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Case Report

Quadruple Valve Replacement for Carcinoid Heart Disease

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Carcinoid heart disease (CHD) is a rare consequence of advanced neuroendocrine tumours (NETs), typically resulting in predominantly regurgitant right-sided valvular disease and heart failure.[1] Aortic and mitral valve involvement is less common.[1] Quadruple-valve replacement (QVR) is rare. Herein, we report a 57-year-old woman with severe quadruple valve CHD, biventricular dysfunction, and interatrial shunt presenting with heart failure and hypoxia. Despite a high disease burden, she underwent QVR, with marked improvement in symptoms and cardiac function.

Novel Teaching Points

- CHD can progress rapidly over months,[1] warranting close clinical follow-up.
- PFO is a recognized mechanism leading to left-sided valvular damage. Guidelines recommend this should be actively sought. If present, it should be closed at the time of surgery, in the absence of irreversible pulmonary hypertension.[1]
- Patch enlargement of the right ventricular outflow tract/pulmonary artery may be necessary to implant the optimal size of pulmonic valve prosthesis.[1]
- Complete heart block is a recognized postoperative risk.[1] Intraprocedural epicardial right atrial and RV pacing wires should be implanted prophylactically.
- QVR for CHD is feasible but requires expertise, meticulous planning, patience, and support. Shared decision making between multidisciplinary teams and the patient is essential.

Case

A 57-year-old woman with New York Heart Association (NYHA) class II dyspnea, menorrhagia, abdominal pain, diarrhea, and weight loss was diagnosed with a small bowel low-grade functional NET, metastatic to the liver. Transthoracic echocardiography (TTE) showed CHD with severe tricuspid and pulmonary regurgitation, moderate aortic and mitral regurgitation, a patent foramen ovale (PFO), and mild right ventricular (RV) and moderate left ventricular (LV) systolic dysfunction. She was declined for cardiac surgery because of high operative risk. Over 5 months, she rapidly declined and was largely bed-bound. Her NYHA class (from II to IV) and home oxygen requirements (from 2 to 9 L/min) increased. Our centre evaluated her for a second surgical opinion.

TTE showed progression of RV dysfunction (now moderate), aortic (now moderate to severe) and mitral (now severe) regurgitation. Right-sided valvular disease persisted (Fig. 1). Cardiac catheterization confirmed severe right-sided heart failure, low output state, and no pulmonary hypertension (cardiac index 1.24 L/min/m^2, right atrial pressure 24/6 mm Hg, RV pressure 32/4 mm Hg, pulmonary artery pressure 22/4 mm Hg, and mixed venous oxygen saturation 47%).

She was evaluated at heart-team rounds with oncology input. Despite cardiac deterioration, her tumour biomarkers (urinary 5-HIAA) declined rapidly (2510 to 490 μmol/L) with octeotride. Considering her poor cardiac but favourable NET prognosis, and her strong preferences, it was decided to pursue QVRs and PFO repair (Fig. 2).

Octreotide infusion was used perioperatively to prevent carcinoid crisis. The heart was protected using cold antegrade and retrograde cardioplegia through cannulas in the ascending aorta and right atrium/coronary sinus, respectively. At the time of aortotomy, 2 polystan cannulas were placed into the coronary ostia to enable near-continuous administration of antegrade cardioplegia, along with intermittent retrograde cardioplegia. Topical ice provided additional RV protection during the cross-clamp time. Core temperature was maintained at 32 oC during the operation.

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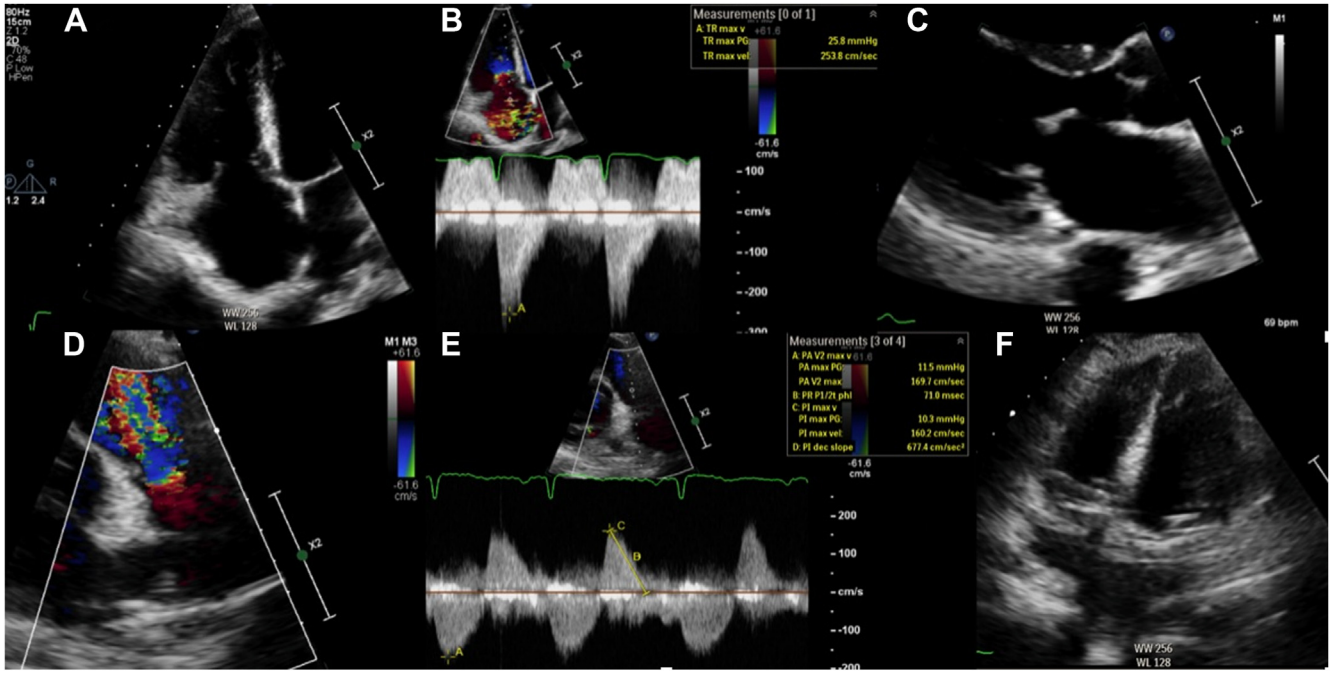

Figure 1. Multivalvular carcinoid heart disease (CHD) with semi-open tricuspid valve (**A**) and severe regurgitation (**B**), restricted mitral valve mimicking rheumatic appearance (**C**), severe pulmonary regurgitation with short pressure half time (**E**), and tricuspid/mitral prostheses with early right ventricular reverse remodelling (**F**).

Intraoperatively, all 4 valves were severely restricted and fibrotic and were not amenable to repair. Following excision of the anterior mitral leaflet, a #25 Magna Ease bioprosthesis (Edwards Lifesciences, Irvine, California, USA) was positioned to avoid the LV outflow tract. The PFO was closed using a running 4.0 prolene suture. The aortic valve leaflets were excised and replaced with a #21 Magna Ease bioprosthesis. Although ischemia time can be reduced by replacing right-sided valves with the clamp off, in this case, replacement was performed with the clamp on because of the often complex anatomy and difficult visualization inherent in carcinoid cases. Right-sided surgery also enables continuous cardioplegia administration so that ischemic time is minimized. The pulmonary valve cusps were excised. To ensure the #23 Magna Ease bioprosthesis would fit properly, an RV infundibuloplasty and pulmonary arterioplasty using bovine pericardium was performed first. The tricuspid valve leaflets were severely restricted, but the valve orifice was still small. The anterior leaflet required excision to accommodate a #25 Magna Ease bioprosthesis. An RV epicardial pacemaker lead was inserted with a tunneled screw. Cross-clamp and cardiopulmonary bypass times were 282 and 319 minutes, respectively.

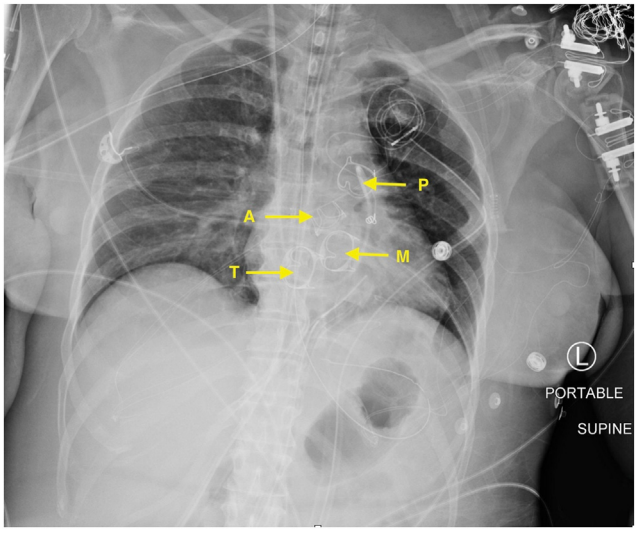

Figure 2. Postoperative chest x-ray showing bioprosthetic aortic (A), mitral (M), tricuspid (T) and pulmonic valves (P). Note absent sternotomy wires.

Intraoperative transesophageal echocardiogram revealed severe RV dilatation and dysfunction. Hemodynamic data confirmed this (central venous pressure 30 mm Hg, mean pulmonary arterial pressure 35 mm Hg, cardiac index 1.3 L/min/m^2). She was 10L positive because of a prolonged pump time and pre-existing RV failure. In addition to standard drains, JP drains were placed in the pericardial space to minimize fluid accumulation and cardiac tamponade. A large left pleural effusion was manually removed. A diaphragmatic incision was made to relieve intra-abdominal pressure. Her sternum was kept open because of RV dysfunction and severe edema. The inferior pericardium was reapproximated. A mesh device normally used for abdominal hernia repair surgery provided temporary sternal coverage. Her coagulopathy was managed with blood products, multiple packings, and topical agents.

Pathologic specimens confirmed changes consistent with CHD of all 4 valves. All leaflets/cusps were fibrotic and thickened. Their surfaces had areas of cellular thickening containing stellate-looking cells and increased mucopolysaccharides with some neovascularization. Right-sided valvular abnormalities were more pronounced, including greater thickening, subvalvular shortening, chordal thickening and fusion, and more abundant leaflet/cusp surface changes.

Postoperatively, she required RV support with multiple pressors and inhaled nitric oxide. Extracorporeal membrane oxygenation was not an option, as it is used as a bridge to destination therapy at our centre. Her coagulopathy and metastatic NET were exclusionary. Her hemodynamics improved when in sinus rhythm. Arrhythmias (atrial fibrillation, junctional rhythm, complete heart block) were managed with antiarrhythmics and transient atrioventricular sequential pacing. The sternum was closed on postoperative day 7, using conventional methods with stainless steel wires reinforced with sternal plates and dressed with a negative pressure dressing. By 2 weeks, on TTE, biventricular size normalized, and function improved (left normal, right mildly to moderately reduced). Following prolonged intubation (caused by pneumonia and severe deconditioning), she was extubated after 3 weeks. She was repatriated to her local hospital by 6 weeks, off oxygen, and ambulating with a walker. Her metastatic NET remained stable during follow-up with urinary 5-HIAA levels of 334 and 321 μmol/L at 2 and 3 months postdischarge, respectively. At 9 months, computed tomography showed decreases in the size of liver metastases and small bowel mass with no new metastatic sites. At 4-, 9-, and 19-month follow-ups, she was still ambulatory, off oxygen, and had a stable NET burden.

Discussion

CHD develops in 20% to 50% of NET patients with carcinoid syndrome.[1] In the presence of metastatic hepatic disease, tumour secretagogues such as serotonin enter the venous circulation.[1] Fibrous plaques deposit and encase the right-sided valves and subvalvular apparatus resulting in marked leaflet thickening, retraction or regurgitation.[1,2] In < 10%, left-sided valvular disease occurs caused by bronchial NET, a PFO, or extremely high levels of circulating vasoactive substances.[1]

CHD has high mortality and can progress rapidly.[1] Cardiac surgery improves symptoms and survival.[1,3] Tricuspid valve replacement (TVR), preferably with a tissue prosthesis, is recommended.[1] In the presence of more than mild pulmonary regurgitation, pulmonary valve replacement (PVR) further improves survival compared with TVR alone.[1] Significant mitral or aortic valve disease may need correction.[1]

There is limited experience with QVR for CHD. In the largest series of patients undergoing QVR for CHD (n = 7), 6 had 4 valves replaced at the same time, 5 with concomitant right ventricular outflow tract enlargement. All survived immediately postoperatively, but 1 died of heart failure on postoperative day 6. Late deaths were reported at 5, 30, and 39 months and caused by progression of carcinoid disease.[4] Although early surgical mortality is high, risk assessment must be individualized, as there are only palliative alternatives.

The 2022 European Neuroendocrine Tumour Society guidelines favour bioprosthetic over mechanical valve replacement for CHD because of higher bleeding risk with anticoagulation caused by concomitant liver disease in most NET patients; need for future invasive procedures to control tumour burden, requiring anticoagulation interruption; and life expectancy in patients with CHD.[1] In our review of QVR for CHD, multivalvular replacement used prostheses that were only mechanical,[4] both mechanical and tissue,[5] and bioprosthetic alone.[6] One report described repair for the left- but not right-sided valves.[7]

To our knowledge, this is the first report of QVR for advanced CHD in Canada. Our patient had a prolonged hospital course because of her advanced NYHA class, RV dysfunction, and physical deconditioning. Despite this, she had early recovery of cardiac function and a good outcome at 19 months follow-up. This is consistent with observations in the largest case surgical series of QVR (n = 7), in which postoperative cardiac function (RV function in 3, LV size in 5) and functional status (n = 6) improved in most patients.[4]

Intraoperatively, the primary obstacle is the length of the operation and the need for meticulous myocardial protection. A clear, well-communicated surgical plan and meticulous attention to operative techniques and hemostasis reduces the risk of procedural delays and setbacks requiring added pump time. Volume management is challenging. Preoperatively, overdiuresis risks volume depletion, renal injury, and hypotension, whereas underdiruesis risks overload compounded by additional fluids given intraoperatively and a long time on cardiopulmonary bypass.

The decision to operate on advanced CHD is complex. Despite our patient's advanced condition, cardiac surgery was undertaken for several reasons. She had a low-grade NET with a favourable response to therapy and, left unoperated, had a dismal prognosis. She lacked significant comorbidities, including risk factors (smoking, preoperative cytotoxic chemotherapy, older age) associated with higher mortality following CHD surgery.[3] Her surgery was performed at a centre experienced with CHD. She strongly desired surgery. This underlines the importance of shared decision making.

Conclusions

Operative management for CHD with quadruple valve involvement is complex and carries high risk. However, QVR is feasible and may be pursued after shared decision making

between multidisciplinary teams and the most important stakeholder, the patient.

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Ethics Statement

The research reported has adhered to the relevant ethical guidelines.

Patient Consent

The authors confirm that a patient consent form has been obtained for this article.

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Disclosures

The authors have no conflicts of interest to disclose.

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