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### Case Report

# Case of Takotsubo cardiomyopathy after tooth extraction – Unusual trigger of a rare syndrome



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#### ABSTRACT

We describe a case of Takotsubo cardiomyopathy in a 75-year-old woman after an elective extraction of 10 teeth of the lower jaw using bilateral mandibular anesthesia. The patient complained of shortness of breath and chest pain after 24 h. Coronary angiography showed smooth normal coronary arteries with thrombolysis in myocardial infarction III flow. Left ventriculography demonstrated apical ballooning. Three months later, the patient is symptom-free, with normal left ventricular function.

We assume that the complex and robust procedures in dentistry together with a systemic absorption of epinephrine are sufficient triggers for the development of Takotsubo cardiomyopathy. In our case, we advocate an external catecholamine exposure rather than an internal catecholamine excess. We need more vigilance when assessing such patients.

<Learning objective: We describe a stress-induced cardiomyopathy with late symptom development despite an uncomplicated tooth extraction. There was only one case of Takotsubo cardiomyopathy with acute symptoms described in the literature, although after complicated tooth extraction. It could be interesting for physicians that the complex and robust procedures in dentistry together with a systemic absorption of epinephrine are sufficient triggers for the development of Takotsubo cardiomyopathy.> © 2014 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

#### Introduction

We describe here a rare case of stress-induced cardiomyopathy, where we want to claim that not only stress-induced internal catecholamine excess but also an external exposition of catecholamine could provoke the above-mentioned cardiomyopathy.

#### **Case report**

An elective extraction of the remaining 10 teeth of the lower jaw was conducted in a 75-year-old woman with a history of controlled hypertension, chronic arthritis, bronchial asthma, and transitory ischemic attack in 2004 without residual effects (Fig. 1A). Patient medication at that moment included: ramipril 2.5 mg, prednisolone 5 mg, as well as budesonide 400  $\mu$ g and

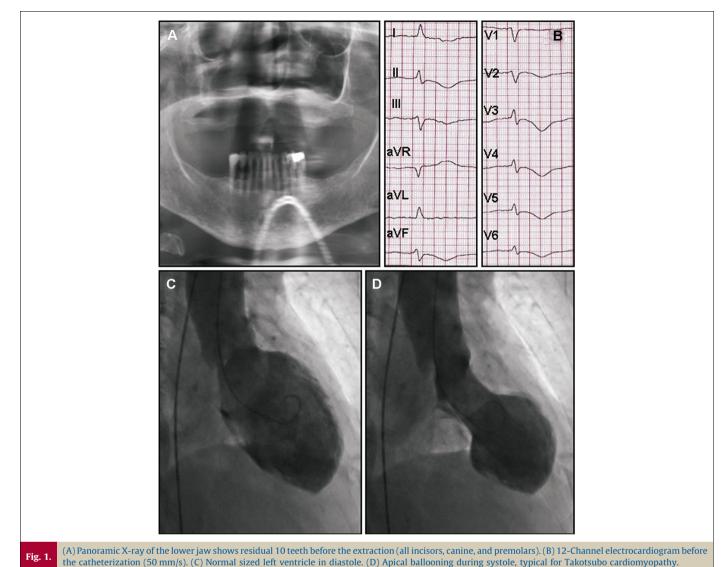
\* Corresponding author at: Division of Cardiology, Schuechtermann Clinic, Ulmenallee 5-11, 49214 Bad Rothenfelde, Germany. Tel.: +49 17670263656; fax: +49 424641598. formaterol 12  $\mu$ g if required (did not use at the extraction day and day before). It was an uncomplicated procedure with bilateral mandibular anesthesia (3 ml of Ultracain-DS was used. 1 ml contains 40 mg articaine hydrochloride and 0.006 mg epinephrine hydrochloride). The whole procedure lasted 45 min. After 24 h the patient complained of shortness of breath and chest pain. The patient denied any type of extraordinary physical or emotional stress during as well as in the postprocedural time until symptoms appeared.

Electrocardiogram (ECG) and troponin I level were normal at the moment of admission in our clinic. In the following 12 h, ECG showed T wave inversion in I, II, III, aVF, and V2–V6 (Fig. 1B), with slightly elevated troponin I level – 0.063 ng/ml (normal values: 0.0–0.028 ng/ml). Transthoracic echocardiography (TTE) showed apical akinesia of the left ventricle with low ejection fraction (EF) 30–35%. We performed a coronary angiography and left ventriculography. Smooth normal coronary arteries with thrombolysis in myocardial infarction III flow, without any sign of vascular disease were found. Left ventriculography demonstrated apical ballooning (apical akinesia with basal hyperkinesias), the typical sign of Takotsubo cardiomyopathy (Fig. 1C and D).

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The patient was treated with clopidogrel, aspirin, bisoprolol, ramipril, and atorvastatin. Three months later the patient was symptom-free, TTE showed significantly improved left ventricular function (EF 55%), and the ECG was normal.

#### Discussion

Takotsubo cardiomyopathy was first described in the 1990s in Japan [1]; it usually occurs in postmenopausal women and is characterized by left ventricular apical ballooning associated with emotional or physical stress. The etiology of the disease remains unclear. Theories described include catecholamine excess, multivessel coronary vasospasm, and a microvascular dysfunction. Typically acute onset of chest pain and/or left ventricular failure occurs; ECG changes are similar to a myocardial ischemia. On the other hand, apical ballooning can be nearly asymptomatic without typical chest pain or dyspnea [2]. Fortunately and most often the left ventricular dysfunction is reversible and associated with favorable prognosis; however, severe complications have been described in some cases [3].

The only known case of Takotsubo cardiomyopathy with acute symptoms after complicated tooth extraction was described recently [4]. There are some reports describing Takotsubo cardiomyopathy after the application of even a small amount of epinephrine [5]. In the case of Vassiliou et al. [4] with the tooth

extraction there is no report of details of the complication of the dental procedure or of the "considerable distress", mentioned by them. In our case on the contrary we have interviewed the female patient, as well as the dentist himself thoroughly:

In the perioperative period both sides have denied to have occurred or observed:

- a. Any type of objective serious or less serious side effects during the procedure, including bleeding, tachy- or bradycardia or other type of hemodynamical hyperreactions, seizures, tachypnea, drowsiness, vomiting, blurred vision, confusion or unconsciousness, etc.
- b. Any type of notable subjective experience of pain, feeling anxious, shaky, dizzy, restlessness, ringing in ears, depression, etc.
- c. The anesthetic dose was usual and there was no necessity of an additional injection of the latter.
- d. The duration of the procedure was usual as well.

That is why the thesis of this case is that the decisive trigger of the Takotsubo cardiomyopathy was an external catecholamine exposure rather than an internal catecholamine excess. This thesis rests on the uncomplicated character of the dental procedure (see above). So, an internal catecholamine excess either could not be at all or should not be sufficient alone to trigger such an extreme cardiologic disaster. How could external catecholamine exposure be a trigger like an internal excess associated with stress?

Activation of the pituitary–adrenal axis is a prominent neuroendocrine response to stressors. Epinephrine secretion increases usually to 300 pg/ml or even less in situations of psychological (mental) stress. The exaggerated neuroendocrine response is observed also with intraoral injections of local anesthetic, oral surgery, or any other type of surgical procedures as well [6]. Plasma catecholamine concentration during myocardial infarction (MI) is usually slightly higher than with any other types of environmental stress. On the other hand, plasma catecholamine concentrations are significantly higher in patients with stress-induced cardiomyopathy as compared to those with MI [7]; epinephrine 1264 pg/ml versus 376 pg/ml and norepinephrine 2284 pg/ml versus 1100 pg/ml, respectively.

In our case, the patient was given 18  $\mu$ g of epinephrine diluted in local anesthetic. Assuming, after the dilution through the whole body (ca. 7000 ml blood volume) it corresponds to more than 2,500,000 pg/ml of epinephrine in the time of injection. This is about 2000 times more than described above in the patients during stress-induced cardiomyopathy and more than 8000 times more than in any other type of environmental stress.

And at last, it should not be forgotten that although a local anesthetic (i.e. epinephrine) during dental procedures should be administered in an infiltrative (submucotic) fashion, accidentally it could be injected in the small vessels as well, producing systemic application of epinephrine, causing an extremely rash elevation of plasma level of epinephrine.

After 3 months the patient recovered and feels good.

#### Conclusion

We assume that the dental procedure itself is a stressor. The local anesthesia with epinephrine together alone could be enough to trigger stress-induced cardiomyopathy. In one of the largest patient cohorts with stress (Takotsubo) cardiomyopathy (136 patients) analyzed by Sharkey et al. [8], the only obvious trigger was sympathomimetic drugs or medical/surgical procedures (but no dental procedure) in about 16% of the patients. However, based on our arguments mentioned above, we find it necessary to begin a discussion about cautiousness and vigilance for a dental procedure or even for any type of infiltrative anesthesia with epinephrine, especially in postmenopausal women.

#### **Conflict of interest**

The authors declare no conflict of interest.

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