have takotsubo cardiomyopathy. herpes simplex virus 1 (HSV-1) encephalitis induced takotsubo cardiomyopathy is a rare presentation with only two cases previously being reported in literature. Our case reinforces the importance of awareness of HSV encephalitis induced takotsubo cardiomyopathy despite its

rare occurrence. We present this case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-24-53/rc).

Case presentation

A 68-year-old male with a past medical history of coronary artery disease status post (s/p) myocardial infarction with one stent placed in the right coronary artery, hypertension, diabetes mellitus, and iron deficiency that presented to the emergency department with a 4-day history of dizziness, confusion, slurred speech, unsteadiness, decrease appetite, and high-grade fevers. He did not endorse at any point numbness, tingling, weakness, photophobia, seizures, rash, neck pain, and headache. He recently returned from a trip to the Rocky Mountain region of the United States. 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 for the 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.

On examination, his vitals were temperature 103.4 °F, blood pressure 171/92 mmHg, heart rate 93 bpm, respiratory rate 16 bpm, and oxygen saturation 95% on room air. On physical exam, he was difficult to arouse, however he was alert and oriented ×2 but not to time. The patient was found to have nuchal rigidity, however Kernig sign and Brudzinski sign was negative. He did not have any focal neurological deficits, cutaneous rashes, or peripheral edema. His cardiac, lung, and abdominal exams were normal. His pertinent initial lab results revealed white blood cell (WBC) count 10.8×10^3/μL, lactate 2.3 mmol/L, erythrocyte sedimentation rate (ESR) 19 mm/h, C-reactive protein (CRP) 2.8 mg/L, troponin 8 pg/mL, and B-type natriuretic peptide (BNP) 58 pg/mL. Urinalysis was negative for infection. Computed tomography (CT) without intravenous (IV) contrast of the brain, abdomen, and pelvis were negative for any acute findings. CT chest without IV contrast along with chest X-ray revealed mild pulmonary vascular congestion. Initial electrocardiogram (EKG) revealed sinus tachycardia with short PR intervals with occasional premature ventricular complexes and incomplete right bundle branch block (*Figure 1*).

Cerebrospinal fluid (CSF) studies from a lumbar puncture revealed a cell count of 100, lymphocyte %: 89, red blood cell (RBC) count: 32/μL, gram stain with few WBCs and no organisms seen, glucose of 83 mg/dL, and protein of 92 mg/dL. He was admitted for possible meningitis and started on broad-spectrum antimicrobial therapy. Subsequently, the CSF was positive for HSV-1; antimicrobial therapy was narrowed to IV acyclovir.

During the patient's third hospital day, he developed worsening mental status. On examination, his vitals were temperature 102.1 °F, blood pressure 162/82 mmHg, heart rate 107 bpm, respiratory rate 25 bpm, and SpO_2 96% on 2 liters nasal canula. He had mild tachycardia, tachypnea, intermittent confusion, and mild lethargy. The rest of his physical exam was within normal limits and he had no focal neurological deficits. CT brain revealed a new hypodensity of the insula frontal and temporal lobe, consistent with encephalitis. A subsequent magnetic resonance imaging (MRI) of the brain revealed patchy areas of fluid-attenuated inversion recovery (FLAIR)/T2 hyperintensities with edema within the right temporal insular cortex and frontal lobe with less advanced edematous change seen in the left insular region (*Figure 2*). An EKG and troponin were complete due to the patient's shortness of breath. EKG revealed normal sinus rhythm with premature ventricular complexes and an incomplete right heart block (*Figure 1*). A troponin level was collected, and it was elevated at 190 pg/mL (normal range, 0–53 pg/mL) and peaked at 640 pg/mL before down-trending. An echocardiogram was obtained and revealed a left ventricle ejection fraction (LVEF) of 20% with severe hypokinesis of all left ventricle segments except the basal segments along with a left ventricular (LV) filling pattern consistent with abnormal relaxation (*Video 1*). A review of his prior echocardiogram from nine months prior

Highlight box

Key findings

- Herpes simplex virus (HSV) encephalitis induced takotsubo cardiomyopathy has been rarely reported in literature.

What is known and what is new?

- HSV encephalitis is the most common sporadic encephalitis in the world, and takotsubo cardiomyopathy is caused by a wide variety of stressors.
- This case report introduces a rare scenario where HSV encephalitis directly causes the development of takotsubo cardiomyopathy.

What is the implication, and what should change now?

- Despite its rarity, this case illustrates the importance that physicians should keep takotsubo cardiomyopathy in their differential diagnosis when a patient presents with HSV encephalitis accompanied by shortness of breath.

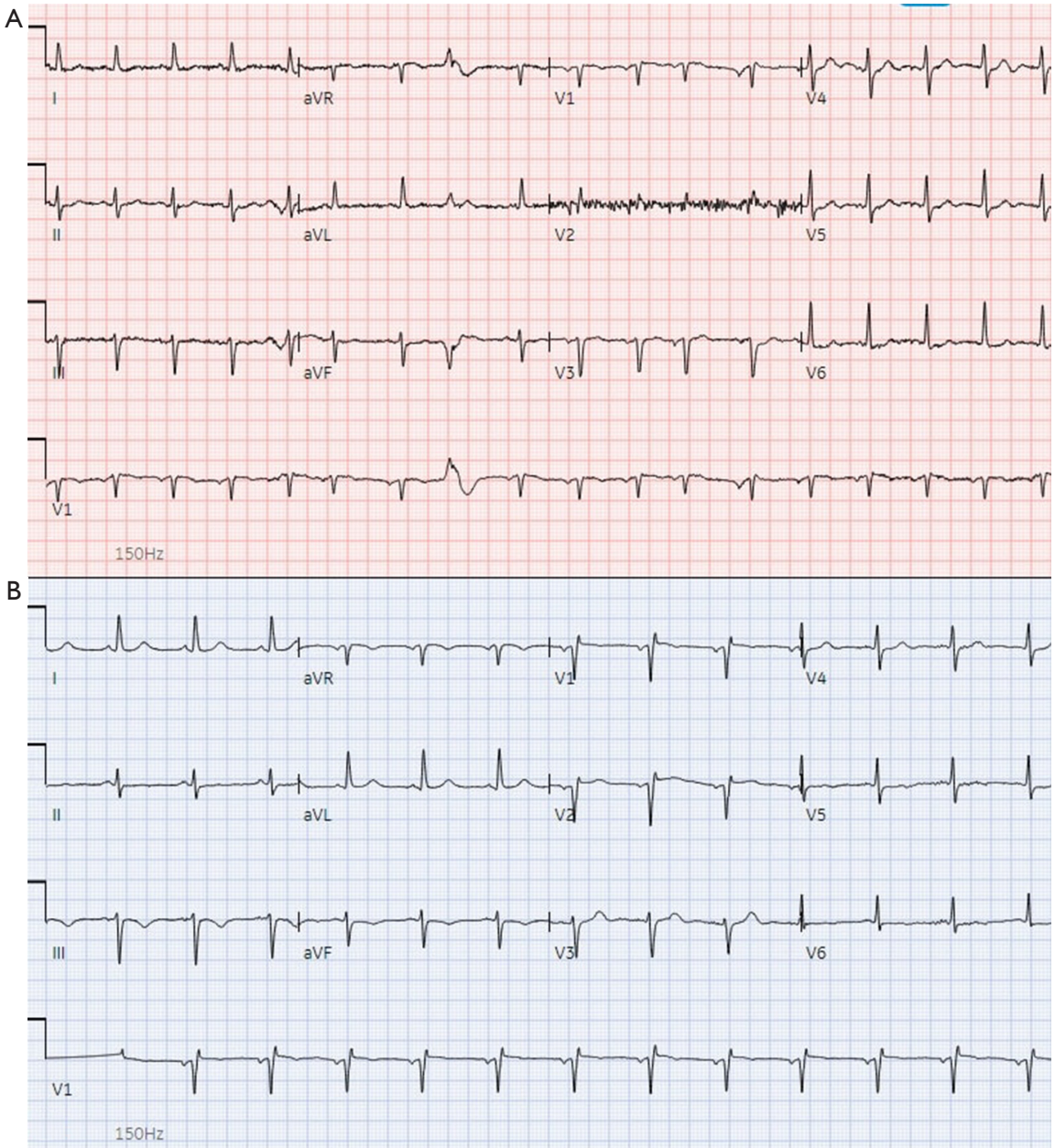


Figure 1 Serial images of electrocardiogram completed on day 1 (A) and day 3 (B) when the patient was found to have takotsubo cardiomyopathy.

revealed his left ventricle was normal in size and function (ejection fraction 60–65%). Given the patient's prior history of myocardial infarction and clinical presentation, cardiac catheterization was recommended and discussed with the patient's family due to the patient's lack of decision-making capacity secondary to persistent encephalopathy. However, they declined further cardiac testing during the hospitalization. He was started on carvedilol and ramipril in the hospital. The patient continued to have improvements in his mental status while hospitalized. At the end of his hospital course, he was discharged to sub-acute rehab. A repeat echocardiogram was complete approximately three weeks following hospitalization, which revealed an ejection fraction of 55% and resolution

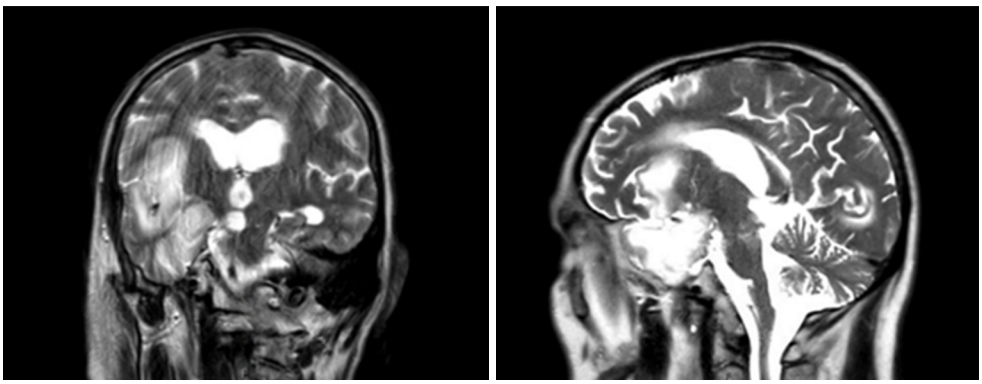
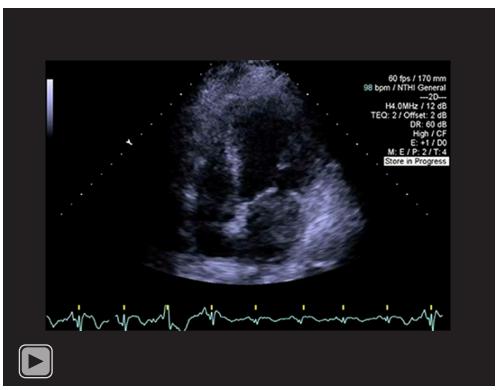


Figure 2 MRI of the brain without intravenous contrast revealing patchy areas of FLAIR/T2 hyperintensities with edema within the right temporal insular cortex and frontal lobe. MRI, magnetic resonance imaging; FLAIR, fluid-attenuated inversion recovery.



Video 1 Echocardiogram revealing left ventricle ejection fraction of 20% with severe hypokinesis of all left ventricle segments except the basal segments along with a left ventricular filling pattern consistent with abnormal relaxation.

of the stress-induced cardiomyopathy. Approximately three months later, the patient underwent a pharmacological nuclear stress test as an outpatient with his cardiologist with results demonstrating no evidence of ischemia or infarction.

Discussion

HSV-1 encephalitis is the most common viral encephalitis worldwide and represents 10–20% of all viral encephalitis cases annually (4). The pathogenesis of HSV-1 encephalitis is not completely understood. One possible mechanism may be related to central nervous system invasion directly from the olfactory tract or trigeminal nerve after having an episode of HSV-1 infection in the oropharynx (5). Another possibility is that there is an *in-situ* reactivation of the HSV-1 in the brain where a previous infection occurred (5). The clinical manifestations of HSV-1 encephalitis can include fever, ataxia, dysphasia, hemiparesis, altered mental status, and headaches (5). A diagnosis can be made via HSV-1 polymerase chain reaction (PCR) test of the CSF (4). Brain MRI will be sensitive in 80–90% of HSV-1 cases and commonly shows temporal lobe involvement with white matter changes. Patients with suspected HSV-1 encephalitis are started on IV acyclovir for 14–21 days in immunocompetent patients, which was done similarly in our patient (4).

Takotsubo cardiomyopathy presents in roughly 1.2% of troponin positive acute coronary syndromes (6). There are several hypotheses regarding the pathogenesis of takotsubo cardiomyopathy. Due to its association with stress, many suggest that the cause could be due to increased catecholamine release causing increased sympathetic activation which leads to cardiac stunning (1,3). Many different stressors have been reported to cause takotsubo cardiomyopathy, including loss of a loved one, arguments, surgery, infections and drug use. There are many different diagnostic criteria for takotsubo, including the Mayo Diagnostic Criteria (7). A diagnosis of takotsubo cardiomyopathy is made when the patient fulfills all four parts of the Mayo Clinic Criteria (7). The criteria include presence of transient regional LV wall dysfunction (dyskinesia, hypokinesia, and akinesia) with deficits extending beyond a single epicardial contribution, new ST elevation or T-wave inversion on EKG or troponin elevation, absence of angiographic evidence of plaque or coronary obstruction, and absence of myocarditis or pheochromocytoma (7). Our patient met three out of the four criteria. Cardiac catheterization was

not performed since the family declined the intervention while the patient was being acutely treated for HSV encephalitis. Treatment of takotsubo is based on clinical presentation (1). Cardioselective beta-blockers and angiotensin converting enzyme (ACE) inhibitors are recommended for treatment in stable patients for 3 to 6 months (1). Imaging with echocardiogram is performed serially to determine resolution of takotsubo (1). Most cases of takotsubo cardiomyopathy resolve in days to weeks (8).

To our knowledge, there are only two other reports of HSV encephalitis induced takotsubo cardiomyopathy (9,10). Other cases have been reported of temporal encephalitis causing takotsubo cardiomyopathy, however it is uncertain if those cases were caused by HSV (11). The diagnosis of takotsubo's cardiomyopathy was made due to high likelihood of stress induced cardiomyopathy due to the hypokinesis in the left ventricle on echocardiogram, modest elevation of troponin, absence of myocarditis and pheochromocytoma, return to baseline cardiac function 3 weeks after on echocardiogram, and negative nuclear stress test results. Our case reinforces the importance for physicians to keep HSV encephalitis induced takotsubo cardiomyopathy in their differential diagnosis despite its rare occurrence.

Conclusions

Further investigation should be done to understand the correlation of HSV-1 encephalitis and takotsubo cardiomyopathy. Physicians should keep takotsubo cardiomyopathy in their differential diagnosis when a patient presents with HSV-1 encephalitis accompanied by shortness of breath and presence of pulmonary vascular congestion on imaging.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-24-53/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-24-53/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 for the 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.

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