Explant Analysis from a Patient Exhibiting Rapid Acceleration of Parkinson Disease Symptoms and Hypercobaltemia Following Metal-on-Metal Total Hip Arthroplasty

A Case Report

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Abstract

Case: A 46-year-old man developed rapidly progressing Parkinson disease symptoms after metal-on-metal total hip arthroplasty, worsening to the extent that he underwent implantation of a right subthalamic deep brain stimulator (DBS). A serum cobalt level of 116 μg/L was measured shortly after DBS implantation, and revision arthroplasty was performed using ceramic-on-polyethylene bearings. After revision, the patient's serum cobalt level fell below 1 μg/L, the Parkinson disease symptoms improved, and he reduced the DBS to its lowest setting. Explant analysis showed substantial material loss from the bearing surfaces of one hip.

Conclusion: Future studies should evaluate the possible link between Parkinson disease symptoms and prosthesis wear-induced hypercobaltemia.

Over one-half of patients undergoing metal-on-metal total hip arthroplasty (THA) using chromium-cobalt bearing surfaces experience blood cobalt concentrations above the ACGIH (American Conference of Government Industrial Hygienists) biological exposure threshold (1 μg/L)[1,2]. In the most severe instances, hypercobaltemia from arthroprosthetic cobaltism may adversely affect the peripheral and central nervous system, thyroid, heart, and hematopoietic system[3]. Neurological and cardiovascular illness from hypercobaltemia secondary to wear or corrosion of chromium-cobalt implants may resolve following revision THA to alternative bearing surfaces[4].

The patient in the present case was informed that information regarding his case would be submitted for publication, and he provided consent.

Case Report

A 46-year-old man presented to an orthopaedic clinic in 2009 with degenerative joint disease in the left and right hips, requiring staggered bilateral THAs. The patient's family history was notable for a father and paternal great-grandfather with Parkinson disease.

The patient underwent a right THA in April 2009. The implant consisted of a metal-on-metal Biomet Magnum M2A, with a 56-mm outer-diameter/50-mm inner-diameter acetabular chromium-cobalt monoblock shell and a 50-mm modular chromium-cobalt head fitted to a titanium stem through a tapered titanium adapter sleeve. The procedure initially alleviated the patient's hip symptoms.

Shortly after the right THA, the patient noticed resting tremor in the left upper and lower extremities, which progressed over the subsequent year, causing him to initiate levodopa therapy in November 2009 and to relinquish his position as a commercial pilot. Following a left THA with the same Magnum M2A components in July 2010, the symptoms worsened to the extent that he was referred to a movement disorders specialist for consideration of deep brain stimulator (DBS) placement. A right subthalamic DBS implantation was completed in June 2012.

In addition to neurological symptoms, the patient reported substantial local discomfort following the left THA. Based on periprosthetic pain and escalation of neurological symptoms, hypercobaltemia with neurocobaltism was suspected. A serum

Disclosure: The authors indicated that no external funding was received for any aspect of this work. On the **Disclosure of Potential Conflicts of Interest** forms, *which are provided with the online version of the article,* one or more of the authors checked "yes" to indicate that the author had a relevant financial relationship in the biomedical arena outside the submitted work.

TABLE I Evaluation of Explant Surface Damage After Revision Total Hip Arthroplasty*

Component	Overall Wear	Burnishing	Scratching	Abrasion	Comments†
Left femoral head	2	2	3	2	Femoral head shows a corrosion crescent roughly 1 × 3 cm; substantial corrosion (4) on the inner taper; minor corrosion (2) on the outer taper
Left cup	2				Articular surface shows an area of corrosion roughly 1 × 1 cm
Right femoral head	2	2	2	2	Articular surface of the femoral head shows an apical scrape (2) and a subtle ellipse; the bore shows corrosion (2)
Right cup	2				Articular surface shows discoloration

*In general, a score of 2 (on the semiquantitative grading scale of 0 to 3) indicates that the damage attribute involves 10% to 50% of the assessed surface, and a score of 3 indicates that >50% of the surface displays the attribute[5]. †Taper corrosion scores follow the standard established by Goldberg et al.[6]. Retrieval artifacts and fretting due to insertion and removal are omitted.

cobalt level of 116 μg/L was measured in July 2012, and the level was 108 μg/L in a repeat measurement in August 2012. In October 2012 (two years after the left THA), the patient reported moderate pain in the right hip and severe pain in the left hip, accompanied by groin pain extending to the posterior aspect of the left thigh and iliotibial band. In addition to accelerated Parkinsonism, he reported blurry vision, memory loss, tongue numbness, and dysgeusia. A provisional diagnosis of arthroprosthetic cobaltism was made and the patient was scheduled for staggered bilateral partial hip revisions. The stem was to be retained, but all articular surfaces were to be replaced.

Revision arthroplasty was performed on the left hip in November 2012 and on the right hip in December 2012 using ceramic-on-polyethylene bearing couples. In both hips, murky yellow serous fluid was encountered during revision surgery, and metal staining was observed in the surrounding tissues. In the left hip, metal debris was encountered in the soft tissues around the rims of the short external rotators and capsule, with accompanying synovitis.

Five weeks after the right hip revision, the serum cobalt level had fallen to 3.2 μg/L. Two weeks later, it had fallen to 0.7 μg/L, below the ACGIH biological exposure threshold[2]. The pain resolved within months of the revision operation, although the patient retained a mildly antalgic gait and tongue irritation. He reported substantial improvement in the Parkinson disease symptoms and reduced the DBS to its lowest setting.

Because of the improvement in symptoms, the patient requested evaluation for DBS removal in November 2013 so that he could return to commercial aviation. By this time, he was noted by a neurologist to have only minimal symptoms in the "off stimulation, off medication" state. However, examination revealed REM (rapid eye movement) sleep behavior disorder and minor asymmetric motor symptoms suggestive of idiopathic Parkinson disease. Given this assessment, a DaTScan (GE Healthcare) was performed, and the results were consistent with a diagnosis of Parkinson disease with left-sided symptoms. Thus, the DBS was left in situ to treat residual motor symptoms at lower settings.

All components retrieved from the revisions were sent to a retrieval laboratory for analysis. Explants were photographed and assessed for gross damage using a semiquantitative grading scale of 0 to 3 that ascribes a score to the percentage of the surface involved with the damage phenomenon[5,6] (Table I).

Following damage scoring, volumetric wear was quantified using a coordinate measurement machine, which measured approximately 70,000 to 120,000 data points on the femoral and acetabular articular surfaces of each component, with a maximum spacing of 50 μm[7] (Table II). The titanium

TABLE II Volumetric Evaluation of Explant Wear After Revision Hip Arthroplasty

Component	Total Volumetric Wear (mm^3)	Volumetric Wear Rate (mm^3/yr)	Maximum Linear Wear Depth (μm)	Linear Wear Rate ($\mu m/yr$)
Left femoral head	9.5	4	27	11.8
Left acetabulum	95	41	138	60
Total for left side	104.5	45		
Right femoral head	2.4	0.7	9.6	2.6
Right acetabulum	0.6	0.2	25	6.8
Total for right side	3.0	0.8		

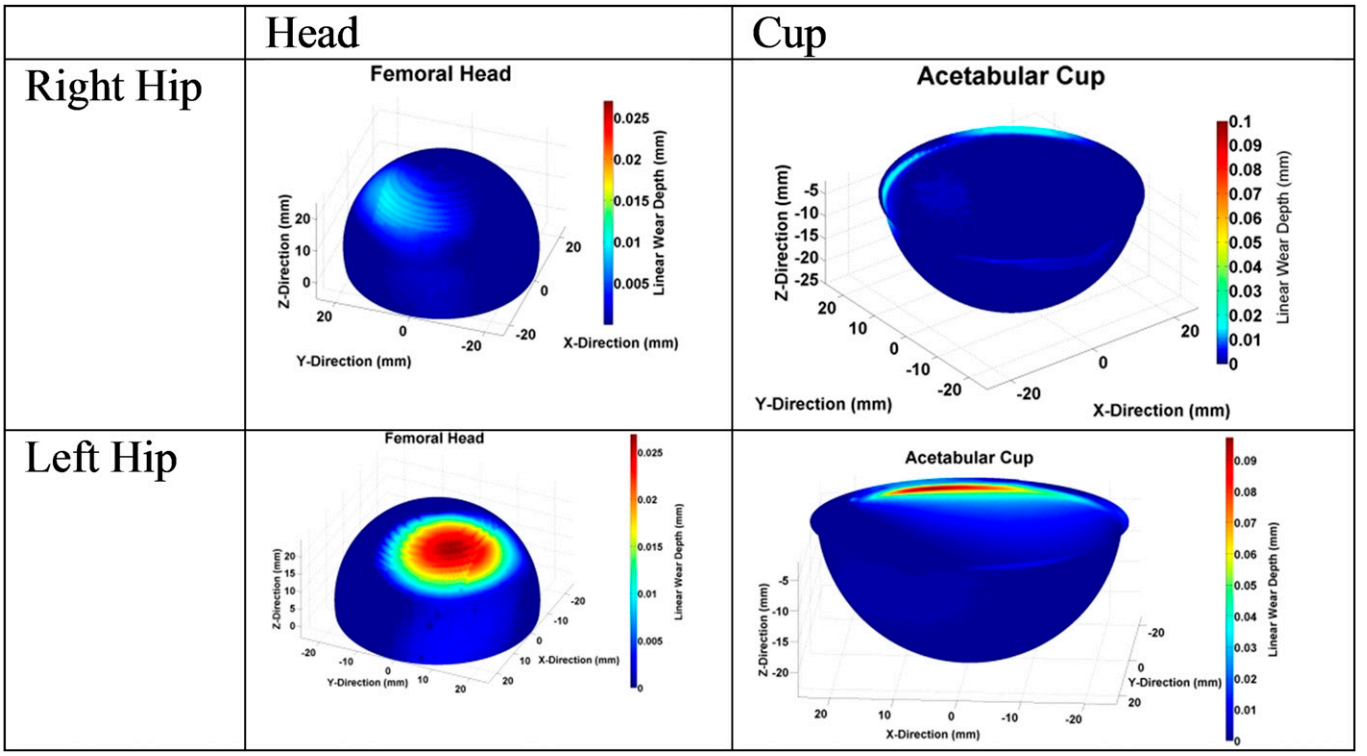

Fig. 1

Volumetric material loss measured with a coordinate measuring machine.

female taper was assessed using 72 axial paths along the interior of the rigidly fixed head[8].

The distributions of material loss on both the right and left bearing surfaces are shown in Figure 1. On the bearing surfaces, the regions of maximum loss corresponded to an elliptical patch on the femoral head and a region close to the rim of the cup. The bore scans exhibited material loss values below the detection limit (<10 μm linear depth). The bore of the left femoral head demonstrated accretion of material near the outermost edge.

Functional follow-up of both hips at 18 months after the right revision surgery showed appropriate recovery. The first author performed an interview and follow-up of the patient 64 months after the right primary THA and 20 months after the right revision hip arthroplasty. Comprehensive record review from the patient's independent neurologist and primary care physician at 18 months after the right revision hip arthroplasty revealed no additional notable findings.

Discussion

Taken cumulatively, the patient's family history of Parkinson disease, his response to levodopa therapy, the results of the DaTScan, and the continued presence of minor motor and non-motor symptoms suggest that the patient has Parkinson disease, which will likely continue in its natural course.

The Parkinson disease symptoms apparently worsened following insertion of a device that exhibited substantial volumetric wear. The linear wear rates of the left femoral head (11.8 μm/yr) and left acetabulum (60 μm/yr) were greater than median linear wear rates reported by Matthies et al. in 2011 (2.71 and 3.85 μm/yr, respectively)[9]. The rates of volumetric loss from the left femoral head (4 mm^3/yr) and left acetabulum (41 mm^3/yr) were also greater than mean rates reported by Matthies et al. in 2013 (3.1 and 2.5 mm^3/yr, respectively)[9]. The left acetabular component exhibited material loss >15 times the latter mean rate, placing it in the top 5% of devices reported in the 2 studies by Matthies et al.[9,10]. Furthermore, their 2013 study affirms that high material loss from the bearing surface is positively correlated with elevated blood metal ion levels, a finding consistent with the current report[10]. Thus, the patient's metal ion levels were likely the result of material loss from the rim and the head of the left acetabular cup (Fig. 1) due to a wear mechanism involving edge-loading and poor metal-on-metal tribological performance.

Following removal of the chromium-cobalt prostheses and normalization of the cobalt level, the patient's clinical state dramatically improved over approximately a year. Remission of severe symptoms is unusual in the absence of drug-induced Parkinsonism, and spontaneous remission is an exclusion criterion for idiopathic Parkinson disease[11]. The patient's medication list was comprehensively screened and did not include any drugs known to cause drug-induced Parkinsonism. Chronologically, reduction of cobalt levels coincided with reduction of symptom severity, but no additional conclusive tests were performed.

A possible biological pathway links hypercobaltemia to symptoms of Parkinson disease. Although, to our knowledge, a population-level epidemiological association between cobalt

exposure and Parkinsonism has not previously been reported, occupational exposure to certain metals, including manganese, copper, and lead, increases the risk of developing Parkinson disease[12,13]. A proposed mechanism suggests that metal-triggered conformational changes in alpha-synuclein increase its propensity to form fibrils, leading to clinical manifestations[14]. In vitro studies have demonstrated that, in addition to metals with known associations with Parkinson disease (e.g., manganese and copper), cobalt directly accelerates the rate of alpha-synuclein aggregation[14]. In addition, research in rat models has shown that intraperitoneal administration of cobalt acetate depletes dopamine concentrations in the basal ganglia, cerebellum, and brain stem[15].

It is important to note that, to our knowledge, acceleration of Parkinson syndrome symptoms directly attributable to cobalt poisoning acting independently in humans has not been described in the literature. Thus, an alternative explanation is that the patient's symptoms may have been exacerbated by cobalt-induced hypoxia-mimesis and reversible cell injury in hypoxia-sensitive cerebellar cells, particularly Purkinje cells, whose functional impairment is known to cause ataxia and tremor[16,17].

The patient's family history of Parkinson disease decreases the likelihood that systemic cobaltism initiated the patient's underlying disease, and recall bias may impede our ability to clarify the timing of symptom onset any further. Although there are other possible explanations for exacerbation of the patient's symptoms, hypercobaltemia due to wear of this patient's metal-on-metal hip prostheses remains plausible both chronologically and biologically. Nevertheless, this link remains speculative, and a clear association has not been documented. Generalization should be limited until future studies can evaluate a possible link and assess the completeness and timing of symptom resolution following revision surgery. ■

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