

## CASE REPORT

# Dementia, epilepsy and polyneuropathy in a mercury-exposed patient: investigation, identification of an obscure source and treatment

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**SUMMARY**

We present a patient aged 54 years with early onset of dementia, epilepsy and peripheral polyneuropathy. A mercury intoxication was diagnosed in 2010, chelation therapy with 2,3-dimercaptopropane-1-sulfonate had failed. A source of exposure could not be identified. MRI showed unspecific hyperintense brain lesions in 2015. She was referred for diagnosis and treatment. Neuropsychological testing indicated severe memory loss and nerve conduction speed measurements showed chronic neurogenically changed potentials. Mercury levels in blood and urine and neuron-specific enolase (NSE) were elevated. A detailed patient history revealed a daily application of mercury-containing skin lightening creams for 6 years. Treatment with 2,3-dimercaptosuccinic acid (DMSA) was started, blood mercury levels were falling during treatment. She was discharged with DMSA prescriptions. A renewed MRI revealed unchanged brain lesions. Blood and urine mercury levels and NSE were falling. Memory function had improved qualitatively and quantitatively.

**BACKGROUND**

Mercury intoxications due to mercury-containing skin cream have previously been reported as well as hyperintense brain lesions in mercury-intoxicated children. It has been described that an elevated neuron-specific enolase (NSE) is sometimes associated with severe mercury intoxications.

2,3-Dimercaptopropane-1-sulfonate (DMPS) and 2,3-dimercaptosuccinic acid (DMSA) have been used as therapy modalities; however, it remains unclear which treatment is superior. It is also being discussed if treatment can be successfully switched from one drug to the other in the case of adverse reactions to one of the drugs.

To the best of our knowledge, this is the first case of an adult with severe neurological symptoms due to a mercury intoxication via a skin lightening cream, corresponding MRI findings and an elevated NSE. This case also demonstrates that DMPS and DMSA can be switched if one drug cannot be used due to adverse effects.

We performed extensive initial investigations and diagnostics and the corresponding diagnostics in the follow-up to allow quantifying the effects of the intoxication and treatment. We could show a measureable improvement of the symptoms as well as the laboratory findings.

**CASE PRESENTATION**

A female patient aged 54 years with an onset of dementia and epilepsy and peripheral polyneuropathy at the age of 49 (2010) was referred to our hospital in 2015. She is born in Morocco, lives there 7/12 months and is analphabetic since she never visited school.

She is status post (s.p.) toxic hepatopathy due to acetaminophen overdose and s.p. hepatitis A. She currently suffers from a minor depression and is treated for epilepsy with oxcarbazepine after having had generalised seizures in 2010. A peripheral polyneuropathy was diagnosed in 2010.

A chronic mercury intoxication was diagnosed in 2010 with mercury-specific skin lesions<sup>1</sup> and elevated blood mercury levels. Treatment with DMPS failed due to adverse dermatological effects in 2013. Under treatment, the initially elevated blood mercury level of 90 µg/L (reference <2) fell to 8.4 and subsequently 2.5. After treatment had to be stopped, the mercury level reincreased to 24 and stayed elevated at 13.3 µg/L until admission to our hospital. Methylmercury was normal at 0.9 µg/L (<1).

Neuropsychological testing (NPT) was conducted in 2013 revealing signs of severe dementia (Neuropsychological Test Battery (NTB) abnormal in 16/18 variables, Mini-Mental-State (MMS) 17/30 points).

Owing to her epilepsy and further progression of her dementia, MRI of the brain was performed in 2015. The T2 sequence showed unspecific hyperintense lesions in the supratentorial region, especially in the frontal superior gyrus, semioval centre and frontal region. Further lesions were seen in the right cerebral peduncle and subcortical temporo-occipital region (figure 1, upper row). Owing to the distribution and localisation of the lesions, an inflammatory cause was considered unlikely and a stroke ruled out.

The MRI revealed no cause for her epilepsy, neither did the EEG. Therefore, the mercury poisoning was assumed to be the most probable cause of the epilepsy.

It is known that chronic mercury poisoning can cause neurocognitive deficits; however, it is unclear if it can cause mood disorders such as, for example, depressions. In our case, it remains unclear if the patient's depression was caused by the mercury poisoning or if it had another cause.

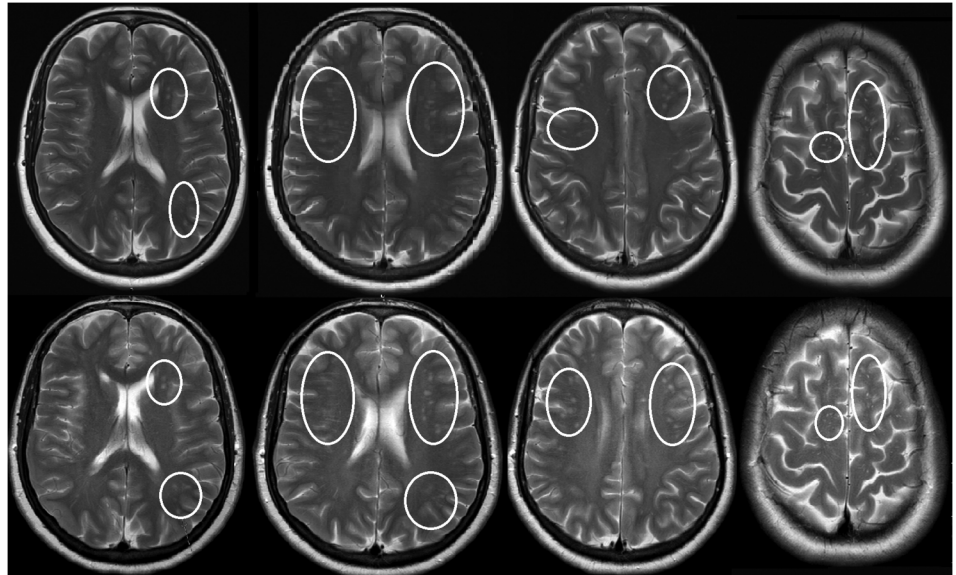
Since the patient partially lives in Morocco, a probable source of mercury exposure was considered environmental, for example, mercury-



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**Figure 1** MRI with unspecific lesions (marked in circles) in T2 sequence at initial presentation (upper row) and corresponding images at follow-up 3 months later (below).



containing fish dishes or the proximity of her residence to a copper mine.

**INVESTIGATIONS**

The physical examination on admission was normal except for mercury-specific skin lesions on shins and calves. A neurological examination revealed pain in all extremities without paraesthesia and paresis. She also suffered from headaches and had pain ‘in her whole body’. Her pallesthesia was not impaired.

The NPT revealed a progress of her dementia: severe deficits were seen especially in her verbal and non-verbal-figurative retentiveness, including recognition. Furthermore, she was oriented to person but not to place, time and situation and had severe concentration issues. The CERADplus-NTB<sup>2</sup>—a test for Alzheimer’s disease—was abnormal in 17/18 variables and she scored 8/23 points in the modified MMS.

Standard laboratory tests in blood and urine, including NSE and proteinuria diagnostics, showed microhaematuria and an

elevated NSE. Further samples were sent to a specific laboratory for mercury and heavy metal analysis (table 1).

An ECG, electromyogram and EEG were normal. Nerve conduction speed measurements showed chronic neurogenically changed potentials in the right anterior tibial muscle but otherwise no abnormalities.

A lumbar puncture was planned and recommended; however, the patient refused this procedure and subsequent cerebral-spinal fluid (CSF) diagnostics.

A detailed patient history was obtained to further identify the source of exposure. The Morocco residence with proximity to the copper mine was ruled out as was the sea-fish consumption (normal methylmercury levels). A daily application of skin lightening creams (Shirley Beauty Cream, Taiwan and IDEAL cream, Lebanon; figure 2) over the last 6 years was considered a possible source. Positive laboratory tests for mercury in cream samples with 420 and 20 000 mg/kg, respectively, confirmed this hypothesis and exposure was stopped immediately.

**Table 1** Notable symptoms, tests and measurements

	2013–2015	First admission May 2015	Follow-up admission 3 months after discharge
Blood		<b>NSE 31.4 µg/L (≤16)</b>	<b>NSE 20.5 µg/L (≤16)</b>
Urine		<b>Leucocytes 25, erythrocytes in sediment 4–10 (0–3)</b>	Normal
Heavy metal analytics (µg/L)	Blood 8/7/13, initial diagnostic: <b>Hg 90 (&lt;2)</b> 9/7/13, during DMPS-therapy: <b>Hg 8.4 (&lt;2)</b> 31/7/14, during DMPS-therapy: <b>Hg 2.5 (&lt;2)</b> 23/1/15, after DMPS-therapy: <b>Hg 24 (&lt;2)</b> 5/3/15, without therapy: <b>Hg 32 (&lt;2)</b> , Methyl-Hg 0.9 (<1)	Blood Admission: <b>Hg 13.3 (&lt;2)</b> Day 5 of DMSA-therapy: <b>Hg 5.2 (&lt;2)</b> Urine <b>Hg 18.4 (&lt;1), Hg qualitative positive; Ir &lt;0.47 (&lt;0.2)</b> , Shirley Beauty cream (Taiwan)—applied for 6 years before first admission <b>Hg 420 mg/kg</b>	Blood After 4 weeks of DMSA-therapy and 2 months without therapy: <b>Hg 2.8 (&lt;2)</b> Urine <b>Hg 3.7 (&lt;1)</b> Ideal cream (Lebanon)—applied for 6 years before first admission <b>Hg 20 000 mg/kg</b>
NCS		<b>Chronic neurogenically changed potentials in right TAM</b>	No examination
NPT/MMS	2013: <b>MMS 17/30, NPT 2/18</b>	<b>MMS 8/23, CERADplus-NTB 1/18</b>	<b>MMS 12/23</b>

Clinical, laboratory and examination results with reference when applicable; italic indicates time of measurement/test; bold indicates abnormal results. CERAD, Consortium to Establish a Registry for Alzheimer’s Disease; EKG, electrocardiogram; Hg, mercury; Ir, iridium; MMS, Mini-Mental-State; NCS, nerve conduction speed; NPT, neuropsychological testing; NSE, neuron-specific enolase; NTB, neuropsychological test battery; TAM, tibial anterior muscle.

**Figure 2** Skin lightening creams containing exorbitantly high mercury concentrations. Left: Shirley Beauty Cream, Taiwan (photographed). Right: ideal cream, Lebanon (source: <http://www.saudi.souq.com>).



## TREATMENT

Treatment with 200 mg oral DMSA three times a day was started and well tolerated. After 5 days of treatment, the blood mercury level had fallen from 13.3 to 5.2 µg/L. The patient was discharged with a DMSA prescription for the next 4 weeks.

## OUTCOME AND FOLLOW-UP

The physical examination remained unremarkable including still present skin lesions. There was no new episode of cerebral seizures. A repeated NPT revealed a qualitative improvement of her dementia also demonstrated in improved MMS testing (score 12/23). Her main improvements were in verbal retentiveness and concentration. This time she was oriented to person, time and situation but not to place.

A depressive episode with somatisation disorder was diagnosed and treatment with vortioxetine and olanzapine was started. The focus of her somatisation was considered the whole-body pain without neurological explanation and we considered the diagnosis of peripheral polyneuropathy unlikely. In order to rule out confounders for the differences in the patient's neurocognitive performance, psychiatric treatment and medication was not started until after the follow-up examination.

Blood laboratory tests remained normal, NSE had fallen from 31.4 to 20.5 ng/mL and mercury from 5.2 to 2.8 µg/L (<2). Urine mercury had fallen from 18.4 to 3.7 µg/L (<1).

A repeated ECG and EEG remained normal.

In a renewed MRI, the pre-existing lesions remained unchanged and one new lesion was seen in the left temporo-occipital subcortical region (T2 sequence, [figure 1](#), lower row).

The patient was discharged with improved memory functions.

## DISCUSSION

The first wide-spread and devastating mass outbreak of mercury intoxications with over 20 000 victims was seen in Minamata disease, which first became evident in 1956 and was caused by methylmercury in contaminated seafood. Symptoms included sensory disturbance, constriction of the visual field, hearing impairment and cerebellar ataxia. MRI findings showed atrophies in the visual cortex, cerebellar vermis and hemispheres and postcentral cortex.<sup>3 4</sup> There was also a high rate of newborns with physical and cognitive deficiencies, attributed to Minamata disease.

Patients with inorganic mercury intoxications show neurological and psychiatric symptoms like fatigue, insomnia, weakness and acrodynia and general symptoms like pruritus,

erythema, renal tubular dysfunction and nephrotic syndrome.<sup>5</sup> One corresponding MRI showed hyperintense lesions in the cerebral white matter, globus pallidus and putamen. NSE levels can be elevated.<sup>5 6</sup> Our patient showed a set of symptoms not classically associated with mercury poisoning but similar MRI lesions and an elevated NSE.

Differential diagnosis for an elevated NSE are on the one side carcinomas-like small cell lung cancer or neuroblastomas and on the other side lesions or infections of the brain, such as meningitis, stroke, intracerebral haemorrhage, multiple sclerosis or Creutzfeldt-Jakob disease.

Differential diagnosis for dementia, seizures and polyneuropathy—among others, can be substance abuse and alcoholism, paraneoplastic neurological disorders, vitamin B<sub>12</sub> deficiency, severe hypothyroidism or neurological manifestations of HIV.

Therefore, it is essential to perform MRI diagnostics in order to rule out some of the mentioned differential diagnosis. In any case of rapidly progressing dementia, MRI diagnostics are recommended. Mercury and its metabolic products cause axon degeneration or cell death and neuron loss. These demyelinating effects can be seen in the T2-weighted MRI sequences.<sup>6</sup> If such lesions are detected, it is important to know that these can be caused by mercury since there is a risk of misdiagnosing patients otherwise.

Skin lightening creams are frequently used, for example, in Africa, the Middle East and Mexico since lighter skin represents a higher socioeconomic status.<sup>7 8</sup> Some creams contain exorbitant high concentrations of inorganic mercury which is readily absorbed through the skin.<sup>9</sup>

So far, only few cases of mercury poisoning due to skin cream have been described and all patients are children. It has been discussed that a child's nervous system is more vulnerable and could therefore more easily be affected by mercury.<sup>5</sup> To our best knowledge, this is the first adult case where chronic administration of mercury-containing skin creams results in neurological symptoms mimicking dementia and MRI changes. Since exposure was chronic and an adult's nervous system is less regenerative, it could explain that our patient's symptoms receded more slowly. This might explain why the MRI remained unchanged in our case. Furthermore, as the mercury exposure in our case persisted over several years, it is unlikely that after the relatively short time of non-exposure and treatment, morphological changes in the MRI would disappear completely.

During chelation therapy, symptoms and MRI findings may transiently worsen.<sup>5</sup> In one case, all symptoms and lesions were completely reversible after treatment was completed.<sup>5</sup>

Recently, it has been discussed that mercury may be an environmental cofactor responsible for Alzheimer's disease.<sup>10</sup> In this case, the chronic mercury exposure mimicked symptoms usually associated with dementia. Our patient could easily have been misdiagnosed with, for example, Alzheimer's disease and not have received the necessary specific treatment.

### Learning points

- ▶ Unspecific findings, such as MRI lesions or elevated NSE, can also be caused by (chronic) mercury poisoning but are frequently attributed to other causes.
- ▶ Identifying and stopping the source of exposure is crucial.
- ▶ Mercury-containing skin creams are used, for example, in Africa, the Middle East and Mexico and regular application can lead to poisoning.

**Contributors** TZ was responsible for patient treatment; NF and FE were the attending physicians. TZ was responsible for the concept and design of the case report. TZ compiled the data and drafted the article. All of the authors reviewed the content and approved the final version.

**Competing interests** None declared.

**Patient consent** Obtained.

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### REFERENCES

- 1 Ozkaya E, Mirzoyeva L, Otkür B. Mercury-induced systemic allergic dermatitis caused by 'white precipitate' in a skin lightening cream. *Contact Derm* 2009;60:61–3.
- 2 Schmid NS, Ehrensperger MM, Berres M, et al. The extension of the German CERAD neuropsychological assessment battery with tests assessing subcortical, executive and frontal functions improves accuracy in dementia diagnosis. *Dement Geriatr Cogn Dis Extra* 2014;4:322–34.
- 3 Korogi Y, Takahashi M, Okajima T, et al. MR findings of Minamata disease—organic mercury poisoning. *J Magn Reson Imaging* 1998;8:308–16.
- 4 Korogi Y, Takahashi M, Sumi M, et al. MR imaging of Minamata disease: qualitative and quantitative analysis. *Radiat Med* 1994;12:249–53.
- 5 Benz MR, Lee SH, Kellner L, et al. Hyperintense lesions in brain MRI after exposure to a mercuric chloride-containing skin whitening cream. *Eur J Pediatr* 2011;170:747–50.
- 6 Abbaslou P, Zaman T. A child with elemental mercury poisoning and unusual brain MRI findings. *Clin Toxicol (Phila)* 2006;44:85–8.
- 7 Adawe A, Oberg C. Skin-lightening practices and mercury exposure in the Somali community. *Minn Med* 2013;96:48–9.
- 8 Centers for Disease Control and Prevention (CDC). Mercury exposure among household users and nonusers of skin-lightening creams produced in Mexico—California and Virginia, 2010. *MMWR Morb Mortal Wkly Rep* 2012;61:33–6.
- 9 Choudhury K, Morris J, Harrison H, et al. Use of skin lightening creams. Dangers from mercury. *BMJ* 2011;342:d1327.
- 10 Mutter J, Curth A, Naumann J, et al. Does inorganic mercury play a role in Alzheimer's disease? A systematic review and an integrated molecular mechanism. *J Alzheimers Dis* 2010;22:357–74.

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