Psychosomatics 2015:56:202–205

Case Reports

Get the Lead Out: Potential Progressive Localized Neural Injury From Retained Cerebral Bullet Fragments Without Systemic Toxicity

Alvaro J. La Rosa, B.S., Clare A. Herickhoff, B.S., Katrina Hickle-Koclanes, B.S., Jason P. Caplan, M.D., Curtis A. McKnight, M.D.

Introduction

The toxidromes of lead and copper have been described clinically since the 19th century. Since then, a number of clinical reports have described disturbances of neurocognitive function in patients with retained bullet fragments and significant blood or cerebrospinal fluid levels of these heavy metals. Lead neurotoxicity has been attributed to disruption of intracellular signaling pathways and the production of free radicals.[1] Copper neurotoxicity is due to severe inflammation, resulting in demyelination and axonal degeneration.[2,3] Here, we describe the case of a 43-year-old white man with retained intracerebral bullet fragments who presented with a 6-month history of accelerated decompensation in cognitive and functional ability with undetectable peripheral lead levels.

Case Report

Mr. S, a 43-year-old right-handed white man, was admitted to the neurology service at our institution directly from an outpatient clinic for evaluation of cognitive and functional decline. He had experienced a gunshot injury 23 years before when a single .22-caliber bullet was accidentally fired into the right side of his head. The composition of the bullet was unknown but was almost certainly lead, based on its near-universal use in civilian ammunition (non-military bullet cores are typically composed of lead with some variation in metal used to jacket the core; recent environmental legislation in some regions has prompted a change from lead to copper bullet cores).[4] The midline of the right cerebral hemisphere was affected and he underwent right craniotomy for decompression shortly after the injury. The locations of bullet fragments made several of them unremovable.

In the months following the injury, he was documented to recover well. He was ambulatory with a cane and spoke fluently. He had some left-sided paresis but maintained most of his range of motion. Medical records and family report both indicated personality changes and poor impulse control evident in that time span consistent with frontal lobe injury. He was prescribed valproic acid at varying dosage over the following years with improvement in impulsivity. Four years after the injury, his family noticed very slow insidious functional decline with worsening neuromuscular weakness and an increasing frequency of falls. Over the next several years, his speech became more difficult to understand and he spoke less.

Received September 15, 2014; revised September 30, 2014; accepted October 1, 2014. From Creighton University School of Medicine—Phoenix Regional Campus, Phoenix, AZ (AJLR, CAH); Creighton University School of Medicine, Omaha, NE (KH-K); Department of Psychiatry, Creighton University School of Medicine at St. Joseph's Hospital and Medical Center, Phoenix, AZ (JPC, CAM). Send correspondence and reprint requests to Jason P. Caplan, M.D., 500 W Thomas Rd, Suite 710, Phoenix, AZ 85013; e-mail: jason.caplan@chw.edu

Valproic acid had been discontinued 6 years before his current admission and a number of other psychotropic trials were subsequently undertaken without benefit. At the time of admission, he was prescribed ascorbic acid 500 mg twice a day, chlorpromazine 50 mg 3 times a day, cyanocobalamin 1000 mcg daily, imipramine 50 mg at night, levothyroxine 50 μg daily, oxybutynin 5 mg daily, and quetiapine 150 mg at night, a regimen that had been consistent for at least 1 year prior. Although his cognition and functionality continued to decline over the subsequent years, little further investigation had been undertaken. Longitudinal computed tomography imaging of the brain showed prior craniotomy, right lateral ventricle *ex-vacuo* dilatation, and retained bullet fragments in the right cerebral parenchyma. The most recent head computed tomography scan was significant for a slowly advancing area of right cerebral encephalomalacia.

His symptoms were noted to have progressed rapidly over the 6 months before admission, now demonstrating left facial paresis, complete plegia of the left upper extremity, and urinary incontinence. Neurocognitively, Mr. S presented as alternately apathetic and impulsive with some hypersexual behaviors. He did not demonstrate any spontaneous speech but could produce soft monosyllabic vocalizations when prompted.

Psychiatry was consulted to assist with management of the psychotropic regimen. On examination, Mr. S was able to make and sustain social eye contact, and he could respond to basic orientation questions with thumbs up/thumbs down with accuracy. He could point to objects in the environment and follow 3-step commands. His speech was dysarthric and consisted of imprecise consonants and repeated phonemes with monotone pitch. On his left side, his quadriceps and peroneal muscle groups had diminished strength and spastic tone with 3+ deep tendon reflexes. His left upper extremity was plegic with spastic tone and contractions. His right upper and lower extremity demonstrated 5 of 5 strength, but with a decreased range of motion owing to spasticity.

Vital signs were stable and there was no evidence on examination of systemic infection. Results of laboratory studies including complete blood count, comprehensive metabolic panel, vitamin B_{12} and folate levels, thyroid-stimulating hormone, and plasma vitamin C were all unremarkable. Additional laboratory studies for heavy metal (including zinc, arsenic, and mercury) toxicity were similarly unremarkable. Whole-blood venous lead was reported as undetectable at <2.0 μg/dL. Electroencephalogram demonstrated a diffuse slowing of the background activity and focal right-hemispheric slowing.

Recommendations included efforts to reduce anticholinergic load. Imipramine was reduced but chlorpromazine dosage was maintained at the request of Mr. S's guardian (discussions regarding the importance of minimizing anticholinergicity were countered with concerns that chlorpromazine had been the most successful medication in managing his symptoms and his dose had been stable over years). These changes and daily rehabilitation services resulted in only negligible improvements. Mr. S was discharged to a group home setting with arrangements to follow up with psychiatry and neurology for further titration of his medications.

Discussion

Although the colic and palsy associated with lead have been recognized since the middle ages, the first clinical description of lead intoxication is credited to the 19th century French physician Tanquérel des Planches.[5,6] His study on the effects of lead inhalation and ingestion allowed for the characterization of the classic symptoms of lead colic, which is characterized by "paroxysms of sharp abdominal pains" with fluctuating states of vomiting and constipation.[6] Further characterization of systemic lead toxicity continued with Bronvin, who described lead poisoning secondary to retention of a lead bullet in the body in 1867, and Machele, who described lead poisoning from retained bullets in the head and brain in 1940.[5] Retained lead bullets as the cause of systemic lead toxicity is a well-explored phenomenon; however, research regarding the direct localized neurotoxic effects of lead represents a small minority of articles within the field of lead toxicity.

Systemic lead toxicity occurs via several mechanisms and results in distinct neurologic and hematologic sequelae. Typically, lead is absorbed through the respiratory and gastrointestinal systems.[7] Once lead reaches the blood, 99% is bound by erythrocytes. The remaining unbound 1% is distributed systemically and enters the kidneys, liver, bone marrow, and central nervous system.[8] The central nervous system is selectively damaged by lead toxicity because cationic lead