A new cutaneous sign of mercury poisoning?

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Chronic mercury poisoning is becoming a health concern because of extensive pollution of water and fish, and the increasing consumption of fish in the human diet. Mercury is extremely toxic to the body, especially the central nervous system, but diagnosis is difficult because of the lack of specific signs. A total of 11 patients were observed to have a nonpruritic or mildly pruritic discreet papular and papulovesicular eruption that correlated with high blood mercury levels. The mercury evidently came from increased seafood consumption. All of the patients improved when they were placed on either a seafood-free diet or chelation therapy. Physicians should suspect mercury poisoning in patients who eat a high-seafood diet who present with an asymptomatic or mildly pruritic papular or papulovesicular eruption. (J Am Acad Dermatol 2003;49:1109-11.)

The diagnosis of mercury poisoning is very difficult as a result of the insidious nature of the disease and the lack of specific signs. I have recently seen 11 patients with an eruption characterized by nonpruritic or mildly pruritic discreet small (1-2 mm) flesh-colored or slightly erythematous papules and papulovesicles that correlated with blood mercury levels and responded well to the lowering of their blood mercury.

RESULTS

The patients ranged in age from 25 to 70 years and the duration of the eruption before diagnosis and the initiation of treatment was from 1 week to 2 years (Table I). Of the patients, 2 had noncutaneous symptoms including dizziness, memory loss, and gastrointestinal bleeding. Blood mercury levels before treatment ranged from 6 to 19 μg/L with a mean of 10 μg/L (normal: <10 μg/L). Prior treatments included topical steroids (9 patients), oral steroids (4 patients), antihistamines (2 patients), and cyclosporine (1 patient), all without success. None of the patients had a personal or family history of atopy (asthma, hay fever, or atopic dermatitis); none had a history of either industrial or incidental exposure to mercury other than seafood, or a history of allergic reactions to any metals. In all, 8 patients had mild pruritus and none had pain.

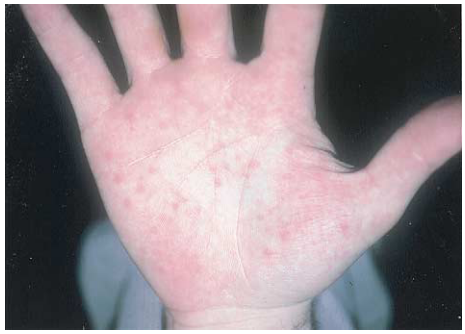

Fig 1. Palm of patient 11 showing discrete erythematous papules and papulovesicles. Note lack of oozing, crusts, or excoriations. Although there is some increased palmar erythema, it differs from pink disease of inorganic mercury poisoning of children by presence of papules and lack of pain.

Physical examination disclosed discrete, flesh-colored or slightly erythematous papules and papulovesicles (1-2 mm) of the palms in all patients (Fig 1), the soles in 1 patient, and the arms (Fig 2) and trunk in 3 patients. Excoriations and crusting were absent.

Biopsies were performed on 9 patients and pathologic examination revealed spongiosis, and a perivascular and diffuse lymphocytic infiltrate. Immunohistochemical studies showed that the cells in the infiltrate stained positively for CD3, CD4, CD5, CD7, and CD8 with negative staining for CD20, consistent with a mixed T-cell infiltrate composed of both helper and suppressor T cells. Direct immunofluorescence showed focal antinuclear staining and indirect immunofluorescence revealed the presence

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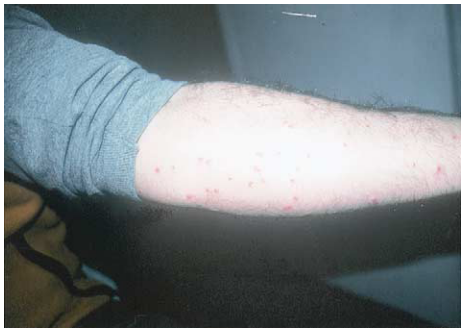

Fig 2. Arm of patient 10 showing discrete scattered (shotgun) 1- to 2-mm papules. Note lack of oozing, crusts, excoriations, or other signs of acute eczema.

of basal cell cytoplasm antibodies, consistent with damage to basal cells and suggesting damage by a cytotoxic agent. Antibodies to DNA, Sm, nuclear RNP, Ro (SS-A), La (SS-B), Jo-1, Scl-70, histone, or $\beta 2$ glycoproteins were not found. Immunofluorescent studies were performed by Beutner Labs, Buffalo, NY.

All patients were treated with a seafood-free diet and 7 patients were treated with chelation therapy with succimer (2, 3-dimercaptosuccinic acid) (200 to 300 mg, 3 times a day).[1] Treatment duration lasted from 1 to 6 months with serum mercury levels, complete blood cell count, and chemistry profile checked every 3 to 4 weeks. All patients responded with a lowering of their blood mercury levels and clearing of the eruption. Treatment was well tolerated with no adverse reactions reported. No concomitant treatment was included.

DISCUSSION

Mercury in all forms is toxic to the body and the signs and symptoms depend on the type of exposure. Elemental mercury, as found in thermometers, lamps, and dental amalgams, is responsible for the least common form of poisoning because it is poorly absorbed from the gastrointestinal tract. However, elemental mercury can vaporize at room temperature and be absorbed through alveoli into red blood cells where it can be converted to mercuric ions. These are toxic to the central nervous system. Inorganic mercury, found in lamps, wood preservatives, disinfectants, explosives, inks, cosmetics, and various chemical products, is absorbed both orally and dermally, and is usually responsible for acute mercury poisoning with central nervous system symptoms. Skin signs in acute inorganic mercury poisoning are rare but may include acrodynia (pink disease), especially in children, and stomatitis. Organic mercury is found as thimerosal, a common medical preservative, and as alkyl mercury in contaminated food, especially seafood. Because of its lipid solubility, it is readily absorbed from the gastrointestinal tract and is widely distributed in the body, including brain, kidney, liver, skin, and erythrocytes. Organic mercury poisoning is usually chronic and skin signs are thought to be either very rare or nonexistent. Neurologic signs and symptoms are common but are difficult to diagnose as they may mimic other diseases including Parkinson's, Alzheimer's, depression, and other psychoses.[2]

Mercury reactions in the skin have been reported in several forms. Mucocutaneous hyperpigmentation can result from chronic absorption and granulomas can develop from mercury injections directly in the skin. Allergic contact dermatitis is the most common form of mercurial reaction in the skin and can occur by both topical and systemic exposure; acrodynia is thought to represent an allergic reaction to parenteral mercury. Allergies to mercury are characterized by painful or pruritic eczematous eruptions. Stomatitis can occur in acute poisoning and is thought to represent direct irritation of the mucosa.[3]

The differential diagnosis in these patients included dyshydrotic eczema (pompholyx), atopic dermatitis, contact dermatitis, and drug eruptions. A careful history should help to differentiate the mercury reaction described here from these other conditions. The lack of pruritus or mild pruritus, and the absence of pain in the mercury eruption may help because pruritus is ordinarily a hallmark of eczematous dermatitis. The lack of contact with any allergens, especially heavy metals, or irritants may also help in distinguishing mercury poisoning from pompholyx, atopic dermatitis, or contact dermatitis. Finally, the absence of more physical characteristic signs of acute eczematous eruptions may help differentiate this eruption from the other disorders.

Mercury is a common pollutant of water, resulting from the burning of coal by power plants, and in the inappropriate disposal from batteries, paints, lights, and industrial by products. Mercury poisoning is becoming more important because of the extensive contamination of water and fish, and the increasing consumption of fish in the human diet.[4] Mercury is cytotoxic, exerting its effect by depleting the thiol reserves in the mitochondria, resulting in cell death.[5] It is extremely neurotoxic, and leads to dizziness, irritability, tremor, depression, and memory loss. It is also toxic to the kidneys and colon, the 2 main sites of excretion.[6] Mercury is released very slowly from the body with a half-life of at least 60 days, resulting in increasing amounts with chronic consumption of contaminated fish.[7] Previous guidelines have indi-

Table I. Types and duration of eruption, associated findings, serum mercury levels, treatment, and response in 11 patients

Patient No.	Eruption/Distribution	Duration	Associated findings	Serum mercury (/L)	Tx	Response
1	Papules/palms	1 mo	None	9	Diet*	Clearing
2	Papules and papulovesicles/ palms	1 mo	Dizziness/rectal bleeding	19	Diet/chelation†	Clearing
3	Papules and papulovesicles/ palms	6 mo	Dizziness/memory loss	11	Diet	Clearing
4	Papules and papulovesicles/ palms	2 mo	None	11	Diet	Clearing
5	Papules/palms	2 mo	None	6	Diet	Clearing
6	Papules/palms	1 y	None	9	Diet/chelation	Clearing
7	Papules/palms	1 y	Macular degeneration	10	Diet/chelation	Clearing
8	Papules and papulovesicles, palms/soles	2 y	None	18	Diet/chelation	Clearing
9	Papules and papulovesicles, palms, arms, chest, abdomen, and back	1 mo	None	11	Diet/chelation	Clearing
10	Papules/palms, arms, legs, chest, abdomen, and back	2 wk	None	14	Diet/chelation	Clearing
11	Papules/palms, arms, legs, chest, abdomen, and back	1 wk	None	7	Diet/chelation	Clearing

Tx, Treatment.
*No seafood.
†Chelation with succimer (2,3-dimercaptosuccinic acid).

cated that mercury toxicity does not occur unless blood levels exceed 15 μg/L but this study suggests that toxicity may occur at levels as low as 6 μg/L or less.[8] Mercury toxicity may be more prevalent than has previously been recognized. A nonpruritic or mildly pruritic papular and papulovesicular eruption, as described here, may be a new cutaneous marker of mercury toxicity.

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