**Argyria in a Pediatric Patient Ingesting Silver Nitrate**

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**Abstract**

Historically used for its putative antimicrobial properties, chronic ingestion of silver can result in argyria, characterized by discoloration of skin and mucous membranes. We report a child with argyria resulting from silver nitrate consumption as alternative treatment for Crohn’s disease. Two years after ingestion stopped, serum silver levels remain elevated.

**Keywords:**

Ingestion; Oral; Blue; Child

**Abbreviations:**

CD: Crohn’s Disease; FDA: Food and Drug Administration

**Body Text**

**Introduction**

Silver has a long history of medicinal uses. Prior to the discovery of bacteria, silver vessels were used to carry water for the ancient Persian kings in the belief that the water would be kept fresher.1 However, today silver is considered by the Food and Drug Administration (FDA) as a “nonessential mineral that has no known physiological functions or benefits when taken orally”.2

Though oral silver preparations have historically been used for their antimicrobial properties, this was not without consequence. Avicenna (980-1037 AD) reported patients developing a bluish discoloration of the eyes associated with the ingestion of silver formulations. In 1840, the term *argyria* was introduced by Fuchs to describe this specific discoloration.3 We report a 10-year-old boy with Crohn’s disease (CD) who developed argyria following chronic silver ingestion.

**Case Presentation**

A 10-year-old Caucasian boy with ileocolonic Crohn’s disease (CD) and multiple food allergies presented with perianal fistula and poor weight gain in the setting of worsening CD. He had been treated with oral azathioprine which had to be stopped due to development of leukopenia. The parents refused all vaccinations after one year of age and were interested in alternative medical and nutritional therapies.

A physical exam revealed a chronically ill-appearing and notably pale boy, with a blue discoloration of his face. In addition to the patient’s current regimen of metronidazole, naltrexone, and other homeopathic remedies, his parents had been giving him silver nitrate solution (600 parts-per-million, marketed for topical use) at a dose of 2.5 mL by mouth three times a day for the past five years.

His parents purchased silver nitrate from an online distributor who specifically claimed that their formulation would not cause blue discoloration of the skin. The patient’s serum level of silver was 257 ng/mL or 2382.5 nmol/L (normal range 0-14 ng/mL) and parents were advised to immediately discontinue silver nitrate. Two months after the parents claimed to have stopped administration of the product, the patient continued to have perioral bluish discoloration and a blue tinge of his face, with a repeat serum silver level of 105 ng/mL (973.4 nmol/L). One year after the initial discovery of chronic silver ingestion, the dermal discoloration had resolved, but the silver level continued to be elevated. The patient’s CD progressed with development of a perianal fistula and abscess and his most recent serum silver level measured 58 ng/mL (537.68 nmol/L) 20 months after stopping the ingestion of silver nitrate (Figure 1).

**Review of Literature and Discussion**

The historical use of silver has been documented in medical literature. In the 1880’s, obstetrician Karl S. Crede proposed the use of silver nitrate 1% eye drops in newborns to prevent gonorrheal ophthalmia. With treatment, the incidence decreased from 7.8% to 0.13%.1 As a result, up until the 1970’s this therapy was advocated a choice of treatment by the United States Centers for Disease Control and the American Academy of Pediatrics and mandated by state law throughout most of the United States to prevent gonorrheal ophthalmia in neonates.4

The use of silver preparations eventually resulted in a unique adverse effect. Argyria originates from the Latin word for silver, argentum, and is characterized by bluish-gray to slate-gray discoloration of tissues caused by deposits of silver granules in the skin and mucous membranes. Generalized argyria may result from absorption through mucosal membranes, injection, inhalation, or ingestion of silver; whereas, localized argyria stems mainly from external contact through the skin. Discoloration of the fingernails, conjunctival membranes, and/or the oral mucosa may also be observed.3

Most of the reports describing argyria due to chronic consumption of silver formulations are in adults and yet still provide little additional data.3, 5-20 Of the few reported children with argyria was an 11-year-old boy with cystic fibrosis who was given colloidal silver to treat his lung disease. His serum silver concentration at the time of diagnosis of argyria was 32 ng/mL (296.7 nmol/L), with a follow-up level of 2.1 ng/mL (19.5 nmol/L) nine months after discontinuation. The skin discoloration resolved.21 The correlation of the concentration of serum silver with argyria is not well established. The lowest level in a patient presenting with discoloration of the skin or nailbeds had a serum level of 8.3 ng/mL (76.9 nmol/L).19 The trend of silver excretion from the body is not well elucidated either. Most reports describe patients with argyria as having just a single serum silver level after terminating ingestion, as we found only two publications documenting multiple levels.20, 21

While argyria is identified by particulate silver accumulation in skin and mucous membranes, other tissues may also be affected. Autopsies of adult patients demonstrated granular deposits of silver within the epidermis, sweat ducts, pituitary gland, myocardium, liver, spleen, adrenals, prostate, thyroid, kidneys, and gray matter of the cerebrum.16, 22 A biopsy of the colonic mucosa performed on a 73-year-old male presenting with argyria and a 5-year history of colloidal silver ingestion revealed silver granules in the lamina propria and basement membrane of the duodenal epithelium.14

The lack of evidence for any benefits to oral use of silver products resulted in warnings against the usage of silver preparations for treatment. In 1975, the United States Pharmacopeia and the National Formulary removed colloidal silver products from their guidebooks, and Goodman and Gillman: The Pharmacological Basis of Therapeutics 1980 edition stated that the “indiscriminate use of colloidal silver solutions…probably does more harm than good”.23 In 1999, the FDA issued a “final rule establishing that all over-the-counter drug products containing colloidal silver ingredients or silver salts for internal or external use are not recognized as safe and effective and are misbranded”.24 The FDA then issued a consumer advisory warning to the public in 2009 describing the risks of argyria associated with the use of silver-containing products, adding that silver supplements may interfere with the proper absorption of certain drugs.2 Currently, the only FDA-approved silver product is silver sulfadiazine 1% topical cream, a prescription drug indicated as an adjunct for the prevention and treatment of wound infection insecond and third degree burns.25

Despite these public alerts, the Internet serves as a means for proprietors to make exaggerated claims regarding the medicinal benefits of silver preparations without revealing potential side effects of their products.26 The FDA and Federal Trade Commission sent warnings to companies who exert false claims that silver “treats”, “cures”, or “prevents” disease, yet these web sites have found ways to avoid responsibility by marketing the products as “dietary supplements”, a category that allows the product to be legally recognized as intended for oral ingestion by The Dietary Supplement Health and Education Act.24, 26 Silver products for oral administration continue to be sold on the Internet, claiming to treat over 600 different diseases and disease-causing pathogens.23, 24 With the recent rise in silver use, the recurrence of argyria may yet again become a familiar clinical diagnosis.

In this report, the parents were administering silver nitrate topical solution orally in the belief that it was preventing and alleviating flares of CD. Elevated serum silver levels decreased upon discontinuation, but after nearly two years have not returned to normal range. We could not find reports of proven efficacy of silver ingestion in adult or pediatric patients for the purpose treating gastrointestinal diseases. The website of the distributor claims that their specific formulation “won’t turn you blue”.27 Unfortunately, due to lack of government oversite and published evidence, the legitimacy of the manufacturer’s declaration appears not to have been challenged.

**Conclusion**

We report the case of a child with clinical argyria resulting from the chronic ingestion of silver nitrate solution administered as an alternative treatment for inflammatory bowel disease. The growing popularity of complementary and alternative medicines could lead to the acceptance of silver-containing compounds as ingestible therapeutic agents without reliable evidence that they are safe and effective. Until there are sufficient data, healthcare providers should be aware that information on the Internet might encourage parents to administer oral silver compounds to their children. Increased awareness about parental practices regarding unregulated products and the need for the FDA to more closely monitor Internet claims about therapy are needed.

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