Type transition and mitral regurgitation of mid-ventricular Takotsubo in a single course

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Takotsubo syndrome (TTS) is a clinical syndrome characterized by acute reversible dysfunction of the left ventricle (LV) usually without significant obstructive coronary artery disease. TTS was classified into apical, mid, basal ventricular, and focal types based on the location of myocardial akinesis [1]. Different types may occur in patients at each recurrent event but are rare in a single course [2]. Mitral regurgitation (MR) is common in the apical type due to systolic anterior motion of the mitral leaflet which is always accompanied by left ventricular outflow tract obstruction (LVOTO) [3] but is rare in the midventricular type. We report a case of midventricular TTS with MR independent of LVOTO and transition to the apical type in a single course.

A 54-year-old woman presented to our emergency department because of acute chest pain and shortness of breath for 6 hours immediately after drinking boiled root soup. Her past medical history included nasopharyngeal carcinoma, receiving chemotherapy for 3 years (5-fluorouracil, nedaplatin, and gemcitabine) and adjuvant radiotherapy, and chronic gastritis for 15 years. Emergency electrocardiogram (ECG) on admission confirmed sinus rhythm with limb lead low voltage and T-wave inversion in leads V3–4 and aVL. Blood testing showed increased troponin I, N-terminal (NT)-pro hormone BNP (NT-proBNP), and creatine kinase isoenzyme of 0.82 μg/l, 1940 pg/ml, and 40.00 U/l, respectively. Subsequent emergency coronary angiography (CAG) at 03:52 am on day 1 showed no evidence of atherosclerosis and obstructive lesions in the coronary arteries (Supplementary material, *Figure S1, S2*). Her chest pain persisted during CAG but without coronary spasm, and a provocation test with acetylcholine was not performed. Left ventriculography demonstrated middle akinesia and basal, apical hypokinesis of the LV, which indicated a possible diagnosis of midventricular TTS, and unexpectedly revealed moderate-severe MR, which was rare in midventricular TTS (Figure 1A, B, Supplementary material, *Video S1*). Echocardiography at 10:30 on day 1 further demonstrated midventricular wall motion abnormality with left ventricular ejection fraction (LVEF) of 41%, severe MR without dynamic LVOTO, and normal right ventricular wall motion. The patient received proton pump inhibitors, spasmolysis, diuretic, and nitroglycerin treatment. Her symptoms quickly disappeared at 5:30 pm on day 1. A bedside transthoracic echocardiography at 07:51 am on day 3 showed significant improvement in mid-ventricular akinesia with LVEF of 58% and reduction of the MR grade from severe to mild (Figure 1C, D, Supplementary material, *Video S2*). Then she gradually improved. Cardiac magnetic resonance (CMR) was performed at 6:40 pm on day 6 and showed good mid left ventricular wall motion but surprisingly found hypokinesia of the apical ventricular wall, which prompted type transition from the midventricular to apical type (Figure 1E, F, Supplementary material, *Video S3*). LVEF was 59% and right ventricular wall motion was normal. Extensive myocardial edema including papillary muscle was found as well (Supplementary material, *Figure S4*). Myocardial edema was evaluated on T2-turbo inversion recovery magnitude sequence in the following way: the myocardial edema ratio [ER] was defined as the ratio between myocardial signal intensity [SI] to skeletal muscle SI, and

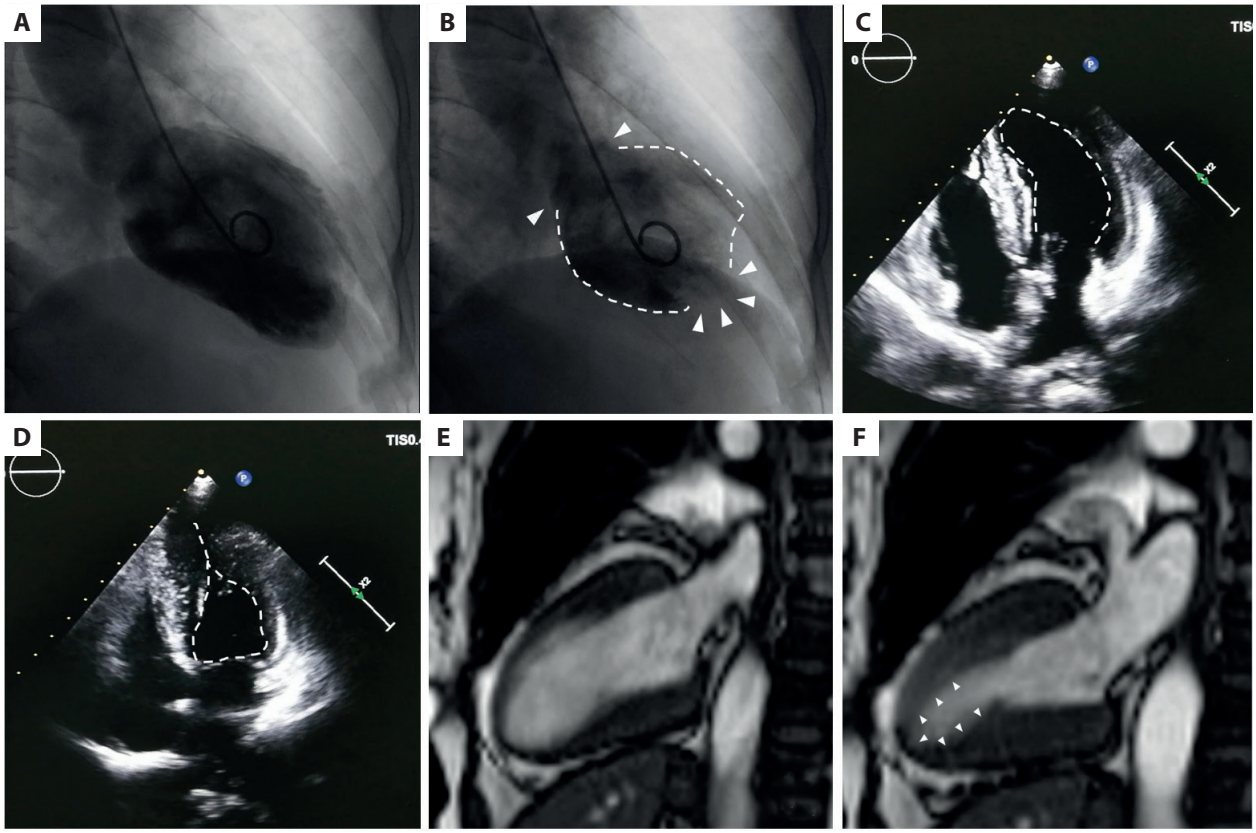

Figure 1. Left ventricular (LV) angiogram of end-diastolic phase (ED) (**A**) and end-systolic phase (ES) (**B**). Mid-LV akinesia (white dotted line) and basal, apical LV hypokinetic (white line and triangles). A bedside transthoracic echocardiography of ED (**C**) and ES (**D**) showed a normal motion of the LV wall (the endocardium was outlined by the white dotted line). Cardiac magnetic resonance cine sequence of ED (**E**) and ES (**F**) showed hypokinesia of apical LV (**F**, white triangles)

an ER ≥1.9 represented edema [4] without late gadolinium enhancement (LGE) (Supplementary material, *Figure S5*). This dynamic multimodal imaging excluded the presence of obstructive or non-obstructive coronary arteries and strongly supported the diagnosis of TTS [5]. Unfortunately, the patient was lost to follow-up.

The dramatic improvement of symptoms of TTS was considered to result from the complete recovery from myocardial akinesia. In the current case, mid-LV akinesis and, surprisingly, even hyperkinesis, disappeared without reappearing, and a new apical LV hypokinesia replaced apical hyperkinesis during convalescence, but the continued improvement of symptoms suggested this is a continuum of a single process, which may provide an insight into the pathogenesis of Takotsubo cardiomyopathy.

In that case, severe MR was found in midventricular TTS which rapidly disappeared with the improvement of cardiac function and did not recur in following apical TTS. This suggested that MR could be a complication of midventricular TTS. Although papillary muscle edema which is considered to be one of the causes of MR was found by CMR on day 6, considering the rapid disappearance of MR, tethering and systolic anterior motion of the mitral valve leaflet caused by asynergic movement of the mid ventricular wall may contribute more to MR than papillary muscle edema.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

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