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Editorial

Unravelling the pathophysiology of spontaneous coronary artery dissections

Descifrando la fisiopatología de la disección coronaria espontánea

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The term *thyroid gland* comes from the Greek word *thyreoeides*, meaning *shield-like*, in reference to the location of the gland in the lower third of the anterior-medial surface of the neck, at the level of the C4 to T1 vertebrae. The thyroid gland was first officially described by Andreas Vesalius (1514-1564) in his collection of books on human anatomy *De Humani Corporis Fabrica Libri Septem*.[1] Vesalius referred to the gland as *glandulae laryngi appositae* (gland attached to the larynx). The term *glandulae thyreoidea* was introduced later by Thomas Warton[2] (1614-1673) in his book *Adenographia*. The thyroid gland does, to a certain extent, act as a shield, as it protects the body from losing functional and metabolic balance and plays a key role in regulating digestion, weight, temperature, and reproduction. Thyroid abnormalities, and hypothyroidism in particular, predispose to cardiovascular diseases such as atherosclerosis. In an autopsy study that conducted a histological analysis of thyroid specimens from 181 patients who had died of heart disease, over one-third of the specimens had evidence of thyroid disease. The most common condition was goiter (uninodular and multinodular), followed by lymphocytic thyroiditis and Hashimoto thyroiditis.[3] In a propensity-matched analysis of patients with coronary artery disease with and without subclinical hypothyroidism, optical coherence tomography showed that patients with hypothyroidism had a higher incidence of lipid-rich plaques and a greater lipid arc.[4]

Spontaneous coronary artery dissection (SCAD) is an uncommon entity that is sometimes underdiagnosed in patients with chest pain and seemingly normal coronary arteries. This event is included in the group of nontraumatic, noniatrogenic, and nonatherosclerotic coronary abnormalities that typically present as acute coronary syndrome, or, less frequently, as arrhythmia or sudden cardiac death.[5] It is a multifactorial disorder that has traditionally been associated with a range of predisposing and precipitating factors. Notable predisposing factors are fibromuscular dysplasia, pregnancy-related factors (recurrent or multiple pregnancies), connective tissue diseases (Marfan syndrome, Loeys-Dietz syndrome, Ehler–Dahlos syndrome type IV, cystic medial necrosis, alpha-1 antitrypsin deficiency, polycystic kidney disease), systemic inflammatory disease (systemic lupus erythematosus, Crohn disease, ulcerative colitis, polyarteritis nodosa, sarcoidosis, Churg-Strauss syndrome, Wegener granulomatosis, rheumatoid arthritis, Kawasaki disease, giant cell arteritis, celiac disease), hormone therapy, coronary artery spasm, and family predisposition. There are also unknown causes. Precipitating stressors include intense exercise, emotional stress, labor, Valsalva-type maneuvers (nausea, vomiting, coughing), recreational drugs (cocaine, amphetamines, methamphetamines), and intense hormone therapy (beta human chorionic gonadotropin or corticosteroid injections).[5,6] SCAD may also be linked to Tako-tsubo cardiomyopathy,[7] as both entities are predominant in women without atherosclerotic lesions and are precipitated by stress. The mean age of presentation, however, is markedly lower in SCAD.

In a recent article published in *Revista Española de Cardiología*, Camacho Freire et al.[8] described an association between SCAD and hypothyroidism in a series of 73 patients[8]; 26% of the patients had hypothyroidism and most of them were women with dissections in more distal segments and in corkscrew coronary arteries. In an earlier series, 13% of 327 patients with SCAD were found to have hypothyroidism.[9] The association between hypothyroidism and SCAD could be clinically relevant and suggests that hypothyroidism could be therapeutically targeted to prevent primary disease or recurrences. Until recently, hypothyroidism was associated with dissections in other arterial territories, such as the aorta and the cervical artery.[10,11] Many questions, however, remain unresolved. First, as recognized by Camacho Freire et al., an association does not imply causation. Second, the potential effects of thyroid replacement therapy and residual thyroid function have not been determined. It is unknown whether hormone replacement therapy could alter the natural history of SCAD, for example, by preventing recurrences. Long-term prospective epidemiological studies of patients with hypothyroidism could help establish the true incidence of this condition and determine whether the association between hypothyroidism and SCAD is due to thyroid dysfunction. One interesting area of study would be to determine the levels at which free thyroxine, triiodothyronine, and thyroid-stimulating hormone increase the risk of coronary dissection. Interventional studies are also needed to investigate the effects of replacement therapy on the prevention of SCAD recurrence. One recent study reported an association between genetically determined thyrotropin levels and atrial fibrillation (AF).[12] In an analysis of 37 154 individuals, the thyrotropin polygenic predictor was positively associated with hypothyroidism and inversely associated with diagnoses linked to hyperthyroidism (eg, toxic multinodular

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goiter). In addition, for each increment in thyrotropin, there was a reduction in the risk of AF. AF risk, therefore, should be taken into account when deciding on a course of treatment for subclinical thyroid disease. As pointed out by the authors of the article on the genetic predictors of thyroid function, the risk of AF could potentially be reduced by antithyroid medications for hyperthyroidism but potentially increased by thyroid hormone replacement for hypothyroidism.[12]

In view of the many associations between endocrine disorders and heart disease, it may be worth following in the footsteps of cardio-oncologists[13] to create cross-disciplinary cardioendocrinology units. Multidisciplinary management of cardioendocrinology or endocrine-cardiology patients could help improve long-term outcomes. A perfect example of how this collaboration might be beneficial would be early identification of ischemic heart disease in patients with diabetes mellitus or diagnosis of cardiomyopathy in patients with autoimmune diseases such as systemic lupus erythematosus.

In conclusion, and considering the association observed by Camacho Freire et al.,[8] hypothyroidism should probably be added to the list of predisposing factors for SCAD and be screened for in patients with compatible clinical and coronary findings.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Vesalius A. Andreae Vesalii Bruxellensis De humani corporis fabrica libri septem. Basileæ: Ex officina Ioannis Oporini; 1543.
2. Wharton T. Adenographia: sive glandularum totius corporis descriptio. Amstelaedami: Sumptibus Joannis Ravesteinii; 1659.
3. Vaideeswar P, Singaravel S, Gupte P. The thyroid in ischemic heart disease: An autopsy study. *Indian Heart J.* 2018;70(Suppl 3):S489–S491.
4. Cai XQ, Tian F, Han TW, et al. Subclinical hypothyroidism is associated with lipid-rich plaques in patients with coronary artery disease as assessed by optical coherence tomography. *J Geriatr Cardiol.* 2018;15:534–539.
5. Saw J, Mancini GBJ, Humphries KH. Contemporary review on spontaneous coronary artery dissection. *J Am Coll Cardiol.* 2016;68:297–312.
6. Macaya F, Salinas P, Gonzalo N, Fernández-Ortiz A, Macaya C, Escaned J. Spontaneous coronary artery dissection: contemporary aspects of diagnosis and patient management. *Open Heart.* 2018;5:e000884.
7. Jiménez Brítez G, Sabaté M, Robles C, García-Granja PE, Amat-Santos IJ, Brugaletta S. Functional and morphological assessment of left anterior descending artery in patients with tako-tsubo syndrome. *Rev Esp Cardiol.* 2018;71:986–988.
8. Camacho Freire SJ, Díaz Fernández JF, Luciana Gheorghe L, et al. Spontaneous coronary artery dissection and hypothyroidism. *Rev Esp Cardiol.* 2018. http://dx.doi.org/10.1016/j.rec.2018.06.031.
9. Saw J, Humphries K, Aymong E, et al. Spontaneous coronary artery dissection. *J Am Coll Cardiol.* 2017;70:1148–1158.
10. Rosenmann E, Yarom R. Dissecting aneurysm of the aorta and hypothyroidism. *Isr J Med Sci.* 1994;30:510–513.
11. Pezzini A, Del Zotto E, Mazziotti G, et al. Thyroid autoimmunity and spontaneous cervical artery dissection. *Stroke.* 2006;37:2375–2377.
12. Salem JE, Shoemaker MB, Bastarache L, et al. Association of thyroid function genetic predictors with atrial fibrillation: a phenome-wide association study and inverse-variance weighted average meta-analysis. *JAMA Cardiol.* 2019. http://dx.doi.org/10.1001/jamacardio.2018.4615.
13. Snipelisky D, Park JY, Lerman A, et al. How to develop a cardio-oncology clinic. *Heart Fail Clin.* 2017;13:347–359.