Cutaneous Mercury Granuloma: A Case Report

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Cutaneous mercury (Hg) granuloma is a rare disorder caused by the traumatic introduction of elemental Hg into skin or soft tissue. Typically, cutaneous elemental Hg deposits cause limited systemic effects. Prominent systemic toxicity may, however, occasionally occur. Herein we report a case of cutaneous Hg granuloma resulting in chronic painful local wounds and systemic toxicity in the form of abdominal pain, visual disturbances, and psychiatric abnormalities. The related literature also is reviewed.

Cutis. 2011;88:189-193.

Case Report

A 42-year-old Hispanic woman presented with painful violaceous nodules and plaques of 2 years' duration on her right forearm and left anterior tibia. The patient admitted to receiving mercury (Hg) injections in these sites for multiple years while residing in Honduras. She reported that the injections of Hg were administered as a treatment of human immunodeficiency virus (HIV) infection. Review of systems revealed nausea, vomiting, chronic nonlocalizing abdominal pain, weakness, headaches, and visual disturbances. Aside from HIV infection diagnosed in 2000, her medical history was remarkable for depression with 4 prior suicide attempts.

Physical examination revealed a 3×4-cm well-circumscribed, indurated, fixed erythematous to violaceous plaque with an eroded nodular component on her right distal volar forearm (Figure 1). A 2×3-cm violaceous plaque was located on her left distal anterior tibia. Pain to palpation and decreased range of motion secondary to pain were present in the involved areas.

Radiographic examination of the extremities revealed metallic particles in subcutaneous tissue in the injection areas (Figure 2). Computed tomography of the right forearm revealed multiple metallic particles in superficial subcutaneous tissue. No fracture or osseous involvement was noted. Results from a chest radiograph were unremarkable.

The lesion on the right forearm was biopsied. Histologic examination showed a foreign body granulomatous reaction surrounding black opaque globules ranging from 7 to 100 nm in diameter (Figure 3). The globules were refractile under polarized light.

The patient's serum Hg level was 300 μg/L (reference range, <5 μg/L). No renal function abnormality was detected on a comprehensive metabolic panel.

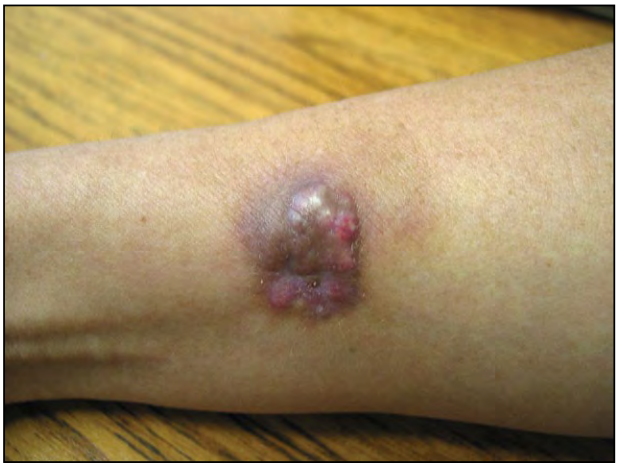

Figure 1. Erythematous to violaceous plaque with an eroded nodular component on the right distal volar forearm.

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The authors report no conflict of interest.

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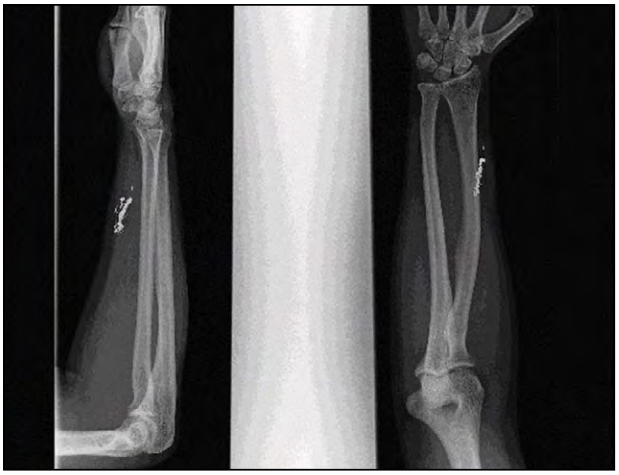

Figure 2. Lateral (left) and anteroposterior (right) radiography of the forearm demonstrated a metallic foreign body that localized to the subcutaneous tissue anterior to the radial diaphysis.

The patient was treated with penicillamine chelation therapy for 3 months, which did not result in a reduction in the serum Hg level. Intraoperative C-arm fluoroscopy-assisted surgical debridement of the involved areas was performed. Intraoperative evaluation of the subcutaneous tissue revealed black particulate matter (Figure 4). The patient reported symptom improvement but was lost to follow-up after Hurricane Katrina.

Comment

Mercury Toxicity—Mercury, a heavy metal, exists in a variety of physical and chemical forms. Two major types are the inorganic and organic species.[1] Inorganic Hg includes elemental metallic Hg, which is a silvery liquid at room temperature that quickly turns to vapor when heated. Exposure to Hg typically occurs via ingestion or inhalation. Rarely, however, Hg exposure occurs via introduction of the elemental metal into skin accidentally or factitiously.

In its liquid form, ingestion of elemental Hg usually is harmless, as negligible amounts are absorbed from the gastrointestinal tract. Humans are most often exposed to elemental Hg in the form of industrial fossil fuel emission, topical medicines, cathartics, dental amalgam, thermometers, sphygmomanometers, barometers, batteries, and Hg-based substances used in ritualistic practices.[2] Inorganic Hg exists in compounds available in some regions and developing countries for the purposes of skin lightening, impetigo, psoriasis, and secondary syphilis.[3]

Clinical manifestations of Hg poisoning depend on the route of entry, chemical state, and subsequent metabolism of Hg compounds. Central nervous system, renal, and gastrointestinal toxicity are the most notable deleterious events. Toxic exposure to elemental Hg results in 3 symptomatic stages.[3] Initially, a flulike syndrome is seen, which is followed by multiorgan symptoms involving the central nervous, respiratory, gastrointestinal,

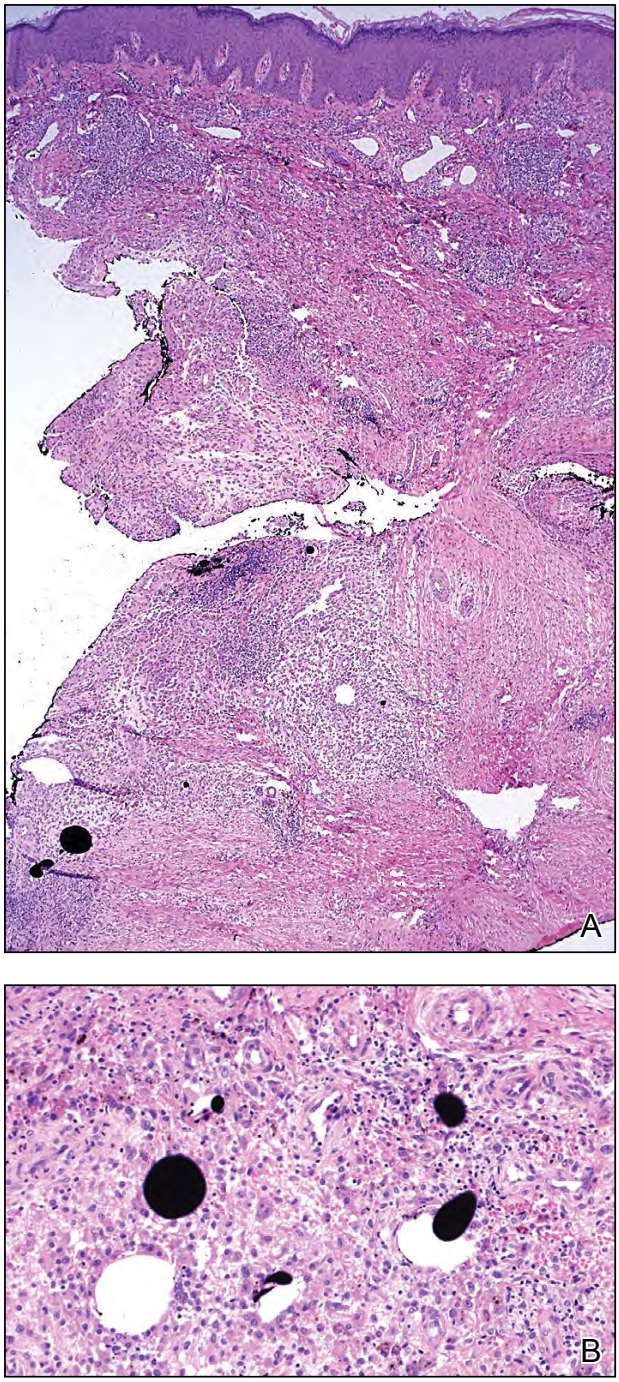

Figure 3. Biopsy from the right forearm demonstrated a foreign body granulomatous reaction surrounding black opaque globules that represented mercury in the dermis (A and B)(H&E; original magnifications ×5 and ×40, respectively).

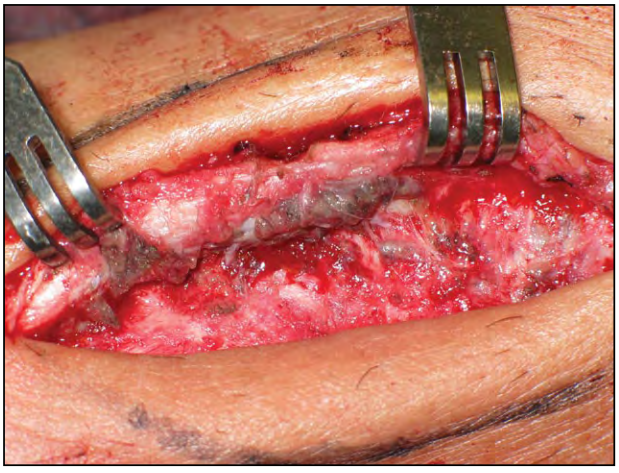

Figure 4. Intraoperative view of black particulate matter localized to the subcutaneous tissue.

and urogenital systems. The third stage consists of neuropsychiatric symptoms that take place over years and have the potential to remain permanent. With chronic exposure, the features of Hg toxicity include ataxia, visual field impairment, seizures, tremor, and paresthesia. Changes in personality and psychiatric symptoms also may occur.[4-7]

Organic Hg consists of phenylmercury, ethylmercury (EtHg), and methylmercury (MeHg). These compounds cross the blood-brain barrier and have a high potential for brain damage. Organic Hg toxicity is more fulminant than inorganic toxicity.[3] Humans are exposed to MeHg via contaminated freshwater and ocean fish and EtHg in the form of thimerosal. Thimerosal contains 49.6% Hg by weight and has been used as a preservative in vaccines routinely given to children.[2] Because of recent concern that EtHg exposure may lead to neurodevelopmental detriments such as autism and attention deficit hyperactivity disorder, thimerosal has been removed from most vaccines in the United States but is still in use in some developing countries. Although the effects of low-dose EtHg are unclear, it recently has been reported that EtHg is less neurotoxic than MeHg.[8]

Cutaneous Hg Granuloma—Cutaneous Hg granuloma is an uncommonly reported disorder that is characterized histopathologically by acute and chronic inflammation, necrosis, foreign body granuloma, and abscess formation.[9] Although subcutaneous Hg exposure is always locally harmful, it carries a lower risk for systemic toxicity than other forms of Hg exposure. In the absence of intravascular Hg injection, clinical signs of Hg toxicity usually are not evident. In the fewer than 100 reports of subcutaneous Hg granuloma presented in the dermatology, toxicology, and general medical literature based on a PubMed search using the terms *cutaneous mercury granuloma*, *subcutaneous mercury granuloma*, *mercury toxicity*, and *cutaneous mercury toxicity*, 5 cases of systemic toxicity have been reported following isolated subcutaneous injection without evidence of elemental Hg dissemination.[3,10-12] Although toxicity is rare following subcutaneous Hg deposition, systemic absorption of metallic Hg from cutaneous sites is evident in the consistently elevated levels of Hg in the blood and urine in the patients reported in the literature. Elevated Hg levels in the urine and blood, therefore, document exposure to Hg but do not closely correlate with the clinical toxicity of Hg. In our patient, an elevated serum Hg level was seen along with signs of systemic toxicity from Hg implantation into the subcutaneous tissues.

Cutaneous Hg exposure occurs most often via penetration by broken Hg thermometers or syringe-sealed anaerobic serum specimen containers in which Hg is used as a sealant.[9,13,14] Ellabban et al[15] described Hg granuloma of the hand in a patient who impaled himself on roof thatching materials that contained Hg as part of a fire-retardant formulation. Mouzopoulos et al[16] described a case of Hg granuloma after red pigment containing henna dye was applied to the forearm for ornamental tattoo placement.

Cases of deliberate cutaneous injection of Hg involve suicide attempts or other attention-getting behavior.[10,17-19] Few reports involve injection of Hg from a belief in the healing or protective properties of the metal. Prasad[20] reported that the injection of subcutaneous Hg is practiced in Honduras to "ward off evil" and to protect against diseases when traveling. The author noted that Hg often is sold for magic or religious purposes in Puerto Rico and Cuba.[20] Our patient stated that subcutaneous elemental Hg injections were administered in Honduras as a "less-stigmatizing" treatment of HIV infection.

When metallic Hg contacts tissue, it slowly oxidizes to Hg salts that are quickly distributed systemically. Mercuric salts have an affinity for and interact with thiol (sulfhydryl) groups and inhibit enzymes containing such groups. The thiol-containing antioxidant glutathione provides the major intracellular defense against Hg-induced neurotoxicity.[21] Because HIV infection induces a glutathione-deficient state, it may be hypothesized that HIV infection predisposes our patient to develop systemic toxic effects secondary to subcutaneous Hg exposure.

Diagnosis—The diagnosis of Hg granuloma is evident when the history is revealing, as seen in our case. In cases in which the history is vague or the patient denies injury by an Hg-containing

object, histopathologic evaluation is of the utmost importance. Clinical differential diagnosis would include other granulomatous processes such as foreign body implantation, deep fungal infection, atypical mycobacterial infection, or mycetoma. Further, neoplasm would have to be ruled out.

Distinctive features on histopathology as described by Lupton et al[10] include the appearance of dark brown to black opaque globules, which usually are spherical. These globules are of varying sizes and numbers. Fibrosis often surrounds the globules. A granulomatous foreign body giant cell reaction accompanied by granulation tissue and a mixed inflammatory infiltrate composed of neutrophils, lymphocytes, eosinophils, plasma cells, and histiocytes usually are present. Epidermal and dermal necrosis with or without ulceration can be seen.

Treatment—Definitive management of subcutaneous Hg granuloma consists of surgical excision of the deposit. Krohn et al[17] recommended the following treatment regimen. First, early and prompt excision of all readily accessible subcutaneous areas where Hg is located should be performed, which allows for lowering the serum Hg level and controls the local inflammatory reaction. Intraoperative radiographic imaging is beneficial, as the Hg tends to disperse when the tissue is manipulated.[22] In our case, fluoroscopic guidance was employed to enhance the Hg deposits. Second, there should be an appropriate monitoring of central nervous system and renal functions. Third, if systemic toxicity is evident, chelation therapy is recommended. Fourth, psychiatric consultation in cases of deliberate self-injection is indicated. Further recommendations include radiographs of postsurgical debridement to assess the extent of Hg removal and postoperative monitoring for 2 years during which blood or urine Hg levels should be followed.[15] In our case, the patient was lost to follow-up after Hurricane Katrina and further serum testing of Hg levels was not performed.

Chelation therapy for the treatment of subcutaneous Hg granuloma is controversial. It is advised when systemic Hg toxicity is evident. Chelating agents available for the removal of systemic Hg include DMPS (2,3-dimercapto-1-propanesulfonic acid), DMSA (2,3-dimercaptosuccinic acid), penicillamine, and BAL (2,3-dimercaptopropanol). DMPS is a derivative of BAL and is considered by the World Health Organization to be first-line therapy for acute and chronic inorganic Hg poisoning.[4] DMPS is available in oral and parenteral preparations. Penicillamine is an oral chelating agent used for lead, arsenic, and Hg poisoning. It is less expensive but not as effective as DMPS. No decrease in the serum Hg level was noted in treating our patient with penicillamine for 3 months. Although DMPS and DMSA have been proven superior to other chelating agents for the removal of systemic Hg, their use is limited, as these agents are unavailable in many countries worldwide.

Conclusion

The introduction of subcutaneous Hg gives rise to systemic toxicity due to absorption evidenced by the elevated serum Hg levels in our patient as well as in all patients reported in the literature. Although elevated serum or urine Hg levels are common in cases of subcutaneous Hg granuloma, systemic toxicity rarely is seen. We hypothesize that the systemic toxicity seen in our patient may be partially due to her glutathione-deficient state secondary to HIV infection, which likely rendered her unable to detoxify the mercuric salts produced by elemental Hg metabolism.

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