White Phosphorus Burns and Arsenic Inhalation: A Toxic Combination

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White phosphorus is a common industrial and military compound, which can cause severe thermal and chemical burns beyond what would be predicted from body surface area alone. The authors present a rare case of a 45-year-old male patient who suffered white phosphorus burns combined with arsenic inhalation because of an industrial accident. The presented case is used to review the history and the toxicities of these chemicals as well as current methods of treatment. A literature review was performed to summarize the current knowledge of white phosphorus burns, as well as arsenic poisoning, and no similar case reports of the two combined were found. The patient ultimately recovered and was discharged, though with significant chronic complications. This case highlights the risk of burns and inhalation injury present in industrial manufacturing jobs, as well as the potential severity of these conditions. The systemic effects of chemicals absorbed across burned skin and via inhalation were the main contributors to our patient's severe illness, and required more intensive treatment than the burns themselves. Arsenic toxicity is rare and could easily have been missed without the appropriate patient history. (J Burn Care Res 2014;35:e128–e131)

CASE

We present the case of a 45-year-old man transferred to our facility after an explosion at a microchip production plant. The facility reported that he had been working in a deactivated area of the plant, but had potential exposures to both white phosphorus and arsenic. He was decontaminated at the scene as well as at the referring hospital for more than 2 hours, where he was also intubated. He had 8% TBSA third-degree burn on his face, neck, and bilateral upper extremities, as well as rupture of the left globe. On arrival, he immediately underwent extensive repeat decontamination with cold water lavage guided by blacklight. A trauma workup for blast injuries was negative, but CT scanning did reveal persistent white phosphorus particles on the face and in both eye sockets (Figure 1). All dressings were kept wet to prevent reignition of particles. Serum arsenic levels were drawn and sent for analysis.

Given the persistence of white phosphorus contamination, the patient was taken to the operating room within 24 hours for planned excision of his facial burns. He first underwent tracheostomy and exploration of his left globe to remove white phosphorus as well as glass particles. During the operation, he developed profound respiratory distress requiring bilateral chest tubes for decompression. Given his instability, the excision of his burns was aborted and further decontamination with surgical scrub brushes was performed instead. He was returned to the intensive care unit in critical condition. During the next

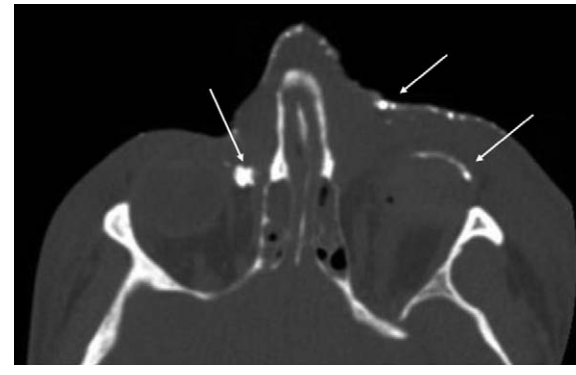

Figure 1. Head CT scan showing white phosphorus particles (white arrows) remaining on the skin and in both eye sockets after three rounds of water decontamination on admission.

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1559-047X/2014
DOI: 10.1097/BCR.0b013e31828c73dd

day, he developed rapidly progressive acute respiratory distress syndrome, which ultimately required veno-venous extracorporeal membrane oxygenation from hospital days 3 to 15. He remained severely hypotensive despite optimal fluid resuscitation, and required multiple vasopressors to maintain adequate perfusion. Hypotension contributed to the development of acute tubular necrosis, and continuous renal replacement therapy was instituted on hospital day 3. He demonstrated mild hyperphosphatemia and hypocalcemia without arrhythmias, and developed acute adrenal insufficiency diagnosed via adrenocorticotropic hormone-stimulation testing. The admission serum arsenic level returned to a level of 856.6 µg/L (upper limits of normal 13.0 µg/L), and he was started on oral chelation therapy with dimercaptosuccinic acid (Figure 2).

His hospital course was notable for mild upper gastrointestinal (GI) bleeding, *Candida tropicalis* fungemia, multiple episodes of bacteremia, and increased liver function tests (maximum total bilirubin 6.0, alanine aminotransferase 240, aspartate aminotransferase 351, alkaline phosphatase 253). Serial excision (hospital days 20–23) and grafting (hospital days 23–30) of his wounds were performed once he stabilized (Figure 3), and on hospital day 27 he required exploratory laparotomy and small bowel resection for obstruction because of an impaction of the oral chelation therapy. A corneal transplant was performed on the left eye, which failed and ultimately required enucleation. Cultures from the globe later grew *C. tropicalis* further. He developed severe peripheral neuropathy as well as symptoms consistent with posttraumatic stress disorder. Despite this, he was taken off ventilatory support, recovered from his acute renal failure (last hemodialysis was performed on hospital day 49), and was transferred to the physical medicine and rehabilitation service. He was later discharged home with home health and physical therapy.

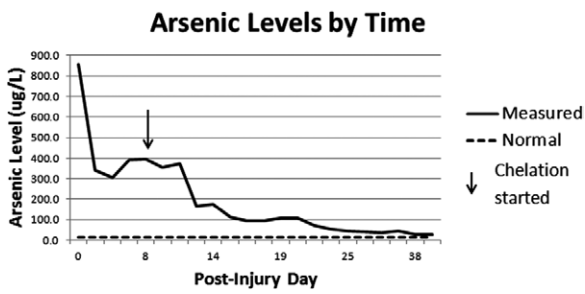

Figure 2. Measured arsenic levels by postinjury day. Normal levels are <13 µ/L.

DISCUSSION

Our case demonstrates the severe tissue destruction that can be caused by white phosphorus burns as well as the toxicity of inhaled and transcutaneously absorbed arsenic. White phosphorus is a chemical compound known primarily for its role in munitions, though it is also commonly used in agriculture (fertilizer, insecticides, and rodenticides), fireworks, electronics (as in our case), and the industrial production of phosphoric acid.[1–4] It burns with a bright yellow flame and produces thick white smoke capable of interference with infrared cameras and weapon-tracking systems; properties that have made it useful in military applications such as smoke screens, tracer bullets, and flares to hand grenades, missiles, bombs, and mortars since World War I. Although still a common instrument of many national military organizations, the usage of white phosphorus against civilians is banned by Protocol III of the United Nations Convention on Certain Conventional Weapons, which limits the uses of incendiary weapons.[5] There have even been case reports of burns caused by white phosphorus released from breakdown of older weapons disposed of in the Baltic Sea.[3] Pertinent to our case, white phosphorus and its less volatile derivative red phosphorus are used as "dopants" (intentionally introduced impurities) to silicon in the production of N-type semiconductors. This modulates the electrical properties of silicon by adding extra electrons for conduction.[6] Arsenic is used in a similar fashion.

The most notable characteristic of white phosphorus is its spontaneous ignition in air at temperatures >30°C (86°F), with oxidation leading to the production of phosphorus pentaoxide (P_2O_5).[1] Further hygroscopic reactions with water form phosphoric acid. These reactions produce large amounts of heat (up to 1300°C) and continue until the substrate is neutralized or entirely consumed. The extreme heat production and generation of phosphoric acid lead to the hallmark combined thermal and corrosive burns of white phosphorus. The depth of injury is determined by the intensity and the duration of exposure, the concentration of the agent, and the specific composition of exposed tissues.[7] This is exacerbated by the lipid solubility of white phosphorus, which enables it to spread rapidly beneath the dermis.[2] In addition, the fumes can cause eye irritation and photophobia. Although the oxidation of white phosphorus is easily extinguished with cold water, it reignites when dried and passes through the GI tract intact, leading to the classic finding of "smoking stools." Finally, exposure is often combined with an explosion leading to a

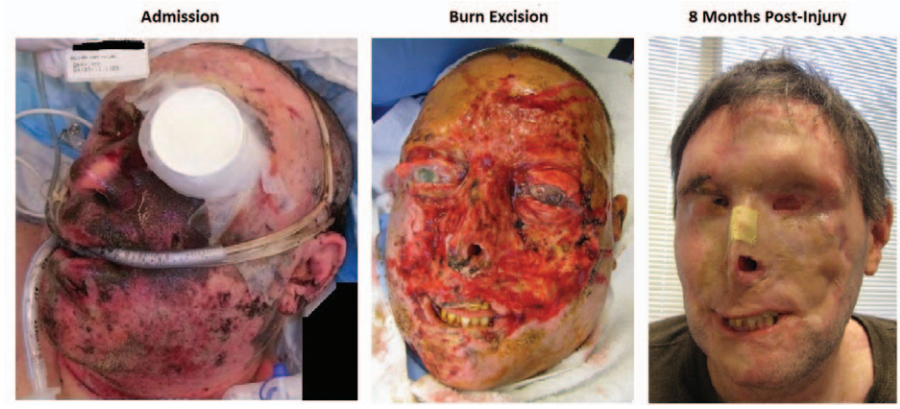

Figure 3. Admission, operative, and follow-up pictures, respectively. Deep excision of the facial burns was necessary to remove all white phosphorus particles.

possible blast injury, as well as the creation of white phosphorus–coated shrapnel that can penetrate deep into tissues and ignite at body temperature.

In addition to causing burns, white phosphorus is easily absorbed through the skin, lungs, and gut, leading to acute intoxication. Toxic effects on multiple organ systems have been reported, with the most serious consequences because of electrolyte imbalances, primarily hyperphosphatemia and hypocalcemia. These disturbances have been implicated in fatal arrhythmias and sudden death as early as 1 hour postexposure in patients with only 10 to 15% of TBSA burns.[8] Other described toxicities include hypoproteinemia, hematuria, renal failure, petechiae, icterus, yellow liver atrophy, seizures, impaired glycogenolysis, and ischemic-like ECG changes.[1–3,7,8] In addition, there is a long-term risk of malignant skin lesions in previously burned areas.

The mainstay of white phosphorus burn treatment is thorough decontamination. This is best accomplished by continuous cold water lavage,[9] which extinguishes burning phosphorus, cools burns, and dilutes phosphoric acid. Identification and removal of white phosphorus can be guided by a blacklight or Wood's lamp that causes particle phosphorescence. Although there is a risk of hypothermia with cold lavage, warm water should be avoided because white phosphorus melts at 44°C and becomes much more difficult to remove. Early debridement is often required for full clearance of embedded particles, particularly when associated with blast injuries and shrapnel. Intensive electrolyte monitoring, workup for potential blast injury (if warranted by the mechanism of exposure), and protection of healthcare workers from contamination are also essential. All bodily fluids must be treated as contaminated and should be disposed of appropriately for at least 48 hours. Historically, copper sulfate has been employed to help identify white phosphorus during decontamination, because the two chemicals react to turn particles black. Unfortunately, copper sulfate is easily absorbed across even unburned skin and can lead to acute copper intoxication, with complications including massive intravascular hemolysis, anemia, renal failure, hepatic necrosis, cardiorespiratory collapse, and death.[2] Because of these risks, the use of copper sulfate is now discouraged. Given that white phosphorus burns are seen most commonly during wartime, consultation with experienced military burn surgeons is encouraged.

The care of our patient was additionally complicated by acute arsenic toxicity, most likely from a combination of absorption across burned skin and inhalation. In addition to its uses in the electronics industry, arsenic commonly occurs in nature, with most exposures worldwide coming through contaminated food or water. It is also a pollutant from mining, an ingredient in agricultural products (pesticides, fungicides, herbicides, etc.), paints and wood preservatives, and an additive in animal feeds where it may be an essential nutrient.[10] Therapeutic medical uses include a historical treatment for syphilis and as a current inducer of apoptosis in acute promyelocytic leukemia.[11]

Inorganic arsenic exists as two main forms: arsenite and arsenate. Arsenite, to which our patient was exposed, is both 60 times more toxic than arsenate and 29 to 59 times more absorbable through unbroken skin.[11,12] Both are also absorbed through the lungs and the GI tract. A multitude of deleterious effects have been attributed to inorganic arsenic—primarily inactivation of enzymes, including those involved with cell migration, wound repair, and the immune response. Ingested arsenic causes hemorrhagic lesions in the GI tract, which present with vomiting, colicky abdominal pain, and bloody, watery diarrhea. When severe, this can lead to massive volume loss, dehydration, circulatory collapse, and death.[11] Patients inhaling arsenic may develop pulmonary edema and respiratory failure. Other

systemic effects include severe peripheral neuropathy mimicking acute Guillain–Barre syndrome, hemolysis and intravascular coagulation, pancytopenia, renal failure, rhabdomyolysis, metabolic acidosis, acute psychosis, encephalopathy, seizures, and cardiomyopathy.[11,13] Long-term effects are primarily related to chromosomal damage leading to malignancies, which may involve almost any organ system. Bronchiectasis, noncirrhotic portal fibrosis, diabetes, and cardiovascular and peripheral vascular disease have also been described.[10,14]

Diagnosis of toxicity requires a high index of suspicion and is confirmed by serum arsenic assays. The assistance of a toxicology specialist is encouraged. Our patient demonstrated significantly increased blood arsenic levels (Figure 2) that were likely extended by his acute renal failure, because arsenic is normally excreted by the kidneys. Chelation in the form of oral dimercaptosuccinic acid was ultimately started, as the preferred intravenous formulation of British antilewisite was not available in the United States. He ultimately developed an obstruction requiring surgery because of impaction of the oral medication in his small bowel. However, serum levels did drop after the initiation of chelation therapy.

In summary, much of our patient's severe illness was attributable to toxicities rather than to his relatively small 8% TBSA burns. Arsenic intoxication almost certainly contributed to his refractory hypotension, respiratory failure, renal failure, and peripheral neuropathy. White phosphorus, in addition to deep burns, caused electrolyte abnormalities and likely exacerbated his renal failure. Chelation therapy for arsenic also had its own side effects. Despite the severity of his illness, our patient was discharged home with family support as well as home physical therapy. He is able to ambulate with the assistance of a walker, though he continues to have severe peripheral neuropathy, distal weakness, and neuropathic pain. He is able to take a regular diet though liquid intake is troublesome, given the scarring and retraction of the lower lip. The vision in his right eye is approximately 20/400, partially because of corneal scarring and neovascularization. He recently underwent a forehead and nasal turndown flap for closure of a nasocutaneous fistula. Plans include fat grafting and possible flap to the left cheek and skin grafting or a musculocutaneous flap to the inner lower lip to help cover the lower teeth. Finally, because of the severity of his burns he is still a potential candidate for a future facial transplant. With accurate diagnosis and high-quality multidisciplinary care, these injuries are treatable.

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