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Cobalt-Chromium Metallosis with Normal ERG: A Case Report and Review

Lola Grillo, BA¹, Huy V. Nguyen, MD¹, Stephen H. Tsang, MD, PhD^{2,3}, Donald C. Hood, PhD^{2,4}, and Jeffrey G. Odel, MD²

¹College of Physicians and Surgeons, Columbia University, New York, NY USA

²Department of Ophthalmology, Columbia University, New York, NY USA

³Department of Pathology & Cell Biology, Institute of Human Nutrition, and Irving Comprehensive Cancer Center, Columbia University, New York, NY

⁴Department of Psychology, Columbia University, New York, NY USA

Abstract

Background—Ocular cobalt toxicity is a rare phenomenon reported with increased frequency due to the rise of cobalt-chromium metal hip implants. We report the case of a 66 year-old previously healthy man who developed decreased vision due to cobalt-chromium toxicity from a metal-on-metal hip arthroplasty. Our objective was to determine whether the origin of his visual loss was due to toxicity of the optic nerve, of the retina, or of both.

Methods—Ocular examination, 10–2 SITA-Standard Humphrey Visual Field (VF), standard full-field electroretinogram (ERG) as indicated by the International Society for Clinical Electrophysiology of Vision (ISCEV), multifocal electroretinogram (mfERG), multifocal visual evoked potentials (mfVEP), and optical coherence tomography (OCT) were conducted.

Results—Ocular examination revealed decreased visual acuity, poor color vision, normal funduscopy, and cecentral scotomas on visual field. As his right eye was amblyopic since childhood, test results from only the left eye are shown. Electrophysiology studies revealed an ISCEV standard full-field ERG with photopic and scotopic responses within normal limits, mfERG with amplitudes and latencies within normal limits, and mfVEP with latencies within normal limits, but with decreased central amplitudes. Peripapillary and macular OCT showed retinal nerve fiber layer (RNFL) and retinal ganglion cell-inner plexiform layer (RGC-IPL) thickness within normal limits.

Conclusion—As decreased color vision and cecentral scotoma on 10–2 VF are most consistent with toxic optic neuropathy, and decreased central amplitudes on mfVEP are suggestive of neural dysfunction, we hypothesize that our patient presented with an early stage of optic nerve toxicity that was not yet apparent as a structural abnormality on OCT.

Corresponding author: Dr. Jeffrey Odel, Edward S. Harkness Institute, 635 W 165th St, New York, NY 10032, (914)426-2700, odel1@aol.com.

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Keywords

Cobalt; chromium; metal; optic neuropathy; arthroplasty

The mechanism of visual loss due to a failed cobalt-chromium hip implant remains obscure. Cobalt and chromium ions leak into the bloodstream and surrounding tissues, resulting in markedly elevated serum levels, particularly in cases where retained ceramic debris from a previous ceramic hip transplant grinds down the metallic implant (1–9). Typically within two years, these patients develop visual loss, sensory-neural hearing loss, hypothyroidism, and cardiomyopathy (1–9). Reported findings in patients with cobalt toxicity include optic atrophy, impaired choroidal perfusion, abnormal macular function, delays on visual evoked potentials (VEP), hyperintensities of the anterior visual pathway on magnetic resonance imaging (MRI), chorioretinal degeneration, hypofluorescent lesions on indocyanine green chorioangiography (ICG), and abnormal electroretinograms (ERG) (1–13). Few patients have been studied with a combination of electrophysiology, optical coherence tomography (OCT), and visual fields. We recently evaluated a patient early in the course of visual loss at the time of replacement of a failed cobalt-chromium implant.

CASE REPORT

A 66-year-old man with a history of childhood amblyopia of his right eye underwent a left total hip arthroplasty with ceramic-on-ceramic pairing. Three years later, the ceramic implant fractured and was replaced with a metal-on-metal implant with a cobalt-chromium femoral head (Zimmer; Warsaw, Indiana). Nine months later, the patient noted that red traffic lights appeared orange. He began to have difficulty seeing at distance and near, and difficulty hearing, requiring hearing aids for normal conversation. He also noted increasing abdominal distention and ankle swelling, left hip pain, pale diarrhea, a rash, incoordination, and subjective loss of mental clarity.

One year following replacement of the femoral head implant, the patient's vision was 20/80, right eye, and 20/30, left eye. He was unable to identify any of the AO-HRR color plates, while pupillary reactions and funduscopy were normal. Visual field testing in the left eye showed cecocentral depression (Fig. 1).

A battery of visual tests were performed. Results are shown only for the left eye, as results from the right eye were inconclusive due to amblyopia. Spectral domain optical coherence tomography (OCT) revealed normal thickness of the retinal nerve fiber layer (RNFL) and retinal ganglion cell-inner plexiform layer (RGC-IPL) (Fig. E1). Full-field electroretinography (ERR) demonstrated normal scotopic and photopic responses (Fig. E2), and mfERG amplitudes and latencies within normal limits (Fig. E3). The mfVEP showed central depression of amplitudes in the left eye (Fig. 2), which corresponded to the cecocentral depression detected on visual field testing.

The patient's symptoms and examination findings raised concern for cobalt toxicity. A serum cobalt level yielded a concentration of 1,078 ug/L (normal < 0.3 ug/L).

The patient underwent revision of the left hip prosthesis. At surgery, ceramic fragments were found in the joint, the cobalt-chromium prosthesis showed significant wear of the head, and metal infiltrates were found on the acetabular cup. The cobalt level measured in the synovial fluid exceeded the maximum recordable value of 1000.0 ug/L. Ten weeks later, the cobalt level in the patient's serum had decreased to 55.9 ug/L. Twelve weeks following surgery, visual acuity was 20/30, left eye and the patient could recognize 3 of 6 color plates. By 18 months following surgery, left visual acuity was 20/25, his vision continued to improve, and the left visual field was normal. His serum cobalt level was 7.4 ug/L.

DISCUSSION

The origin of visual loss due to cobalt toxicity has long been debated. Currently, five case studies reported optic nerve atrophy based upon fundus exam, of which two reported abnormal VEP testing (Table 1; 8–12). An additional case was reported with an abnormal VEP, but did not include a fundus exam (1–2). None of these cases had ERG testing. In contrast, three cases found retinal toxicity, two with abnormal ERG and one with photoreceptor thinning on OCT (Table 2; 3–6). Two of these three reported normal VEP testing, isolating toxicity to the retina (3–4).

Our case stands in contrast to the recently reported cases of retinal cobalt toxicity. Weber et al described a woman with a history of hip prosthesis and decreased vision OU with an ISCEV-standard full-field ERG showing significant cone dysfunction (6). Similarly, Apel et al reported a case of arthroprosthetic cobaltism with persistent abnormalities in all phases of ERG including a negative b-waveform, suggesting inner retinal pathology (4). In contrast, the ISCEV standard full-field ERG conducted on our patient's non-amblyopic eye showed normal flicker timing and amplitude, with both photopic and scotopic wave-forms within normal limits (Fig. E2). Additionally, the multifocal ERG showed amplitudes and latencies within normal limits (Fig. E3) and the OCT of the macula reveals the outer retinal layers to be of normal shape and contour (Fig. E1). Therefore, we conclude that it is unlikely that the outer layers of the retina have been affected by cobalt toxicity.

The decreased central amplitudes of the mfVEP are consistent with dysfunction somewhere along the anterior or posterior visual pathways. As the mfVEP tests macular function, we cannot fully rule out early retinal toxicity that has yet to manifest on the mfERG or full-field ERG. However, the cecocentral depression on visual field testing and loss of color vision out of proportion to reduced visual acuity are most consistent with a toxic optic neuropathy (14). Although the OCT demonstrated that inner retinal layers (RNFL and RGC-IPL) were of normal thickness, it is possible that toxic damage to the ganglion cells and their axons had not yet resulted in thinning. Possibly our patient had thick RNFL and RGC+ layers that did not show demonstrable loss of fibers at the time of OCT testing. We conclude that we may have detected an early stage of optic nerve toxicity that is not yet structurally apparent on OCT.

Proposed mechanisms of cobalt toxicity may explain involvement of both the optic nerve and retina. Optic neuropathy due to cobalt toxicity is attributed to defective mitochondrial oxidative phosphorylation, similar to that seen in Leber hereditary optic neuropathy and

dominant optic atrophy (15). Because RGCs lack myelin, they may be prone to damage from mitochondrial dysfunction, where defects in the respiratory chain lead to oxidative stress and, ultimately, apoptosis (16). Cobalt also is known to block calcium-dependent synaptic transmission between photoreceptors and second-order neurons, inhibiting the negative feedback in the outer retina that leads to glutamate release to bipolar and horizontal cells (17).

Animal studies have shown evidence of cobalt toxicity in both the retina and the optic nerve. Cobalt was found to suppress rod signal transmission in the outer plexiform layer in super perfused, isolated carp retina and diminish the rod- and cone-driven b-wave responses in frog retina (18). Evans et al (19) showed complete elimination of rod-photoreceptor contribution to the ERG b-wave in frog retina exposed to cobalt. Hara et al (20) found photoreceptor cells progressively underwent apoptosis with time and under dose-response relationship following intravitreal injections of cobalt-chloride in mice and rats. In contrast, Apostoli et al (16) found severe ganglion cell depletion, diffuse areas of optic nerve damage, and axonal swelling following daily dosage of rabbits with intravenous cobalt, with severity of damage related to dose and time of exposure.

Only a portion of patients with high serum cobalt levels develop symptoms of toxicity, and these symptoms vary from patient to patient. This may be due to albumin binding capacity, which affects the amount of free cobalt in the blood and generation of free radicals by cobalt (21). In addition, as cobalt toxicity has been linked to mitochondrial dysfunction, it is possible that some patients may develop a compensating increase in mitochondrial mass and are less susceptible to cobalt toxicity, just as unaffected carriers of the Leber genotype were found to have a greater mitochondrial mass when compared with their affected relatives (22).

In conclusion, a normal ERG in a patient with history of metal-on-metal hip prosthesis does not rule out cobalt toxicity, particularly when it is accompanied by other symptoms such as tinnitus, deafness, peripheral neuropathy, incoordination, depression, cardiomyopathy, and hypothyroidism (2). It is important to perform a complete work-up including ISCEV-standard full field ERG, mfERG, mfVE, and OCT in patients losing sight and suspected of having cobalt toxicity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Statement of Authorship

Category 1:

a. Conception and design Lola Grillo

Donald Hood

Huy Nguyen

Jeffrey Odel

Stephen Tsang

b. Acquisition of data

Lola Grillo

Huy Nguyen

Jeffrey Odel

Stephen Tsang

c. Analysis and interpretation of data

Lola Grillo

Donald Hood

Huy Nguyen

Jeffrey Odel

Stephen Tsang

*Category 2:***a.** Drafting the manuscript

Lola Grillo

Donald Hood

Huy Nguyen

Jeffrey Odel

Stephen Tsang

b. Revising it for intellectual content

Lola Grillo

Donald Hood

Huy Nguyen

Jeffrey Odel

Stephen Tsang

*Category 3:***a.** Final approval of the completed manuscript

Lola Grillo

Donald Hood

Huy Nguyen

Jeffrey Odel

Stephen Tsang

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Figure 1.
Cecentral visual field depression is present in the left eye (Humphrey 10-2).

Figure 2.

The multifocal VEP responses centrally (A) are significantly smaller than normal (B, red boxes) consistent with depressed central visual field sensitivity (C, red area). VEP, visual evoked potential

TABLE 1

Cases of ocular cobalt toxicity localized to the optic nerve

Report	Type of exposure	Time to symptom onset in months	Highest measured Co level, ug/L (serum nl < 0.9)	Symptoms, exam findings, and ancillary tests	Tissue abnormality	Visual tests
Licht et al. (10)	73 g cobalt-chloride over 3 yr period: Treatment for pancytopenia and hypercellular bone marrow	Unknown	Undocumented	Nausea/vomiting, cardiomyopathy	Optic nerve atrophy OU; Impaired chorioidal perfusion	Abnormal VF OD Abnormal fluorescein angiography
Meecham and Humphrey, (11)	Industrial raw cobalt powder exposure for 20 mo. working 50 hrs/wk	13	Blood: 234 Urine (24-hr collection): 119	Tinnitus, deafness, vertigo, decreased visual acuity (VA)	Optic nerve atrophy with temporal pallor OU	Delays on VEP OU; improved with decline in serum cobalt
Steens et al. (1)	Metal-on-ceramic hip arthroplasty	24	Serum: 398	Sight and hearing impairment, numbness of feet, dermatitis	Optic nerve macular malfunction OU	Clinical exam only
Rizzetti et al. (3) Pazzaglia et al. (4)	Metal-on-ceramic hip arthroplasty	5	Blood: 549 Plasma: 90 CSF: 11.4 Urine (24-hr collection): 1,187	Visual and hearing loss, hypothyroidism EMG: mild lower limb amplitude reduction 3 months later- wheelchair bound due to lower limb weakness	Optic nerve, tract, and/or visual cortex dysfunction, OU (fundus exam not described)	VEP: Irregular cortical visual responses; MRI of brain with hyper-intensity of optic nerves and tracts
Tower, (2)	Metal-on-metal hip arthroplasty (ASR system, DePuy [*])	11	Serum: 122 CSF: 2.2 Joint fluid: 3,200	Dermatitis, hip pain, anxiety, headache, tinnitus, hearing loss, incoordination	Optic nerve atrophy OU	Clinical exam only
Bhardwaj et al. (12)	Oral ingestion of two 9 cm cattle magnets (5–38% cobalt)	Unknown	Blood: 112.4 Urine (24-hr collection): 473.2	Decreased color vision and VA, generalized malaise, hypothyroidism, tachycardia, polycythemia	Optic nerve atrophy OU Bilateral RPE dysfunction	Delays on VEP OU Abn. VF OU Abn. EOG OU
Current case	Metal-on-metal hip arthroplasty (Zimmer)	9	Serum: 1,078	Decreased color vision and VA, hearing loss, hypothyroidism, ataxia, dermatitis, cognitive decline	Optic nerve dysfunction OS	Normal ERG, mfERG, OCT; mfVEP with decreased central amplitude OS

* Articular Surface Replacement Implants (ASR): metal-on-metal Co-Cr hip implant by DePuy Orthopaedics; internationally recalled in 2010. VA, visual acuity; VF, visual field; MRI, magnetic resonance imaging; VEP, visual evoked potential; EOG, electro-oculogram; mfERG, multifocal electroretinography; mfVEP, multifocal visual evoked potentials; RPE, retinal pigment epithelium; EMG, electromyogram.

TABLE 2

Cases of ocular cobalt toxicity localized to the retina

Case report	Type of exposure	Time to symptom onset in months	Highest measured cobalt level in ug/L (serum normal < 0.9)	Symptoms, exam findings, and ancillary tests	Tissue abnormality	Visual tests
Ng et al. (5)	Bilateral metal-on- metal hip arthroplasty (ASR system, DePuy *)	24	Serum: 44.6	Paracentral scotoma in OS, dysgeusia	Chorio-retinal degeneration; RPE dysfunction OS	Normal VEP, normal ERG (slightly reduced amplitudes OS compared to OD) OCT: degenerative alterations of RPE in OS
Apel et al. (6)	Metal-on-ceramic hip arthroplasty (DePuy femoral head)	48	Plasma: 446.4	Decline in vision, general malaise, pericardiomypathy, hypothyroidism, motor axonopathy	Retinopathy	Abnormal photopic and scotopic ERG, normal VEP 18 months post- revision: ERG improved to near normal, VEP: Delays OU
Weber et al. (8)	Metal-on-ceramic hip arthroplasty	14	Blood: 411	Visual and hearing loss, depression, weight loss, paresthasias in hands and feet, imbalance	Retinopathy	VF: Bilateral central scotoma; ERG: severe cone dysfunction

* Articular Surface Replacement Implants (ASR): metal-on-metal Co-Cr hip implant by DePuy Orthopaedics; internationally recalled in 2010 VEP, visual evoked potential; ERG, electroretinography; OCT, optical coherence tomography.