Case report

Acute coronary syndrome: Uncommon presentation of multiple endocrine neoplasia

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1. Introduction

Multiple endocrine neoplasia type 2 is a rare genetic syndrome [1] with an incidence of less than 0.2% among the general population [2–4]. The elevated circulating catecholamines can lead to different cardiovascular effects [5]. The serious and fatal cardiovascular complications of these tumors are because of the potent effects of catecholamines, especially noradrenaline. Hypertension, tachycardia, pallor, headache and anxiety usually dominate the clinical presentation, although some patients are asymptomatic [6]. Therefore, in the evaluation of non-ischemic, non-valvular cardiomyopathy or cardiogenic shock of unknown origin, we should consider the presence of multiple endocrine neoplasia type 2, as differential diagnosis as good as other states of adrenergic hyperstimulation, even in the absence of symptoms of catecholamine excess. This work has been reported in the line with the SCARE criteria [7].

2. Presentation of the case

A 49-year-old ex-smoker and insulin-dependent diabetic had been admitted in our department with myocardial infarction and angiographically normal coronary arteries a year ago. His presentation was complicated by severe left ventricular (LV) dysfunction with ejection fraction of 30%. The patient made spontaneous recovery (Fig. 1). A cardiac magnetic resonance imaging established the diagnosis of myocarditis. The evaluation to determine a cause was unremarkable. The evolution was reassuring without any medical treatment (the patient didn't receive treatment for acute coronary syndrome). The patient represented a year later with atypical exertional chest pain and stage III New York Heart Association dyspnoea rapidly progressing to stage IV. This was associated with several episodes of vomiting. Through physical
examination, vital signs were recoded as normal blood pressure of 110/70 mmHg, normal pulse rate of 87 beats per minute, respiratory rate of 28 breaths per minute and 90% oxygen saturation on room air. Cardiac examination revealed crackles Killip II with no signs of right heart failure. General examination demonstrated a right thyroid nodule. Electrocardiogram findings revealed depressed ST segment in anteroseptal territory and suspended ST segment in AVR. Also, the initial laboratory analyses revealed Troponin at 2656 ng/l (N:26). Trans-thoracic Echocardiography (TTE) showed akinesia of the basal and middle segments of all walls, severe LV dysfunction, ejection fraction at 15%, restrictive mitral flow and dilated Vena Cava. Coronary angiography revealed normal coronary arteries. A few days in to the hospitalization the patient developed haemorrhage due to intestinal bleeding as a result of dual anti-platelet therapy. His condition deteriorated due to cardiogenic and the haemorrhagic shock but stabilized with general supportive intensive care management, vasoactive agents and four units of packed red cells as his haemoglobin dropped from 17 g/dl to 7 g/dl. The abdominal computed tomographic scan revealed bilateral adrenal mass (Figs. 2, 3) and segmental circumferential thickening of the right colic wall. The colonoscopy found an ulcerative process 21 cm away from the anal margin of which the histological study find moderately differentiated adenocarcinoma. At the discovery of the thyroid nodule, a cervical ultrasonic identify thyroid nodule TIRADS 5 with suspicious lymphadenopathy. Laboratory analysis revealed normal thyroid stimulating hormone (TSH) and thyroxin values, anti thyroperoxidase antibody were normal, TSH receptor auto anti-bodies and calcitonin were
higher. A chest computed tomography (CT) scan shows heterogeneous thyroid. Trans thoracic Echocardiography 3 weeks later showed overall systolic and segmental function at 65% (Fig. 4) alteration of the overall longitudinal strain at $-15\%$ affecting the basal segments. Because of adrenal incidentaloma presence, the diagnosis of pheochromocytoma was evoked and confirmed by the dosage of urine metanephrines. It revealed an elevated level of normetanephrines at 4.44 μmol/day and metanephrines level at 5.52 μmol/day. After extensive discussion by a multidisciplinary team of cardiologists, visceral surgeons, anaesthesiologist and endocrinologists, the decision was made to resect the adrenal mass, colon cancer and thyroid tumor in a single sitting after preoperative optimisation. He had bilateral pheochromocytoma and medullar thyroid carcinoma confirmed by histopathological evaluation suggested the diagnosis of multiple endocrine neoplasia type 2 (Fig. 5). The patient remained haemodynamically stable throughout the operation and afterwards. He recovered without complications and was discharged from the hospital on post-operative day three with only calcium supplement. After a 6-month follow up the patient’s symptoms resolved and his ejection fraction remained at 65\% without any medical treatment.

The patient remains under regular follow-up with no recurrence of clinical signs and a normal TTE.

3. Discussion

This case highlights the importance of thorough investigation to determine the aetiology of MINOCA. Differential diagnoses for MINOCA include plaque disruption, coronary artery spasm, thromboembolism, coronary dissection, takotsubo cardiomyopathy, unrecognized myocarditis and other forms of type-2 myocardial infarction. While according to the European Society of Cardiology guidelines, diagnostic criteria and investigation pathway for MINOCA doesn’t include the pheochromocytoma as one of the differential diagnoses for MINOCA, may be due to the low incidence and prevalence of pheochromocytoma making screening invaluable in terms of cost and benefits.

Regarding clinical presentation, the overproduction of catecholamine is associated with the presence of hypertension in about 60\% of patients, but only 1 in 4 patients present with the classic triad of headache, palpitations and diaphoresis [8] [9]. A recent review has reported even a lower rate of triad symptoms (around 4\%) in patients with diagnoses of adrenergic cardiomyopathy. The absence of hypertension or suggestive symptoms found in more than 30\% of the cases of pheochromocytoma is due to predominant secretion of adrenaline, dopamine and inactivation of noradrenaline inside the tumor as occurred in the case above.

Epinephrine is a catecholamine with greater affinity for the $\alpha$-adrenergic and $\beta$-adrenergic receptors. At low doses, epinephrine
produces tachycardia via β1 receptors in the heart and hypotension via β2 receptors in the vessels. The serious and potentially fatal cardiovascular complications of pheochromocytoma are due to the potent effects of catecholamines, especially noradrenaline [10]. Persistent high levels of catecholamine have been related with the deregulation of beta-adrenergic receptors, myofibril dysfunction and reduction of the contractile units [10,11]. Actually, it also has been related to increased sarcolemma permeability, with increased cytosolic concentration of calcium and with even direct myocardial necrosis [12]. In addition, the maintained adrenergic stimulation generates an intense vasoconstription and coronary spasm, which aggravates the myocardial damage. In fact, focal myocardial necrosis and inflammatory cells are present in 50% of patients who died with a pheochromocytoma, and these findings could be related to clinically significant ventricular dysfunction. Patients with pheochromocytoma may present with various disturbances in rhythm [13], conduction and ventricular repolarization on the ECG [14,15], usually have normal or decreased ventricular systolic function on echocardiography, with only around 10% presenting with catecholamine-induced cardiomyopathy, as occurred in our case. Diagnostic exams in suspected multiples endocrine neoplasia type 2 include measurements of urine catecholamines and urine metanephrines (normetanephrine and metanephrine) to look for a pheochromocytoma has been shown to be reversible after surgical resection of focal myocardial lesions. Nevertheless, catecholamine-induced cardiomyopathy due to pheochromocytoma has been shown to be reversible after surgical resection of the tumor. Functional myocardial recovery after adrenalectomy has been described in cases of mild myocardial damage, but it is not possible in case of massive necrosis or extensive myocardial fibrosis, where the prognosis becomes poor [20].

4. Conclusion

In this case we highlight the importance of thorough history taking and investigation for the underlying an aetiology of MINOCA and we demonstrate that multiple endocrine neoplasia should be considered as a differential diagnosis. The prognosis depends greatly on an early diagnosis and a prompt medical and surgical treatment, which are unfortunately often delayed because of the challenging diagnosis in many cases.

Declaration of competing interest

The authors declare no conflicts of interest regarding the publication of this paper.

Acknowledgements

The authors express their sincere gratitude to all the participants of the study.

Funding

None.

Ethical approval

Not required for this case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

All the authors approved the final draft of the manuscript. Dr. Kissami Ibtissam wrote the manuscript and conducted the literature review. Dr. Mehdi Berrajaa helped in data collection and analysis. Professor Jadi Rachid operated the patient and provided imaging data. Professors Ibrahim Housni conducted the pre-operative medical management. Professors Nabila Ismart and Noha Elouafi supervised the writing and reviewing of the manuscript.

Registration of research studies

Not required.

Guarantor

Dr. Kissami Ibtissam.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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