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Risk of sudden cardiac death in a case of spontaneous coronary artery dissection presenting with thyroid storm

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Abstract. – OBJECTIVE: Spontaneous coronary artery dissection (SCAD) is a spontaneous separation of the coronary artery wall whose etiology appears to be poorly understood. SCAD is a rare cause of acute coronary syndromes, and it is a life-threatening condition.

CASE REPORT: We report the case of a young woman who developed SCAD during a thyroid storm (TS).

RESULTS: To the best of our knowledge, this is the first reported case of SCAD during a TS, and it suggests a possible association between high levels of circulating thyroid hormones and SCAD susceptibility.

CONCLUSIONS: Early identification of SCAD predisposing factors is important to identify high-risk patients. In patients presenting to the emergency department because of chest pain with a history of dysthyroidism, early determination of thyroid hormones and troponin could prevent certain forms of sudden cardiac death.

Key Words:
Coronary artery dissection, Chest pain, Acute coronary syndrome, Myocardial infarction, Computed tomography, Coronary angiography, Cardiac magnetic resonance, Thyroid storm.

Introduction

Spontaneous coronary artery dissection (SCAD) is a spontaneous separation of the coronary artery wall that is not iatrogenic or due to trauma[1]. SCAD is an intramural hematoma that forms a false lumen and obstructs coronary perfusion distally to the lesion. SCAD is a rare cause (0.1%-4%) of acute coronary syndromes (ACS) and it is a life-threatening condition. It affects women in >90% of cases. Due to its low prevalence, most data have been obtained from case reports and small studies. The underlying etiology of SCAD appears to be multifactorial and poorly understood; for this reason, there is no consensus on the best treatment[1].
We describe the case of a 45-year-old woman affected by SCAD during a thyroid storm (TS). We suppose that the SCAD in our patient was related to high thyroid hormones circulating levels.

Case Report

A 45-year-old woman was admitted to our Emergency Department (ED) because of chest pain. Smoking was the only cardiovascular risk factor. Past medical history included chronic autoimmune thyroid disease. On arrival, the patient was sweaty, agitated and tachycardic (heart rate 120 bpm), with a blood pressure of 140/80 mmHg and a normal body temperature (36.5°C) and SpO_2. The patient also complained nausea and abdominal pain. Electrocardiogram (EKG) showed normal sinus rhythm at 85 bpm, normal atrioventricular and intraventricular conduction and normal ventricular repolarization with QTc of 395 msec. Laboratory tests were within normal limits, documenting hemoglobin 14.6 g/dl, white blood cells 8290/μL, creatinine 0.6 mg/dl, potassium 3.8 mEq/L, magnesium 2.46 mg/dl, troponin I 10 ng/L. After three hours, the patient developed multiple episodes of ventricular fibrillation treated with DC-shock (200

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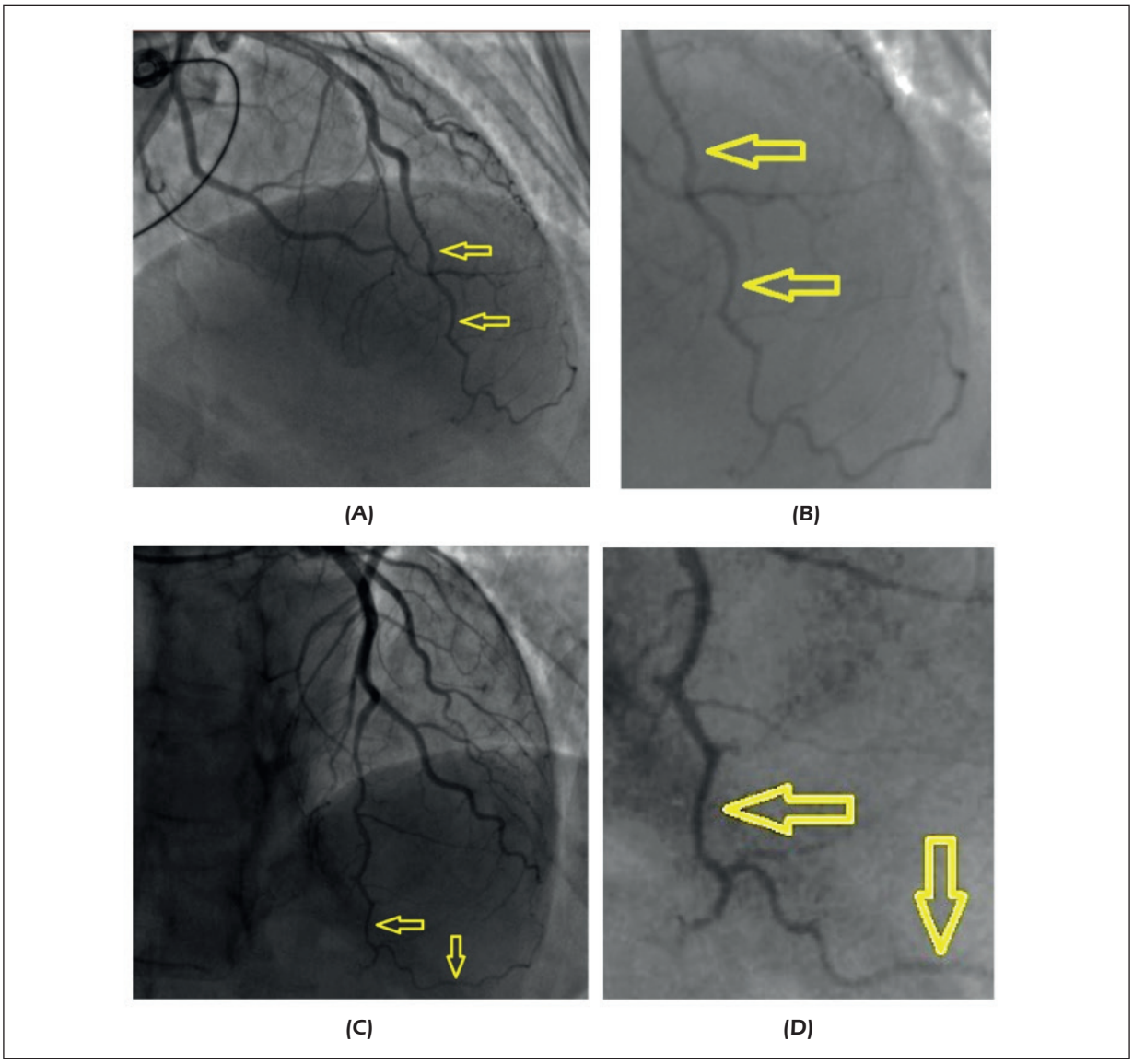

Figure 1. Coronary angiogram shows spontaneous coronary artery dissection (SCAD). (**A**) SCAD of mid and distal segments of left anterior descending artery (LAD) (yellow arrows); (**B**) Magnification of the SCAD region presented in (**A**) (yellow arrows). (**C**) SCAD of distal LAD branches (yellow arrows). (**D**) Magnification of the SCAD region presented in (**C**) (yellow arrows).

J), followed by a successful restoration of sinus rhythm. Repeat EKG showed sinus rhythm at 80 bpm, ST-segment elevation in the anterior leads and diffuse ventricular repolarization abnormalities, indicating anterior ST elevation myocardial infarction (STEMI). Transthoracic echocardiogram (TTE) documented apical akinesia with severe left ventricular dysfunction and an ejection fraction (EF) of 35%. The patient immediately underwent coronary angiography through right radial access. Selective angiography of the left coronary artery showed a long SCAD of the mid and distal segments of the left anterior descending (LAD) coronary artery, with an intramural hematoma secondary to a spiral dissection (Figure 1). No significant coronary artery disease was observed in the right coronary artery. The patient remained asymptomatic for chest pain, and in consideration of the distal location of the SCAD, we opted for a conservative approach with medical management. Blood tests showed an elevated troponin I level (42910 ng/L). During the first day of hospitalization, the patient developed fever (39.5°C peak) with diaphoresis, sinus tachycardia, hypotension, anxiety, nausea, vomiting, diarrhea, and abdominal pain. Blood tests showed thyrotoxicosis, with fT4

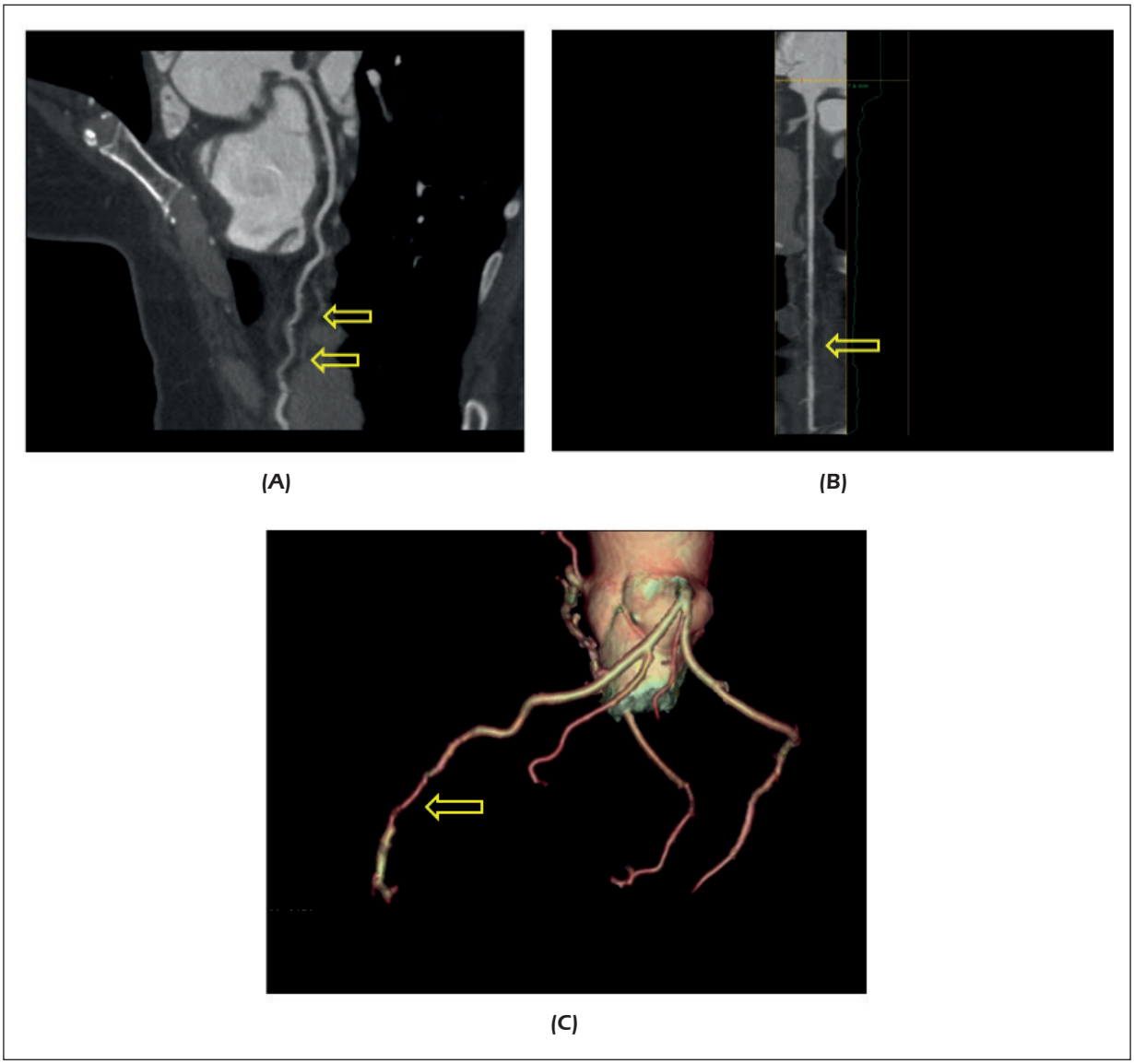

Figure 2. Cardiac computed tomography showing dissection of the left anterior descending (LAD) artery. (**A-B**) Curved planar reconstructions: LAD mid segment is irregular, and presents a smaller caliber, where it is possible to observe the thrombotic false lumen (yellow arrows); (**C**) Volume Rendering reconstruction shows the smaller and irregular tract of LAD, site of dissection (yellow arrow).

2.19 ng/dl (reference range 0.8-1.75 ng/dl), fT3 5.1 pg/ml (reference range 2.3-4.2 pg/ml), TSH 0.01 µIU/ml (reference range 0.35-4.5 µIU/ml), anti-thyroid peroxidase antibodies (anti-TPO-Ab) 631 IU/mL (reference range 0-35 IU/mL), anti-thyroglobulin antibodies (anti-TG-Ab) 291 IU/mL (reference range 0-40 IU/ml) and anti-TSH receptor antibodies (anti-TSHR-Ab) 23.7 IU/L (reference range 0-1.5 IU/L). These values were compared with previous laboratory tests performed 3 months earlier, which showed fT4 1.89 ng/dl, fT3 3.9 pg/mL, TSH 0.8 µIU/mL, anti-TPO-Ab 85.2 IU/mL, anti-TG-Ab 71.8 IU/mL and anti-TSHR-Ab 3.2 IU/L. A total score of 60 was calculated using the Burch-Wartofsky point scale, confirming a diagnosis of thyroid storm, and a treatment with propylthiouracil was immediately started. The thyroid ultrasound exam revealed an enlarged gland, with an irregular pseudonodular appearance and an isoechoic nodule. Prior to discharge, a cardiac computed tomography (CT) was performed, documenting a reduced caliber of the distal LAD with luminal compression due to an intramural hematoma (Figure 2). The patient was discharged with appropriate medical therapy (bisoprolol 2,5 mg daily, clopidogrel 75 mg daily, furosemide 25 mg daily,

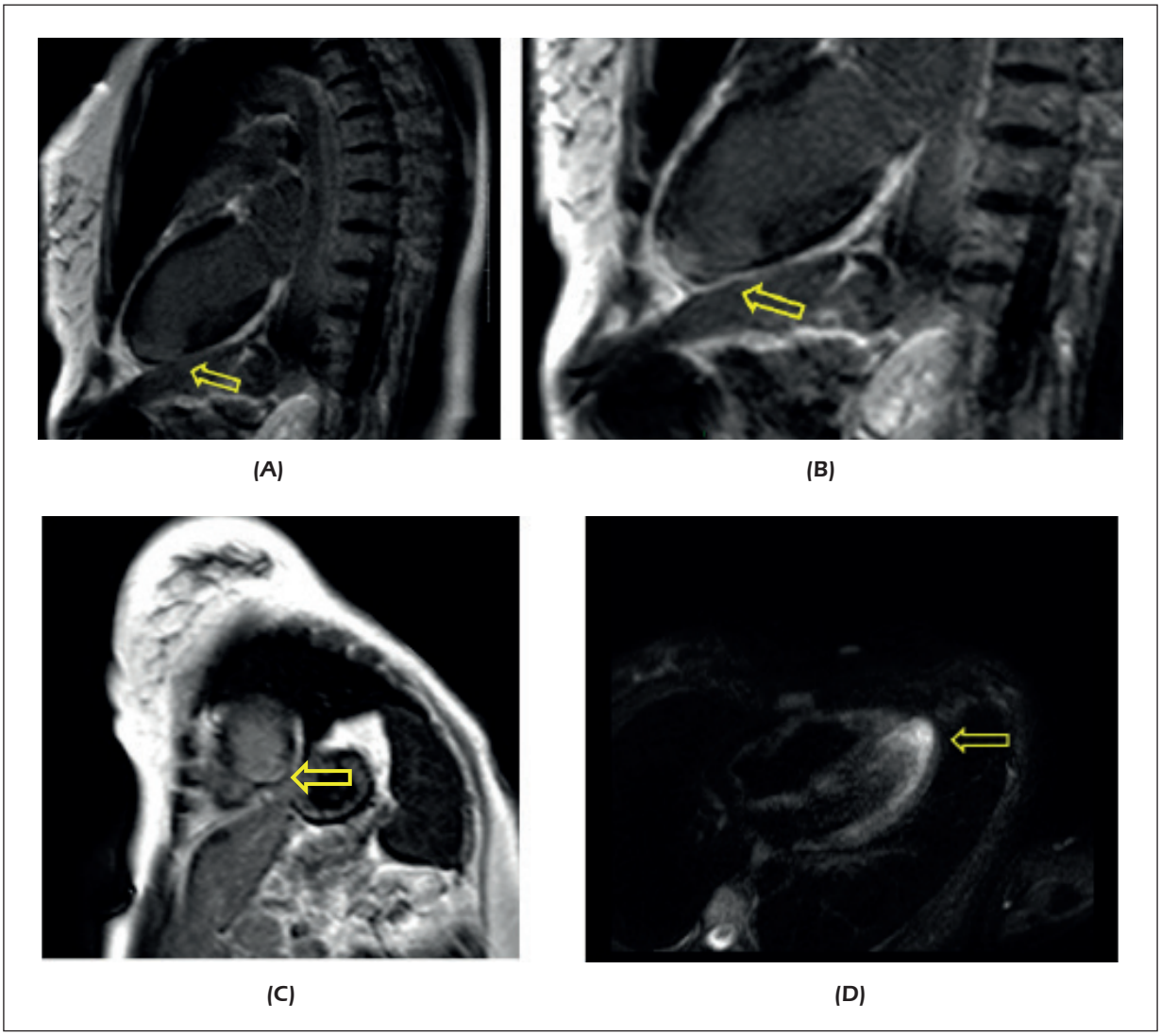

Figure 3. Cardiac magnetic resonance performed at 30 days follow-up. (**A-C**) T1 post Gadolinium sequence shows a post ischemic infero-apical late gadolinium enhancement (LGE) in two-chambers view (**A-B**, yellow arrows) and short axis view (**C**, yellow arrow); (**D**) Short Tau Inversion Recovery (STIR) sequence documents a wide infero-apical post ischemic edema (yellow arrow).

spironolactone 25 mg daily and propylthiouracil 400 mg daily). Thirty days later, a cardiac magnetic resonance (CMR) was performed, which showed normal global left ventricular systolic function (EF 68%), thin and dyskinetic infero-apical segments with a patchy area of subendocardial late-gadolinium enhancement (LGE) involving more than 75% of the myocardial wall thickness, compatible with infero-apical post-infarction scar, and a large infero-apical edematous area in the Short Tau Inversion Recovery (STIR) sequence (Figure 3). At three months-follow up, the patient was in good and stable clinical conditions and TTE showed mild apical hypokinesia with an overall improved left ventricular systolic function and EF 55%. One year later, cardiac CT documented normal caliber of the distal LAD and disappearance of the intramural hematoma (Figure 4).

Discussion

To the best of our knowledge, this is the first reported case of SCAD during a TS. A possible link between SCAD and chronic hypothyroidism has recently been suggested[2], however this association has not yet been confirmed in other studies of SCAD. This could be a serious combination leading to an increased risk of sudden cardiac death, especially in young people and women, as this

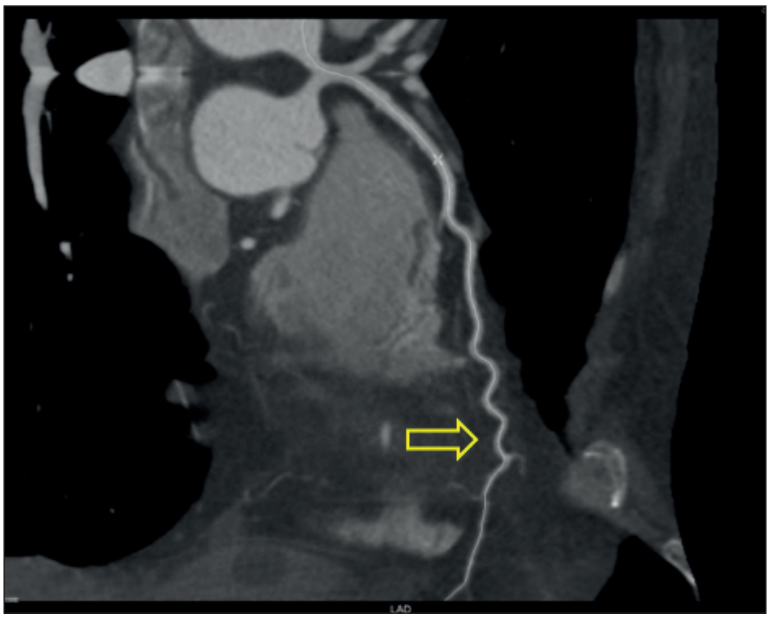

Figure 4. Cardiac computed tomography performed at 12 months follow-up. Normal caliber of distal LAD (yellow arrow) and disappearance of intramural hematoma.

population group suffers mostly from these two diseases.

We propose that a re-exacerbation of autoimmune thyroid disease may have predisposed this patient to a SCAD. Two potential mechanisms for arterial wall separation initiation have been proposed: the intimal tear hypothesis and the medial hemorrhage hypothesis[1]. The underlying etiology of SCAD appears to be multifactorial. The main potential predisposing factors for SCAD are fibromuscular dysplasia, pregnancy-related SCAD, connective tissue disorders, systemic inflammatory disease, coronary artery spasm and hormonal therapy[1].

TS is a debilitating complication of thyrotoxicosis resulting from thyroid hormones overproduction[3]. TS occurs in 1-2% of individuals with hyperthyroidism and most patients develop cardiovascular manifestations, including severe cardiac arrhythmias. Usually, the increase of troponin levels in this condition may be related with tachycardia, coronary artery spasm or Takotsubo cardiomyopathy[4].

Considering that the blood tests performed in our patient showed TSH suppression with high levels of thyroid hormones and anti-thyroid antibodies, we can speculate that the TS may have triggered the SCAD. Therefore, we hypothesize a link between the high levels of circulating thyroid hormones and SCAD susceptibility.

Iodinated contrast media used in coronary interventional procedures result in massive iodide exposure to the thyroid gland. Although people with normal thyroid activity usually experience no ill effects, patients with pre-existing thyroid disease may experience thyrotoxicosis with rapid onset after the iodinated contrast injection. Prophylaxis is not recommended, but patients at high risk to develop iodine-induced hyperthyroidism should be carefully monitored after iodinated-contrast studies[5].

In our patient, CMR and TTE performed at 1- and 3-months follow-up, respectively, documented significant improvement in the myocardial function, with normal global left ventricular systolic function. Possible mechanisms responsible for this improvement include spontaneous reperfusion, appropriate medical therapy for heart failure, but also the cardiac reparative response induced by the acute increase in thyroid hormones[6-8].

SCAD should be considered as one of the various cardiac manifestations of TS. A biological explanation for the observed association could be endothelial dysfunction due to the pro-oxidative stress effects of thyroid hormones causing coronary artery dissection[9].

Conclusions

SCAD is a severe and sometimes life-threatening clinical condition that raises management is-

sues. Given the low incidence of SCAD amongst the population and its association with many predisposing factors, it not easy to find a common molecular pathway leading to this clinical condition. In the contest of an ACS, the recognition of specific clinical or laboratory characteristics could be important for an early identification of SCAD, and a careful analysis of possible predisposing factors could be a crucial turning point to prevent it. Interventional procedures involving iodine-containing contrast agents may precipitate acute thyrotoxicosis in patients with a history of thyroid diseases. TS is a medical emergency associated with significant mortality, and most patients usually develop severe cardiac arrhythmias. Early determination of thyroid hormones and troponin can be lifesaving in patients presenting with chest pain and a history of dysthyroidism. Furthermore, a personalized, multi-modality imaging approach is crucial to determine optimal diagnostic evaluation and therapeutic management.

Authors' Contributions

S.M., D.L. (Davide Lauro) and A.A. designed the research study. D.L. (Dalgisio Lecis) and F.R.P. performed the research. D.Y. provided help and advice on conceptualization. V.C. analyzed the data. M.C. and V.C. provided help and advice on images selection. D.L., F.R.P. and S.M. wrote the manuscript. A.A. and D.Y. supervised the manuscript reviewing and editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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Conflict of Interest

The authors declare no conflict of interest.

Informed Consent

Written informed consent has been obtained from the patient to publish this paper.

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References

1) Saw J, Mancini GB, Humphries KH. Contemporary Review on Spontaneous Coronary Artery Dissection. J Am Coll Cardiol 2016; 68: 297-312.
2) Camacho Freire SJ, Díaz Fernández JF, Gheorghe LL, Gómez Menchero AE, León Jiménez J, Roa Garrido J, Cardenal Piris R, Pedregal González M, Bastante T, García Guimaraes M, Vera A, Cuesta J, Rivero F, Alfonso F. Spontaneous coronary artery dissection and hypothyroidism. Rev Española Cardiol (Eng Ed) 2019; 72: 625-633.
3) Ylli D, Klubo-Gwiezdzinska J, Wartofsky L. Thyroid emergencies. Pol Arch Intern Med 2019; 129: 526-534.
4) Nai Q, Ansari M, Pak S, Tian Y, Amzad-Hossain M, Zhang Y, Lou Y, Sen S, Islam M. Cardiorespiratory Failure in Thyroid Storm: Case Report and Literature Review. J Clin Med Res 2018; 10: 351-357.
5) Dunne P, Kaimal N, MacDonald J, Syed AA. Iodinated contrast-induced thyrotoxicosis. CMAJ 2013; 185: 144-147.
6) Pantos C, Mourouzis I. Thyroid hormone receptor α1 as a novel therapeutic target for tissue repair. Ann Transl Med 2018; 6: 254.
7) Mourouzis I, Mantzouratou P, Galanopoulos G, Kostakou E, Roukounakis N, Kokkinos AD, Cokkinos DV, Pantos C. Dose-dependent effects of thyroid hormone on post-ischemic cardiac performance: potential involvement of Akt and ERK signalings. Mol Cell Biochem 2012; 363: 235-243.
8) Lourbopoulos AI, Mourouzis IS, Trikas AG, Tseti IK, Pantos CI. Effects of Thyroid Hormone on Tissue Hypoxia: Relevance to Sepsis Therapy. J Clin Med 2021; 10: 5855.
9) Mancini A, Di Segni C, Raimondo S, Olivieri G, Silvestrini A, Meucci E, Currò D. Thyroid Hormones, Oxidative Stress, and Inflammation. Mediators Inflamm 2016; 6757154.