Silver Woman and Silver Man after Ingestion of Silver Solution: How about Silver Mouse?

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Dear Editor:

Argyria is a rare skin disease caused by deposition of silver granules due to exposure by the ingestion of colloidal silver in dietary supplements, drugs, or topical silver-containing preparations¹⁻³. Herein, we present two cases of argyria by drinking silver solution and an animal study with feeding mice using the same solution¹.

In the first case, a 24-year-old woman presented with a bluish to grayish discoloration on her face and nails that had been ongoing for 1 year (Fig. 1A). She had been taking approximately 1.5 L/d of silver solution made by commercial silver solution generator that was purchased with intent of whitening her skin. Oral mucosa, tongue,

and conjunctiva were spared. The silver concentration in her serum, urine, and skin, as determined by inductively coupled plasma emission spectrometry that was performed at the Thermo Jarrell Ash Co. The patient's silver concentration levels were 74.6 ng/ml in her serum, 9.5 ng/ml in her urine, and 24.1 μ g/ml in her skin, (reference values <15 ng/ml in serum, <1 ng/ml in urine). A light microscopic examination of a punch biopsy specimen taken from the patient's back showed multiple small, round, brown-black granules deposited in basement membrane surrounding eccrine and sebaceous glands (Fig. 2A ~C). In addition, her mother who had also lived with her and taken the solution, showed similar cutaneous

Fig. 1. Diffuse blue-gray pigmentation of the faces of Patient 1 (A) and 2 (B) as compared with the hand of a healthy individual.

Received June 8, 2012, Revised July 22, 2012, Accepted for publication August 26, 2012

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Fig. 2. Biopsy specimens of the patients (patient 1: A~C, patient 2: D~F): Numerous, tiny dark granules (arrows) deposited in the peri-adnexal areas (H&E, A, D: $\times 100$; B, E: $\times 400$) and multiple black granules near the basement membrane of eccrine glands and hair follicles (Gomori methenamine-silver, C, F, $\times 100$).

manifestations, but refused to undergo further evaluation. In case 2, a 51-year-old man visited our department complaining of progressive grayish pigmentation on face and trunk (Fig. 1B). A detailed history determined that he had ingested a silver solution for a year as a health food supplement. The silver levels in his serum, urine, and skin were elevated (127.7 ng/ml, 31.4 ng/ml and 35.8 μ g/ml, respectively). A histopathologic examination from his chin revealed numerous tiny dark black granules near eccrine gland, hair follicles, periadnexal areas, and pilosebaceous units (Fig. 2D~F).

The hallmark of systemic silver toxicity is a slate-gray, metallic skin discoloration. Having views on these 2 cases, we designed a preliminary study using a mouse model.

To establish the relationship between duration and amount of silver, we electrolyzed distilled water using a silver anode to produce solution containing the colloidal silver oxide. As the patients had done, we fed 5 Balb/c mice about 15~30 ml of the silver solution per week and one mouse was fed distilled water as a control for 2 months. Biopsies were performed on skin, brain, kidneys, livers, lungs, and ovaries from the 2 mice. However, no silver granules were detected in any organ, and the levels were not higher than in naïve controls. Our presumption is the differences in metabolism between rodents and humans, or by an insufficiency of silver-containing supplement related with a dose-dependent impact^{4,5}. Although we failed to devise a murine model, this study implies that

cutaneous features were just not by genetic susceptibility, but a result of exposure to a soluble silver compound. Accordingly, we caution against the ingestion of silver solutions, which are widely used as a health supplement in Korea.

ACKNOWLEDGMENT

This work was supported by a 2-year research grant of Pusan National University.

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