CASE STUDY

Altered Mental Status in an Elderly Woman with Concurrent Takotsubo Syndrome and Polymyalgia Rheumatica: A Case of Treatable Geriatric Delirium

Hien Nguyen, MD; Connie Le, MD; Hanh Nguyen, MD; Nam-Tran Nguyen

Abstract

We present a unique case of a patient, aged 80 years, who presented with delirium and takotsubo syndrome. Also known as "broken heart syndrome" because it often originates following an emotional stress, takotsubo syndrome may be difficult to distinguish from myocardial infarction because of similar symptoms and demographics. However, the distinction of these opposing diagnoses is significant because takotsubo syndrome is associated with more favorable prognosis for complete recovery, especially with early diagnosis and expedient supportive therapy. To our knowledge, we present the first case of takotsubo syndrome in which the diagnosis was made in an elderly patient presenting with delirium and in the absence of the hallmark symptoms of chest pain and dyspnea. Finally, we describe this patient's coexistent diagnosis of polymyalgia rheumatica and speculate on its possible theoretic relationship to takotsubo syndrome.

Introduction

Takotsubo syndrome has historically been considered quite rare but currently is suspected to be underdiagnosed, because the estimated incidence is approximately 1.7% to 2.2% of patients presenting with acute myocardial infarction (MI).[1,2] It is important that physicians be familiar with this diagnosis because the elderly are rapidly becoming a large segment of the population. An enigmatic condition first described in 1990, takotsubo syndrome has the cardinal symptoms of angina and dyspnea, mimicking acute coronary syndrome.[1,2] We present a case of rapidly reversible delirium heralded by the diagnosis of concurrent takotsubo syndrome and polymyalgia rheumatica (PMR).

Case Report

A black woman, age 80 years, with type 2 diabetes and hypertension was admitted to the hospital because of an acute change in sensorium evolving over two days, with abrupt aberrant sleep-wake cycles (agitated and awake at nighttime; sleeping in the daytime), fluctuating disorientation to family members, and refusal of food. At admission, it was found that her medications included mirtazapine, lisinopril, metformin, atenolol, simvastatin, and aspirin. A full review of organ systems revealed a five-pound weight loss, fatigue, myalgias, and low-grade fevers over the preceding month. The patient reported no chest pains, shortness of breath, headaches, abdominal pains, or falls at any time period before or during her acute decompensation. However, later during her hospital stay, a family member reported that the patient's sister had recently died.

At admission, she was febrile, with a temperature of 100.3°F, and this continued intermittently throughout her hospitalization. Examination showed her blood pressure to be 73/49 mm Hg, her pulse to be 90 beats/minute, and her respiratory rate to be 22 breaths/minute. She had leukocytosis (30,000 cells/mm^3), mild acute renal insufficiency (creatinine of 1.8 mg/dL), normal acid-base values, and slightly elevated liver enzyme levels. Her erythrocyte sedimentation rate was elevated, at 91 mm/h, and her C-reactive protein level was elevated, at 153 mg/L. Findings were normal on flow cytometry studies and on tests to evaluate for connective-tissue diseases, including antinuclear antibody, rheumatoid factor, anti-SSA, anti-SSB, cytoplasmic antineutrophil cytoplasmic antibodies, perinuclear antineutrophil cytoplasmic antibodies, hepatitis, cryoglobulins, and anticardiolipin antibody. Findings on blood cultures for infectious etiologies and on tests for mononucleosis, lyme disease, thyroid disease, syphilis, human immunodeficiency virus, tuberculosis, and *Clostridium difficile* infection were all normal. Neither whole-body computed tomography (CT) scanning of the chest, abdomen, and pelvis nor positron-emission tomography, indium white-blood-cell scanning, or gallium scanning revealed occult infection or malignancy.

An initial electrocardiogram revealed new acute deep T-wave inversions in all precordial leads, along with an old right bundle-branch block (Figures 1 and 2). Initial creatine kinase MB fractions and troponin levels were normal, as were follow-up serial cardiac enzyme levels. An initial echocardiogram demonstrated mild concentric left ventricular hypertrophy with a severely depressed ejection fraction of 20% and prominent apical ballooning (Figure 3). Complete restoration of cardiac ejection fraction was confirmed by echocardiography one week later (Figure 4). Cardiac CT scans demonstrated normal coronary vasculature, other than minimal coronary calcifications. Findings on a nuclear stress test were normal, with an ejection fraction of 58%. Thus, the consulting cardiologist recommended medical management. Initially, cardiac catheterization was contemplated, but it was not completed because cardiac function was rapidly reversible and because of benign findings on noninvasive evaluations. In the interim, the patient was treated with standard supportive therapy, including oxygen, acetylsalicylic acid, and intravenous hydration for hypotension.

Once infectious etiologies were excluded, a rheumatology consultant initiated corticosteroidal therapy at a dose of 20 mg of prednisone daily because of concern about the possibility of PMR, which was based on the patient's clinical presentation and strikingly elevated levels of markers for inflammation. The patient's cognition, laboratory-test findings, and

Hien Nguyen, MD, is an Internist at the Camp Springs Medical Center in Temple Hills, MD, and an Attending Internist at the Washington Hospital Center in Washington, DC. E-mail: hientrinhnguyen@yahoo.com. **Connie Le, MD,** is an Attending Internist at the Fairfax Hospital in Fairfax, VA. E-mail: drconniele@aim.com. **Hanh Nguyen, MD,** is a Resident at the University of California Irvine Medical Center in Irvine, CA. E-mail: hanhnguyenmd@gmail.com. **Nam-Tran Nguyen** is a Pre-Baccalaureate Student at the Westminster School in Annandale, VA. E-mail: namtrannguyen@aol.com.

functional status improved rapidly within less than one week, so she was transferred to subacute care with indefinite continuation of the prednisone dosage.

Discussion

Delirium

To the best of our knowledge, the case we present here is the first reported case of takotsubo syndrome in which delirium, in the absence of chest pain and shortness of breath, was the primary and unexpected manifestation. Our findings are in contrast with those of Malone et al,[3] who reported that delirium may be the initial presentation for MI, the closest correlate of takotsubo syndrome. In that study of very old patients with acute MI, delirium developed in 28%; delirium was only rarely the initial presentation for MI.

Delirium involves acute global changes in cognition and consciousness. Its causes can be placed into four broad categories: metabolic, toxic, structural, and infectious.[4] An alternative classification scheme is medical, chemical, surgical, or neurologic.[4] However, delirium often has multiple causes, as was the situation with our patient, who had multiple preexisting medical comorbidities and presented with multisystemic disease. We believe that her delirium was primarily caused by metabolic derangements (hypotension, renal insufficiency, and transient heart failure). A frequent iatrogenic cause of delirium in the elderly is overmedication with, for example, tricyclic antidepressants and antiparkinsonian drugs. Elderly persons are especially at risk for delirium because of preexisting cognitive impairment, medical and psychiatric comorbidities, functional impairments, and polypharmacy.[3,4]

Takotsubo Syndrome

A diagnosis of takotsubo syndrome is based on four criteria developed by the Mayo Clinic: transient hypokinesis or akinesis of the left ventricle, sparing the apex; exclusion of obstructive coronary disease; electrocardiographic changes, including ST segment or T-wave inversions, and/or mild cardiac enzyme elevations; and exclusion of pheochromocytoma or myocarditis. The syndrome is sometimes called "broken heart syndrome" because of its high correlation with a stressful life event. Diagnosis is important because cardiogenic shock, pulmonary edema, dysrhythmia, left ventricular thrombus or free wall rupture, and death (mortality, 1.7%–2.3%). Takotsubo syndrome is also known as the broken heart syndrome because a stressful emotional stressor is often the trigger for the disease.[5]

In spite of the well-defined symptomatology of takotsubo syndrome, its diagnosis may be challenging because of ethnicity-, age-, and sex-related differences in presentations. Although 90% involve postmenopausal women older than 67 years, occurrences have been

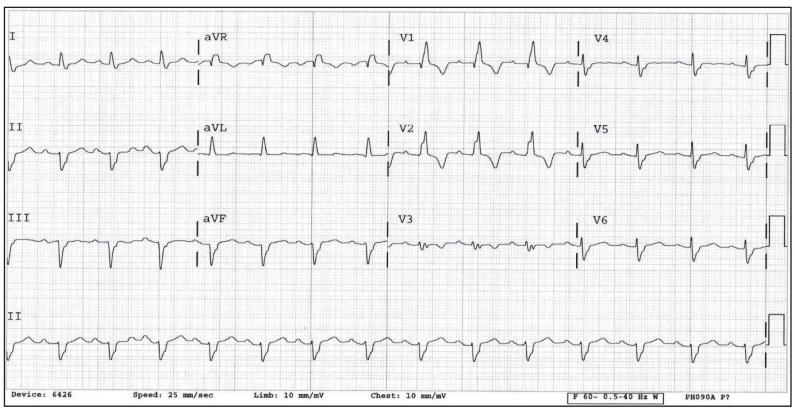

Figure 1. Initial echocardiogram demonstrating apical ballooning and depressed ejection fraction of 25%, confirming the diagnosis of takotsubo syndrome.

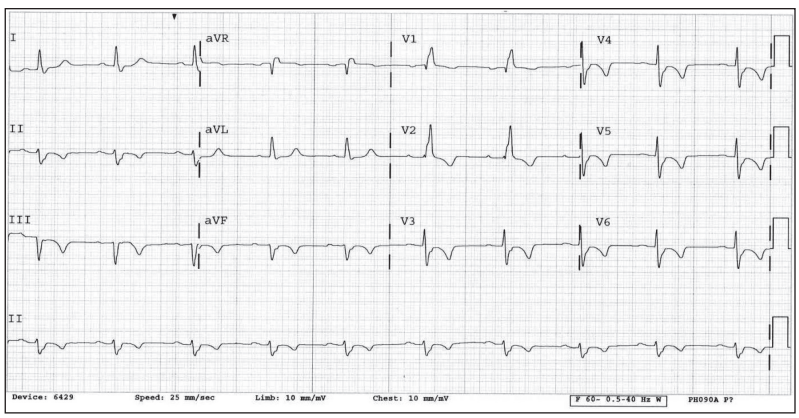

Figure 2. Follow-up echocardiogram showing complete recovery of cardiac function with an ejection fraction of 55%.

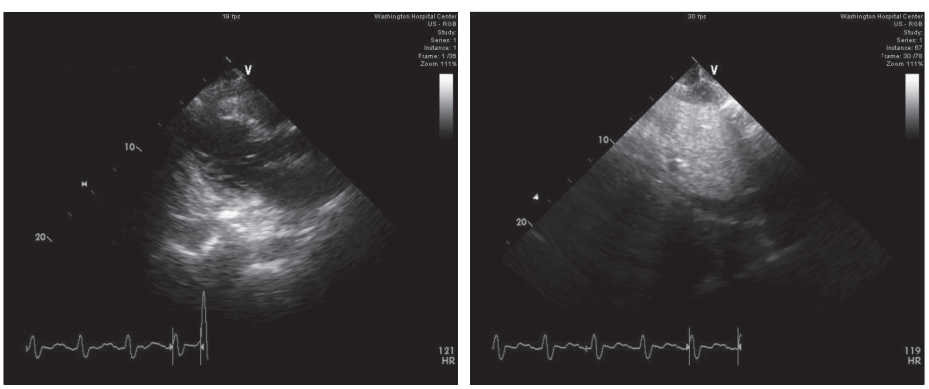

Figure 3. (left) Baseline electrocardiogram obtained in the outpatient setting before the patient's hospitalization. Figure 4. (right) Initial electrocardiogram obtained at the time of hospitalization revealing acute deep diffuse T-wave inversions and supporting the diagnosis of takotsubo syndrome.

described in persons ranging in age from 2 to 80 years. In a recent case series in the US, 57% of patients were Asian, 40% were white, and 3% were of other ethinicity.[1,2,5-7]

Recently, Pezzo et al reported[6] that blacks may present with dyspnea and without chest pain; our patient presented atypically with delirium and without angina or dyspnea. Other atypical presentations for takotsubo syndrome described in other case series include seizures, epigastric pain, or nausea and vomiting, but these patients also had concurrent chest pain and dyspnea.[6]

Therapy for takotsubo cardiomyopathy is generally supportive but may include aggressive treatment such as the use of inotropic agents or an intra-aortic balloon pump if there is severe or refractory hypotension. In most patients, the left ventricular ejection fraction normalizes within two months.[6]

Polymyalgia Rheumatica

PMR is characterized by fever, weight loss, fatigue, depression, proximal muscle pain and stiffness, and gel phenomenon and is seen more commonly in women older than age 50 years.[8] Our patient's elevated levels of inflammation markers and systemic symptoms strongly suggested a diagnosis of PMR concurrent with takotsubo syndrome, an association not previously reported.[8] The diagnosis of PMR was strengthened when corticosteroids rapidly resolved her cognitive difficulties and aberrations on laboratory findings.

We speculate that there may be an association between takotsubo syndrome and PMR in the presence of a sympathetic nervous system dysfunction; this relationship is not unprecedented. There are two case reports in the medical literature describing reflex sympathetic dystrophy syndrome coexisting with PMR.[9,10] Indeed, the most preeminent theory for the pathogenesis of takotsubo syndrome is a sympathetic hyperactivity, such as may occur from acute emotional or physical stress.[9,10] However, it is entirely possible that the development of concurrent takotsubo syndrome and PMR was simply coincidental in this elderly patient, whose age group is associated with a higher incidence of both medical conditions independently.

A review of the literature illustrates two distinct cases of takotsubo syndrome associated with other acute conditions in which corticosteroids were interestingly prominent in the resolution of this cardiomyopathy, such as is illustrated in our case. Ukita et al reported resolution of takotsubo syndrome after corticosteroid therapy; the syndrome had developed during an acute adrenal crisis because of isolated adrenocorticotropin deficiency.[11] Radhakrishnan and Granato reported resolution of this cardiomyopathy after corticosteroid therapy; it had developed during thyroid storm.[12]

PMR has not been previously described with delirium to our knowledge, and it is most closely related to temporal arteritis. Pascuzzi et al reported that a patient with temporal arteritis had a primary presentation of delirium—delusional thinking without concomitant headache or visual loss.[13] We acknowledge, though, that our patient presented with other metabolic impairments that we believe contributed strongly to the development of delirium.

Conclusion

We presented the case of a patient with rapidly reversible delirium heralded by concurrent takotsubo syndrome and PMR. Both conditions are uncommon in general and even rarer when diagnosed concurrently in a single patient. Furthermore, our patient is black, a group that is not typically considered prone to PMR. Scandinavian people have been reported to have the highest rate of PMR, whereas black and Hispanic groups have the lowest rates.[14] Less than 2% of patients diagnosed with takotsubo syndrome are black, with the majority being of Asian descent.[7]

Our case demonstrates valuable teaching points in the challenging management of delirium in an elderly patient. Delirium can have multiple etiologies, and atypical presentations for common medical conditions are commonplace in elderly patients presenting with delirium. Further research may be useful in searching for a possible relationship, based on sympathetic dysfunction, between takotsubo syndrome and PMR. This research will likely be facilitated by the rapid acceleration in the world's geriatric population and an accompanying increase in the incidence of both of these medical conditions. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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