

A Case of Argyria: Multiple Forms of Silver Ingestion in a Patient With Comorbid Schizoaffective Disorder

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Argyria is a rare cutaneous manifestation of silver deposits in the skin, characterized by a grayish blue discoloration, particularly in sun-exposed areas. We report the case of a patient with a history of schizoaffective disorder and type 2 diabetes mellitus who presented with argyria of the face and neck. The patient had a history of ingesting colloidal silver proteins (CSPs) for approximately 10 years as a self-prescribed remedy for his medical conditions.

Colloidal silver protein has gained popularity among patients who seek alternative medical therapies. Argyria is the most predominant manifestation of silver toxicity. It is unclear if our patient began taking CSP because of his schizoaffective disorder or if silver toxicity may have induced somatic delusions; however, it is important for physicians to have a thorough understanding of alternative therapies on the market. We present a detailed background on silver ingestion and its systemic effects.

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Argyria is a rare disorder characterized by a permanent grayish blue discoloration of the skin. It often is the result of occupational exposure or self-administration of silver-containing products for unproven medicinal purposes. Silver

is an elemental compound often found in drinking water, various sources in industry, and alternative medicine compounds. Silver was first used medically in 980 AD; it was believed to provide a means of blood purification, to treat heart palpitations, and to serve as an adjunct treatment of epilepsy and tabes dorsalis.¹ In the 1900s, silver began being used as a popular treatment of infections. However, reports of unsolicited side effects diminished its popularity as a mainstay solution for many ailments. Silver recently has regained popularity, with an increase in Internet claims promoting the use of oral colloidal silver proteins (CSPs) as mineral supplements and as a way to prevent and treat many diseases.²

We present a patient with argyria as a consequence of multiple forms of silver ingestion in an attempt to treat his type 2 diabetes mellitus and schizoaffective disorder. We also briefly review the effects of silver and the clinical basis of argyria.

Case Report

A 60-year-old man presented to the psychiatric inpatient unit as petitioned by the police. The patient had a history of schizoaffective disorder and noncompliance of his medications, including thiothixene for his schizoaffective disorder and glyburide for type 2 diabetes mellitus. He began using oral CSP approximately 10 years prior because he “wanted something less toxic than allopathic medicines.” He had a history of utilizing alternative medical treatments such as cinnamon instead of glyburide, placing garlic cloves on wounds, and using “magnetic fields to guide gallstones out of the gallbladder.” He had discovered that CSP preparations were used as alternative treatments of various illnesses and had subsequently ordered mass quantities of CSPs from alternative medicine Web sites. He reported that he ingested up to 2 gallons of CSP per day to prevent colds, gallbladder disease, and appendicitis. He also

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maintained an authentic silver dollar coin between his buccal mucosa and buccal gingiva to enhance absorption of silver particles. He also admitted to injecting silver nitrate into his scrotum because “it’s supposed to be good for infection.”

His medical history included type 2 diabetes mellitus with poorly controlled blood glucose, long-term tobacco dependence, gallstones, hiatal hernia, and hypercholesterolemia. His psychiatric history included a diagnosis of schizoaffective disorder for which he was prescribed thiothixene. Because of his long-term history of not complying with his thiothixene treatment regimen, he had been admitted to multiple inpatient psychiatric hospitals. At the time of presentation, he was only taking the CSP and was admittedly noncompliant with thiothixene and glyburide.

He presented to the psychiatric inpatient unit with a generalized silvery sheen limited to his face and neck (Figures 1 and 2). The sclerae of his eyes appeared blue-gray. The remainder of his skin was a normal skin tone, except for areas that lacked normal skin pigmentation on his scrotum surrounding the sites of CSP injection.

Results of the heavy metal screen, including arsenic, mercury, and lead, were all below the laboratory reference ranges. His serum level of silver was 11 $\mu\text{g/L}$ (reference range, $<5 \mu\text{g/L}$). The patient refused a punch biopsy of the skin.



Figure 2. Lateral view of argyria on the face and neck.

Comment

Silver—Silver is a naturally occurring element in the earth’s crust with considerable strength, malleability, and electrical and thermal conductivity. It has been used for thousands of years with numerous applications, including use as coinage, a material for tools, a chemical catalyst, an electrical conductor, and a medicinal ingredient.³ At low concentrations, silver cations have been shown to have microcidal effects. This antibacterial activity is related to direct binding to biotic molecules as well as the disruption of hydrogen ions and thus the pH balance. Additionally, silver cations inhibit enzymatic activities and provoke protein denaturation.⁴

For many years, claims have been made that the oral administration of silver can serve as a cure-all. In the late 19th century and early 20th century, CSPs were used as oral medications to treat a variety of ailments, including syphilis, epilepsy, and nasal allergies. Colloidal silver proteins are gelatinous suspensions of finely divided elemental silver prepared by mixing silver nitrate, sodium hydroxide, and gelatin, and diluting the mixture with water to a desired concentration.⁵ Due to health concerns and the emergence of more effective therapies, the use of CSP preparations eventually fell out of favor. In 1999, the US Food and Drug Administration issued a final rule that all over-the-counter drug products containing colloidal silver ingredients or silver salts were not generally recognized as safe and effective

Figure not
available online

Figure 1. Frontal view of argyria on the face and neck.

and were misbranded.² However, the topical use of silver sulfadiazine, a silver salt, remained among the initial treatments in patients with burn injuries. Adding silver sulfadiazine to burn dressings kills bacteria and increases the rate of reepithelialization.⁶

The US Environmental Protection Agency published an oral Reference Dose, which estimates the daily exposure that is unlikely to be associated with an appreciable risk for certain toxic effects during a lifetime. The oral Reference Dose for argyria is 5 mg/kg daily, with the critical dose estimated at approximately a total accumulation of 8 g.⁷ After oral administration of silver, up to 10% can be absorbed in the small intestine.⁸ The absorbed silver is transported in the blood bound to plasma proteins, such as albumin and globulins.¹ A portion of the silver is transported as a salt and can be deposited in various tissues after it is reduced to its metallic form. The amount of silver deposited is directly proportional to the blood supply of the organ.¹ Absorbed silver is widely distributed in the body, and the highest concentrations of deposition are in the skin, liver, spleen, and adrenals.⁴ Argyria occurs with generalized deposition of silver in the skin and mucous membranes, characterized by a gray to grayish blue staining of the skin.

Argyria—Argyria is the most obvious effect of silver overexposure or ingestion. Generalized argyria can result from either simple mechanical impregnation of silver particles in the skin or inhalation and oral absorption of particulate silver. Local routes of silver absorption occur through the conjunctivae or oral mucous membranes and more directly ingestion of CSP preparations.³ Argyria develops in stages, beginning with a gray-brown staining of the gingiva that progresses to hyperpigmentation and bluish gray discoloration in sun-exposed areas. Later, sclerae, nail beds, and mucous membranes become hyperpigmented. The degree of discoloration is correlated to the amount of silver absorbed or ingested.⁹ The threshold dose for silver accumulation and retention resulting in generalized argyria considerably varies among individuals.³

Cases of localized argyria also can occur. Ocular argyrosis (deposition into the eyes) is the most common type of localized argyria that manifests as a permanent gray to brownish discoloration, limited to the eye.¹ Deposits of silver can occur in the cornea and the anterior capsule of the lens.⁷ Argyrosis frequently was reported from prolonged use of colloidal silver disinfectant eyedrops, but because these drops are no longer used, the incidence has decreased. Localized argyria also can occur on the tongue and gingiva and is described in patients with silver dental amalgams.^{10,11}

There are no pathologic changes or inflammatory reactions visible at the histologic level from silver deposition or impregnation. Silver granules initially are found within fibroblasts and macrophages, then extracellularly along the basement membrane of blood vessels, sweat glands, dermoepidermal junction, and alongside erector pili muscles. The blue-gray discoloration of the skin occurs from the silver itself and increased melanin production. The proposed mechanism for this process is similar to photographic image development because the silver complexed with proteins is reduced to the elemental form through photoactivation. In the presence of light, silver further stimulates melanogenesis, increasing melanin in light-exposed areas,^{3,12} which could explain the mechanism behind increased pigmentation on sun-exposed areas.

With the exception of argyria, no pathologic changes have been shown among patients with low-dose silver exposure.⁷ When silver is administered at higher doses, either orally or intravenously, there is evidence of adverse health effects. In animal experiments, it has been suggested that silver intoxication can influence central nervous system (CNS) function by accumulating in neurons and resulting in hypoactivity, following parenteral administration of silver salts. Additionally, in experiments performed in the late 19th century, the intravenous administration of inorganic silver showed notable effects on the CNS, marked by weakness and rigidity of the legs, loss of voluntary movement, and abnormal conduction of the heart.⁸

Diagnostic Testing—Urine and serum concentrations of silver can be measured as indices of silver exposure. In patients without a history of medicinal silver ingestion or occupational exposure, the serum silver concentration reference range is less than 2.3 µg/L and the urinary silver concentration reference range is less than 2 µg per day (24-hour urine collection).¹³

Treatment of Argyria—Treatment of argyria remains limited, and the overall cessation of silver ingestion remains paramount. Chelators (eg, British anti-Lewisite, D-penicillamine) have proven ineffective in treating both silver toxicity and argyria.^{14,15} The use of hydroquinone cream 4% may slightly reduce the number of silver granules in the upper dermis and around the sweat glands as well as diminish the number of melanocytes.¹⁶ Decreased sun exposure and use of sun protection and opaque cosmetics have shown limited reduction in pigmented appearance on sun-exposed areas.³ However, breakthroughs in laser therapies may prove beneficial. A study using a Q-switched Nd:YAG laser successfully improved the appearance of argyria both clinically and microscopically.¹⁷ The concentration

of brown-black granules and dermal melanin was decreased along the collagen bundles and surrounding eccrine glands. The study was limited to localized argyria and the effectiveness in larger, more generalized disease must still be evaluated.¹⁷

Clinical Case—Although our patient presented with a history of schizoaffective disorder, it is unclear if argyria affected his psychologic state. There has been 1 other report in the literature documenting a patient who presented with argyria because of somatic delusions,¹⁸ and 1 single study showed CNS hypoactivity in rats with prolonged silver ingestion.¹⁹ One study suggests a hypothesis that ingestion of large amounts of silver may cause convulsive seizures.²⁰ However, no established link presently exists between argyria and psychologic or neurologic alterations. According to a PubMed search of articles indexed for MEDLINE using the search terms *argyria*, *psychiatric*, *schizophrenia*, *delusions*, *mental illness*, and *neurologic*, an established link is not shown.

Conclusion

Our case demonstrates interesting issues facing medicine today. The use of alternative therapies, though popular in the media, should not be undertaken without adequate research and testing. Furthermore, physicians should be acutely aware of the various possible home remedies on the market and be able to appropriately advise patients on the benefits and risks. As modern society continues to evolve, the perception of alternative medicine continues to gain popularity. Although alternative medicine may possibly provide some symptomatic relief, these remedies must be carefully monitored and used with extreme caution, as the long-term consequences of such treatments remain in question.

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