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Case Report

From Hip to Heart: A Comprehensive Evaluation of an Infiltrative Cardiomyopathy

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ABSTRACT

Infiltrative cardiomyopathies are an increasingly recognized cause of heart failure warranting systematic evaluation. Given overlap of clinical and imaging findings among etiologies of infiltrative cardiomyopathies, comprehensive evaluation, including a history and physical examination, advanced cardiac imaging, and sometimes endomyocardial biopsy, is required for diagnosis. We report a case of infiltrative cardiomyopathy in which endomyocardial biopsy confirmed diagnosis of cobalt-induced cardiomyopathy. The novel teaching points highlighted by this case report include identification of heavy-metal toxicity as a cause of infiltrative cardiomyopathy, and the outline of a diagnostic approach and management for cobalt-induced cardiomyopathy.

RÉSUMÉ

Le fait que les cardiomyopathies infiltrantes sont de plus en plus reconnues comme la cause de l'insuffisance cardiaque justifie une évaluation systématique. Puisque les résultats cliniques et d'imagerie se recoupent entre les étiologies des cardiomyopathies infiltrantes, l'évaluation exhaustive, y compris les antécédents et l'examen physique, les techniques avancées en imagerie cardiaque et parfois la biopsie endomyocardique, est nécessaire au diagnostic. Nous présentons un cas de cardiomyopathie infiltrante pour lequel la biopsie endomyocardique a permis de confirmer le diagnostic d'une cardiomyopathie induite par le cobalt. Parmi les points à enseigner illustrés dans cette observation, on cite la reconnaissance de la toxicité des métaux lourds comme une cause de cardiomyopathie infiltrante, et la vue d'ensemble de l'approche diagnostique et de la prise en charge de la cardiomyopathie induite par le cobalt.

Infiltrative cardiomyopathies (ICs) are an increasingly recognized subset of nonischemic cardiomyopathy. Cobalt toxicity has been identified as a cause of subacute IC and can be accompanied by noncardiac features such as thyroid goiter and polycythemia. We report a case in which a thorough evaluation of IC reached the diagnosis of a rare cobalt-induced cardiomyopathy.

Case

A 67-year-old woman with a history of bilateral hip replacement surgery 10 years prior and systemic hypertension was transferred to our tertiary-care center for evaluation of new-onset biventricular systolic dysfunction after presenting to an outside hospital with shortness of breath of 3-week duration. She was noted to be tachycardic, with a heart rate of 119 beats per minute, and borderline hypotensive, with blood pressure of 94/62 mm Hg. An electrocardiogram demonstrated sinus tachycardia, low voltage, and right bundle branch block without acute ST-segment or T-wave changes (Supplemental Fig. S1). Lab tests were significant for elevated N-terminal pro-brain natriuretic peptide (N-terminal pro b-type natriuretic peptide) of 6033 pg/mL and mildly elevated troponin levels of 0.35 ng/mL. Chest computed tomography with contrast ruled out a pulmonary embolism but was notable for mediastinal and bilateral hilar lymphadenopathy (Supplemental Fig. S2). An echocardiogram revealed a left ventricle (LV) ejection fraction of 20%-25%, with global hypokinesis, a LV wall thickness of 1.1 cm, and a large circumferential pericardial effusion with features concerning for tamponade (Supplemental Figs. S3 and S4). She underwent pericardiocentesis, which yielded bloody

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Novel Teaching Points

- Heavy-metal toxicity can be a cause of infiltrative cardiomyopathy.
- This report outlines an approach to diagnosis and management of cobalt-induced cardiomyopathy.

fluid with elevated neutrophils but no evidence of malignancy on cytology. Bacterial, fungal, and acid-fast bacilli cultures of the pericardial fluid were negative. Left and right heart catheterization demonstrated normal coronary arteries (Videos 1 and 2, view videos online), and elevated filling pressures (right atrium—15 mm Hg; pulmonary capillary wedge pressure—30 mm Hg) with a low cardiac index of 1.5 L/min per m^2, respectively, which was consistent with cardiogenic shock. She was transferred to the intensive-care unit, where she was started on dobutamine infusion at 2.5 mcg/kg per minute, which was increased to 5 mcg/kg per minute, along with loop diuretic therapy.

Further investigations showed normal thyroid stimulating hormone, thiamine, and ferritin levels. Evaluation for plasma cell dyscrasia was unremarkable, and a rheumatologic workup was also negative. Given the clinical concern for sarcoidosis and malignancy, a mediastinal lymph node biopsy was performed, which showed mild lymphocytic infiltration without granulomatous inflammation or malignancy. Cardiac magnetic resonance imaging with gadolinium demonstrated diffuse late gadolinium enhancement throughout the LV (Supplemental Fig. S5).

A comprehensive review of systems (ROS) obtained upon admission was notable for bilateral hip replacement surgery, and was negative for a low-protein diet or alcohol use. Serum cobalt and chromium levels were obtained and found to be significantly elevated, at 121 mcg/L (normal level $\leq$ 1 mcg/L) and 46.2 mcg/L (normal level $\leq$ 5 mcg/L), respectively, raising the suspicion level for cobalt-induced cardiomyopathy. An endomyocardial biopsy (EMBx) demonstrated lymphocytic infiltrate without evidence of granulomatous inflammation or amyloid protein deposition. Electron microscopy of the myocardium showed mitochondrial changes concerning for heavy-metal toxicity. Bilateral hip magnetic resonance imaging showed abnormal periarticular soft tissue of the left hip, and complex fluid in the left iliopsoas bursa consistent with pseudotumor formation. This condition was identified as the source of spillage of heavy-metal ions into the blood circulation. Following a patient-centered multidisciplinary discussion, the patient underwent revision of the left cobalt-alloy hip prosthesis with a ceramic hip prosthesis. The patient was placed on oral N-acetyl cysteine chelation therapy and discharged with continuous dobutamine infusion at 5 mcg/kg per minute. At the 1-month follow-up clinic visit, serum cobalt levels had declined to 33.1 mcg/L; however, echocardiogram revealed persistence of severe LV systolic dysfunction. The patient was readmitted to the hospital with worsening heart failure symptoms, and milrinone 0.25 mcg/kg per minute was added to the dobutamine infusion of 5 mcg/kg per minute. Serum cobalt levels further decreased to <11 mcg/L. She was urgently evaluated for advanced heart failure therapies, owing to failure to wean dual inotropic therapy, and underwent successful orthotropic heart transplantation. Electron microscopy of the explanted native heart showed cardiomyocytes with large lipid droplets (Fig. 1A) and enlarged distorted mitochondria (Fig. 1B). Myocardial tissue cobalt levels obtained from the native heart were elevated at 0.95 mcg/g (reporting limit: <0.018 mcg/g), consistent with cobalt-induced cardiomyopathy.

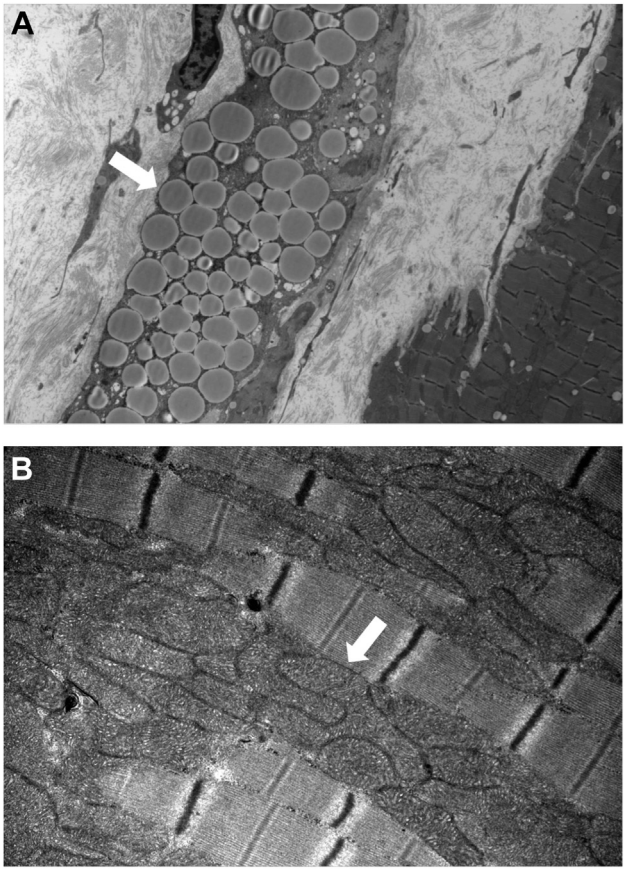

Figure 1. (**A**) Electron microscopy image illustrates large lipid deposits within the cardiomyocyte. (**B**) Electron microscopy image illustrates distorted mitochondria within the cardiomyocyte.

Discussion

Cobalt toxicity has been described in heavy beer drinkers as "Quebec beer-drinker's cardiomyopathy," because cobalt was used to stabilize foam in beer. In patients with a cobalt-alloy prosthesis, corrosion of the joint can generate metal debris that circulates in the bloodstream and leads to deposition in distant organs.[1,2] However, the threshold at which serum and tissue levels of cobalt cause cardiomyopathy is undefined.[3]

Reaching a diagnosis of cobalt-induced cardiomyopathy involves a comprehensive evaluation for infiltrative causes of cardiomyopathy, including a thorough medical history and ROS. In our case, the patient presented with new-onset, rapidly progressing heart failure symptoms. Her past medical history was significant for history of bilateral hip replacement surgery, which may not have appeared relevant on the initial presentation. Subsequently, the findings of low-voltage QRS complexes on electrocardiogram, circumferential pericardial effusion

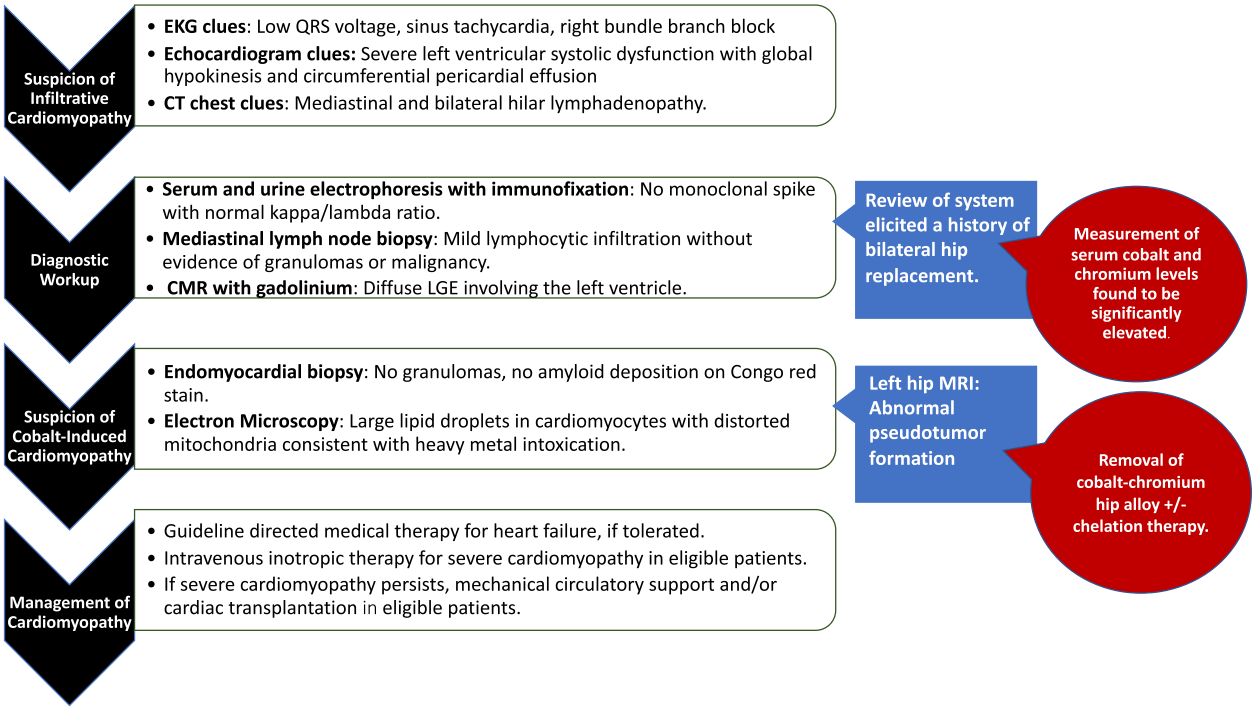

Figure 2. Diagram shows the diagnostic workup and management of cobalt-induced cardiomyopathy. CMR, cardiac magnetic resonance; CT, computed tomography; EKG, electrocardiogram; LGE, late gadolinium enhancement; MRI, magnetic resonance imaging.

seen on echocardiogram, mediastinal and bilateral hilar lymphadenopathy seen on computed tomography of the chest, and cardiac magnetic resonance features (diffuse late gadolinium enhancement) raised the suspicion of IC. Once the suspicion for IC had been raised, the history of bilateral hip replacement redirected the diagnostic process to measurement of serum cobalt and chromium levels, as cases of cobalt-induced cardiomyopathy have previously been described in patients with cobalt–chromium hip alloys. Serum cobalt levels of >7 parts per billion were an indication for hip magnetic resonance imagine, despite an absence of joint symptoms. EMBx to identify or rule out the cause of IC became critical in this evaluation, with electron microscopy increasing our suspicion of heavy-metal toxicity. Electron microscopy of the EMBx in this case was not classic for cobalt toxicity (absence of dense osmophilic intramitochondrial particles) but did show mitochondrial changes of early heavy-metal toxicity. Pathologic examination of the native heart posttransplantation did reveal classic features of heavy-metal toxicity, along with elevated tissue cobalt levels.

Management of cobalt-induced cardiomyopathy due to a cobalt-alloy prosthesis hinges on the removal of the cobalt source, which may lead to improvement in cardiac function, as seen in some patients.[4,5] The role of chelating agents remains unclear.[3] Whether cobalt-induced cardiomyopathy should also be managed with guideline-directed medical therapy for heart failure remains undetermined. Once cobalt cardiomyopathy has progressed to end-stage heart failure, cardiac transplantation is the preferred long-term treatment, as in the case of our patient. Therapy with left ventricular assist devices can be challenging in these patients, owing to the presence of concomitant right ventricular failure or to small left ventricular size with accompanying thickened myocardium. The diagnostic workup and management of cobalt-induced cardiomyopathy is illustrated in Figure 2.

Conclusion

Cobalt-induced cardiomyopathy is a potentially reversible cause of IC, with the diagnosis hinging on comprehensive evaluation for IC, including a thorough ROS assessing for history of joint-replacement surgeries. This condition should be suspected in patients with nonischemic cardiomyopathy with a history of cobalt–chromium alloy arthroplasties. Treatment includes routine heart failure management and removal of the cobalt source; the role of chelation therapy remains unclear. Once the condition progresses to end-stage heart failure, cardiac transplantation is the treatment of choice for eligible patients.

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Disclosures

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2021.06.010.