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Case Report

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Heart failure heralded by hip pain: A case of cobalt cardiomyopathy after hip arthroplasty

Patrick Tran; Raunak Banerjee; Mithilesh Joshi; Prithwish Banerjee*

Cardiology Department, University Hospitals Coventry and Warwickshire, Clifford Bridge Road, Coventry CV2 2DX, UK.

***Corresponding Author: Prithwish Banerjee**
Cardiology Department, University Hospitals Coventry and Warwickshire, Clifford Bridge Road, Coventry CV2 2DX, UK.
Email: prithwish.banerjee@uhcw.nhs.uk

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Keywords: Cobalt cardiomyopathy; Heart failure; Hip replacement; Metal toxicity.

Abbreviations: CMR: Cardiac Magnetic Resonance; DCM: Dilated Cardiomyopathy; LVEF: Left Ventricular Ejection Fraction; TSH: Thyroid Function Test.

Abstract

Background: The 2021 European Society of Cardiology guidance on heart failure lists metal toxicity as one of the rare causes of cardiomyopathy, citing iron and copper as examples. Another trace metal element that can induce a rapid-onset form of cardiomyopathy is cobalt. When released into the systemic circulation at excessive levels, this bivalent nanoparticle can cause neuronal and cardiomyocyte damage. Given its wear-resistant properties, cobalt-chromium was a popular alloy used in orthopaedic prostheses, but it was not until the last decade that its potential toxicity was realized.

Case presentation: A 61-year-old retired nurse presented to the orthopaedic clinic with left hip osteoarthritis, for which she underwent a cobalt-chromium metal-on-metal hip replacement. Two years later, she was admitted to the coronary care unit with acute heart failure and pulmonary oedema, for which she received intravenous furosemide. Few weeks prior to admission, she reported exertional breathlessness and bilateral ankle swelling. NT-pro B-type natriuretic peptide was elevated at 377 pmol/L (3195 pg/ml). Bedside echocardiography demonstrated a severe globally hypokinetic left ventricle and bi-atrial dilatation. Autoimmune screen, iron studies and viral serology were unremarkable. Invasive coronary angiography showed normal coronary arteries. Cardiac magnetic resonance (CMR) ruled out myocarditis, infarction or infiltration. Serum cobalt levels came back significantly raised at 550 nmol/l (reference range <11 nmol/l) as did the chromium level at 166 nmol/l (reference range <41 nmol/l), confirming cobalt toxicity. After the revision arthroplasty, serum cobalt and chromium levels declined near-normal levels. Repeat CMR demonstrated significant improvement in biventricular systolic function with a reduction in left ventricular end-diastolic volume.

Conclusions: Cobalt-induced cardiomyopathy is a rare but serious complication of cobalt-chromium hip replacements. More cases are likely to emerge due to their peak use in the early 21st century with reports of toxicity manifesting as late as 10 years post-implant. However, with low awareness of this phenomenon, there may still be patients with non-ischaemic DCM in which the link to failing cobalt prostheses remains unnoticed.

Background

Cobalt forms an integral part of the vitamin B12 complex (cobalamin) which is essential for normal cellular function. However, when present in large doses, this trace mineral can cause DNA damage and cellular apoptosis [1]. Its cytotoxic effects were first noted in the mid-1960s, when breweries started adding cobalt as a foam stabilizer to beer, resulting in some heavy beer drinkers developing thyroid, neurological and cardiac dysfunction [2]. Cobalt is also known for its wear-resistant properties and as an alloy, cobalt-chromium was widely used in the manufacture of orthopaedic metal prostheses. It was not until the high failure rates and reported cases of cobalt toxicity that led to it being phased out and replaced by polyethylene and ceramic-on-ceramic arthroplasties. Yet, many patients still have cobalt hip replacements. Clinicians should thus remain vigilant of the potential delayed presentations of metal toxicity. The Medicines and Healthcare products Regulatory Agency have published guidance on blood screening for cobalt toxicity, stating a level >7 ug/L as suggestive of soft tissue metal reaction [3]. Our case report highlights the unique features of cobalt cardiomyopathy and the early warning signs that may facilitate timely diagnosis and management of this potentially reversible cause of heart failure.

Case presentation

A 61-year-old retired nurse presented to the orthopaedic clinic with left hip osteoarthritis, for which she underwent a metal-on-metal hip replacement. The left femoral head was replaced by a cobalt-chromium alloy sphere and fitted into a metallic acetabular socket (Figure 1A). She was doing well until three years later when she developed left-sided groin pain. Ultrasonography revealed signs of iliopsoas tendonitis and a pseudo-tumour, described as an inhomogeneous hypoechoic mass near the left greater trochanter, measuring 2.85 x 2.87 cm (Figure 1B). Since her groin pain resolved after a steroid injection, no further action was taken for the pseudo-tumour. Two years later, she was admitted to the coronary care unit with acute heart failure and pulmonary oedema, for which she received intravenous furosemide. Few weeks prior to admission, she reported exertional breathlessness and bilateral ankle swelling. Exercise tolerance was largely limited by right hip osteoarthritis. Compared to a pre-operative Electrocardiogram (ECG), that showed sinus rhythm, admission ECG revealed new-onset atrial fibrillation. An ECG taken a year prior to admission showed premature ventricular complexes and signs of bi-atrial enlargement, raising suspicion of a surreptitious cardiomyopathic process in the preceding year (Figure 2).

NT-pro B-type natriuretic peptide was elevated at 377 pmol/L (3195 pg/ml). Bedside echocardiography demonstrated a severe globally hypokinetic left ventricle and bi-atrial dilatation. Apart from mild functional mitral and tricuspid regurgitation, no significant valvular abnormalities were noted (Video 1). Cardiac Magnetic Resonance (CMR) confirmed a moderately dilated left ventricle with global hypokinesia, resulting in severely impaired systolic function (ejection fraction 20%). Right ventricle was mildly dilated with mild systolic dysfunction. There was no myocardial late gadolinium enhancement to suggest myocarditis, infarction or infiltration. Myocardial T2* was 38 ± 1.15 ms and liver T2* was 24.8 ± 0.9, excluding iron overload (T2* <20 suggests iron overload). Liver signal intensity was normal. Overall findings indicated dilated cardiomyopathy (DCM) but the aetiology was unclear on the scan.

To investigate its cause, she underwent a series of inpatient tests. Invasive coronary angiogram showed normal coronary arteries. Autoimmune screen (ANA, ANCA, dsDNA, rheumatoid factor, complements, immunoglobulins) and viral serology (EBV, CMV, HIV, hepatitis B and C) came back negative. Renal function (creatinine 62 µmol/L) was normal, as were liver function tests, iron studies (ferritin 78 µg/l, haemoglobin 111 g/l), HbA1c and thyroid stimulating hormone (TSH) (2.61 mU/l) levels. Given the presence of a peri-prosthetic pseudo-tumour around the hip replacement, metal ion toxicity was later entertained. Serum cobalt levels came back significantly raised at 550nmol/l (reference range <11 nmol/l) as did the chromium level at 166nmol/l (reference range <41 nmol/l), indicating cobalt toxicity.

Before a formal diagnosis of cobalt cardiomyopathy was reached, it was necessary to rule out other causes of heart failure such as coronary artery disease. She was an ex-smoker of 15 pack-years but denied a history of chest pain. Coronary angiography and CMR excluded myocardial ischaemia. Office and admission BP have consistently been below 130/80, excluding a hypertensive cause. In terms of drugs and other toxins, she did not consume alcohol and apart from modified-release morphine and gabapentin for analgesia, she was not on any regular medications prior to admission. Tachycardia-mediated cardiomyopathy was considered, but prior ECGs and resting heart rates recorded in the outpatient clinics were invariably within the normal range. Regarding less common causes, infiltrative disease and myocarditis were excluded on CMR, which was performed promptly during admission to ensure any transient acute myocardial oedema and inflammation to suggest acute myocarditis were not missed. Autoimmune disease was ruled out by the negative antibody screen and absence of clinical features of connective tissue disease e.g. lupus or scleroderma. There was no family history of cardiomyopathy or neuromuscular weakness to suggest mitochondrial or storage disorders. Overall, the combination of non-ischaemic DCM, hypercobaltaemia and signs of metallosis around the prosthetic joint made cobalt cardiomyopathy the most likely diagnosis.

She was discharged on guideline-directed medical therapy for heart failure and anticoagulation for atrial fibrillation. More importantly, to confirm the diagnosis of cobalt-induced cardiomyopathy, it was vital to demonstrate myocardial recovery after removal of the cobalt source. She was therefore listed for an urgent left hip revision arthroplasty, which was performed a few months later.

On entering the fascia planes above the left hip, profuse black fluid was encountered, blackening the surrounding joint capsule, gluteus and iliopsoas muscles. This indicated extensive tissue metallosis. The bone was otherwise healthy and viable. After thorough debridement of the necrotic tissue, the hip joint was subsequently revised. The fluid and tissue samples were sent for histology. This demonstrated prominent macrophagic infiltration and foreign body multinucleated giant cells in the skeletal muscle with loss of myofibril filaments, consistent with metallosis. Microbiology showed scanty polymorphs but no growth after extended incubation. A repeat CMR, cobalt level

and clinical follow-up were arranged after 6 months.

After the revision arthroplasty, serum cobalt and chromium levels declined to 12 nmol/l and 32 nmol/l respectively. Repeat CMR demonstrated significant improvement in biventricular systolic function (LVEF 44% and RVEF 52%) with a reduction in left ventricular end-diastolic volume (end-diastolic volume 158 mls) (video 2). Bi-atrial enlargement was still present, along with mild mitral and tricuspid regurgitation. Although there are no published ranges in T2* values for assessing myocardial cobalt or chromium overload, myocardial T2* was found to increase to 72 ± 11 ms (previously 38 ms), perhaps reflecting a reduced cobalt exposure to the myocardium. The onset of atrial fibrillation would have also added to the residual left ventricular systolic impairment and hence she was referred for an elective DC cardioversion. Over the following 12 months, the patient's symptoms steadily improved and she now manages to walk her dog without experiencing exertional breathlessness.

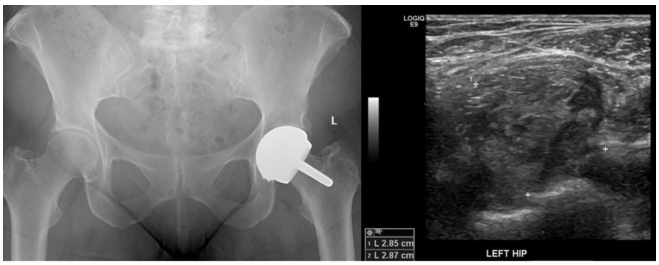

Figure 1: Pelvic X-ray and USS.

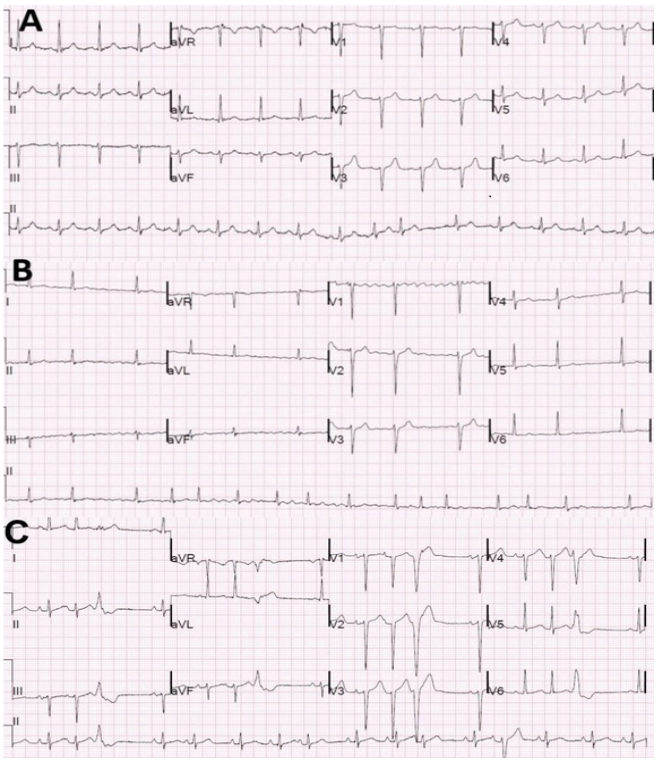

Figure 2: ECG.

Discussion

Cobalt-induced cardiomyopathy is a rare but serious complication of cobalt-chromium hip replacements. More cases are likely to emerge due to their peak use in the early 21st century with reports of toxicity manifesting as late as 10 years post-implant [4]. However, with low awareness of this phenomenon, there may still be patients with non-ischaemic DCM in which the link to failing cobalt prostheses remains unnoticed. In fact, there have been cases of referrals for heart transplantation and young fatalities due to late diagnosis [5,6]. Choi et al (2019) reported one case being diagnosed only at the time of heart transplantation, while another managed to avoid transplant surgery by virtue of a timely diagnosis and consequent revision hip surgery [7]. It is therefore helpful to be aware of specific features of cobalt toxicity to prompt early recognition and treatment of this potentially reversible cardiomyopathy.

Initially, patients may present with features of metallosis around the joint replacement in the form of joint pain, swelling, instability and destruction. Due to a type IV hypersensitivity reaction, a pseudo-tumour may develop (i.e. a non-infectious, non-neoplastic mass) [8]. Localized metallosis does not only occur in metal-on-metal prosthesis, but also in metal-on-polyethylene or metal-on-ceramic prosthesis due to excessive wear on the cobalt-chromium head [5,7]. A pseudo-tumour suggests localized tissue reaction and does not always result in systemic toxicity as seen in one patient with a pseudo-tumour and femoral invasion but with normal metal ion levels [8]. As cobalt accumulates systemically, neurological symptoms, such as tinnitus, tremor and hearing and vision impairment, and thyroid dysfunction may arise [2]. Interestingly, as cobalt stimulates erythropoiesis, some cases may exhibit polycythaemia [9]. Fung et al reported 8 cases of cobalt cardiomyopathy associated with hypothyroidism, polycythaemia and weight loss [10]. A combination of these features may serve as early clues to systemic cobalt toxicity, but they are not highly sensitive, as reflected in our patient who had normal levels of haemoglobin and TSH.

No definitive diagnostic tool exists for cobalt-induced cardiomyopathy. While the majority of cases have serum cobalt levels >250 µg/L, others have exhibited levels as low as 13 µg/L; hence the serum level and its cardiotoxic effect is not strongly correlated [4]. On the other hand, ECG and cardiac imaging are sensitive but not specific. Early cardiac dysfunction may manifest as sinus tachycardia or atrial fibrillation, as seen in our patient's ECG [1]. Other non-specific findings include poor R wave progression and small QRS voltages, which may indicate the uncommon incidence of global pericardial effusion [1]. More frequently observed on echocardiography are atrial enlargement, left ventricular hypertrophy, biventricular dilatation and systolic dysfunction [2,7]. CMR is valuable in excluding other causes of non-ischaemic DCM and is often used to assess for myocardial iron overload. Despite sharing similar magnetic properties to iron, the use of CMR T2* has not been validated in detecting myocardial deposition of cobalt [12]. Interestingly, we observed an improvement in this patient's T2* values as the serum cobalt levels normalized after revision hip arthroplasty, suggesting that T2* levels below average (normal average value >52 ms) may indicate cobalt deposition.

Conclusion

A high index of suspicion for cobalt cardiomyopathy is required for patients with unexplained left ventricular systolic dysfunction who have previously underwent a cobalt-chromium joint replacement, associated with signs of metallosis in the form joint pain, swelling or instability. This is a potentially reversible cause of cardiomyopathy after prompt removal of the cobalt source.

Declarations

Consent for publication: Written consent has been obtained from the patient described in this case.

Availability of data and materials: All data generated or analysed during this study are included in this published article

Competing interests: The authors declare that they have no competing interests

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