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ALS, mercury exposure, and chelation therapy

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To the Editor

We welcome and support the suggestions of Praline et al. [1] regarding the potential link between sporadic amyothrophic lateral sclerosis [sALS] and repeated overexposure to metallic mercury vapor.

Presumably, mercury appears to be involved in some cases of sporadic ALS [2,3], even though the literature shows conflicting results [4,5].

However, we would like to make the following points about their important case report.

First, metallic mercury vapor is both neurotoxicant and nephrotoxicant. Upon overexposure, mercury vapor may cause a nephrotic syndrome with proteinuria and – in some individuals – may thus lead to renal failure [6].

Given the very high levels of mercury in patient's urine (7282 μm/g creatinine), therefore, it would be informative to know more about the kidney conditions.

Second, the authors hypothesize that amounts of elemental mercury vapor [Hg^0] released from the pressure device's rubber might have been absorbed and deposited into the skin. We think that this possibility is extremely unlikely. Although mercury vapor may be adsorbed through the skin, however, its rate of absorption is believed to be only 2.2% [7].

Instead, we deem plausible that the patient was repeatedly exposed to elemental mercury vapor primarily via inhalation. Once carried to lungs, about 80% mercury vapors are absorbed and subsequently distributed to all tissues [8].

To our knowledge, X-ray image cannot rule out the presence of metallic mercury into the skin. Unlike metallic mercury vapor injected into soft tissues, when adsorbed onto skin surface, mercury vapor is unable – in our view – to form a network of mercury droplets large enough to provide sufficient radiopacity to X-ray.

Finally, in their discussion, the authors correctly point out that chelation therapy with the dithiol chelator *meso*-2,3-dimercaptosuccinic acid "DMSA must be initiated shortly after exposure to prevent accumulation and avoid toxicity." However, in their case report, chelation treatment with DMSA was started approximately 7 months after the last mercury vapor exposure.

We cast doubts about the efficacy of postexposure treatment delay with DMSA to prevent and/or to treat the metallic mercury toxicity. Studies in animal models have shown that neither DMSA nor any other chelating or mobilizing agents were able to ameliorate the brain burden of mercury [9,10].

Specifically, as yet, no evidence is available about the use of DMSA and its substantial reduction of the mercury levels in nervous system after exposure to metallic mercury vapor [9].

Further evidence against the use of chelating agents among patients with sALS came from an investigation in animals. The treatment with DMSA after exposure to inorganic mercury caused an increased elevation of mercury into motor axons presumably owing to redistribution of mercury, which was mobilized from non-neural tissues (e.g., kidneys and liver) [10]. It has been found that the metabolism of copper may be altered in humans after administration of DMSA [11]. Of particular interest, decreased cerebrospinal fluid and serum copper levels have been reported to be associated with sALS [12].

As a consequence, DMSA – as well as various mercury chelating agents – may cause worsening of patient's condition. This fact should be taken into account when using DMSA as chelators in persons with sALS [10]. Other investigators also cautioned regarding the use of chelators in sALS patients [10,13].

In strikingly contrast, previously published cases of amyotrophic lateral sclerosis after acute overexposure to elemental mercury resolved spontaneously without using any chelation treatment, within a few months after removal of sources of mercury [14,15].

These considerations raise the provocative question of benefits of chelating agents in persons who have sALS associated with overexposure to mercury.

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