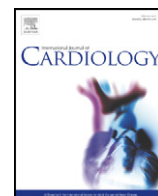




Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Tako-tsubo cardiomyopathy after administration of intravenous epinephrine during an anaphylactic reaction

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ARTICLE INFO

Article history:

Received 25 October 2010

Received in revised form 7 December 2010

Accepted 9 December 2010

Available online xxxx

Keywords:

Tako-tsubo cardiomyopathy

Cardiomyopathy

Epinephrine-induced cardiomyopathy

Tako-tsubo cardiomyopathy was first described as a transient left ventricular apical ballooning syndrome in Japanese about 19 years ago [1]. Clinically, the entity often mimics signs and symptoms of acute coronary syndromes. On the individual level, pathophysiological consequences of increased catecholamines are not sufficiently understood. However, functional alterations of the presynaptic sympathetic neurotransmission seem to play an important role. In the majority of cases, non-invasive and invasive imaging shows either an apical (typical pattern) or a mid-ventricular (uncommon pattern) dys- or akinesia of the left ventricle [2]. Most frequently wall-motion abnormalities are fully reversible within a few days. Although the prognosis of tako-tsubo cardiomyopathy depends on the triggering factors, the mortality of these patients is higher as compared to the expected mortality for the general population [3].

A 37-year-old woman suffered from a bee sting and developed local itching and spreading hives. She immediately presented to a local primary care physician, who administered 1 mg epinephrine (1:10,000) intravenously, 1 mg epinephrine in NaCl 0.9% p.i. and 250 mg prednisolone. After the application of epinephrine, the ECG showed ventricular bigeminy. A few minutes after administration of the drugs, the patient developed shortness of breath, coughing and bloodstained sputum. A few minutes later, she developed symptoms

of shock with a drop in systolic blood pressure to 80 mm Hg and an increase in heart rate to 110 bpm. Auscultation of the lungs revealed bilateral rales. The patient was given intravenous fluids, 250 mg prednisolone i.v., 8 mg dimetindine, and 50 mg ranitidine and was immediately transferred to our emergency department.

Upon presentation in our emergency department, the patient complained about chest pain and palpitations. The chest X-ray showed pulmonary oedema. Electrocardiography revealed ST-segment elevation in lead V1 and reduction of R waves in leads V2–V4 (Fig. 1). Abnormal laboratory findings obtained at admission included elevated troponin I level (1.10 ng/mL), which increased to 3.35 ng/mL after 8 h (normal ≤ 0.04 ng/mL) and creatine kinase level (150 U/L up to 218 U/L; normal ≤ 140 U/L) and CK-MB fraction (24% of CK; normal $< 6\%$), and D-dimer level (5.36 mg/L; normal ≤ 0.50 mg/L). Initial echocardiography demonstrated hypokinesia of the apicoseptal wall with almost normal global left ventricular function. Coronary angiogram excluded coronary artery disease. Left ventriculography revealed an extensive apical ballooning with a hypokinesia of anterior and posterior segments and a slightly impaired global left ventricular. The magnetic resonance imaging confirmed hypo-/akinesia of the anterior, posterior and lateral wall accompanied again by a ballooning of the left ventricle without late enhancement after gadolinium application. At this stage, “inverse tako-tsubo cardiomyopathy” was diagnosed.

The medical treatment included the usual heart failure therapy including beta-blocker, ACE inhibitor, and aldosterone antagonist.

A 70-year-old female patient presented with clinical signs and symptoms of an acute coronary syndrome in the emergency room. The patient had experienced a wasp sting 45 min ago. Based on her history of hypersensitivity to wasp venom, she was treated for an evolving anaphylactic reaction with prednisolone (250 mg i.v.), clemastin (2 mg i.v.) and cimetidin (200 mg i.v.). Due to subjective swelling of the throat the patient received 0.3 mg i.v. epinephrine. Immediately after application, the patient developed severe chest pain, tachycardia and vomiting. At that time, the ECG showed transient ST-segment elevation involving the leads I, aVL and V2–V4. Because of preliminary diagnosis of acute coronary syndrome, the patient was transferred to the next hospital with PCI capabilities. At the time of admission, the symptoms were less pronounced, blood pressure measured 120/60 mm Hg, and heart rate was 65 bpm. The ECG revealed sinus rhythm, T-wave inversion in leads I, aVL and V2 to V4, and a prolonged QT interval. The troponin T levels were elevated (0.15 $\mu\text{g/L}$, normal < 0.10 $\mu\text{g/L}$) with a normal creatine kinase (117 U/L, normal 15–174 U/L).

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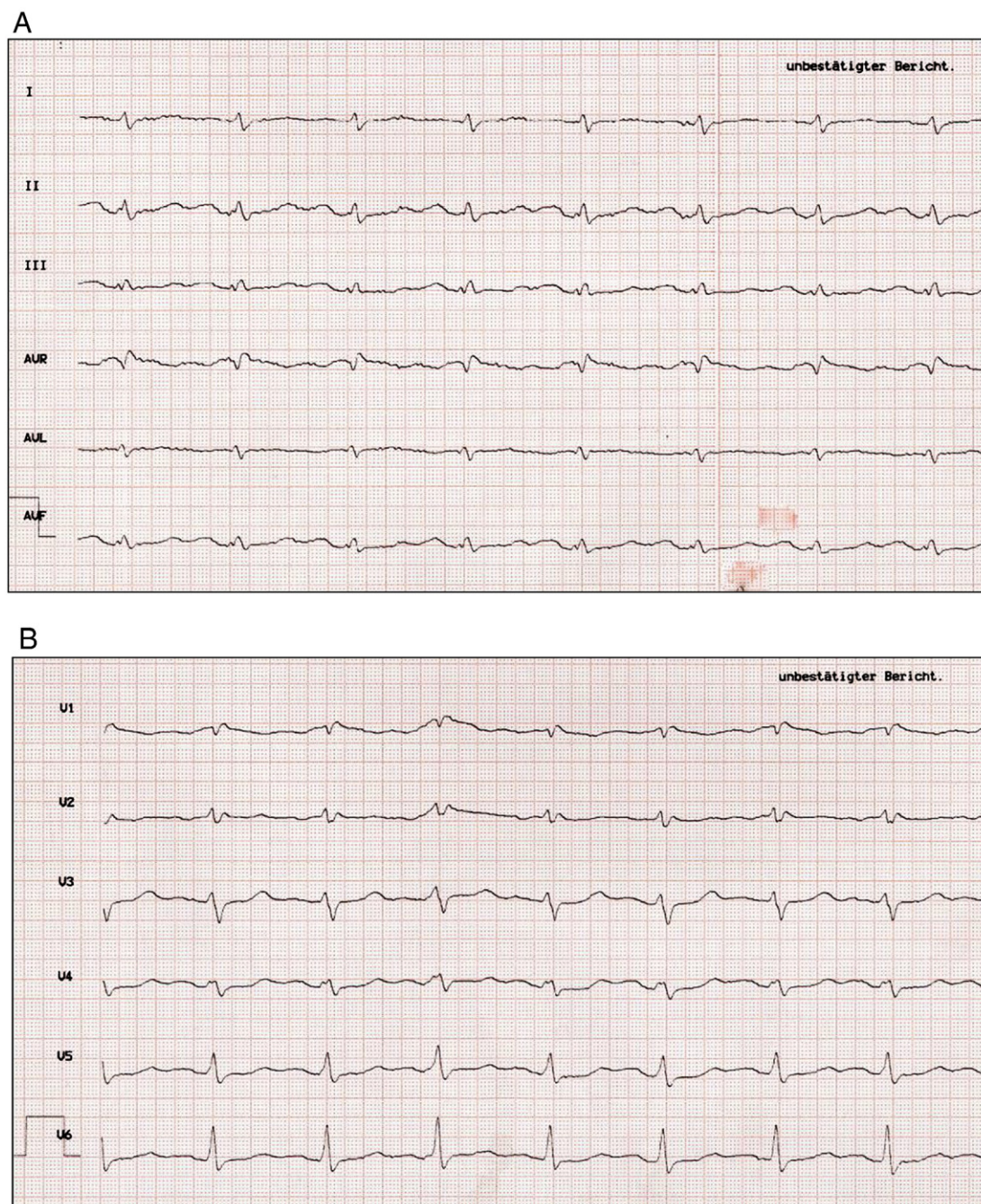


Fig. 1. A and B: 12-lead electrocardiogram of the first case registered at hospital admission.

Transthoracic echocardiography showed apical and anteroseptal wall motion abnormalities and a moderately reduced global ejection fraction (LVEF 45%). Coronary angiography was performed and significant coronary artery disease was excluded. Left ventriculography, however, demonstrated a clear apical akinesia, indicating typical apical ballooning. Cardio-vascular magnetic resonance imaging confirmed a focal signal increase indicating myocardial oedema of anterior and anteroseptal segments (Fig. 2). Based on these findings, tako-tsubo cardiomyopathy of typical apical type was diagnosed. The patient was treated with beta-blockers, ACE inhibitors, and aspirin.

Despite of a large number of primarily clinical studies addressing the pathophysiology of tako-tsubo cardiomyopathy the exact mechanisms underlying the development of the disease remain unclear.

Here, we report two distinct cases where epinephrine was administered to prevent anaphylactic reactions following a bee or

wasp sting. In both cases, the application led to a sudden onset of clinical signs and symptoms of an acute coronary syndrome. After invasive exclusion of coronary artery disease, tako-tsubo cardiomyopathy was diagnosed by clear wall motion abnormalities, as visualized in echocardiography, left ventricular angiogram and magnetic resonance imaging.

According to the immediate clinical response to catecholamine administration, a pathophysiological link is strongly suggestive. The regional metabolic and contractile responses to catecholamine infusion are greater in the apical myocardium than in the basal region since the density of beta-adreno receptors decreases from apex to base [4]. These regional differences could contribute to an increased vulnerability of the left ventricular apex to sudden surges of circulating catecholamine levels and, hence, would explain the specific contractile wall motion abnormalities observed in tako-tsubo cardiomyopathy. Further concepts regarding

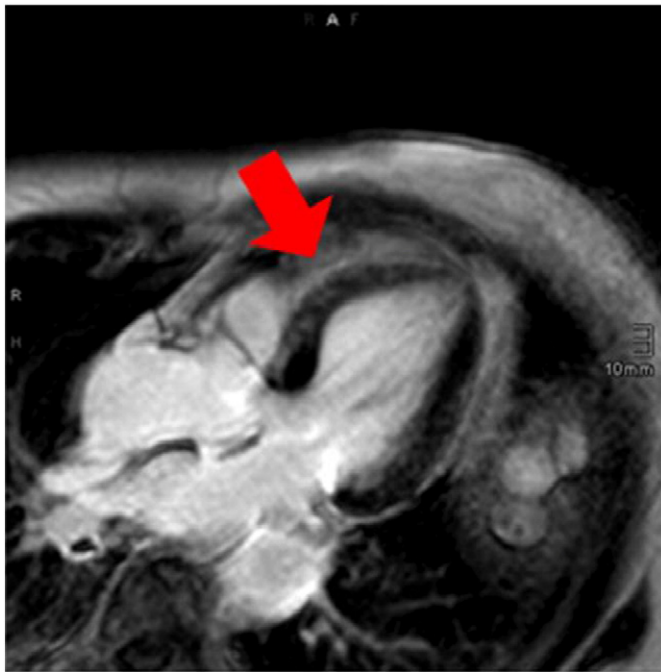


Fig. 2. Contrast enhanced MRI (T1) of case #2. Late gadolinium enhancement (LGE) indicating edema anterolateral.

the pathophysiology of tako-tsubo cardiomyopathy include coronary vasospasm [1], disturbances in myocardial microcirculation, and calcium metabolism [5].

Currently, there is no specific treatment of tako-tsubo cardiomyopathy which can be offered other than the usual heart failure therapy including beta-blockade, ACE inhibition and diuretics.

In summary, our report describes the importance of tako-tsubo cardiomyopathy as a possible differential diagnosis to acute coronary syndrome. The possibility of iatrogenic induction, as reported in our cases, should be recognized in everyday clinical practice.

Acknowledgement

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [6].

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