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Severe Cardiomyopathy Due to Arthroprosthetic Cobaltism: Report of Two Cases with Different Outcomes

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Abstract

Cobalt-induced cardiomyopathy is a well-known but uncommon disease, and the physician must maintain a high index of suspicion in order to make a timely diagnosis. We report two patients with cobalt-induced cardiomyopathy. Both patients developed progressively worsening symptoms of cobalt toxicity following revision of a fractured ceramic-on-ceramic total hip replacement to a metal-on-polyethylene bearing. In both patients, echocardiography showed LV hypertrophy, biventricular systolic dysfunction, and a large amount of pericardial effusion. Due to decompensated heart failure, both patients were initially considered candidates for heart transplantation. One patient was diagnosed with cobalt-induced cardiomyopathy before transplantation. He received cobalt chelation therapy and revision surgery, which led to complete recovery of heart function. In the other patient, the diagnosis was not made until the time of heart transplantation. The gross examination of the explanted heart revealed typical features of cobalt cardiotoxicity, which was then diagnosed as cobalt-induced cardiomyopathy. These cases emphasise the importance of early diagnosis and prompt treatment of cobalt intoxication.

Keywords Cobalt · Cardiomyopathy · Metallosis · Heart failure · Prognosis · Transplantation

Introduction

Cobalt cardiotoxicity has been recently described in patients who have undergone hip replacement and experienced prosthesis-mediated intoxication [1–4]. Metallic degradation of joint arthroplasties can release alloys (e.g. cobalt, chromium, titanium, and aluminium) into the bloodstream. In excess, cobalt blocks cellular metabolism and can damage multiple organs. Several case reports have been presented attributing a wide range of symptoms to elevated cobalt concentrations. Most reported symptoms are either neurological, cardiological, or endocrinological [4–10]. Many cases occur after off-label replacement of broken ceramic hips by metal parts [2, 11, 12]. Retained ceramic microparticles are believed to cause wear on the metal parts, resulting in metallosis [13].

Previous case reports noted that heart failure can improve after cobalt toxicity from an orthopaedic prosthesis is identified and the source is removed [2]. The present report describes rare cases of two patients who developed severe cardiomyopathy and advanced heart failure after revision total hip replacement for fracture of a ceramic liner. One patient subsequently experienced complete cardiac recovery after early diagnosis and prompt management; the other patient underwent heart transplantation due to delayed diagnosis. We present a comprehensive workup regarding the diagnosis of cobalt-induced cardiomyopathy, including echocardiography, magnetic resonance imaging, pericardial fluid analysis, and pathologic features.

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Case Reports

Case 1

In January 2016, a 52-year-old man was referred to our cardiology centre for advanced heart failure management. His past medical history was positive for hypertension treated with amlodipine 5 mg daily. An alcoholic, he had a history of osteonecrosis of the femoral head, for which he underwent bilateral total hip replacement. In 2002, he underwent left total hip arthroplasty with a ceramic head-on-polyethylene liner implant, followed by right total hip arthroplasty with a ceramic-on-ceramic bearing joint in 2005. In August 2014, the ceramic inner socket liner for the left hip prosthesis fractured and was replaced with a new bearing surface comprising a cobalt–chromium alloy head and a polyethylene liner. At that time, a preoperative echocardiogram revealed normal biventricular systolic function with an estimated left ventricular ejection fraction (LVEF) of 65%. Left ventricular (LV) thickness was normal (posterior wall thickness in diastole [LVPWd], 1.0 cm). After revision surgery, he showed improvement initially but developed progressive hip pain with activity after a few months. Numbness and pain in the left hip were gradually exacerbated. One year after revision surgery (September 2015), the patient reported dyspnoea on exertion, progressive inefficiency, and fatigue. Neurologically, he had painful dysesthesia and paraesthesia distal to the left hip, proximal dominant muscle weakness, and bilateral sensorineural hearing loss. He particularly complained of orthopnea requiring urgent admission via the emergency room. An echocardiogram 15 months after revision surgery revealed moderate concentric LV thickening (1.2 cm) with moderately reduced systolic function (LVEF, 44%). Right ventricular (RV) systolic function was preserved with mild tricuspid regurgitation. There was a large amount of pericardial effusion, measuring 26 mm in thickness anteriorly and 12 mm posteriorly, without any sign of cardiac tamponade. The patient initially was considered to have idiopathic dilated cardiomyopathy. He was treated with intravenous diuretics, with improvement of symptoms, and discharged with treatment with an angiotensin-converting enzyme (ACE) inhibitor, a beta-blocker, digitalis, and diuretics. Attempts to add neurohormonal therapy were limited by elevated creatinine level and recurrent decompensation. LVEF decreased substantially to 32% within the following 2 months. Follow-up transthoracic echocardiography revealed continued decrease in LVEF with thickened LV wall and serial increases in left atrial and LV dimensions (Table 1). Cardiac magnetic resonance imaging showed biventricular dysfunction and delayed contrast imaging showed no delayed enhancement

Table 1 Serial change in echocardiographic parameters in cobalt-induced cardiomyopathy

	IVSd (mm)	LVPWd (mm)	LVIDd (mm)	IVSs (mm)	LVPWs (mm)	LVIDs (mm)	LVEF (%)	LA (mm)	E/E′	MR	TR	TR velocity (m/s)	Pericardial effusion
Aug-14	10	10	54	18	17	28	65	44	9.4	Trivial	Mild	2.5	No
Oct-15	12	12	57	17	17	45	44	49	14.19	Trivial	Mild	3.37	Large
Dec-15	13	12	53	14	15	48	32	50	20	Trivial	Mild	2.34	Large
Jan-16	12	12	57	13	15	51	13	53	12	2	4	2.5	Moderate
May-16	13	13	58	17	18	46	35	42	9	1	1	2.7	Moderate
Jun-16	12	12	60	19	19	35	49	41	26	Trivial	Trivial	2.8	Small
Aug-16	12	11	52	14	15	37	56	43	9	Trivial	1	2.3	Minimal
Dec-16	12	12	53	15	17	36	63	44	7	Trivial	1	2.4	No

IVSd interventricular septal thickness at end-diastole, *LVPWd* left ventricular posterior wall thickness at end-diastole, *LVIDd* left ventricular internal dimension at end-diastole, *IVSs* interventricular septal thickness at end-systole, *LVPWs* left ventricular posterior wall thickness at end-systole, *LVIDs* left ventricular internal dimension at end-systole, *LVEF* left ventricular ejection fraction, *LA* left atrium, *E* mitral peak early diastolic filling velocity, *E′* mitral annulus early diastolic motion, *MR* mitral regurgitation, *TR* tricuspid regurgitation

lesion. A T2-weighted image showed no definite abnormal signal intensity lesion. One month prior to admission to our centre, the patient needed inotropic support with dobutamine due to hemodynamic instability. He was transferred to our centre for advanced heart failure management.

At admission to our hospital, electrocardiography showed sinus tachycardia (104 bpm) with poor R-wave progression. Accounting for LV mass (334 g), a relatively low voltage was observed. Chest radiography showed globular enlargement of the cardiac shadow (cardiothoracic ratio, 73%), resulting in a water bottle configuration, hazy hilar enlargement, and bilateral pleural effusion. Echocardiography showed symmetrical increases in LV and RV wall thickness (LVPWd, 13 mm) with severe biatrial enlargement. The LV was not dilated, but systolic function was severely decreased (LVEF, 13%). The estimated pulmonary artery systolic pressure was 25 mm Hg plus right atrial pressure (estimated at 15–20 mm Hg based on the appearance of the inferior vena cava). There was a moderate amount of pericardial effusion without any signs of hemodynamic significance. No evidence of myocardial ischaemia was detected by electrocardiogram, cardiac enzymes, or echocardiogram. Laboratory data showed polycythemia (haemoglobin level, 18.3 g/dL), mild elevation of C-reactive protein (1.8 mg/dL), hyponatraemia (118 mmol/L), hyperkalemia (5.5 mmol/L), azotemia (1.3 mg/dL), and liver function test abnormalities suggesting passive hepatic congestion (aspartate aminotransferase, 251 U/L; alanine aminotransferase, 232 U/L; alkaline phosphatase, 76 U/L; and total bilirubin, 2.3 mg/dL). B-type natriuretic peptide was elevated to 1686 pg/mL. The troponin I level was normal (0.373 µg/L), and creatine kinase–muscle/brain (CK-MB) was slightly elevated (9.9 ng/mL). An audiogram showed high-frequency hearing loss.

Initially, the causative role of the mentioned disorders was ignored, and the patient was suspected of having AL-type cardiac amyloidosis or autoimmune disease because of rapidly progressive heart failure, relatively low voltage on the electrocardiogram, concentric LV thickening, biatrial enlargement, and pericardial effusion. However, the results of the following tests were normal or negative: thyroid function test, autoantibodies, and serum and urine free light chain. In the absence of amyloidosis, the only other pattern that would be consistent with his condition was diffuse, fulminant myocarditis of toxic origin lacking clinical evidence of an infectious origin. During workup, the patient presented with progressive left hip pain and complaint of discomfort from a mass on the left groin. A simple radiograph (Fig. 1), an enhanced computed tomography (CT) study, and orthopaedic consultation were performed. The image finding showed a huge mass combined with a haemorrhagic component lining the acetabular area extending to the psoas compartment. The mass was highly suspected to be a metal-related granuloma, indicating severe metallosis.

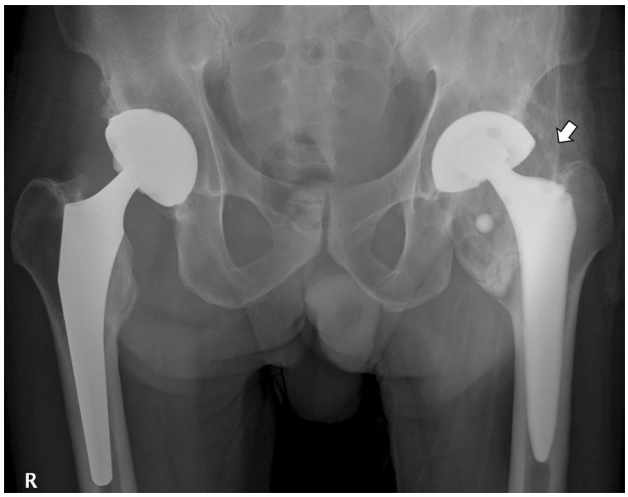

Fig. 1 Anteroposterior pelvis radiograph demonstrating radiodense area around the hip joint extended intrapelvic cavity

The cobalt level in aspirated fluid was 397,800 µg/L, and the chrome level was 236,000 µg/L. Additional workup was initiated, and in a heavy metals screening, the cobalt level in serum was 489.5 µg/L (normal range, 0–3.9 µg/L) and the chrome level was 84.2 µg/L (normal range, 0–3.0 µg/L). Cobalt-induced cardiomyopathy was suspected based on the clinical, laboratory, and imaging features. The patient had been considered ineligible for prosthesis removal surgery due to high operative cardiac risk, and from the time of the diagnosis of cobalt-induced cardiomyopathy to the removal of the prosthesis (68 days), therapy with a chelating agent (ethylene diamine tetraacetic acid [EDTA]) was administered at regular intervals of about 7 days. The cobalt level following the first EDTA administration decreased to 393 µg/L, but the patient was inotrope-dependent for 2 months, with a profoundly depressed LV function. Four months after admission, the patient became hemodynamically stable, but his cobalt level was 223.5 µg/L, which was significantly higher than the normal range. Since his vital signs were stable on low-dose inotropes (dopamine, 0.5 µg/kg/min) and echocardiography showed slightly improved LV systolic function (LVEF, 35%), he underwent a second revision surgery to remove the prosthesis and metallosis. During surgery, a massive metallosis and debris of the metal femoral head were found due to the visible presence of ceramic debris particles left over from the first revision surgery (Fig. 2). The black tissue was thoroughly removed, and the operative field was carefully cleaned. Exchange arthroplasty was performed with a new ceramic-on-ceramic bearing prosthesis, and the soft tissues contaminated with metal debris were removed as completely as possible. The patient tolerated the surgery without complications, and his postoperative period was without incident. Dobutamine and furosemide were discontinued. Shortly after hip replacement, the patient's plasma

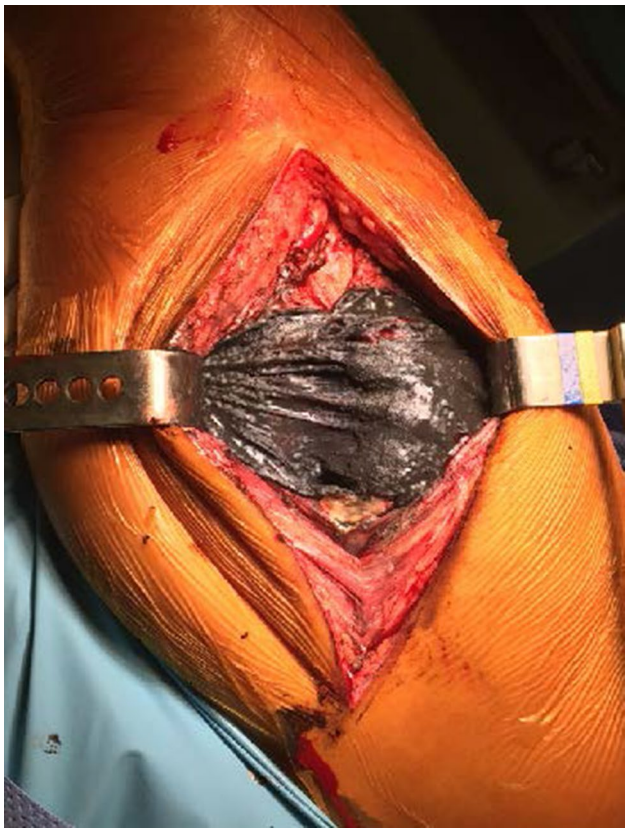

Fig. 2 Intraoperative finding showing dark staining of the surrounding soft tissue around the greater trochanter consistent with metallosis

cobalt and chromium concentrations decreased further to 111.0 and 34.5 µg/L, respectively, but not enough to allow chelation therapy to be stopped. This finding suggested that residual metallosis remained in the muscle and joint space after surgical debridement. Therefore, chelation therapy was maintained for 3 months after surgery, at which time the cobalt level was decreased to 30.17 µg/L. A repeat echocardiogram obtained 1 month after revision surgery showed normal systolic function of the LV (LVEF, 58%). LV hypertrophy regressed, as evidenced by a 24.9% decrease in LV mass index and a 15.4% reduction of relative wall thickness. RV function was normalised. There was small amount of pericardial effusion, and the inferior vena cava was not dilated with normal inspiratory collapse (Fig. 3). At a recent follow-up, the patient was stable, with no signs of local or systemic effects of cobalt. His neurological symptoms were improved, allowing him to walk without assistance.

Case 2

In April 2017, a 46-year-old man presented at the emergency department of our institution with New York Heart Association (NYHA) functional class 3 dyspnoea and orthopnea. He had essential hypertension and chronic kidney disease stage 3a (glomerular filtration rate, 30 mL/min/1.73 m^2), which had been diagnosed a year previously. He also had a history of osteonecrosis of the femoral head, for which he underwent bilateral total hip arthroplasty. In 2003, the patient underwent left total hip arthroplasty with a ceramic head-on-ceramic liner implant, followed by right total hip arthroplasty with a ceramic-on-ceramic bearing joint in 2004. In 2008, the ceramic head for the right hip prosthesis fractured and was replaced with a new bearing surface comprising a ceramic-on-metal prosthesis. During surgery, right ceramic head fracture and local metallosis were found. Four years later, in 2012, the right ceramic head was fractured again while he was playing soccer. The patient underwent a

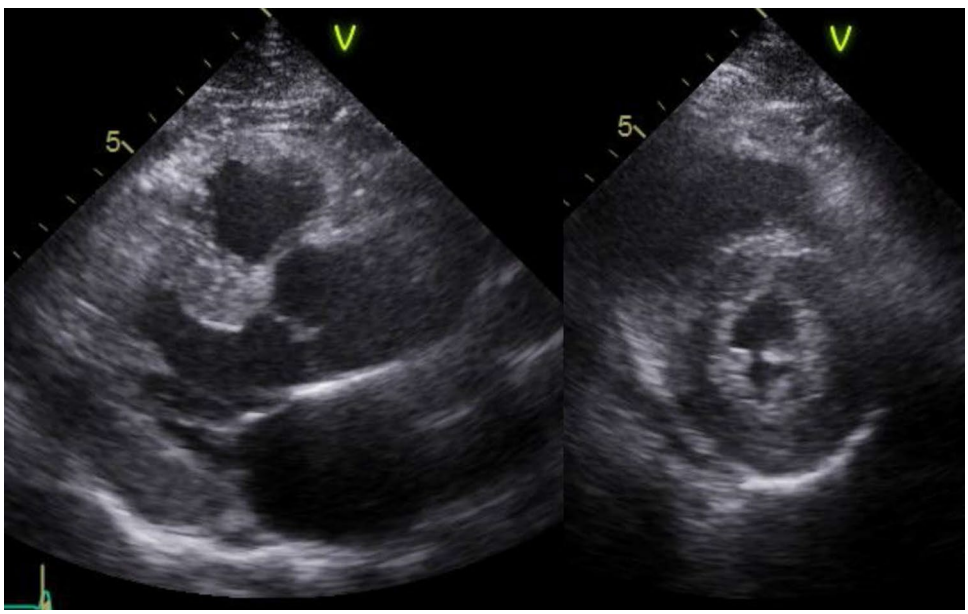

Fig. 3 An echocardiography obtained 1 month after revision surgery of patient 1. Parasternal long and short axis view showing complete recovery of left ventricular (LV) systolic function (LV ejection fraction, 58%) and regressed LV hypertrophy

second revision surgery. Multiple fractured particles of the ceramic head were observed on the medial surface of the fractured head. During the second revision surgery, the fractured ceramic head and the polyethylene liner were replaced with a 32-mm cobalt–chromium medium neck and a polyethylene liner. The surgical wound was repeatedly thoroughly cleaned. Six years after the second revision surgery, he developed sudden dyspnoea (NYHA functional class 3).

At admission, electrocardiography showed a sinus tachycardia (102 bpm). Chest radiography showed cardiomegaly (cardiothoracic ratio, 66%), hazy hilar enlargement, and bilateral pleural effusion. Echocardiography showed symmetrical increases in LV and RV wall thickness (LVPWd, 13 mm) with biatrial enlargement. The LV was not dilated, but systolic function was severely decreased (LVEF, 24%). There was a moderate amount of pericardial effusion with hemodynamic significance (Fig. 4). Laboratory data were normal except for azotemia (2.9 mg/dL) and B-type natriuretic peptide (> 5000 pg/mL; normal value < 100 pg/mL). The troponin I level was normal (0.406 µg/L), and CK-MB was slightly elevated (17.6 ng/mL).

Initially, the patient was suspected of having an infiltrative cardiomyopathy, such as cardiac amyloidosis. However, the results of the following tests were normal or negative: thyroid function test, autoantibodies, and serum and urine free light chain. At that time, there was no clinical suspicion of cobalt-induced cardiomyopathy, and endomyocardial biopsy results showed nonspecific myocardial degeneration and fibrosis, and negative Congo-red stain. There was no inducible ischaemia on thallium single-photon emission computed tomography.

The patient was treated with diuretics with improvement of his symptoms and discharged with a beta-blocker, digitalis, and diuretics. ACE inhibitors were not prescribed due to unstable kidney function. Despite medical therapy, the patient repeatedly decompensated within the following 7 months. In September 2017, he visited the emergency department again for acute severe resting dyspnoea. Cardiac tamponade was diagnosed based on clinical and typical echocardiographic findings, and pericardiocentesis was performed, yielding 700 mL of serous fluid. Laboratory tests of the fluid showed 89 mg/dL glucose, 4.9 g/dL total protein, 652 IU/L lactate dehydrogenase, and 20.9 IU/L adenosine deaminase. Bacterial culture of the fluid showed no bacterial infection. Cytologic examination of the fluid showed no malignant cells, a red blood cell count of 800/mm^3, and a white blood cell count of 744/mm^3, with 61% polymorphonuclear leukocytes and 31% histiocytes. He was listed for combined heart and kidney transplantation for advanced heart and renal failure. His multiorgan failure subsequently progressed rapidly to include acute kidney injury, and 12 days before transplantation, he required continuous renal replacement therapy for fluid balance and metabolic control. Despite the administration of multiple high-dose inotropes, severe hemodynamic instability required venoarterial extracorporeal membrane oxygenation support on the day before transplantation. Refractory cardiogenic shock and acute kidney injury on chronic renal failure were the indications for combined heart and kidney transplantation. Kidney and heart donor grafts were available from a deceased 44-year-old woman who was ABO compatible. The postoperative course was uneventful. The gross examination of the explanted heart revealed a slightly increased heart weight (370 g) considering his small body stature. The LV was dilated, and the wall measured up to 2.1 cm in thickness. The RV wall and septum measured 1.2 and 1.8 cm in thickness, respectively. Microscopically, there were increased lipofuscin pigments and myocyte vacuolisation (Fig. 5). These were not specific findings but one of finding of cobalt-induced cardiomyopathy. At the electron microscopic level, swelling of the mitochondria (ranging 810–1500 nm) and occasional distortion of the cristae and outer membrane were noted. In addition, a pathognomonic feature of cobalt toxicity was found, comprising dense, osmophilic, intramitochondrial particles ~ 0.3–0.4 µm in diameter (Fig. 6).

A routine postoperative CT scan of the pelvis after kidney transplantation revealed a low-density mass with calcified rim and internal inhomogeneous hyperdensity in the right iliacus muscle, suggestive of metallosis. The first surveillance endomyocardial biopsy on post-transplantation day 29

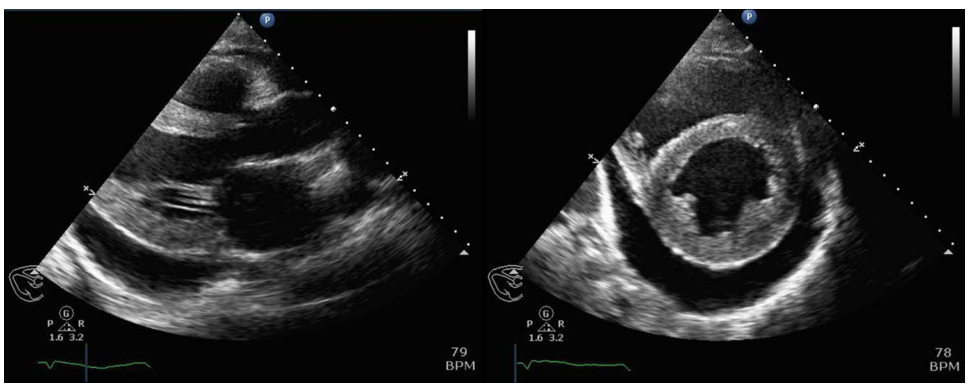

Fig. 4 An echocardiography of patient 2 at initial presentation. Parasternal long and short axis showing severe left ventricle (LV) dysfunction with thickened LV wall. Note large amount of pericardial effusion

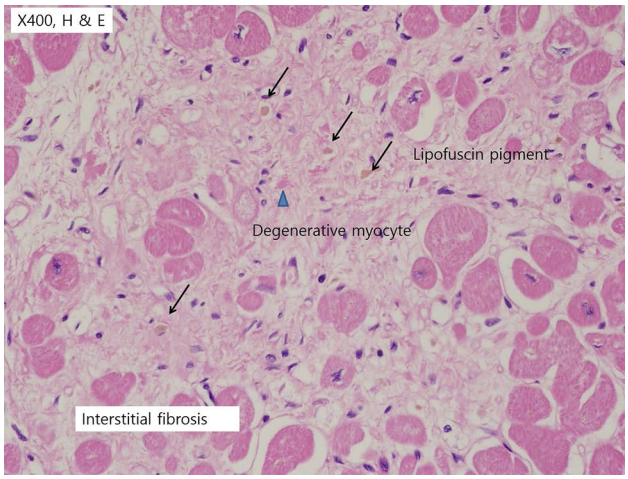

Fig. 5 High magnification of heart biopsy, showing marked increase in interstitial fibrosis replacing myocardial tissue, myocyte with cytoplasmic vacuolation and lipofuscin pigment [hematoxylin–eosin (H&E) stain, original magnification ×40]

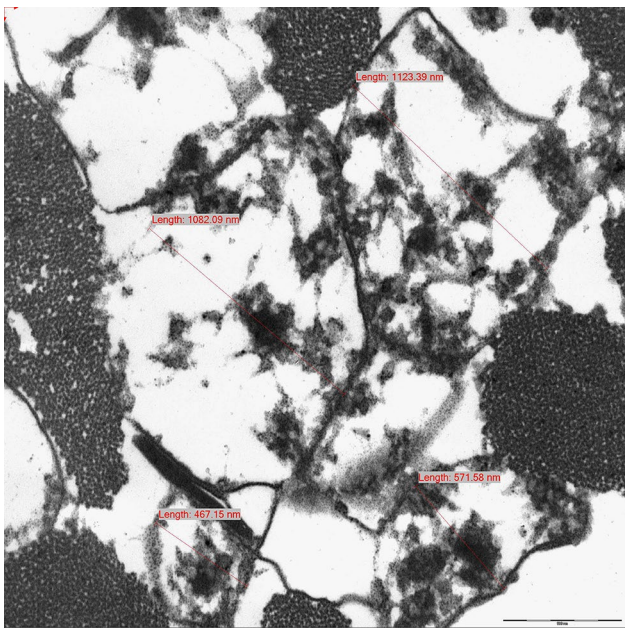

Fig. 6 Electron microscopic presentation of heart biopsy, showing swollen mitochondria, dilated sarcoplasmic reticulum, and intramitochondrial particle which is a pathognomonic features of cobalt toxicity. (×40,000)

showed increased lipofuscin pigments and focal myocyte vacuolisation. In a heavy metals screening, the cobalt level in the serum was 111.98 µg/L and the chrome level was 98.76 µg. Taken together, these findings strongly suggested cobalt-induced cardiomyopathy. A second revision surgery was performed on post-transplantation day 30. Wear of a steel ball head by ceramic fragments in the polyethylene acetabular cup was found. Massive irrigation and reimplantation of a Zimmer Continuum 58-mm outer diameter acetabular shell with a BIOLOX 36-mm option head was performed. Metallosis at the iliacus was not visualised by the posterolateral approach and therefore could not be completely removed. Chelation therapy was maintained for 3 months after surgery, at which time the cobalt level was decreased to 30.17 µg/L. Endomyocardial biopsy 4 months after transplantation showed no evidence of rejection or cobalt intoxication. The patient's cardiac function is normal, and with rehabilitation, he has reported improvement in his quality of life.

Discussion

We report two cases of cobalt-induced cardiomyopathy after revision total hip replacement for fracture of a ceramic liner. In the first case, removal of the prosthesis resulted in dramatic clinical and echocardiographic recovery, whereas in the second case, the diagnosis was not made until after heart transplantation. Our cases illustrate the importance of early recognition and management of cobalt toxicity. In a patient with cardiomyopathy with neuropathy, hypothyroidism, and a prior hip replacement, especially with hip pain, a toxicology workup should be considered.

Cobalt cardiac toxicity was first characterised in the early 1960s as 'Quebec beer-drinkers' cardiomyopathy' and was attributed to a cobalt-based foam-stabilising agent [14, 15]. The clinical presentation during that epidemic was quite similar to that in the cases presented here, with a rapidly progressive cardiomyopathy after the onset of symptoms in otherwise fairly healthy persons. Despite the absence of cardiac risk factors, both our patients presented with severe biventricular heart failure, which was distinguished by its abrupt onset; the presence of pericardial effusion; the presence of low voltage on the electrocardiogram with the absence of cardiac arrhythmias; rapid clinical progression leading to cardiogenic shock and a high mortality rate (of 10–40%) [15, 16]. In recent years, several cases of presumed cardiomyopathy related to cobalt implants used in arthroplasty have been described in the literature [1, 4, 17]. These cases have typically involved overt prosthetic failure or resurfacing of the metal-on-metal prosthesis [18], and in most cases, the cardiomyopathy was reversible with removal of the prosthesis [1]. In patients who undergo metal-on-metal hip arthroplasty, corrosion and wear produce metal debris in the form of nanoparticles, which can enter the bloodstream with subsequent release of cobalt ions [19–21].

Arthroprosthetic cobaltism has been reported to cause dilated cardiomyopathy and progressive myocardial dysfunction. In contrast to the often-reported impairment of myocardial contractile function, our first case report

describes an initial diastolic dysfunction with relatively preserved ejection fraction. Several reports reported impaired diastolic function resulted from cobalt toxicity [7, 22, 23]. The patient later developed progressive LV chamber dilatation and reduced contractile function, which responded well to treatment with removal of the metallosis and chelation therapy. The underlying mechanisms of myocardial damage by cobalt remain poorly understood. A suggested action mechanism is depression of oxygen uptake in the myocardial mitochondria by cobalt [24]. This action may result from cobalt-induced inhibition of the sulfhydryl groups of α-ketoglutarate and pyruvate to succinyl CoA and acetyl CoA, respectively [25]. Because cobalt has a high affinity for sulfhydryl groups, the protective effect of proteins and amino acids probably results from the sequestration of free cobalt in the cell. Other proposed mechanisms of toxicity include cobalt-induced damage to the transmembrane transport system [26, 27], resulting in increased intracellular calcium concentrations, and chronic inhibition of sympathetic tone [28, 29].

In both cases, the clinical and echocardiographic data strongly suggested an infiltrative cardiomyopathy. Concentric LV thickening in the absence of uncontrolled hypertension and aortic stenosis suggests a cause other than hypertrophy. The findings are suggestive of an infiltrative cardiomyopathy, including cardiac amyloid. However, laboratory and genetic tests ruled out common causes of infiltrative cardiomyopathy (e.g. amyloidosis or Fabry's disease). Review of the histologic images from the second patient's explanted heart showed diffuse myocardial degeneration with fibrous infiltration of the myocardium in the absence of inflammatory cell infiltration. Interstitial fibrosis, vacuolation within myocardial fibres, and lipofuscin accumulation are nonspecific findings but have been reported in histologic examination of a Quebec group of workers [16, 30]. Echocardiographic findings from both our patients showed hyperechoic myocardium. In myocardial infarction, the thick and densely packed mature myocardial scar appears hyperechoic [31]; this probably explains hyperechoic myocardium. The underlying mechanism of pericardial effusion is not yet fully understood, but the production of massive pericardial effusion from cobalt administration in several animal species has been reported [32]. Aspirate from the pericardial effusion had the characteristics of an exudate in our patient.

Cobalt and chromium chelation therapy in patients receiving metal-on-metal hip implants has been described in a few cases [33, 34]. Chelating agents such as EDTA, sodium 2,3-dimercaptopropane sulfonate, dimercaprol, and *N*-acetyl cysteine have been used [35–38]. EDTA is used to bind metal ions in the practice of chelation therapy mainly for mercury and lead poisoning. It binds to a metal cation through its two amine and four carboxylate sites [39], enhancing metal elimination through renal excretion. At present, the efficacy and role of these agents in therapy for arthroprosthetic cobaltism remain anecdotal. In our cases, EDTA chelation therapy reduced elevated blood levels of cobalt and chrome but not enough to allow the therapy to be discontinued. We believe that revision surgery with the removal of cobalt–chromium metal heads and liners or cups in the setting of cobalt toxicity appears to be the best option for definitively lowering cobalt levels because it completely removes the source of cobalt [40]. Sustained permanent damage to the myocardium [9] and a progressive decline in cardiac status resulting in death have been reported [1]; therefore, early recognition and prompt management are crucial.

Arthroprosthetic cobaltism is a rare but devastating known consequence of metal-on-metal total hip arthroplasty. The possibility of this diagnosis should always be in the forefront of clinicians' minds when confronted with a patient with metal-on-metal total hip arthroplasty and rapidly progressing heart failure that cannot be attributed to other more common systemic diseases. These two cases show the devastating cardiomyopathy that can occur and the potential recovery that can be achieved after explantation of the implants.

References

1. Gilbert, C. J., et al. (2013). Hip pain and heart failure: The missing link. *Canadian Journal of Cardiology, 29*(5), 639e1–e2.
2. Machado, C., Appelbe, A., & Wood, R. (2012). Arthroprosthetic cobaltism and cardiomyopathy. *Heart, Lung and Circulation, 21*(11), 759–760.
3. van Lingen, C. P., et al. (2013). Clinical manifestations in ten patients with asymptomatic metal-on-metal hip arthroplasty with very high cobalt levels. *Hip International, 23*(5), 441–444.
4. Oldenburg, M., Wegner, R., & Baur, X. (2009). Severe cobalt intoxication due to prosthesis wear in repeated total hip arthroplasty. *The Journal of Arthroplasty, 24*(5), 825 e15–e20.
5. Cheung, A. C., et al. (2016). Systemic cobalt toxicity from total hip arthroplasties: Review of a rare condition Part 1—History, mechanism, measurements, and pathophysiology. *The Bone & Joint Journal, 98-b*(1), 6–13.
6. Gessner, B. D., et al. (2015). A systematic review of systemic cobaltism after wear or corrosion of chrome-cobalt hip implants. *Journal of Patient Safety, 0*, 1–8
7. Tower, S. S. (2010). Arthroprosthetic cobaltism: Neurological and cardiac manifestations in two patients with metal-on-metal arthroplasty: A case report. *The Journal of Bone and Joint Surgery, 92*(17), 2847–2851.
8. Catalani, S., et al. (2012). Neurotoxicity of cobalt. *Human & Experimental Toxicology, 31*(5), 421–437.
9. Mosier, B. A., Maynard, L., Sotereanos, N. G., Sewecke, J. J. (2016). Progressive cardiomyopathy in a patient with elevated cobalt ion levels and bilateral metal-on-metal hip arthroplasties. *The American Journal of Orthopedics, 45*(3), E132–E135.
10. Zywiel, M. G., et al. (2013). Fatal cardiomyopathy after revision total hip replacement for fracture of a ceramic liner. *The Bone & Joint Journal, 95*(1), 31–37.

11. Allen, L. A., et al. (2014). Clinical problem-solving. Missing elements of the history. *The New England Journal of Medicine, 370*(6), 559–566.
12. Samar, H. Y., et al. (2015). Novel use of cardiac magnetic resonance imaging for the diagnosis of cobalt cardiomyopathy. *JACC Cardiovasc Imaging, 8*(10), 1231–1232.
13. Kempf, I., & Semlitsch, M. (1990). Massive wear of a steel ball head by ceramic fragments in the polyethylene acetabular cup after revision of a total hip prosthesis with fractured ceramic ball. *Archives of Orthopaedic and Trauma Surgery, 109*(5), 284–287.
14. Morin, Y., Tetu, A., & Mercier, G. (1971). Cobalt cardiomyopathy: Clinical aspects. *British Heart Journal, 33*(p. Suppl), 175–178.
15. Morin, Y., Tetu, A., & Mercier, G. (1969). Quebec beer-drinkers' cardiomyopathy: Clinical and hemodynamic aspects. *Annals of the New York Academy of Sciences, 156*(1), 566–576.
16. Alexander, C. S. (1972). Cobalt-beer cardiomyopathy. A clinical and pathologic study of twenty-eight cases. *The American Journal of Medicine, 53*(4), 395–417.
17. Tilney, R., Burg, M. R., & Sammut, M. A., (2017). Cobalt cardiomyopathy secondary to hip arthroplasty: An increasingly prevalent problem. *Case Reports in Cardiology, 2017*, 5434571.
18. Pandit, H., et al. (2008). Pseudotumours associated with metal-on-metal hip resurfacings. *The Journal of Bone and Joint Surgery British, 90*(7), 847–851.
19. Polyzois, I., et al. (2012). Local and systemic toxicity of nanoscale debris particles in total hip arthroplasty. *Journal of Applied Toxicology, 32*(4), 255–269.
20. Gill, H. S., et al. (2012). Molecular and immune toxicity of CoCr nanoparticles in MoM hip arthroplasty. *Trends in Molecular Medicine, 18*(3), 145–155.
21. Papageorgiou, I., et al. (2007). The effect of nano- and micron-sized particles of cobalt-chromium alloy on human fibroblasts in vitro. *Biomaterials, 28*(19), 2946–2958.
22. Tower, S. (2010). Arthroprosthetic cobaltism: Identification of the at-risk patient. *Alaska Medicine, 52*, 28–32.
23. Sotos, J. G., & Tower, S. S. (2013). Systemic disease after hip replacement: Aeromedical implications of arthroprosthetic cobaltism. *Aviation, Space, and Environmental Medicine, 84*(3), 242–245.
24. Heggtveit, H. A., Grice, H. C., & Wiberg, G. S. (1970). Cobalt cardiomyopathy. Experimental basis for the human lesion. *Pathologia et Microbiologia (Basel), 35*(1), 110–113.
25. Dingle, J. T., et al. (1962). The biological action of cobalt and other metals. II. The mechanism of the respiratory inhibition produced by cobalt in mammalian tissues. *Biochimica et Biophysica Acta, 65*, 34–46.
26. Rona, G., (1971). Experimental aspects of cobalt cardiomyopathy. *British Heart Journal, 33*(Suppl), 171–174.
27. Harrow, J. A., Das, P. K., & Dhalla, N. S. (1978). Influence of some divalent cations on heart sarcolemmal bound enzymes and calcium binding. *Biochemical Pharmacology, 27*(22), 2605–2609.
28. Barceloux, D. G. (1999). Cobalt. *Journal of Toxicology: Clinical Toxicology, 37*(2), 201–206.
29. Unverferth, D. V., et al. (1984). The evolution of beta-adrenergic dysfunction during the induction of canine cobalt cardiomyopathy. *Cardiovascular Research, 18*(1), 44–50.
30. Seghizzi, P., et al. (1994). Cobalt myocardiopathy. A critical review of literature. *Science of the Total Environment, 150*(1–3), 105–109.
31. Tabel, G. M., et al. (2006). Collagen fiber morphology determines echogenicity of myocardial scar: Implications for image interpretation. *Echocardiography, 23*(2), 103–107.
32. Mohiuddin, S. M., et al. (1970). Experimental cobalt cardiomyopathy. *American Heart Journal, 80*(4), 532–543.
33. Giampreti, A., Lonati, D., & Locatelli, C. A. (2014). Chelation in suspected prosthetic hip-associated cobalt toxicity. *Canadian Journal of Cardiology, 30*(4), 465.e13.
34. Devlin, J. J., Schwartz, M., & Brent, J. (2013). Chelation in suspected prosthetic hip-associated cobalt toxicity. *Canadian Journal of Cardiology, 29*(11), 1533.e7.
35. Smith, S. W. (2013). The role of chelation in the treatment of other metal poisonings. *Journal of Medical Toxicology, 9*, 355–369.
36. Pazzaglia, U. E., et al. (2011). Cobalt, chromium and molybdenum ions kinetics in the human body: Data gained from a total hip replacement with massive third body wear of the head and neuropathy by cobalt intoxication. *Archives of Orthopaedic and Trauma Surgery, 131*(9), 1299–1308.
37. Repo, E., et al. (2011). Capture of Co(II) from its aqueous EDTA-chelate by DTPA-modified silica gel and chitosan. *Journal of Hazardous Materials, 187*(1–3), 122–132.
38. Giampreti, A., et al. (2016). *N*-acetyl-cysteine as effective and safe chelating agent in metal-on-metal hip-implanted patients: Two cases. *Case Reports in Orthopedics, 2016*, 8682737.
39. Asapoglu, N. K., Toprak, A. B.,M. S., Koseoglu, Y., & Bayrakdar, H. (2000). Synthesis and characterization of NiFe ~ 2O ~ 4 nano-octahedrons by EDTA-assisted hydro-thermal method. *Turkish Journal of Chemistry, 30*, 659–666.
40. Kwon, Y. M., et al. (2014). Risk stratification algorithm for management of patients with dual modular taper total hip arthroplasty: Consensus statement of the American Association of Hip and Knee Surgeons, the American Academy of Orthopaedic Surgeons and the Hip Society. *The Journal of Arthroplasty, 29*(11), 2060–2064.