CARDIAC SARCOIDOSIS MIMICKING TAKOTSUBO SYNDROME

Belma Pojskić[1*], Herwig Schmidinger[2], Amra Macić-Džanković[3]

[1] Department for Internal Diseases –Cardiology Cantonal Hospital Zenica, Crkvice 67, 72000 Zenica, Bosnia and Herzegovina

[2] University Clinic for Internal Medicine II, AKH, Vienna, Austria

[3] General Hospital "Abdulah Nakaš" Sarajevo, Kranjčevićeva 12, 71000 Sarajevo, Bosnia and Herzegovina

[*] Corresponding author

Abstract

An unusual case of cardiac sarcoidosis is described. A woman with biopsy proven lung sarcoidosis was presented on admission in hospital as ventricular tachycardia and non Q myocardial infarction. Ultrasound of the heart and coronarography examination presented Takotsubo syndrome, "ballooning heart", and normal blood vessels. Cardiac sarcoidosis and Takotsubo syndrome are diseases where definitive etiological factor was not found. This case report suggests the existence of their similar pathogenesis. As far as we know, this is the first described connection between Takotsubo syndrome and cardiac sarcoidosis.

KEY WORDS: cardiac sarcoidosis, Takotsubo syndrome

Introduction

There has been reported a new syndrome regarding heart failure and cardiac contractile abnormalities in the last few years, known as Takotsubo syndrome or a brocken heart syndrome. It is mimicking acute myocardial infarction and it's etiology is unknown (1).Cardiac sarcoidosis is present at 5% patients with sarcoidosis and is manifested as a cardiomyopathy with loss of muscular function or tachy-brady arrythmias or as sudden death. To this date, many reports concerning ethyology of cardiac sarcoidosis and Takotsubo syndrome have been published, but the clinical data are still incomplete. As far as we know, this is the first described case of cardiac sarcoidosis presented as Takotsubo syndrome, what could indicate common patophysiology.

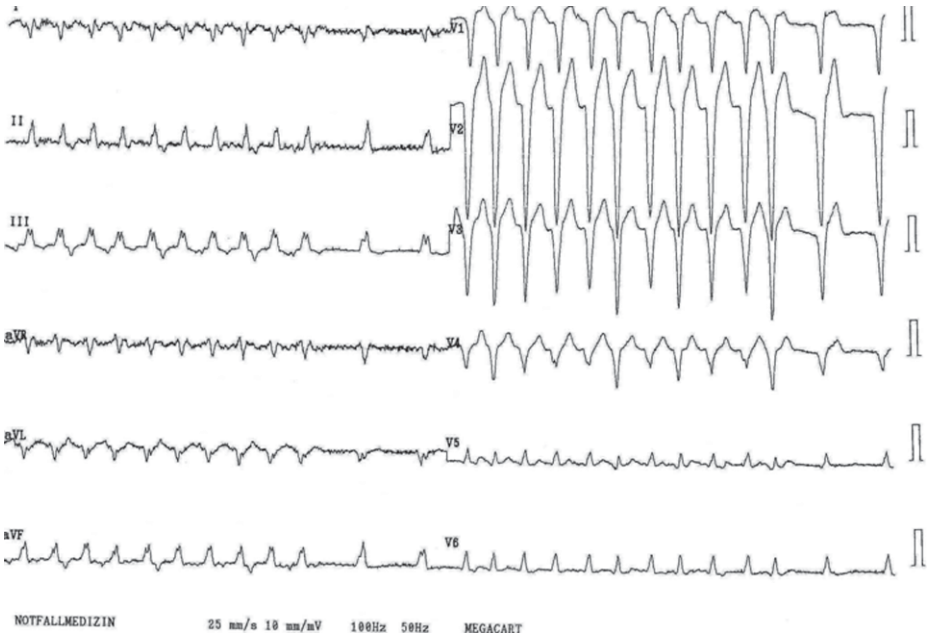

FIGURE 1. ECG on admission- ventricular tachycardia

Material and Methods

A representative case involved a 48-year-old woman with a medical history of pulmonary sarcoidosis. We described her previous medical history, ECG patterns presented as acute coronary syndrome on the admition in hospital as well as each medical procedure during her staying in hospital, including recommended therapy.

Case report

A 48 year old woman was admitted to hospital as an emergency because of sudden chest discomfort which awaked her during the night. This was followed by transient acute chest pain lasting approximately 20 minutes and slight dyspnoa . She was investigated because of sarcoidosis 6 months before the event. Her spirometry was normal with normal forced vital capacity and expiratory volume. Transbronchal lung biopsy confirmed presence of granulomas and diagnosis of sarcoidosis. She was observed without therapy. She did not smoke cigarettes. Her father had coronary heart disease, diabetes, high cholesterol. On admission she was presented with a dyspnoa and irregular tachycardia with heart rate of 174/min which is recognized as ventricular tachycardia with ST segment elevation in precordial leads, and appearing of ventricular escape beats (Figure 1).

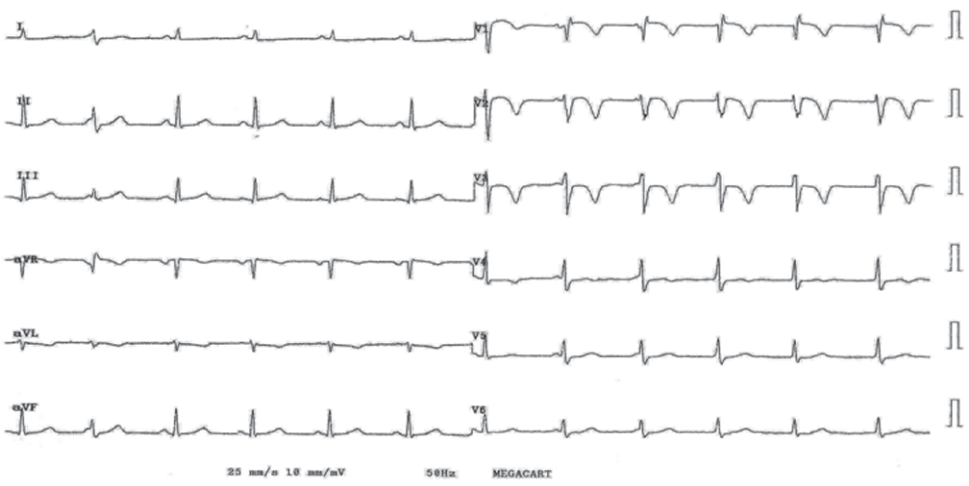

FIGURE 2. Changes in ECG after restoring sinus rhythm

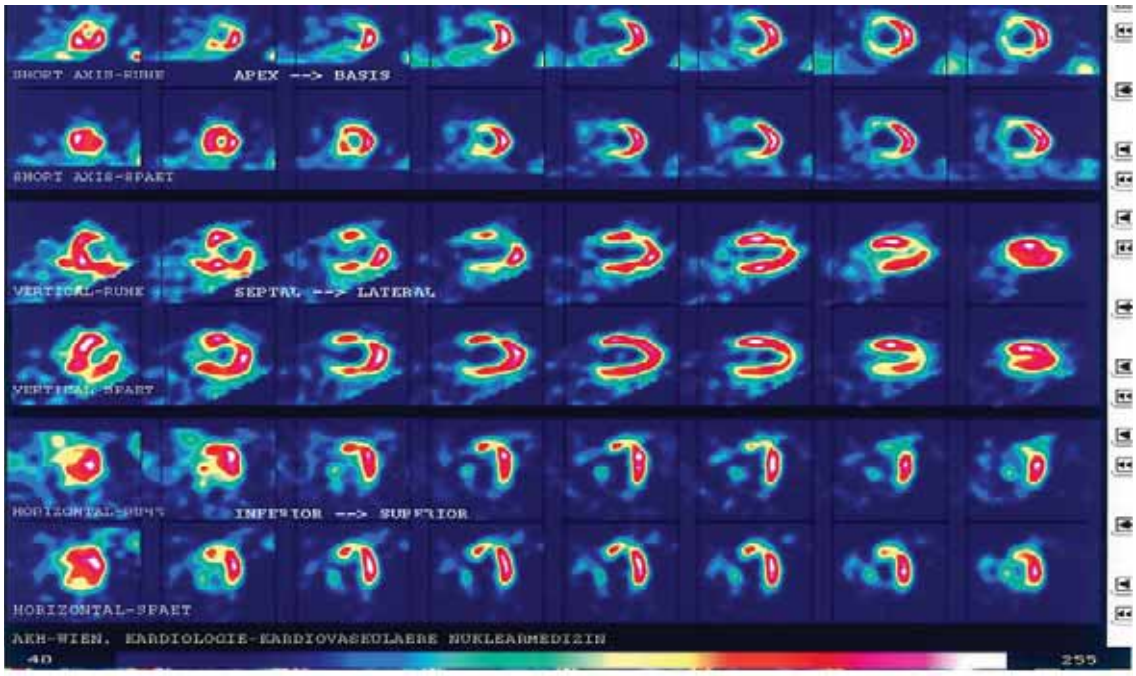

FIGURE 3. Thallium stress test of the heart shows mid and proximal septal-anterior ischemia during the stress

Examination showed blood pressure 125/95 mm Hg, heart rate 124-174 beats/min, and normal sounds in lung fields. The patient was initially treated with intravenous Amiodaron and Ajmalin. Clinical evolution was rapidly favourable, with restored sinus rhythm. ECG showed sinus rythm, QRS upright in V1, inversion T up to 7 mm in V1 to V3 (Figure 2). Repeated ECG showed an evolution towards major repolarisation abnormalities in V1 to V3. Baseline (erythrocithies, thrombocities, leucocythies) concentration were normal, with presence of neutrophil(-ic) polynucleosis 78%, slight increased ALAT 53U/l, LDL 272U/l, gamma GT 39U/l. Troponin T had a small rise as 0,07 and proBNP was 1448,0 pg/ml . Echocardiography revealed hypokinesia of the medium and apical segments of the septal and anterior wall with abnormal septum moving in basal part. Chamber sizes were normal, although right ventricle had upper limit (30mm).Right ventricle function was normal. Left ventricular function was decreased, as well as diastolic function due to restrictive changes. There was mitral regurgitation regarding to dilatation of valve ring, and slight tricuspid regurgitation (pulmonary blood pressure 36 mmHg). Thallium stress test confirmed ultrasounds findings, and presented clear ischemia in mid and apical part of anterior wall (Figure 3)

Angiographic examination was performed the next day. There was found no evidence of clinically significant coronary disease decreased systolic function with ejection fraction 39,6%, and abnormal wall motion of the mid and distal LV, i.e. "apical ballooning" (Figure 4).

Endomyocardial biopsy was performed, and oral corticosteroids were recommended. Cardiac granulomas were not found. Patient was discharged with sotalol and cortison in the therapy. On the discharge, she was feeling well, and ECG had showed premature ventricular beats. There was recommendation for further follow up.

Discussion

The clinical course of Takotsubo cardiomyopathy is similar to that of an acute myocardial infarction. It is characterized with acute substernal chest pain, ST-segment elevation and/or T-wave inversion, systolic dysfunction (ejection fraction 29±9%), with abnormal wall motion of the mid and distal left ventricle (known as "apical ballooning"), absence of significant coronary disease by angiography and psychological stress triggering the cardiac events (1,2,3,4,5). Etiology is unknown till now, but it is an evidence that there is association between simpathetic stimulation and myocardial stunning. Plasma catecholamines have been elevating during the week (6). That can be reason for vasoconstriction of epicardial coronary arteries (7). The other possible mechanism is microvascular spasm or direct myocyte injury through cyclic AMP–mediated calcium overload what is proved in animal models (8,9,10,11). Myocardal biopsies in the majority of patients show

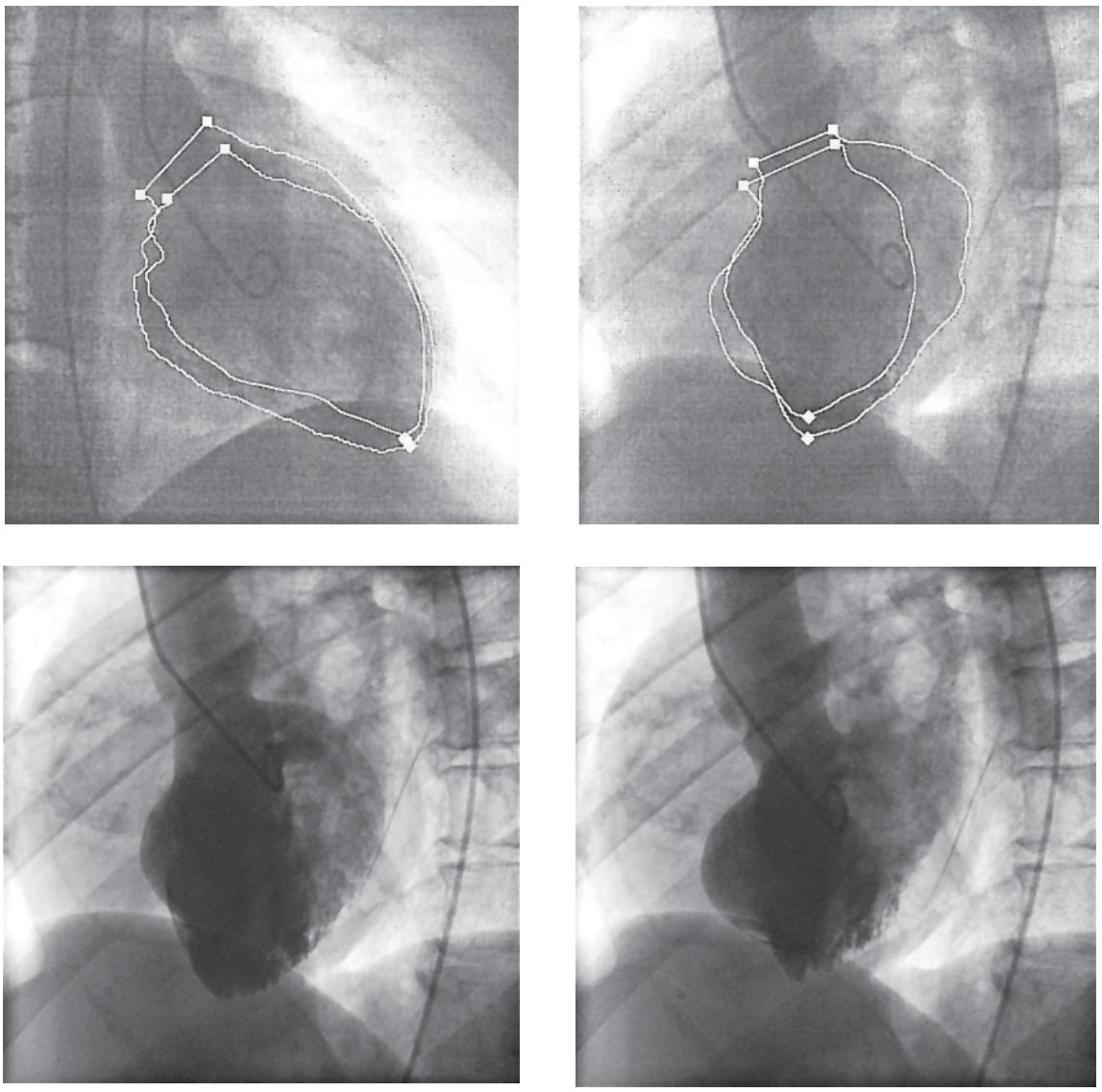

FIGURE 3. Thallium stress test of the heart shows mid and proximal septal-anterior ischemia during the stress

mononuclear inflammatory infiltrates, suggesting that the elevation of catecholamines is a link between injury of myocites and emotional stress6. The incidence of Takotsubo is estimated to be 1% to 2% of patients presented with an acute myocardial infarction. A good course of Takotsubo cardiomiopathy is well known (12). On the other hand, an early diagnosis of cardiac sarcoidosis is important , although it can be difficult (13). The diagnosis is contemplated, because it is usually not confirmed with specific diagnostic tests. Granulomatous lesions in the heart were found on biopsy in 20% do 37% patients (14,15). The prognosis for patients with clinically diagnosed cardiac sarcoidosis is probably poor, and estimated survival range from 2 to over 5 years (16,17,18,19). The fibrogranulomatous lesions of the myocardium appear in segmental areas, and endomyocardial biopsies have uncertain results. We have presented the patient with cardiac sarcoidosis, which appeared on admission as Takotsubo syndrome. Clinical course was typical for acute coronary syndrome. Angiography findings were according to Takotsubo syndrome. The emotional stress was lacking element for fulfilling criteria for diagnosis of Takotsubo syndrome. The history of previous lung sarcoidosis directed medical approach to cardiac sarcoidosis. Although endomyocardial biopsy did not confirm granulomatose disease, corticosteroid therapy, the mainstay of treatment of sarcoidosis, was prescribed to the patient (20). Sarcoidal granulomas are structured masses composed of macrophages, epithelioid cells, giant cells, and T cells. They may persist, resolve, or lead to fibrosis (21) .But, endomyocardial biopsy has a low diagnostic yield (less than 20%) because of their patchy arrangement, and granulomas are more likely to be located in the left ventricle and basal ventricular septum than in the right ventricle, where biopsies are usually performed (22). Postulating of thrombotic

etiology for Takotsubo syndrome does not preclude the possibility of catecholamine-mediated augmentation. The other possible mechanisms include the specific coronary anatomy, a transient intraventricular gradient increase in circulating catecholamines (23). No consensus exists regarding appropriate therapy for Takotsubo cardiomyopathy. Actually, the number of reported cases is still low and the disorder is possibly underdiagnosed.

Conclusion

There is possibility that in basis of Takotsubo syndrome and cardiac sarcoidosis lies the same or similar etiopathogenic mechanism.

Cardiac sarcoidosis is a serious disease. Fifty percent of patients have disturbances of rhythm, conduction or repolarization, and sometimes all of them Sudden death can be the first sign of this disease. No definitive etiology was found ,too. But it is obvious that chronic inflammatory response in sarcoidosis or some other common process has an influence on Takotsubo shape of cardiomyopathy.

Since there, no case of cardiac sarcoidosis mimicking Takotsubo syndrome has been reported before. The occurrence of this pattern of cardiac sarcoidis as we presented may point to a further etiological investigations.

Cardiac sarcoidosis has poor prognosis and Takotsubo syndrome a favourable one. Would Takotsubo appearance of sarcoidosis have better prognosis, following up of patient will present.

References

(1) Pavin D., Le Breton H., Daubert C. Human stress cardiomyopathy mimicking acute myocardial syndrome. Heart 1997;78:509-511

(2) Brandspiegel H.Z., Marinchak R.A., Rials S.J., Kowey P.R. A broken heart. Circulation 1998;98:1349-1349.

(3) Kawai S., Suzuki H., Yamaguchi H., et al. Ampulla cardiomyopathy (`Takotsubo' cardiomyopathy) -- reversible left ventricular dysfunction: with ST segment elevation. Jpn. Circ. J. 2000;64:156-159. [Erratum, Jpn. Circ. J. 2000;64:237

(4) Villareal R.P., Achari A., Wilansky S., Wilson J.M. Anteroapical stunning and left ventricular outflow tract obstruction. Mayo Clin. Proc. 2001;76:79-83.

(5) Tsuchihashi K., Ueshima K., Uchida T., et al. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. J. Am. Coll. Cardiol. 2001;38:1-3

(6) Wittstein S.I, Thiemann R.D, Lima A.C.J., Baughman L.K. et al. Neurohumoral features of myocardial stunning due to sudden emotional stress, N. Engl. J. Med . 2005;352:1923-1925,

(7) Lacy C.R, Contrada R.J., Robbins M.L., et al. Coronary vasoconstriction induced by mental stress (simulated public speaking). Am. J. Cardiol. 1995;75:503-505

(8) Bybee K.A., Prasad A., Barsness G.W., et al. Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning syndrome. Am. J. Cardiol. 2004;94:343-346

(9) Mann D.L., Kent R.L., Parsons B., Cooper G. Adrenergic effects on the biology of the adult mammalian cardiocyte. Circulation 1992;85:790-804.

(10) Singal P.K., Kapur N., Dhillon K.S., Beamish R.E., Dhalla N.S. Role of free radicals in catecholamine-induced cardiomyopathy.Can. J. Physiol. Pharmacol. 1982;60:1390-1397

(11) Bolli R., Marban E. Molecular and cellular mechanisms of myocardial stunning. Physiol. Rev. 1999;79:609-634.

(12) Fazio G., Barbaro G., Sutera L.,et al. Clinical findings of Takotsubo cardiomyopathy: results from a multicenter international study. Cardiovasc. Med. (Hagerstown). 2008;9(3):239-244.

(13) Guttilla D., Pizzuto C., Azzarelli S., Palecek T., Di Gesaro G., Lombardi R., Akashi Y.J., Novo S., Hirose Y., Ishida Y., Hayashida K., et al. Myocardial involvement in patients with sarcoidosis: an analysis of 75 patients. Clin. Nucl. Med. 1994;19:522-525

(14) Silverman K., Hutchins G., Bulkley B. Cardiac sarcoidosis: a clinico-pathological study of 84 in selected patients with systemic sarcoidosis. Circulation 1978;58:1204-1211

(15) Hunninghake G.W., Costabel U., Ando M., et al ATS/ERS/WASOG statement on sarcoidosis: American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and other Granulomatous Disorders. Sarcoidosis Vasc. Diffuse Lung. Dis. 1999;16:149-173

(16) Roberts W., McAllister H., Ferrans V. Sarcoidosis of the heart: a clinicopathologic study of 35 necropsy patients (group 1) and review of 78 previously described necropsy patients (group II). Am. J. Med. 1977;63:86-108

(17) Flemming H., Bailey S. Cardiac sarcoidosis. In: Sarcoidosis and other granulomatous disorders Vol. 73, (James D.G. ed.), 1994; pp. 323-334

(18) Iannuzzi C.M, Rybicki A.B., Teirstein S.A. Sarcoidosis. N. Engl. J. Med. 2007; 357:2153- 2165

(19) Nunes H., Bouvry D., Soler P., Valeyre D. Sarcoidosis. Orphanet. J. Rare Dis. 2007;2:46-51

(20) Newman S.L., Rose S.C. Maier A.L. Sarcoidosis, N. Engl. J. Med. 1997; 336:1224-1236

(21) Uemura A., Morimoto S., Hiramitsu S., Kato Y., Ito T., Hishida H. Histologic diagnostic rate of cardiac sarcoidosis: evaluation of endomyocardial biopsies. Am. Heart J. 1999;138:299-302

(22) Ibanez B. Takotsubo Syndrome: A Bayesian approach to interpreting its pathogenesis. Mayo Clin. Proc. 2006;81(6):732-735