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# First Epileptic Seizure Induced by Occupational Nickel Poisoning

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**Summary:** Toxic causes of seizures are numerous: alcohol and other substances of abuse, drugs, and industrial and household products. However, in the absence of a clearly suggestive history and/or associated symptoms and signs, identification of the toxic origin of new-onset seizures may be extremely difficult. We report here the case of a patient admitted in our hospital after a single generalized tonic–clonic seizure. The remarkable coincidence that a colleague of his, with whom he was working to clean the same workshop, had been admitted 1 week earlier for respiratory distress, coma, and de novo nonconvulsive focal status epilepticus, led us to consider a possible toxicologic etiology. Urine analysis revealed a high nickel concentration, suggestive of acute nickel poisoning. **Key Words:** Seizures—Poisoning—Nickel.

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## CASE REPORT

The patient was a 43-year-old man admitted to our hospital after an inaugural generalized tonic–clonic seizure. His medical and surgical history was unremarkable. The patient did not take or had not recently stopped any medication. He did not abuse alcohol or any other substance and did not recently modify his sleep or food habits. No familial history of epilepsy was known. He had worked for a couple of weeks in a car body–repair workshop where he was cleaning the ceilings of the building. On admission, physical and neurologic examinations were normal, except for a mild drowsiness attributed to a postictal state. No meningeal signs were seen. Prolactin and lactate levels were high on admission, 36.8 ng/ml (2.5–11) and 122.8 mg/dl (9–16), respectively. HbCO was normal (<5%). Glycemia and other routine blood analyses were within normal values. EEG performed a few hours later showed diffuse slow waves. Brain CT and MRI scans were normal. A diagnosis of first idiopathic generalized seizure was presumed, until we were informed that a colleague of the patient, with whom he was working to clean the same workshop, had been admitted 1 week earlier in the same hospital for respiratory distress, coma, and de novo nonconvulsant focal status epilepticus [global aphasia and continuous periodic left temporal epileptiform discharges on EEG, with remarkable improvement of language within a few minutes and resolution of epileptiform anomalies on the EEG performed a few hours later after intravenous injection of 5 mg valium and 1,250 mg phenytoin (PHT)]. This 34-year-old male colleague was already discharged, with no clear cause of his focal epilepsy despite an extensive biologic, infectious, and radiologic workup. With the second case of seizures a week apart in two patients employed in the same workshop, we considered a possible toxicologic etiology. Urine analysis revealed a high nickel concentration (18.7 $\mu$g/g creatinine, n = 2) on day 2. Urinary thiocyanate and 2-thiothiazolidine-4-carboxylic acid (TTCA, a metabolite of carbon disulfide) were normal (3.4 mg/g creatinine and not detected, respectively). The patient evolved uneventfully and was discharged on day 4. Six months later, he is still seizure free without any treatment.

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## DISCUSSION

Acute nickel poisoning occurs after inhalation of great amounts of nickel, most often in the form of nickel carbonyl [$Ni(CO)_4$], more rarely in the form of Ni, $Ni_3S_2$, NiO, or $Ni_20_3$ (1–3). $Ni(CO)_4$ is formed in the refining process of nickel and used as a catalyst in the production of petroleum, plastic, and rubber. Most acute $Ni(CO)_4$ poisonings occur in industrial environments, most often after pipe leaks or accidental discharges (2,3). A potential source of $Ni(CO)_4$ was not immediately apparent in the incriminated workshop, suggesting that other forms of nickel might be involved. Possible sources of Ni in the atmosphere of a car body–repair workshop are from fuel oil combustion and spray paints. The car body–repair workshop had hired the patient and his colleague for a very short period to perform a good cleaning of the ceilings. During this short period, no other worker was present in the workshop, and we could not identify a definite source of Ni poisoning. We therefore hypothesize that our patient could have been intoxicated by some form of Ni brought in suspension into the air by the cleaning of the workshop. The initial effects of acute nickel intoxication include irritation of the respiratory tracts and nonspecific symptoms (headache, dizziness, etc.). In patients with severe poisoning, intense pulmonary and gastrointestinal toxicity develops. Diffuse interstitial pneumonitis and cerebral edema are the main causes of death. Convulsions occur occasionally, sometimes terminally (1–3).

The colleague of our patient was already discharged, and it was probably too late to detect nickel in blood or urine. We could therefore not formally demonstrate the etiologic link between the two stories. It is, however, very tempting to evoke the possibility that in the first patient, who had been exposed during the same period to the same environment, acute respiratory distress, coma, and left temporal status epilepticus also were due to nickel intoxication. Focal seizures, especially from the temporal lobes, have been reported exceptionally with poisonings with methanol, carbon monoxide, lithium, or domoic acid (4–7). They suggest a higher susceptibility of the temporal cortex to potentially epileptic agents. In rats, when applied directly to the cerebral cortex, nickel is one of the most potent focal seizure-inducing metals (8). However, in humans, to our knowledge, focal seizures have not been described after nickel intoxication. In the particular case of inhaled nickel, focal accumulation of this metal in the temporal lobe cannot, however, be excluded. Studies with nickel and other metals, such as manganese, indicate that in their volatile form, these metals can be taken up in the primary olfactory neurons and be transported transneuronally to olfactory bulbs and even further into other areas of the brain (9). Animal studies suggest that inhibition of the glutamate transporter may be one mechanism explaining the seizures induced by nickel exposure (10).

In conclusion, we have reported the case of a patient with tonic–clonic seizure most probably induced by occupational nickel poisoning. This case underlines the importance to keep in mind the possibility of toxic-induced seizures in a patient with new-onset seizures of unknown etiology.

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