

Systemic Argyria Secondary to Breath Freshener "Jintan Silver Pills®"

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ABSTRACT

A case of generalized argyria secondary to "Jintan Silver Pills®" is described. Jintan Silver Pills® are made of natural extracts and coated with silver, and they are very popular as one of the breath fresheners in Japan. The patient has extreme blue-gray pigmentation of her skin. Histopathologically, the fine black granules were present in greatest number in the basement membrane zone surrounding the sweat glands and scattered diffusely through the dermis. She has taken about five hundred Jintan Silver Pills® a day for nineteen years. Her total intake of silver was calculated to be about 350g, which can be sufficient for producing argyria.

Systemic argyria is a relatively uncommon disease which results from exposure to silver medicinally or industrially. The pigmentation of the skin is blue-gray in color and is most intense on exposed surfaces. It has been described that many cases have followed the use of silver salts for the irrigation of nasal or urethral mucous membranes, and its use tends to be limited recently¹⁾.

This paper describes a patient with generalized argyria secondary to taking tremendously excessive Jintan Silver Pills®, which are very popular as one of the breath fresheners in Japan.

CASE REPORT

A woman aged 57 years was admitted to our institute in May, 1984 for the purpose of rehabilitation following right thalamic bleeding. On admission, the patient's skin was blue-gray; the pigmentation was most striking in the sun-exposed areas, but was present to a lesser extent over the entire skin. Physical examination was negative except for a left hemiparesis. The laboratory studies showed unremarkable. On inquiry she admitted having taken about five

hundred Jintan Silver Pills® a day from 1965 till 1984. In 1975 the patient noticed that a bluish discoloration appeared on her face at first.

A specimen of the skin was taken from the forehead to confirm the diagnosis of argyria. Paraffin sections showed the presence of finely granular black pigment in the dermis. In contrast, the granules were not seen in the epidermis or its appendages. As well as being diffusely scattered throughout the dermal connective tissue, the granules were present in greatest number in the basement membrane of the sweat glands (Fig. 1). After a diagnosis of argyria was made, treatment with a daily dose of 1000 mg of calcium disodium edetate (Bleian®) was started in August 1984. After 5 months therapy, no clear cut change could be noted.

COMMENTS

Systemic argyria is caused by prolonged ingestion of silver salts or their prolonged application to the mucous membranes¹⁾. Slow administration can result in the massive storage of the metal in the body. Silver can be absorbed by the mucosa into the blood stream and deposited in the tissues. The soluble silver (albuminate, chlo-

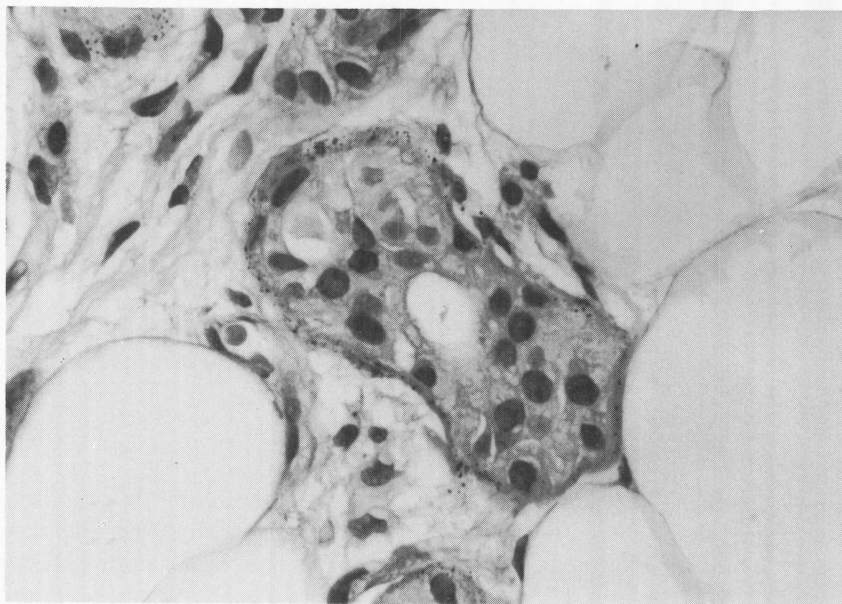


Fig. 1. Sweat glands showing concentration of silver granules in the membrane propria

ride or ion) may be released from tissue stores into blood stream and excreted in the urine, feces and saliva²⁾. However, an insoluble form as oxide, sulfide or metallic silver remains in the tissues⁷⁾. No inflammatory reaction occurs in the skin or viscera in cases of argyria. Argyria is characterized by a slate-gray discoloration of the skin, especially in the exposed areas. Pigmentation may appear after a few months or over 20 years accordingly to the degree of exposure.

In Japan until 1972, most cases reported in the literature had followed the use of silver-containing preparation (Alsilin[®]) for the treatment of gastro-intestinal irritation. In 1973 Sato⁸⁾ described the first case report secondary to taking breath fresheners (Jintan Silver Pills[®]). Since then there have been only 10 Japanese cases reportedly resulting from Jintan Silver Pills[®] ³⁾.

Jintan Silver Pills[®] have been very popular as one of the breath fresheners for a long time in Japan. Their major components are natural extracts, such as licorice, gambir, sweet hydrangea and more than 10 other kinds of raw materials, and they are coated with silver. Silver is employed to keep the coating thinner. The mean silver content of its coating is 0.1 mg per pill. Pharmacologically one should restrict the

maximum quantity of 100 pills per day.

The minimum amount of silver necessary to cause the discoloration of the skin in argyria is not exactly known. However, by Oae⁴⁾, the minimal oral dosage ingested to yield systemic argyria has been estimated to be about 90g. In our patient, she has been taking about 500 pills per day, namely the daily intake of 50mg of silver, for about 19 years. The total intake of silver is calculated to be about 350g, which can be sufficient for producing argyria.

Although all silver-containing preparations should be controlled, Jintan Silver Pills[®] are easily obtained at pharmacies or drug stores in Japan. Therefore there might be an increase in the number of patients suffering from argyria in the near future.

The most common site of accumulation of silver is the skin, although visceral deposits also occur, especially in the kidneys, liver and spleen⁷⁾. Although Potter⁶⁾ attributed numerous maladies to argyria, present understanding is, in general, that the systemic distribution of silver can be linked with no systemic toxicity other than the pigmentation. However, the most puzzling problem concerning her pigmentation was that since its presence caused this patient a great deal of embarrassment, her social activities were much more restricted. Unfortunately,

because the pigment is elemental silver, it is generally accepted that chelating agents such as dimercaprol and calcium disodium edetate are ineffective⁵⁾ and the pigmentation is permanent as well as this present case.

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