A Case of Acute Heart Failure Probably Associated With Venlafaxine Use

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Venlafaxine is a bicyclic antidepressant that significantly inhibits the reuptake of both serotonin and norepinephrine, and to a lesser extent dopamine, and lacks notable muscarinic-cholinergic or adrenergic effects.[1] The common adverse effects associated with venlafaxine use include nausea, somnolence, insomnia, dry mouth, dizziness, nervousness, constipation, sweating, anorexia, asthenia, blurred vision, abnormal ejaculation or orgasm, erectile dysfunction, and impotence.[2] Recently, some concerns have been raised regarding a potential higher incidence of cardiac adverse effects with venlafaxine use in comparison with selective serotonin reuptake inhibitors (SSRIs).[3] The pattern of cardiovascular side effects reported with venlafaxine use includes vascular headache, angina pectoris, hypotension, dose-dependent blood pressure elevation, syncope, sinus bradycardia, first-degree arterioventricular block, bundle branch block, and acute heart failure. To date, only a few case reports[4,5] have described acute heart failure associated with its use, most often at toxic doses. This report describes a case of drug-induced heart failure associated with venlafaxine at a therapeutic dose.

Case Report

Mr A was a 45-year-old man working in the Middle East who returned home after developing psychiatric symptoms characterized by low mood, reduced interest, lack of enjoyment, negative thoughts, impaired biological functions, and poor concentration. The symptoms were precipitated by financial losses due to mismanagement of his business by his partner. He had a history of a similar episode 10 years ago, which improved with medications for 3 months. He consulted a psychiatrist and was diagnosed with recurrent depressive disorder, current episode severe without psychotic symptoms. He was prescribed oral amitriptyline 12.5 mg/d and chlordiazepoxide 5 mg 3 times/d, along with oral olanzapine 2.5 mg/d. Given the lack of response, oral venlafaxine 75 mg/d was added, the dose of amitriptyline was reduced to 10 mg/d, and chlordiazepoxide and olanzapine were stopped. He had no significant medical comorbidities. There was no family history of psychiatric illness.

Mr A presented to the emergency department (ED) of the nearby hospital after 1 week of starting venlafaxine with complaints of breathlessness, palpitation, and sweating. He was admitted to the hospital, and investigations (echocardiography) revealed global left ventricular dysfunction with noncoronaries. He gradually developed anuria, and his serum creatinine level increased to 7.3 mg/dL. He was transferred to our hospital due to worsening of symptoms. At the time of presentation to the ED, he was conscious and oriented. His heart rate was 99 beats/minute, and his blood pressure was 130/80 mm Hg. The respiratory system examination revealed bilateral crepitant rales. Laboratory investigations revealed hyperammonemia (127.8 ug/dL), high serum creatinine (7.96 mg/dL), and high alanine transaminase (2,210 U/L) and aspartate aminotransferase (1,421 U/L). Sputum culture and sensitivity revealed the growth of *Klebsiella* species. Ultrasonographic examination revealed bilateral increased renal cortical echo texture with accentuated corticomedullary differentiation. High resolution computed tomography (CT) scan of the lungs showed consolidation with air bronchiogram in the left lower lobe, lingual subsegmental atelectasis of the left lower lobe, and mild left pleural effusion. CT scan of the brain showed chronic lacunar infarct in the left caudate nucleus. Echocardiogram showed concentric left ventricular hypertrophy, global left ventricular hypokinesia, moderate to severe left ventricular dysfunction, mild mitral regurgitation, and mild pericardial effusion.

Mr A was diagnosed with decompensated heart failure with moderate to severe left ventricular dysfunction and left lower lobe consolidation with hepatic dysfunction, as well as acute kidney injury. He was hypoxic at admission and was treated with noninvasive ventilation. He improved within 1 week and was extubated. He was treated with hemodialysis, antiplatelets, digoxin, calcium supplements, antibiotics, and other supportive medications. A psychiatric evaluation was conducted given his underlying depression. He was diagnosed with a severe depressive episode, and oral mirtazapine 7.5 mg was started. Mr A symptomatically improved with treatment, and deranged laboratory values gradually improved as well. He was discharged 13 days after admission.

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Discussion

The case described here had documented evidence of deterioration in ventricular function coincident with the use of venlafaxine in a previously healthy man. Mr A developed acute heart failure within a week of starting venlafaxine, and he had no comorbid medical risk factors. The depressive disorder and severe stress associated with financial crisis might have contributed to the presentation. There are multiple reports[6,7] of stress cardiomyopathy among patients with stress. Amitriptyline also can be considered as an added risk factor, as there are reports of cardiotoxic effects of tricyclic antidepressants.[8] However, the temporal association of the event with the introduction of venlafaxine is well established in our case.

Although a large-scale population study reported no significant increase in the incidence of cardiovascular side effects with venlafaxine use when compared with SSRIs, there are multiple reports[4–7] of a variety of cardiotoxic effects with venlafaxine use, and most of the severe cardiac side effects were reported in large overdose. However, hypertension and tachycardia are observed after moderate venlafaxine exposures.[9] There are multiple previous reports[3] indicating conduction abnormalities with venlafaxine overdose, suggesting that it is a arrhythmogenic agent. However, the possibility of venlafaxine-related acute heart failure without changes in cardiac conduction even after an overdose has been suggested.[5]

Mr A developed acute cardiac failure with no documented evidence of changes in cardiac conduction at a therapeutic dose. The pathophysiologic mechanism associated with venlafaxine-induced cardiac failure with preserved conduction function is not fully known. However, a potential explanation could be catecholamine-induced myocardial damage along with the inhibition of norepinephrine and dopamine reuptake.[5] Moreover, increased levels of norepinephrine and serotonin can accelerate cardiac sympathetic activity, leading to a mild increase in heart rate and systemic blood pressure. Another possibility is that epinephrine has the potential to trigger an intracellular signaling switch through β2-adrenoceptors on cardiomyocytes of the ventricles causing a positive inotropic response.[10]

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