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INTERMEDIATE

CASE REPORT: CLINICAL CASE

Carcinoid Crisis–Induced Acute Systolic Heart Failure

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ABSTRACT

Carcinoid crisis is a life-threatening manifestation of carcinoid syndrome characterized by profound autonomic instability in the setting of catecholamine release from stress, tumor manipulation, or anesthesia. Here, we present an unusual case of carcinoid crisis leading to acute systolic heart failure requiring mechanical circulatory support. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:2068–71) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENT ILLNESS

A 59-year-old woman with a stage IV, World Health Organization grade 2 ileal neuroendocrine tumor was referred for transcatheter arterial chemoembolization (TACE) of extensive bilobar hepatic metastases (Figure 1A). Two years prior, she underwent ileocolectomy and began octreotide depot injections (escalated to 60 mg/month) to manage diarrhea and flushing from carcinoid syndrome. Transthoracic echocardiography performed 1 month prior to TACE revealed normal biventricular size and function.

LEARNING OBJECTIVES

- To review and be aware of the perioperative management of carcinoid crisis.
- To discuss the management of acute systolic heart failure in the setting of carcinoid crisis.
- To recognize how high-dose octreotide could exacerbate cardiogenic shock.

The patient's admission vital signs were normal. Pre-operative findings were unremarkable aside from mildly abnormal liver function test results. Pre-procedurally, she received an octreotide infusion at 150 μg/h as well as H1- and H2-blockers for carcinoid syndrome prophylaxis. During the TACE procedure, performed under general anesthesia, an emulsion of doxorubicin and mitomycin followed by embolization was administered to the largest lesions in hepatic segments 2 and 4. Her intraoperative course was notable for tachycardia and hypertension managed with beta-blockade. Given concern for carcinoid crisis secondary to TACE, the patient's octreotide infusion was increased to 300 μg/h. The procedure was completed uneventfully, and she was admitted to the

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hospital for a planned 24-h course of continuous octreotide at 150 μg/h followed by subcutaneous injections of octreotide 150 μg 3 times daily until discharge. Within 12 h of hospital admission, the patient developed progressive shock and respiratory failure requiring high-flow nasal cannula. Physical examination disclosed bilateral rales, cool extremities, and tachycardia without murmurs or jugular venous distension.

MEDICAL HISTORY

The patient additionally had a history of hypertension, hyperlipidemia, and depression.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis included cardiogenic shock from acute coronary syndrome, acute systolic heart failure, and carcinoid crisis.

INVESTIGATIONS

Lactate was 4.8 mmol/l (normal range: 0.5 to 2.2 mmol/l), troponin 6.5 μg/l (normal range <0.05 μg/l), and B-type natriuretic peptide 475 pg/ml (normal range <82 pg/ml). Chest radiography revealed new diffuse interstitial opacities consistent with pulmonary edema. Electrocardiography showed sinus tachycardia with new ST-segment elevation and T-wave inversions in leads V_1 and V_2. Transthoracic echocardiography disclosed severely depressed left ventricular function (ejection fraction <20%) with akinesis of apical segments and preserved contraction of basal segments (Videos 1A and 1B).

MANAGEMENT

Dobutamine and vasopressin were administered for cardiogenic shock. The patient was emergently taken to the cardiac catherization laboratory for coronary angiography, which revealed diffuse coronary vasospasm without significant atherosclerotic plaques (**Figure 2**, Videos 2A and 2B). On inopressors, her cardiac index (CI) by thermodilution was 1.15 l/min/m^2, left ventricular end-diastolic pressure 40 mm Hg, and systemic vascular resistance (SVR) 5,213 dyn·s·cm^{-5}. Because of concern for catecholamine excess, the dobutamine and vasopressin infusions were discontinued in favor of milrinone and nitroprusside. The patient's CI improved to 1.44 l/min/m^2 during the peak nitroprusside challenge. The octreotide infusion was increased to 500 μg/h, and intermittent octreotide boluses of 500 μg were administered to widen her narrow pulse pressure from presumed catecholamine-driven vasoconstriction.

Despite these interventions, cardiogenic shock persisted (CI 1.3 to 1.5 l/min/m^2), resulting in anuric renal failure necessitating continuous renal replacement therapy. The troponin level rose above the laboratory's upper limit of detection (>81 μg/l). The patient thus returned to the cardiac catherization laboratory several hours later for placement of a percutaneous axillary ventricular assist device (Impella CP, Abiomed, Danvers, Massachusetts) under general anesthesia. Despite Impella flow rates of 3.5 l/min with mean arterial pressure of 60 to 70 mm Hg, her cardiac output as measured by thermodilution remained <2.0 l/min, with SVR of 3,700 dyn·s·cm^{-5}. This discrepancy was believed to

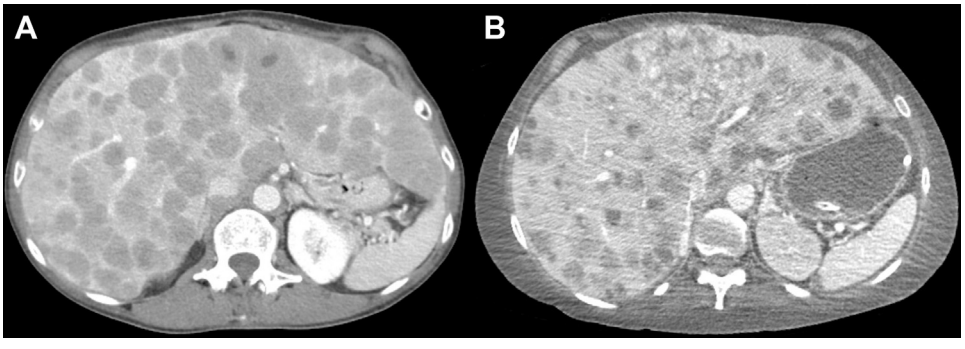
ABBREVIATIONS AND ACRONYMS

CI = cardiac index

SVR = systemic vascular resistance

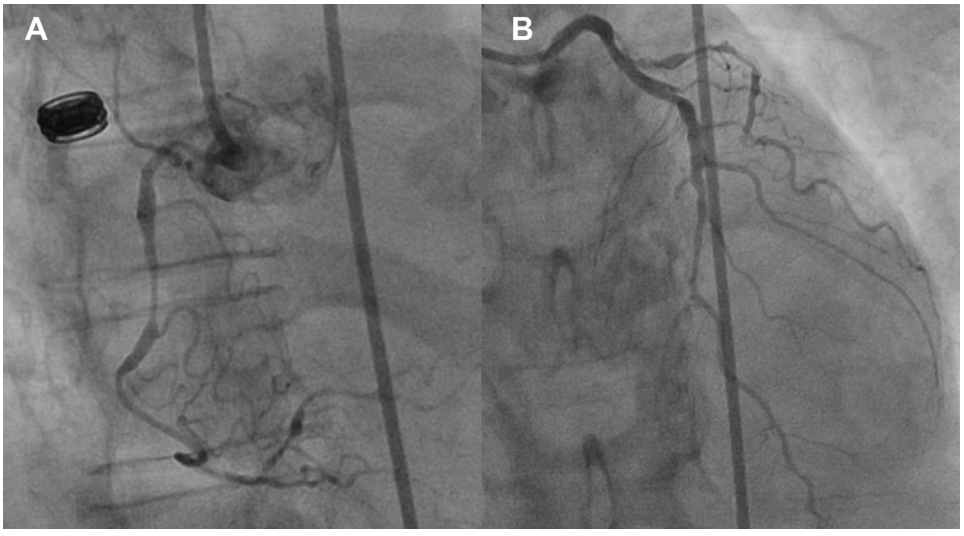
TACE = transcatheter arterial chemoembolization

FIGURE 1 Contrast-Enhanced Computed Tomography of the Abdomen



(A) Before transcatheter arterial chemoembolization (TACE), with nearly 70% of liver parenchyma replaced by hepatic metastases. **(B)** Two weeks post-TACE, with extensive hepatic necrosis of both embolized and untreated lesions.

FIGURE 2 Coronary Angiogram With Femoral Arterial Access



(A) Right coronary artery angiography showing diffuse vasospasm. **(B)** Left coronary artery angiography showing diffuse vasospasm throughout the left main coronary artery, left anterior descending coronary artery, and left circumflex coronary artery.

be due to severe systemic vasoconstriction exacerbated by high doses of octreotide. As a result, the octreotide infusion was slowly weaned to 50 μg/h. With unchanged Impella settings, cardiac output measured by thermodilution improved to 3.3 l/min, and SVR decreased to 1,500 dyn·s·cm^{-5}.

Over the following week, the patient's cardiac function completely recovered, permitting discontinuation of milrinone and removal of the Impella device (Video 1C). She was extubated to ambient air. She required hemodialysis for 5 weeks. Chromogranin A level decreased from 10,000 ng/ml (normal range 0 to 160 ng/ml) prior to TACE to 3,000 ng/ml on postoperative day 21. Contrast-enhanced computed tomography performed 2 weeks following TACE showed extensive necrosis of both untreated and embolized liver lesions (**Figure 1B**). The patient's hospital course was complicated by delirium, critical illness myopathy, upper gastrointestinal bleeding, and small bowel obstruction, all of which were managed conservatively.

DISCUSSION

Acute systolic heart failure due to carcinoid crisis has been rarely described, with catecholamine excess postulated as a potential etiology (1). Our patient's markedly elevated troponin levels suggested widespread cardiac ischemia resulting in apical akinesis and severe global hypokinesis. This was likely driven by diffuse coronary vasospasm from carcinoid crisis-induced serotonin and catecholamine surge. We thus opted for noncatecholamine inopressors, afterload reduction, and temporary mechanical circulatory support to minimize iatrogenic catecholamine toxicity. We simultaneously treated carcinoid crisis with high-dose octreotide infusion.

Octreotide has been used for both carcinoid crisis prophylaxis and treatment. Pre-operative prophylaxis with subcutaneous octreotide (150 to 500 μg) is often administered either immediately preoperatively or up to 2 weeks pre-procedurally (2). Prophylactic octreotide infusion of 50 to 100 μg/h and treatment infusion of up to 300 μg/h have both been described (3). Notably, tachyphylaxis to octreotide can occur. Our patient required progressively higher doses of octreotide than have been previously described (4).

Although important for the management of carcinoid crises, the physiological effects of octreotide carry some risk. Increased systemic and pulmonary pressures and decreased cardiac output can occur within 30 min of intravenous octreotide administration (5). As our patient's carcinoid crisis resolved, the high-dose octreotide infusion likely contributed to markedly elevated SVR. Like all mechanical circulatory support devices, the ability of the Impella CP device to provide forward flow (up to 4.0 l/min) is sensitive to systemic afterload, with higher left

ventricular-aortic pressure gradients resulting in lower pump flow (6). In this case, severe systemic vasoconstriction contributed to persistently low cardiac output despite mechanical circulatory support. While on high-dose octreotide, our patient's cardiac output measured by thermodilution (1.8 l/min) was consistently lower than the flow reported on the Impella monitor (3.5 l/min). This mismatch resolved once the octreotide infusion was weaned and SVR improved.

Finally, our patient's cardiogenic shock likely contributed to worsened carcinoid crisis through positive feedback mechanisms. The extent of hepatic tumor necrosis seen on subsequent imaging was more pronounced than expected after focal TACE. This suggests that severe hepatic hypoperfusion from cardiogenic shock triggered diffuse necrosis of liver metastases supplied exclusively by the hepatic artery (**Figure 1B**). This extensive tumor necrosis markedly increased the severity and duration of the carcinoid crisis, which in turn increased the severity of cardiac failure.

FOLLOW-UP

The patient was discharged to a rehabilitation facility after a 7-week hospitalization. Four months following TACE, the patient reported no symptoms of the carcinoid syndrome. Her cardiac and renal function have recovered, and she continues to rehabilitate from her critical illness myopathy.

CONCLUSIONS

This case offers several insights into the diagnosis and management of circulatory failure from carcinoid crisis. We are among the first to describe acute systolic heart failure from carcinoid crisis due to both catecholamine excess and diffuse coronary vasospasm. We postulate that noncatecholamine inopressors and mechanical circulatory support can mitigate iatrogenic catecholamine excess. Our experience indicates that high-dose octreotide administration can result in increased systemic afterload that worsens circulatory shock and limits the efficacy of mechanical circulatory support devices. Clinicians should maintain a high index of suspicion for iatrogenic systemic vasoconstriction when administering high-dose octreotide for carcinoid crisis.

AUTHOR DISCLOSURES

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KEY WORDS acute heart failure, cardiac assist devices, inotropes

APPENDIX For supplemental videos, please see the online version of this paper.