Innovative approach to a functional mediastinal paraganglioma with anomalous coronary supply: a case report

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Received 1 August 2019; first decision 17 September 2019; accepted 5 March 2020; online publish-ahead-of-print 17 April 2020

Background
Mediastinal paragangliomas (PGs) are rare and particularly challenging neuroendocrine tumours. Clinical presentation is heterogeneous and tumour resection can be challenging due to bleeding and the risk of catecholamine surges in functional tumours.

Case Summary
A 36-year-old man with multiple cardiovascular risk factors was admitted with subacute heart failure. Investigations revealed a large non-metastatic functional mediastinal PG irrigated mainly by a left circumflex coronary anomalous feeder branch. The surgical risk was deemed very high due to patient comorbidities, tumour vascularization, and close relation to major thoracic structures. A multidisciplinary team decided to perform embolization of the anomalous coronary branch followed by peptide-receptor radionuclide therapy with 177-LuDOTATE aiming to decrease tumour size and perioperative risk. Follow-up studies showed a reduction in tumour vascularization, size, and hormonal production.

Discussion
The innovative strategy of combining embolization of the anomalous feeder branch with radionuclide therapy proved to be a promising approach.

Keywords
Mediastinal paraganglioma • Coronary embolization • Radionuclide therapy • Neuroendocrine tumour • Case report

Learning points
• Functional mediastinal paragangliomas (PGs) are extremely rare. They pose serious challenges in surgical resection due to the risk of catecholamine surges and extensive blood loss.
• Embolization of the feeding artery prior to resection is a promising strategy to minimize perioperative bleeding in thoracic PGs.
• Peptide-receptor radionuclide therapy is increasingly recognized as an effective therapy in neuroendocrine tumours and is a solid option for patients with tumours considered inoperable.

Introduction
Mediastinal paragangliomas (PGs) are extremely rare neuroendocrine tumours. Clinical presentation varies and tumour resection can be challenging due to bleeding and hormonal secretion during tumour manipulation.1–3 In patients with very high surgical risk, innovative adjunctive strategies should be considered to try to reduce complications during surgery.
**Timeline**

| **Clinical presentation (Day 0)** | • 36-year-old man with: multiple cardiovascular risk factors, schizophrenia  
• Symptoms at presentation: dyspnoea, palpitations, and atypical chest pain  
• Initial evaluation in the emergency room: rapid atrial flutter, signs of congestive heart failure  
• Transthoracic echocardiography: extrinsic compression on the left atrium, moderate systolic dysfunction  
• Coronary angiography: no epicardial coronary disease, large vascularized mass supplied mainly by an anomalous branch from the left circumflex coronary artery  
• Contrast computed tomography (CT): mediastinal mass of 61 × 53 × 33 mm  
| **Imaging studies (Days 0–1)** | • Hormonal analysis: elevation of 24-h urinary and plasmatic normetanephrine values  
• Whole-body 123-MIBG scintigraphy: isolated enhanced uptake in the mediastinum  
• Large non-metastatic functional mediastinal paraganglioma with a left circumflex coronary anomalous feeder branch  
• Multidisciplinary discussion: Initial surgical risk considered high  
| **Functional studies (Days 1–5)** | • Three-step strategy to decrease risk: α and β blockade, embolization of the anomalous coronary branch, radionuclide therapy (1 cycle every 3–5 months)  
| **Diagnosis** | • Outpatient consult (monthly): symptomatic improvement, no arrhythmia recurrence  
| **Therapeutic approach (Months 0–1)** | • Contrast CT (1 and 11 months after embolization): successful embolization, slight decrease in tumour size  
| **Follow-up (Months 1–18)** | • Echocardiography (6 months after presentation): improvement in left ventricular function  
• Death (suicide) before surgery (18 months after initial presentation)  

**Case presentation**

A 36-year-old man presented to the hospital with subacute onset heart failure, palpitations, and atypical chest pain. He had schizophrenia (with an admission 10 years prior for paranoia and suicidal behaviour) and several cardiovascular risk factors, including hypertension, smoking habits, dyslipidaemia, and obesity (body mass index 48 kg/m²). His medication included bisoprolol 2.5 mg o.d., ramipril 5 mg o.d., simvastatin 20 mg o.d., metformin 1000 mg b.i.d., lamotrigine 25 mg o.d., risperidone 4.5 mg o.d., and lorazepam 2.5 mg o.d.

Upon initial examination, he was tachycardic at 150 b.p.m., had a blood pressure of 110/55 mmHg, and a peripheral oxygen saturation of 90%. Heart sounds were rapid with no murmurs, jugular venous pressure was raised at 45°; there were bilateral pulmonary rales and pedal oedema. Electrocardiogram revealed rapid atrial flutter (150 b.p.m.) and non-specific ST changes (Figure 1). A transthoracic echocardiogram was done in the emergency room and excluded left atrial appendage thrombus, allowing for safe cardioversion (1 synchronized 150 Joules shock) that successfully reverted the patient back to sinus rhythm. The transthoracic echocardiogram performed at the echo laboratory disclosed an extrinsic compression on the left atrium and left ventricular (LV) moderate systolic dysfunction with global hypokinesia (Supplementary material online, Video S1).

Given the patient’s risk factors and clinical presentation, a coronary angiography was performed to evaluate for coronary disease. There was no epicardial coronary disease, but the angiography showed a large vascularized mass located posteriorly to the heart. The mass was supplied mainly by an anomalous feeder branch arising from the left circumflex coronary (Figure 2; Supplementary material online, Video S2).

Contrast computed tomography (CT) scan revealed a large mediastinal mass (61 × 53 × 33 mm) with heterogeneous arterial-phase enhancement and compression of the left atrium (Figure 3A). The poorly defined borders of the mass suggested local invasion of the pulmonary arteries and the pericardium. These CT findings raised the suspicion of a PG. There were no other masses or suspicious ganglia in the thoracic, abdominal or pelvic compartments.

Hormonal analysis showed significant elevation of 24-h urinary and plasmatic normetanephrine values, revealing that this was a functional (catecholamine-secreting) PG. A subsequent whole-body 123-MIBG scintigraphy confirmed an isolated enhanced uptake in the mediastinum.

The final diagnosis was consistent with the presence of a large non-metastatic functional mediastinal PG, with a left circumflex coronary anomalous feeder branch. Catecholamine secretion and direct mass effect were the most likely causes for atrial flutter and subsequent tachycardiomyopathy.

Anticoagulation with rivaroxaban (20 mg o.d.) was started. Alpha and beta blockade was achieved by adding the alpha-blocker phenoxymenzamine (10 mg initially slowly titrated until 30 mg/day) to the selective beta-blocker bisoprolol (2.5 mg o.d.). The case was subsequently discussed at a multidisciplinary meeting with the cardiology and neuroendocrine thoracic tumours teams.
Surgical risk was deemed high due to (i) patient comorbidities (metabolic syndrome, LV dysfunction, and schizophrenia), (ii) tumour vascularization and proximity to major thoracic structures, and (iii) risk of catecholamine surges. The team’s approach to try to optimize the patient prior to surgery, namely by trying to decrease tumour size and the risk of perioperative complications, consisted of three steps. The first was alpha and beta blockade, the second was to perform embolization of the anomalous coronary branch, and the third was peptide-receptor radionuclide therapy with 177-Lu-DOTATE.

The patient’s 68-Galium-DOTANOC positron emission tomography scan showed high expression of somastostatin receptors (Figure 4), making him a good candidate for radionuclide therapy.

Cardiac catheterization was performed via radial artery. For the embolization procedure, the interventional cardiologists used the EBU 3.5–4 (Medtronic) guiding catheter, the BMW guidewire (Abbott), and the microcatheter finecross (Terumo). Two hydrocoils (AZUR) were deployed in the anomalous branch of the circumflex artery achieving significant reduction in distal flow (Supplementary material online, Video S3). Subsequently, the patient underwent radionuclide therapy with 177-Lu-DOTATE and completed two cycles during the following year (1 cycle every 3–5 months).

A CT coronarography performed 1 month after the procedure and confirmed the successful embolization of the anomalous branch. A second follow-up CT was performed after the second cycle of radionuclide therapy (11 months after embolization) (Figure 3B). It confirmed a reduction both in tumour vascularization and size (from $61 \times 53 \times 33$ mm to $59 \times 50 \times 29$ mm). The patient was followed monthly via outpatient consultations. His symptoms slowly improved and there was no evidence of arrhythmia recurrence. Echocardiography was done every 6 months and showed an improvement in LV function (39–50% in LV ejection fraction by Simpson’s biplane). Hormonal analysis revealed a decrease in catecholamine levels [plasmatic normetanephrine (upper limit of normal < 983): initial value: 4530 pmol/L, at 12 months: 4420 pmol/L; urinary normetanephrines (normal-range: 480–2424): initial value 10454 nmol/day, at 12 months: 8894 nmol/day]. Genetic testing for SDHAF2, SDHB, SDHC, SDHD, MAX, TMEM127, and VHL genes was negative.

The adjunctive strategies to reduce surgical risk showed positive results. Unfortunately, the patient expired due to unrelated causes (suicide) before the procedure (18 months after initial presentation).
Figure 3  (A) Computed tomography contrast scan showing a heterogeneous mass of $6.1 \times 5.3$ cm in close proximity with the pulmonary arteries, the aorta, and the left atrium, with mass effect. Imaging characteristics were consistent with a mediastinal paraganglioma. (B) Follow-up computed tomography contrast scan (11 months after embolization): confirmed the successful embolization of the left circumflex coronary anomalous feeder branch and a slight decrease in tumour size from the initial to $61 \times 53 \times 33$ mm to $59 \times 50 \times 29$ mm.

Figure 4  68-Galium-DOTANOC positron emission tomography scan confirming isolated mediastinal uptake and high expression of somastostatin receptors.
Discussion

Paraganglioma’s located within the mediastinum are exceptionally rare, accounting for <2% of cases, and the majority being non-functional tumours.\(^1\)\(^,\)\(^2\) According to the World Health Organization, PGs are not classified as benign or malignant but rather they represent a spectrum of metastatic potential. Patients with larger tumours, extra-adrenal locations and SDHB mutations are at higher malignancy risk.\(^6\) Genetic testing is mandatory in all PG cases since mutations are found in the majority of pheochromocytoma and PG patients with family history but also in at least one-third of patients with sporadic tumours.\(^4\) Establishing a hereditary syndrome is crucial for the earlier diagnosis of patients’ relatives.

Paraganglioma’s pose diagnostic and therapeutic challenges. Clinical presentation may be related to compressive effects or to catecholamine secretion.\(^2\)\(^,\)\(^3\) With typical imaging results and according to functional studies, tissue diagnosis should be avoided due to the risk of bleeding and of catecholamine surges (acute release of catecholamine’s into the bloodstream causing sudden severe hypertension and tachycardia).\(^4\)\(^-\)\(^6\)

Alpha and beta blockade therapy prior to tumour manipulation minimizes the risk of surges.\(^2\)\(^,\)\(^5\)\(^,\)\(^6\) Guidelines recommend complete surgical resection in non-metastatic PGs.\(^5\)\(^,\)\(^6\) However, high rates of significant perioperative bleeding and even death have been observed in tumours with close proximity to the heart and major vessels.\(^1\)\(^,\)\(^8\) Embolization strategies to minimize blood loss during resection were studied in head and neck PGs\(^5\)\(^,\)\(^10\) but are only recently starting to be applied in mediastinal PGs with few case reports available.\(^1\)\(^,\)\(^5\)\(^,\)\(^13\) In this case, embolization of the main feeder branch intended to reduce tumour vascularization and the risk of perioperative bleeding.

Peptide-receptor radionuclide therapy for neuroendocrine tumours with expression of somatostatin receptors has growing evidence of safety and efficacy.\(^1\)\(^,\)\(^15\) Higher expression of somatostatin receptors correlates with better responses; in few cases complete remission was achieved.\(^1\)\(^5\) Given the rarity of PGs experience is limited. Response to therapy is variable and might be delayed. Therefore, caution is advised in interpreting early follow-up CT scans. In this case, the goal with radionuclide therapy was to decrease tumour size and hormonal production to provide the best possible conditions for surgery. Even though surgery did not occur, the early controls performed showed positive signs (no metastasis, slight size reduction and successful embolization). By decreasing tumour-related surgical risk, these strategies offer promising results for suitable PG tumours initially considered inoperable or for patients at very high surgical risk.

Schizophrenia correlates with higher risk of cardiovascular disease, related to lower treatment of cardiovascular risk factors and to anti-psychotic drug use that increases arrhythmia risk.\(^1\) In this case, the mechanism of death (suicide) was unrelated to arrhythmia or coronary disease. However, chronically elevated catecholamine’s levels can cause mood swings and might have contributed to aggravate the symptoms of schizophrenia. The stress from having a severe diagnosis in a mentally fragile patient added to high circulating catecholamine’s levels probably played a role in this unfortunate outcome. Clinicians need to be vigilant to identify patients potentially at risk.

This case describes a very rare tumour with an unusual coronary supply. Our innovative strategies, combining coronary artery embolization with radionuclide therapy, were effective in decreasing tumour vascularization, size, and hormonal production. This is a promising approach for suitable PG tumours among patients at very high surgical risk.

Lead author biography

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Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: Patient’s next of kin (father) provided verbal and written consent for the publication of this case report.

Conflict of interest: none declared.

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