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13. Charcot–Marie–Tooth disease type 1A with 17p11.2 duplication. Clinical and electrophysiological phenotype study and factors influencing disease severity in 119 cases. Nazha Birouk,1 Riadh Gouider,1 Eric Le Guern,2 Michel Gugenheim,1 Sandrine Tardieu,2 Thierry Maisonobe,1 Nadine Le Forestier,1 Yves Agid,2 Alexis Brice2 and Pierre Bouche1


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PHACT vs FICTION

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Abstract:

Introduction and objective: Prosthetic hip-associated cobalt toxicity (PHACT) is a rare cause of cobalt toxicity from metal-on metal (MoM) total hip prosthesis. There are few reports of PHACT and only one case report from our review that reported tremor as a presenting symptom.7

Case presentation: This is a report of a 44 year old male with history of hip replacement. He presented to PCP with progressive worsening of muscle weakness, fatigue and tremor of two months duration. After an extensive work up was performed and reviewing current literature, serum cobalt level was eventually performed and was found to be high. Resolution of the symptoms with concomitant decrease in serum cobalt was noted.

Discussion: PHACT being a diagnosis which is rare and done by exclusion, it is important to make it a part of the differential diagnosis. As our patient also has the diagnosis of Charcot Marie Tooth, it is important to prevent anchoring heuristic bias and evaluate the patient from fresh eyes especially with a history of MoM device placement.

Conclusion: The symptoms did resolve on removing the MoM device which does imply that PHACT can be regarded closer to a fact when compared to a fiction.

Keywords: Cobalt Toxicity, Metal on Metal Prosthesis, Tremor
Introduction:

Prosthetic hip-associated cobalt toxicity (PHACT) is a rare cause of cobalt toxicity from metal-on-metal total hip prosthesis. Symptoms of cobalt toxicity include sensorineural hearing impairment, vision loss, cognitive impairment, cardiac failure, neuropathy, and hypothyroidism. The following criteria have been suggested for the diagnosis of PHACT:

(1) Elevated cobalt levels due to a prosthetic hip.
(2) At least two levels consistent with cobalt toxicity.
(3) Exclusion of other etiologies.

Objective:

PHACT is a rare disease and tremor has been reported in only one case. This report is to highlight this manifestation of this rare disease and the importance of considering PHACT in any patient presenting with a tremor, months to years after the implantation of a MoM device.

Case report:

A 44 year old male with history of hip replacement presented to PCP with progressive worsening of muscle weakness, fatigue and tremor of two months duration.

The patient has past medical history of: Charcot Marie Tooth (CMT) type 1 A, Hypogonadism and Hip Osteoarthritis and had foot surgery for CMT and Hip replacement with a metal on metal prosthesis five years back.

Physical Exam:

Vital signs, chest, abdomen and heart exam were within the normal limits.

New onset high frequency low amplitude, intentional tremor of truncal and upper extremities is noted. Strength was decreased all over as well as proprioception and vibration in feet; Patient was chronically areflexic from his CMT.

Workup:

After exhaustive work up and referrals, worsening of CMT, androgen deficiency and factitious disorder were considered.

Adequate testosterone replacement and thorough psychiatric evaluation didn't improve the tremor.

Meanwhile, patient started complaining of hip pain, with his history of metal on metal hip joint Prosthesis and refractory tremor; cobalt levels were checked.
**Imaging and Laboratory studies:**

Cobalt: 37 ng/ml (N = 0.0-0.9)

MRI brain was negative.

Nerve conduction study: severe chronic hereditary demyelinating neuropathy such as CMT 1A. However the temporal dispersion noted suggests an acquired inflammatory component.

Testosterone, Albumin and Chromium levels were within normal limits.

Right Hip MRI showing metallic artifact indicating a Metal on Metal Hip Prosthesis.

**Intervention:**
Removal of metal on metal hip prosthesis, it was replaced with Polyethylene and Oxinium Prosthesis.

Laboratory work and exam findings twelve weeks after intervention:

Cobalt: 2.6 ng/ml (N= 0.0- 0.9)

Complete resolution of tremor was noted.

Discussion:

While the use of metal-on-metal (MoM) hip devices in the USA is declining due to safety concerns,\(^1\) it is estimated that about 1 million MoM devices have been implanted worldwide in the past two decades.\(^2\) All such devices in the USA contain cobalt alloys. Normal wear and tear experienced by these devices has demonstrated release of metal microparticles and ions into systemic circulation.\(^4\) Concerns about device safety have caused product recalls and clinical guidelines by the Food and Drug Administration.\(^5\)

This case of prosthetic hip-associated cobalt toxicity (PHACT) is significant for a few reasons. First of all, little is known about PHACT and few cases have been reported. A systematic review carried out by Devlin et al in 2013 found only 10 cases, which met their criteria.\(^1\) It is hypothesized by the authors that the prevalence of suspected PHACT will increase in the coming years due to a growing population of patients who have had MoM devices for many years as well as an increased index of suspicion in treating physicians. In this regard, this case certainly highlights the likelihood of PHACT being initially overlooked as a diagnosis.

Perhaps most significant about this case was the patient’s chief complaint of tremor. Of the ten cases reported by Devlin et al, nine of them had neurologic manifestations yet only one of them presented with a tremor. In a 2012 review of neurological involvement of cobalt toxicity by all routes of ingestion by Catalini et al, only one out of eleven cases (the same case in fact) demonstrated tremor.\(^6,7\) Neurologic dysfunction due to cobalt toxicity by any route (the historic routes being cobaltous chloride infusion for hematopoiesis, industrial exposure, and consumption of beer containing excess cobalt\(^8\)) presents similarly to that seen in PHACT. The most common neurotoxic symptoms include hearing loss, visual impairment, and polyneuropathy. The mechanism by which cobalt causes neurotoxicity is controversial and likely multifactorial. Cobalt is known to be directly cytotoxic to neurons, disrupt oxidative phosphorylation, alter neurotransmitter regulation, phosphorylate MAP kinases, and repress the p53 gene.\(^6\) And more recently, metal ions on cell- mediated immunity, lymphocyte reactivity and chemokine secretions have been demonstrated among other actions.\(^10,11,12\)

Tremors are quite common with an estimated worldwide prevalence of essential tremor alone reaching as high as 5 percent of the population.\(^9\) Also, CMT type 1A Neurological manifestation does include kyphoscoliosis, postural hand tremor, hypoacusia, motor and sensory loss and areflexia of upper and lower extremities, pes cavus.\(^13\) This case, however, displayed a temporal relationship of device implantation followed by clinical symptoms as well as serum abnormalities, which were both relieved by removal of the device.
The discussion would not be completed if reports against PHACT were not reviewed. Retrospective and case studies measuring ERY have reported evidence against implant derived cobalt toxicity.\textsuperscript{14} Also in a self-reported cross sectional study, the neurological symptoms did not correlate to the elevated cobalt levels.\textsuperscript{15} This could be attributed to the rarity of this condition and the lack of concrete guidelines.

This case is a good example of anchoring heuristic bias and how it can affect patient outcomes. This patient’s known diagnoses of CMT as well as hypogonadism lead to exhaustive workup and referrals. As the patient’s condition failed to improve, he underwent both testosterone replacement and psychiatric therapy for possible diagnoses of androgen deficiency and factitious disorder respectively.

**Conclusion:**

This original case report describes a novel presentation of a poorly understood and rarely reported phenomenon. The diagnosis of PHACT can be complicated as its etiology and symptoms span numerous clinical specialties. During the evaluation of tremors, especially in individuals with MoM implantation, PHACT should be considered as a differential diagnosis. Additional studies and reports would be beneficial in forming better guidelines for diagnosis and treatment to improve patient care.
References:

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