Between 1992 and 1996, a man from the UK, in his early 40s, worked in Bosnia. He had been well, except for his longstanding asthma, nasal polyps, and eczema, but developed persistent abdominal pains and periodic fatigue, unrelated to exertion, for which no medical cause was identified. In 1997, the patient had a cholecystectomy for right hypochondrial tightness, and a Nissen’s fundoplasty for Barrett’s oesophagus. However, his fatigue and discomfort became so severe that he retired involuntarily. In 1999, the patient spent 12 months in Kosovo. By now, he had increasing cramps of the abdominal muscle wall and viscera, altered bowel habit, and weight loss of 19 kg. In 2001, he developed morning stiffness of his back, knees, and elbows, facial paraesthesias, and nocturia. In 2003, the abdominal tightness developed into truncal flexion jerks; later, he developed spasms in his left arm and hips.

In 2004, we observed a stiff gait, abdominal myoclonus, and an enhanced (neurological) startle response. MRI of the head and spine showed nothing of note. Blood tests revealed slightly high concentrations of creatinine (138 μmol/L), bilirubin (20 mmol/L), and γ-glutamyl-transferase (121 U/L); the blood film and concentration of C-reactive protein were normal. Ultrasonography and CT of the abdomen, and analysis of CSF, showed no abnormality. Further blood tests showed a normal concentration of angiotensin-converting enzyme, and absence of antibodies to nuclear factor, neutrophil cytoplasm, DNA, endomyosiun, and neurones; results of electrophoresis were normal. The blood lead concentration was undetectably low. However, we found high concentrations of IgA (5·4 g/L), IgE (475 IU/mL), cardiolipin (62 U/mL), and antibodies to glutamic acid decarboxylase (GAD) (3·3 U/mL; normal <1·0 U/mL). Electromyography showed focal continuous motor unit activity, and abnormal exteroceptive spinal reflexes. We sought further neurological opinions; provisional diagnoses included stiff person syndrome—given the stiffness, muscle spasms, and antibodies to GAD—and propriospinal myoclonus. Treatment with baclofen, and a trial of intravenous immunoglobulin, provided temporary, symptomatic relief.

We found proteinuria (0·2 g per 24 h) and erythrocyturia (2·4×10⁶ cells per 24 h). Histopathological examination of a kidney biopsy sample showed mesangial expansion and dominant mesangial IgA, without vasculitis—findings diagnostic of (partly autoimmune) IgA nephropathy. In the liver, we found steatosis, and a non-caseating granuloma. Electron microscopy of kidney and liver tissue showed giant mitochondria, without cristae. Even without osmium staining, the mitochondria had high electron densities consistent with heavy-metal deposition (figure); we also saw a nuclear inclusion (webfigures 1–4). Spectrometry showed intense signals from lead-207, lead-208, uranium-235, and uranium-238, distributed throughout the cells, rather than localised in organelles. We gave the patient intravenous calcium sodium edetate; thereafter, we prescribed 2,3-dimercaptopropanoesic acid, 250 mg twice daily, which he still takes. Urinary excretion of lead was 50–180 μg per month initially, and 400 μg per month with oral treatment. Nephritis resolved, kidney function and neurological health improved, and concentrations of antibodies to GAD returned to normal. Within 12 months of starting treatment, the patient was able to work. We intend to continue treatment until heavy-metal excretion is undetectable.

Some people in war zones develop unexplained neurological or psychiatric syndromes. Little information exists on tissue heavy-metal sequestration in war zones. Spectrometry allowed us to find substantial metal deposits that would otherwise have been unrecognised. The ratio of 239U to 235U, at about 10:1, was consistent not with depleted uranium from ordnance (99·7% ²³⁵U), but with enriched, fissile uranium. Natural lead isotope ratios were found. We suspect that our patient’s food was grown in soil contaminated with lead and uranium (many international workers ate food grown outside Bosnia). Heavy-metal toxicity results in part from disruption of cellular metabolism; we surmise that mitochondrial dysfunction in part caused the illness. Heavy-metal poisoning can also induce autoimmunity, which was detected, and resolved with our patient’s recovery. Our diagnostic methods may prove pivotal in assessment for metal poisoning.

References

**Figure:** Evidence of heavy-metal poisoning

(A) Electron micrograph, showing metal deposits resembling those caused by staining; magnification ×29 000. (B) Laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) of ²³⁸U. See webfigures for other isotopes.