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Delayed multifocal recurrent stress-induced cardiomyopathy after antidepressants withdrawal

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ABSTRACT

Stress-induced cardiomyopathy is an acute disease characterized by a large left ventricular apical dyskinesia ("apical ballooning"), triggered by intense emotional or physical stress, acute illnesses or, rarely, by alcohol or opiates withdrawal. Connection to stress and apical asynergy suggest a catecholamine-mediated pathogenesis.

We recently observed a typical apical stress-induced cardiomyopathy, arising two weeks after a long-lasting antidepressant treatment withdrawal and recurring, a week later, with evidence of inferior wall akinesia.

The reported case has several unusual features: 1) both episodes were not preceded by relevant triggering event (except antidepressant discontinuation); 2) early heterozonal relapse was observed; 3) the latency between antidepressant discontinuation and stress-induced cardiomyopathy onset is unusually long.

The lack of relevant triggering stress and the evidence of multifocal asynergies could support the hypothesis of a non-catecholaminergic pathogenesis. Moreover, the long latency after antidepressant withdrawal may suggest that prolonged antidepressant treatments may have delayed pathological consequences, possibly related to their known neuroplastic effects.

Introduction

Stress-induced cardiomyopathy (SIC) is an increasingly diagnosed clinical condition, largely prevalent in post-menopausal women, characterized by acute chest pain and/or dyspnea, reversible left ventricular dysfunction, ECG changes mimicking an acute myocardial infarction and a mild increase of cardiac necrosis biomarkers.[1–3] Typical left ventricular systolic feature of SIC is a large dyskinetic area involving the apex and the neighboring segments, giving the syndrome the name "apical ballooning." Due to the resemblance of systolic ventriculograpic images to a traditional Japanese octopus fishing pot, the term "takotsubo syndrome" is also widely used.[1–3] Atypical localizations have been also described, with akinetic-dyskinetic proximal ("reverse" takotsubo)[4] or inferior segments,[5] diffuse hypokinesia[1] or, finally, with biventricular apical involvement.[6]

During early phases, various complications are frequent: arrhythmias (ranging from isolated ventricular premature beats to ventricular fibrillation), left ventricular failure and pulmonary edema, apical thrombosis (with associated thromboembolic phenomena), papillary muscle rupture.[1–3]

In spite of the impressive onset, the prognosis of SIC is usually good, with almost complete recovery of systolic function within a few weeks; recurrences are uncommon.[7]

The onset of SIC is usually preceded by an intense and extraordinary emotional or physical stress, but it has also been reported during or after invasive diagnostic procedures, surgical interventions, in cases of massive bleeding, sepsis or during severe acute hypoxia.[1–3] A few reports have also been published regarding sporadic cases of SIC associated to withdrawal syndrome from alcohol[8] or opiates[9] and, in single reports, from benzodiazepines[10] and from GABAb receptor agonist Baclofen (administered by continuous intrathecal infusion).[11]

Case report

A 65-year-old woman admitted to an Emergency Department due to repeated fainting episodes that occurred during and immediately after a fitness session in a gym. She was engaged in

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light aerobic exercise on a bicycle when she experienced dizziness and began to feel weak, lightheaded and nauseated. She stopped exercising and went to the locker room, where she had two fainting spells, falling down thus provoking a slight wound to her left temporal region.

At the Emergency Room evaluation, she complained of weakness and mild dyspnea. Physical examination reported rhythmic heart beats (heart rate 62 bpm), mild hypotension (arterial blood pressure 100/60 mm Hg); no sign of acute heart failure. ECG showed (Fig. 1) normal sinus rhythm; QS complex with mild ST segment elevation in leads V2 and V3; negative T waves in leads I, aVL and V2–V6.

The patient had been in physiological menopause since the age of 51, had never smoked and had no history of arterial hypertension, hypercholesterolemia or diabetes. She also had no history of cardiac or circulatory diseases; three months before this episode she underwent an ECG on effort before starting physical activity, excluding ischemic heart disease. She had been suffering from a severe depression since the age of 40; in the last 8 years she had been continuously treated with a combination of antidepressants, both tricyclic and serotonin-specific reuptake inhibitors (SSRI), neuroleptics, antiepilectics and benzodiazepines. Her daily prescribed drug schedule was imipramine 25 mg BID, amitriptyline 10 mg UID, paroxetine 20 mg UID, perphenazine 2 mg UID, gabapentin 300 mg TID, trazodone 12 mg UID, delorazepam 0.25 mg UID; all drugs were taken orally. This treatment actually led the subject into a remission of depression over the last two years. For this reason, 15 days before the repeated fainting episodes, consultant psychiatrist planned a hospital admission to discontinue antidepressive therapy; paroxetine was gradually reduced until discontinuation over a 3-day-period, while all other drugs except gabapentin (hold at the same dose) were stopped. Diazepam and metadoxine were continuously infused intravenously during the first 3 days, then hydroxyzine 25 mg UID was started. The patient tolerated this procedure well and was discharged in good clinical and psychological health.

At admission in the cardiac intensive care unit, the patient was asymptomatic. Medical therapy with fondaparinux (2.5 mg UID s.c.),

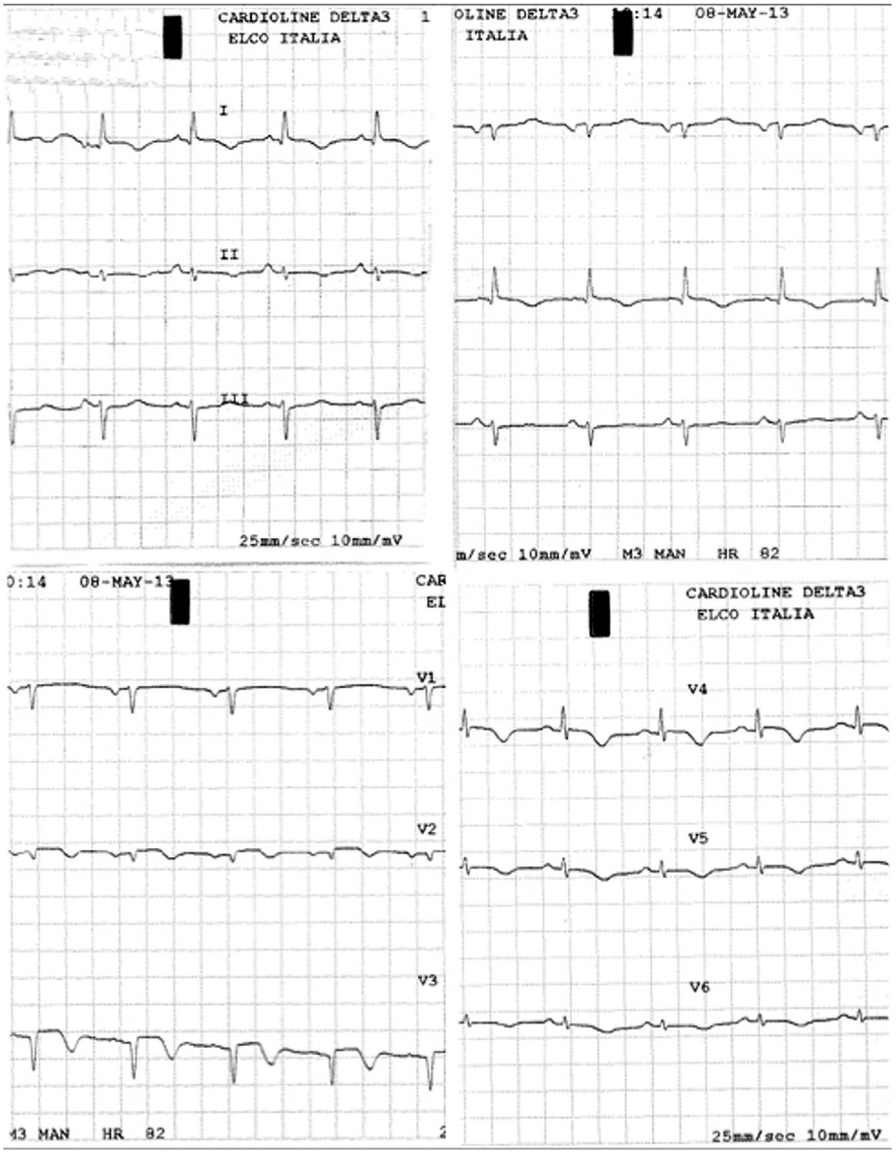

Fig. 1. ECG at admission during the first SIC episode. Mild ST segment elevation in leads V2 and V3 and negative T waves in leads I, aVL and V2–V6 are evident.