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Original Article

Dissolution of tungsten coils does not produce systemic toxicity, but leads to elevated levels of tungsten in the serum and recanalization of the previously occluded vessel

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Abstract *Aim:* To evaluate the failure of mechanically detachable spirals produced from tungsten (MDS, Balt, Montmorency, France) and the toxicity of elevated levels of tungsten in the serum subsequent to their implantation. *Methods:* We reviewed findings in 21 patients in whom tungsten coils had been used to occlude pathologic vessels, aneurysms and fistulas between 1996 and 1999. We achieved clinical follow-up, and measured renal and hepatic function, in 14 of the 21 patients. *Results:* Decreased radiopacity of the coils was observed in 9 of 13 patients who had follow-up fluoroscopy during repeat cardiac catheterization. Repeat angiography of the vessel occluded by the coil was performed in 7 patients, 5 of whom showed recanalization. Levels of tungsten in the serum were analyzed 6 to 35 months after implantation of coils in 8 patients. The mean concentration was 6.43 μg/l, with a range from 2 to 14.4 μg/l, normal values being less than 0.2 μg/l. *Conclusion:* Tungsten coils may dissolve over time and lead to markedly elevated levels of tungsten in the serum, with recanalization of previously occluded vessels. Despite lack of clinical and laboratory data in patients with elevated levels of tungsten in the serum, our study suggests that the clinical use of mechanically detachable coils produced from tungsten should no longer be recommended.

Keywords: Aneurysm; carotid artery; arteriovenous malformation; embolization; interventional radiology

For more than three decades, embolization using coils has been the standard technique for catheter occlusion of pathologic vessels, aneurysms, and fistulas. Currently available coils are produced from stainless steel matching categories 304 and 316-L of the American Iron and Steel Institute, platinum, and tungsten. Due to its high radiopacity, tungsten is an attractive material for use as an endovascular coil. Even tiny filaments of tungsten can be clearly localized on fluoroscopy. Furthermore, its thrombogenicity[1] leads to a high primary rate of success, with no residual shunting after implantation of the coil. Recently, decreased radiopacity of mechanical detachable coils made of tungsten (MDS, Balt Extrusion, Montmorency, France), and elevated levels of tungsten in the serum, were reported subsequent to the occlusion of intracranial aneurysms, collateral vessels, and varicose veins.[2–5]

To assess whether similar findings could be observed in patients treated with coils for the occlusion of aorto-pulmonary or venous collateral channels, coronary artery fistulas, persistent arterial ducts, and vessels nourishing hepatic hemangioendotheliomas, we reviewed data from patients in whom tungsten coils had been implanted at our institution between the years 1996 and 1999. We searched for signs of clinical pathology in all patients with elevated levels of tungsten in the serum, both clinically and by testing renal and hepatic function.

Patients and methods

From August 1996 to October 1999, we occluded pathologic vessels by insertion of coils in 104

*It is with great regret that we report that Professor Hausdorf died subsequent to the completion of this manuscript.

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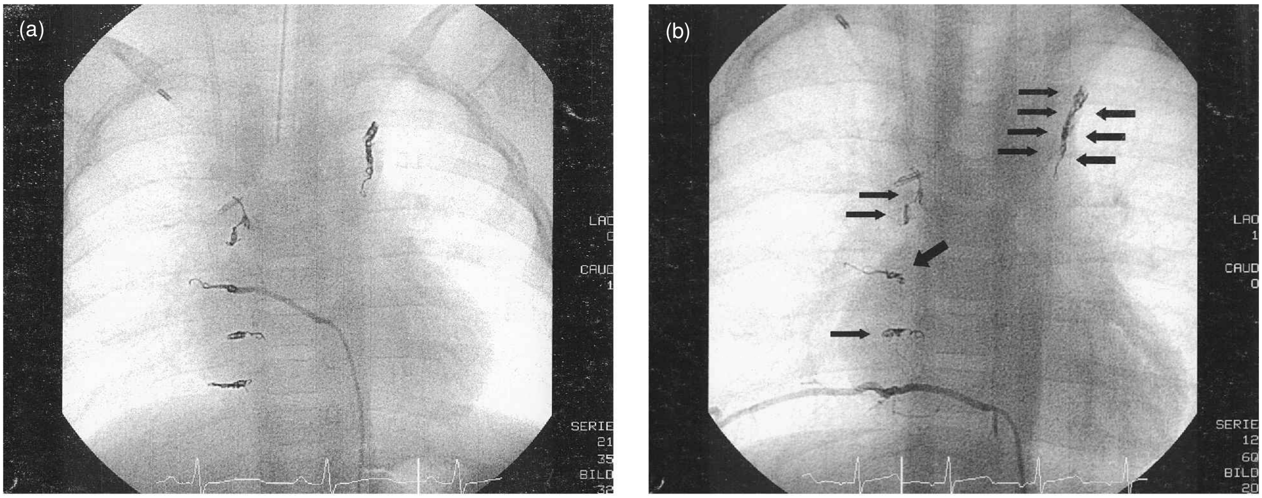

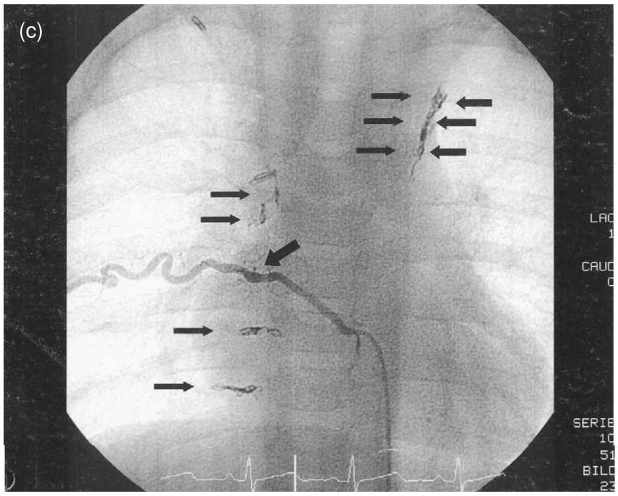

Figure 1.
Angiography (a) immediately after implantation of seven detachable coils for occlusion of aorto-pulmonary collateral arteries in our third patient. There is complete occlusion of the aorto-pulmonary collaterals. Follow-up angiography after 8 months (b and c) revealed recanalization of all the collateral arteries. Note the decreased radiopacity and blurred contour of the tungsten coils (arrows).

patients. The channels were aorto-pulmonary or venous collaterals due to cyanotic congenital cardiac malformations in 28 patients, coronary arterial fistulas in 2 patients, and vessels nourishing hepatic hemangioendotheliomas in 4 patients. Persistent arterial ducts were occluded in 70 patients. A total of 219 coils were implanted, 132 of these being mechanically detachable coils produced from stainless steel, the steel satisfying category 304 of the American Association for Iron and Steel category, and the coils being the "Flipper" variant manufactured by Cook at Bjaeverskov in Denmark. The remaining 87 coils were made of tungsten, being the mechanical detachable spirals produced by Balt at Montmorency, France. All patients with ducts had them closed with detachable steel coils, but 87 tungsten coils of different sizes were implanted, either exclusively or in addition to the detachable Cook coils, in 21 of 34 patients with aorto-pulmonary or venous collateral channels, coronary arterial fistulas or hepatic hemangioendotheliomas. Angiography after the implantation confirmed complete occlusion of the chosen vessel in all patients. Follow-up fluoroscopy, using the same fluoroscopic equipment, was available to evaluate the radiopacity of the tungsten coils in 14 of these 21 patients. Chest radiographs were available in an additional 2 patients. To study recanalization of the previously occluded vessels, follow-up was available in 11 of the 21 patients. Of these, 7 patients were examined angiographically during repeat cardiac catheterization, while an additional 4 of the 21 patients with hepatic hemangioendotheliomas were evaluated by color-coded duplex abdominal sonography. The mean age of the 21 patients in whom tungsten coils were implanted was 97 months, with a range from 2 days to 38 years. The mean body weight was 26.3 kg, with a range from 2.45 to 80 kg.

Levels of tungsten in the serum were analyzed in 8 of the 21 patients after obtaining consent of their parents to draw an additional 2 ml of blood during a venous puncture as part of their routine check-up.

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Blood was drawn using teflon cannulas, and was transferred into standard containers with no further addition of anticoagulants. Levels of tungsten were determined by inductive coupled plasma mass spectrometry focusing on the isotope 184 (Labor Schiwara, Hafer Sende, Bremen, Germany). Normal values were taken from the cohort studied by Minoia et al.[6] The other 13 of the 21 patients who were previously referred to our institution for occlusion of vessels using coils were not available for follow-up in terms of laboratory data. Of these 13 patients, the parents of 8 refused to consent to further checks since their children were in good clinical condition. The other 5 patients were lost to follow-up.

Routine follow-up laboratory findings were available in 14 of the 21 patients, including complete blood count, creatinine, blood urea nitrogen, enzymes, clotting factors II and V, gamma-GT, bilirubin, alkaline phosphatase, total protein, and electrolytes. Complete physical examinations and electrocardiograms were performed in 16 of the 21 patients, but the other 5 patients, as already indicated, were lost to follow-up.

Results

Implantation of the coils resulted in a mean load of tungsten of 0.22 g, with a range from 0.05 to 0.52 g. The mean ratio of implanted tungsten to body weight was 18.5 mg tungsten per kg body weight, with a range from 4.9 to 45.0 mg/kg. Follow-up with fluoroscopy in the 14 in whom tungsten coils had been implanted showed a decreased radiopacity (Fig. 1) of at least one of the coils implanted in 9 of 14 patients when compared qualitatively with the digitally recorded appearance at implantation (Fig. 1a). Review of the chest radiographs in two further patients performed 3, 4, and 6 months after the implantation showed no change in the radiopacity of the implanted coils. Repeated angiography in 7 patients demonstrated recanalization of 1 to 4 of the previously occluded vessels in 5 patients (Figs 1b, c). In all recanalized vessels, the coils showed a decreased radiopacity. Color-flow duplex-sonography demonstrated no recanalization of the occluded vessels in the 4 patients with hepatic hemangioendotheliomas. The levels of tungsten in the serum were markedly elevated in all 8 patients in whom it was possible to measure levels, ranging from 2.0 to 14.4 μg/l, with a mean of 6.43 μg/l, compared to normal values of less than 0.2 μg/l (Figs 2–4). No patient complained of unexplained symptoms on follow-up physical examination. Routine laboratory tests, performed in 14 of the 21 patients, were all within normal limits. The results are summarized in Table 1.

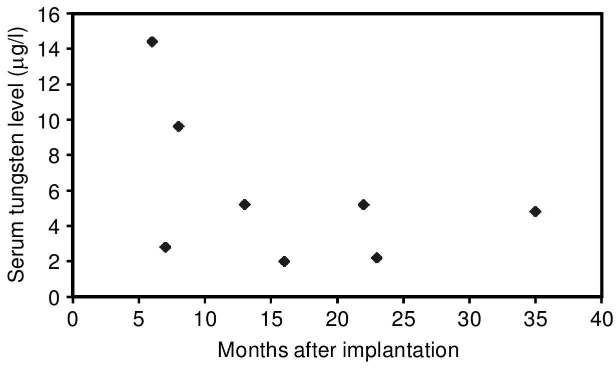

Figure 2.
Levels of tungsten in relation to time after implantation.

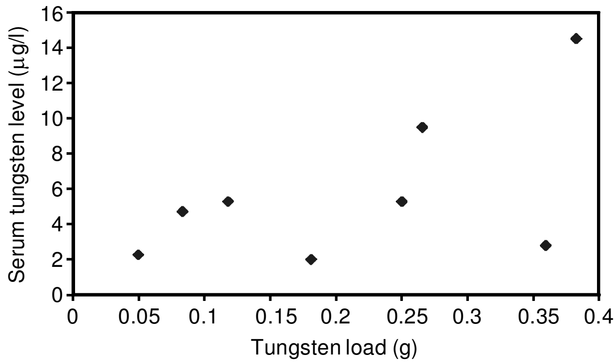

Figure 3.
Levels of tungsten in relation to the weight of the tungsten coils implanted.

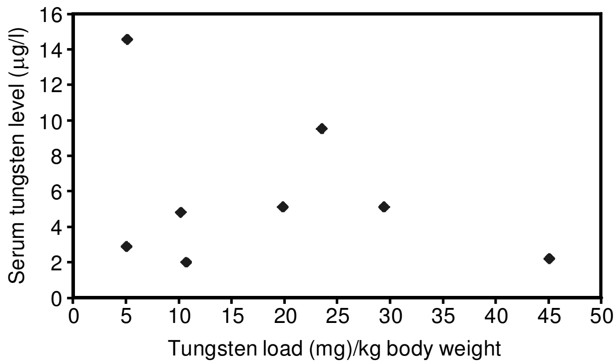

Figure 4.
Levels of tungsten levels in relation to weight of tungsten implanted per kg of body weight.

Discussion

We have demonstrated that tungsten coils undergo dissolution subsequent to their implantation for occlusion of vessels, and that the dissolution results in recanalization of the previously occluded vessel. The degradation of the tungsten coils produced elevated levels of tungsten in the serum, albeit that

Table 1. Clinical data and follow-up of the patients in whom mechanical detachable spiral tungsten coils were implanted between 1996 and 1999.

At implementation													
Patient	Age	Body weight (kg)	Follow-up after (months)	X-ray	Fluoro-scopy	Radio-pacity	Sono-graphy	Angio-graphy	Recanali-zation	Number of MDS coils implanted	Total weight of coils (g)	Serum tungsten level (μg/l)	Renal and liver function test
1	7 mon	6.1	13	+	+	Decreased	−	+	+	2 × MDS 2 × 50 1 × MDS 4 × 80	~0.12	5.2	WNL
2	13 mon	8.5	22	+	+	Decreased	−	−	−	1 × MDS 5 × 150 1 × MDS 2 × 50 1 × MDS 6 × 300	~0.25	5.2	WNL
3	24 mon	11.3	8	+	+	Decreased	−	+	+	2 × MDS 4 × 80 4 × MDS 5 × 80 1 × MDS 5 × 150	~0.25	9.62	WNL
4	3 mon	4.7	22	+	+	Decreased	−	−	−	1 × MDS 5 × 100	~0.05	2.2	WNL
5	18 y	70	7	+	+	Decreased	−	−	−	4 × MDS 7 × 100 1 × MDS 4 × 80	~0.36	2.8	WNL
6	4 mon	4.0	16	+	+	Normal	−	−	−	3 × MDS 4 × 80 1 × MDS 3 × 50 1 × MDS 2 × 50	~0.18	2.0	WNL
7	23 y	77	6	+	+	Decreased	−	+	+	2 × MDS 2 × 50 3 × MDS 3 × 50 3 × MDS 4 × 100 1 × MDS 5 × 100	~0.38	14.4	WNL
8	12 mon	7.8	35	+	+	Decreased	−	+	−	1 × MDS 2 × 50 1 × MDS 4 × 80	~0.08	4.8	WNL
9	1.5 mon	2.50	3	+	+	Normal	+	−	−	1 × MDS 3 × 50 1 × MDS 5 × 150	~0.12	No consent	WNL

10	38 y	80	3	+	+	Decreased	−	+	+	1 × MDS 2 × 25 1 × MDS 3 × 50 1 × MDS 4 × 80 3 × MDS 3 × 80 5 × MDS 5 × 100 1 × MDS 5 × 150	~0.53	No consent	WNL
11	2 mon	4.1	7	+	−	Normal	+	−	−	4 × MDS 5 × 100	~0.21	No consent	WNL
12	47 mon	17.6	5	+	+	Normal	−	+	−	2 × MDS 3 × 50 2 × MDS 3 × 80 2 × MDS 5 × 150	~0.32	No consent	WNL
13	2 d	3.5	8	+	−	Normal	+	−	−	3 × MDS 3 × 80 2 × MDS 5 × 100 2 × MDS 5 × 150	~0.39	No consent	WNL
14	17 y	53	1	+	+	Normal	−	−	−	1 × MDS 5 × 100	~0.05	No consent	WNL
15	5 mon	7.0	4	+	+	Normal	+	−	−	1 × MDS 2 × 50 1 × MDS 3 × 50 4 × MDS 5 × 100 4 × MDS 7 × 100	~0.55	No consent	No consent
16	7 y	21	12	+	+	Decreased	−	+	+	1 × MDS 3 × 50 1 × MDS 3 × 80	~0.08	No consent	No consent
17	22 mon	11.3	Lost to FU							1 × MDS 6 × 300	~0.15		
18	16 y	50	Lost to FU							2 × MDS 10 × 300	~0.32		
19	15 y	37	Lost to FU							1 × MDS 5 × 150	~0.08		
20	17 y	55	Lost to FU							2 × MDS 5 × 150	~0.16		
21	6 y	20.6	Lost to FU							2 × MDS 5 × 100	~0.11		

Abbreviations: FU: follow-up; WNL: within normal limits

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no adverse clinical effects were identified during follow-up of the patients.

In keeping with our own findings, to date there are no reports of clinical evidence of toxicity or unexplained clinical symptoms in patients in whom fluoroscopy is suggestive of degradation of tungsten coils.[2–5] To date, the only reported sign of clinical toxicity associated with high levels of tungsten in the serum involves a 19-year-old patient who was discovered convulsing and unconscious after ingesting tungsten-contaminated wine. Tungsten was measured at 5 mg/l in the serum, and analysis of gastric contents revealed levels of 8 mg/l.[7] He recovered after one day, but developed transient renal failure with tubular necrosis. The authors attributed these findings to the elevated levels of tungsten, albeit that this conclusion was questioned by others.[8]

There is currently a lack of concise data on the toxicity and clearance of tungsten in humans. The role of tungsten in occupational exposure to metal dusts, named "hard-metal" – lung disease, leading to pulmonary interstitial fibrosis, remains unclear. The local deleterious effects of tungsten on the lung seem to be dependent of the interaction with cobalt-particles,[9,10] and may therefore not be transferred to the intravascular compartment. Tungsten is reported to be poorly soluble in water, and therefore resorption was assumed to be sparse.[11] Concentration of tungsten in the blood, toenails, urine and pubic hair, nonetheless, is elevated in asymptomatic workers exposed to tungsten dust as compared to normal subjects.[12] No systemic toxicity occurred in humans after ingestion of 25 to 80 g of tungsten powder, used as substitute for barium in radiological examinations.[13]

An important finding in our study is the observation of recanalization of the vessels previously occluded by the tungsten coils. It is possible that the recanalization is related to the dissolution of the coil. Dissolution of the coil, in contrast, may also be related to the recanalization of the vessel. In occluded vessels, the pH will decrease due to local acidosis secondary to metabolic processes and lack of oxygen carriers, leading to a stabilized oxide layer on the tungsten coil, called passivation. In contrast, a constant flow of blood around the coil may accelerate its degradation by keeping the pH at a level higher than 7.4. The concept of residual flow within the vessel may explain our observation that, within the same patient, one coil shows a decreased radiopacity while another implanted in a different vessel does not. Another possible explanation of the latter finding could be a different composition of the coils, such as different contaminants in the tungsten, different working, and different surfaces of the coils with different lot numbers, with differing corrosion characteristics.

Due to the retrospective nature of our study, we were unable to define levels of tungsten in the serum prior to implantation. Since we did not identify any other potential cause of elevated levels in any of our patients besides the implantation of tungsten coils into the vasculature, we compared the levels with existing normal values.[6] Recanalization was observed in 5 of 7 patients. Repeated angiography, however, was performed in only 7 of our 21 pertinent patients, since this procedure was not part of our routine follow-up in patients having implantation of tungsten coils.

In conclusion, we have shown that mechanical detachable coils made of tungsten may dissolve over time, leading to recanalization of the previously occluded vessel and markedly elevated levels of tungsten in the serum. The clinical use of these coils, therefore, can no longer be recommended, even though, as yet, there is lack of evidence for direct toxicity of tungsten. Patients in whom tungsten coils have already been implanted should be followed thoroughly, measuring levels of tungsten in the serum and evaluating both hepatic and renal function. Repeated angiography may be warranted if decreased radiopacity is observed.

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