Cardiac paraganglioma: A challenging diagnostic and treatment dilemma

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In their recently published clinical vignette, Redzek et al. [1] reported an interesting case of cardiac primary neuroendocrine tumor in a previously asymptomatic 38-year-old female, presenting with heavy chest pain, ST depression in inferolateral leads on electrocardiogram, and elevation of high-sensitive troponin I. Tumor's location (intrapericardial, near the right atrium, surrounding the right coronary artery), radiological features, and the absence of metastatic disease, as well as histopathology and immunohistochemistry findings, indicate paraganglioma (PGL) [1]. As cardiac PGLs are extremely rare, accounting for <0.3% of mediastinal tumors and 1%–3% of primary cardiac tumors, we would like to write a short comment [2].

Paragangliomas are uncommon neuroendocrine tumors that arise from chromaffin cells located outside of the adrenal gland. In the heart, PGLs either arise from branchiomeric paraganglia (in the roots of the great vessels including the pulmonary artery, pulmonary vein, vena cava, and aorta), or visceral autonomic paraganglia (the interatrial or interventricular groove) [3]. Although cardiac PGLs have been observed in all heart chambers, the most prevalent are left atrial PGLs, followed by aortic body tumors [2].

Clinical symptoms of PGLs are heavily influenced by the tumor's metabolic profile, which is most typically caused by mutations in predisposing genes. In a multi-institutional case series, it was reported that underlying mutations in the succinate dehydrogenase (SDH) B/C/D (SDHx genes) were implicated in around 77% of cardiac PGLs [2]. Redzek et al. [1] stated that the patient had no family history of PGL. Nevertheless, it should be emphasized that negative family history does not exclude the hereditary background of the disease because, in the case of *SDHD* gene mutations, the phenomenon of maternal imprinting occurs and there may also be incomplete disease penetration [4]. Therefore, patients with confirmed cardiac PGLs should be tested at the same time for predisposing germline mutations, particularly SDHx. Accordingly, we wonder whether the patient [1] had genetic testing. PGLs are either symptomatic or asymptomatic and may be biochemically active or inactive. In general, PGLs are classified into three biochemical phenotypes: noradrenergic, adrenergic, and dopaminergic. As cardiac PGLs are predominantly associated with SDHx mutations, they often present with the noradrenergic biochemical phenotype, with typical symptoms such as hypertension, sweating, diaphoresis, palpitations, headache, and dizziness. Only around 18% of patients present with chest pain or distress [2], which probably caused diagnostic difficulties in the reported case [1]. As the tumors are usually fed by coronary arteries, angina could be present as a result of coronary steal syndrome [4].

We would also like to draw attention to the metastatic potential of these tumors. Unfortunately, except for the existence of distant metastases, there are no exact histological features, immunohistochemical stains, or molecular criteria that point towards the diagnosis of malignancy [2]. The incidence of malignant cardiac PGLs is estimated at 6% [4]. Distant metastases may appear even after many years, and therefore these patients require a long-term follow-up in both imaging and hormonal examinations. The most notable predictor of aggressive clinical behavior is the presence of a germline *SDHB* mutation, as this mutation predisposes to familial para-

ganglioma-pheochromocytoma syndrome type 4 (PGL4), which is tightly associated with the extra-adrenal location of PGLs with high metastatic potential [5]. This is another strong argument in favor of all patients with cardiac PGL undergoing genetic testing.

Diagnosis of PGLs is mostly achieved with a multimodality approach including biochemical investigation, radiological and nuclear imaging. A biopsy is not recommended, especially in biochemically positive PGLs with a typical positivity of nuclear medicine imaging, due to extensive vascularity of cardiac PGLs, which makes the biopsy unsafe [2].

Surgery is the gold standard for treating cardiac tumors. However, PGLs can infiltrate cardiac tissues and coronary arteries, so resection may be difficult or even impossible, and cardiac transplantation may be necessary as the last option [2]. The authors should be commended for taking up this challenge and for successful surgery.

In conclusion, we would like to highlight that cardiac PGLs are rare tumors with significant surgical demands and that even though the complete surgical excision can be challenging, it remains the mainstay of treatment. We would also like to emphasize the importance of considering a genetic etiology in every case of cardiac PGL.

Article information

Conflict of interest: None declared.

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