Argyria from Overindulgence of a Breath Freshener

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ABSTRACT:

ROJANAPANTH P. ARGYRIA FROM OVERINDULGENCE OF A BREATH FRESHENER.

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We report a 53-year-old woman who presented with a blue-gray discoloration on her face and bluish discoloration of lunulae of all her nails. She admitted a 10-year-history of taking too many pellets of a breath freshener, Jintan™ silver pellet pills. Skin biopsy revealed round, black-colored, fine granules deposition at basement membrane of sweat glands and connective tissue. Scanning electron microscopy and energy dispersive x-ray spectroscopy (SEM/EDS) of the skin biopsy demonstrated the presence of silver and selenium. These findings were diagnostic of generalized cutaneous argyria. She was treated with Q-switched 1064-nm Nd:YAG laser with excellent improvement.

Key words: argyria, silver, Q-switched Nd:YAG laser

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บทคัดย่อ :

ภัทรีวัลย์ โรจนพันธุ์ ณัฐพร สัมปัตตะวนิช กอบกุล อุณหโชค ภาวะเกิดพิษจากเกลือเงินจากการรับประทานลูกอมดับกลิ่นปากเกินขนาด วารสารโรคผิวหนัง 2561; 34: 217-224.

แผนกผิวหนัง กองอายุรกรรม โรงพยาบาลพระมงกุฎเกล้า

รายงานผู้ป่วยหญิงอายุ 53 ปีมาด้วยผิวบริเวณใบหน้าและรอยโค้งที่วงเล็บทุกเล็บเปลี่ยนเป็นสีฟ้าเทา ผู้ป่วยมีประวัติรับประทานลูกอมดับกลิ่นปากยี่ห้อยินตันจำนวนมากมานาน 10 ปี ผลพยาธิวิทยาจากผิวหนังมีสารสีดำทรงกลมสะสมที่บริเวณฐานของต่อมเหงื่อและเนื้อเยื่อเกี่ยวพัน ผลการแยกสารจากชิ้นเนื้อด้วยเครื่องจุลทรรศน์อิเล็กตรอนและเครื่องวิเคราะห์สเปกตรัมพบแร่เงินและแร่ซีลีเนียม จึงให้ผลการวินิจฉัยเป็นผื่นผิวหนังอาจัยเรียแบบเป็นทั่ว ผู้ป่วยได้รับการรักษาด้วยเลเซอร์คิวสวิชเอ็นดีแย็ก ตอบสนองต่อการรักษาเป็นอย่างดี

คำสำคัญ : ผื่นอาจัยเรีย, แร่เงิน, เลเซอร์คิวสวิช

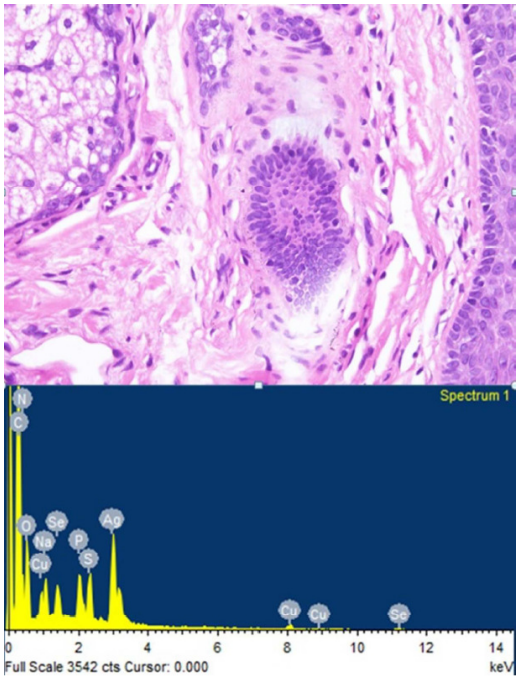
Introduction

Argyria (from the Greek word argyros, which means silver) is a rare disease characterized by blue to slate-grey discoloration of the skin and/or mucous membranes following the exposure to silver compounds.[1,2] The most common risk factor of argyria is occupational exposure such as mining, welding, silversmithing, antique restoration, jewelry manufacturing and photographic development. However, the condition has been reported after acupuncture, colloidal silver ingestion in alternative health practices and topical use of silver- containing products.

Cutaneous argyria can be manifested as localized and generalized form. Localized form is due to the impregnation of silver into the site of direct contact. Generalized form is caused by the systemic absorption of silver leading to wide deposition in the skin, nails, eyes, and mucosa.

Even though these blue-grey skin lesions are often biopsied and sent for histopathological examination, the diagnosis is often missed since low-power microscopic examination is usually unremarkable and the fine silver particles are often overlooked in higher power examination. Thus the diagnosis of argyria is challenging, especially when clinical information is inadequate. Not only argyria is a challenge in the diagnosis but also the treatment is problematic since argyria does not usually respond to chelating agents and topical medication.

Diffuse blue-gray patches on the face and blue lunulae of all fingernails



Histopathological findings showed silver accumulation in the basement membrane of eccrine sweat glands and SEM/EDS showed silver component in the tissue

After treatment with Q-switched 1064-nm Nd:YAG laser showed good result in only one session

Our case

A 53-year-old woman with no significant medical history presented with a blue-grey discoloration on the face for 10 years. The patient was a clerk who had the history of using breath freshener, "Jintan^{TM} silver pellet pills", around 10 packs per day for 10 years prior to her skin problem and discontinued for 5 years. Physical examination revealed diffuse blue-gray patches on the face and blue lunulae of all fingernails and toenails. The rest of the body, sclera and oral mucosa were normal. A 4-mm punch biopsy was taken from a cheek and revealed fine small, round, black-colored, granules deposition in the basement membrane of sweat glands and connective tissue sheaths around hair follicles. The definite diagnosis was

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finalized after scanning electron microscopy and energy dispersive x-ray spectroscopy (SEM/EDS) analysis of the skin biopsy which demonstrated the presence of silver and selenium in the skin lesion.

Discussion

Argyria has a high incidence in the 19th and 20th centuries due to the use of silver compounds.[3,4] The most common cause is occupational exposure, involved in silver mining, jewelry, and photographic processing. It has also been reported following surgical and dental procedures, topical treatment, body jewelry, acupuncture and alternative medicine.[5] Because of the increasing use of alternative medicine that often contains the silver compounds, the incidence of argyria is increasing. Silver solution is regarded to have anti-bacterial, anti-viral, anti-cancerous, and health-promoting properties.[1] The amount of silver reported to cause generalized argyria ranges from 4 to 5 g.[6] In Japan, generalized argyria due to breath freshener "Jintan™ silver pellet pills", as in our patient, has been reported.[7]

The pathogenesis of cutaneous argyria is not fully known.[4] Generalized argyria is the result of systemic absorption of silver, mostly in the small intestine, but the respiratory mucosa or broken skin can also be the routes. Silver is transported by blood and deposited in all body tissues with the highest concentration in the skin, liver, spleen and adrenal glands.[2,8,9]

In the skin, silver particles deposit around eccrine glands. They combine with elemental sulfur to form black silver sulfide particles using sunlight which acts as a catalyst in the same way as photography processing. Thus, the discoloration usually develops in sun-exposed areas such as the face and hands.[1,8,10,11,12] In addition, silver can stimulate melanocyte tyrosinase activity, which would contribute to hyperpigmentation.[13]

The typical clinical presentation of generalized cutaneous argyria is permanent blue-gray macules or patches in the sun-exposed area.[3] Due to the Tyndall effect, the brown silver particles in the dermis appear blue-gray through the skin.[1] Diagnosis is often challenging because it looks like melanocytic lesions and dermoscopy shows a nonspecific blue homogeneous pattern.[5,14]

Histopathologic examination shows normal epidermis with silver accumulation in the basement membrane of sweat gland and dermis. It is characterized by dark small granules distributed around eccrine sweat glands and elastic fibers. Silver deposits on collagen fibers may be swollen and ochre-coloured called pseudo-ochronosis pattern.[3,5,15] Immunohistochemistry does not help in the

diagnosis but immunostaining can be used to rule out a melanocytic lesion.[3]

Microanalytical techniques such as scanning electron microscopy (SEM) and energy dispersive x-ray spectroscopy (EDS) can be used to identify chemical elements in a biopsy and give the definitive diagnosis. SEM exposes a tissue sample to electrons altering the elements at the atomic level and resulting in an emission of x-rays, which are measured by EDS. Since each element has characteristic emission patterns, the type of element can be identified. In our case, SEM/EDS analysis of the skin biopsy presented both silver and selenium. Selenium is an essential micronutrient which plays a role in the metabolism and detoxification of silver and results in the deposition of silver–selenide complexes.[3]

The clinical differential diagnosis of generalized argyria includes cyanosis, Addison's disease, haemochromatosis, Wilson's disease, ochronosis, methaemoglobinaemia and metastatic melanoma. The ingestion of gold, bismuth, chlorpromazine, amiodarone, or antimalarial agents may produce a similar skin lesion. [1,16]

Although generalized argyria is a benign condition and hardly associated with health risk, it can cause a cosmetic problem and psychosocial stress.[17] Silver particles may deposit in the liver, kidneys, gastrointestinal tract and can rarely produce thrombocytopenia and neurological symptoms.[1,4]

There have been various modalities to treat argyria without any good response. Silver selenide complexes are inert and cannot be chelated by British anti-Lewisite (BAL) or intralesional injection of sodium thiosulfate or potassium ferrocyanide that can be used in some metal intoxication. Topical depigmenting agents e.g. hydroquinone and dermabrasion have shown poor results.[12,17,18] Sun protection and sunscreen can lighten the lesions but have limited effect.[17]

The most promising treatment is the use of Q-switched 1064-nm laser. Q-switched Nd:YAG is weakly absorbed by natural chromophores such as melanin, hemoglobin, and water, so it can penetrate into the deep dermal exogenous chromophores and absorbed by the silver granules. The mechanisms of argyria treatment by Q-switched lasers may be the same as tattoo removal. The laser is absorbed by silver particles and photoacoustically explodes the pigment particles. Macrophages engulf the fragments and particles are removed via the lymphatic system. Other mechanisms may include the suppressive effects of laser toning on activated melanocytes.[1,12,17,19]

Our case was treated with a Q-switched 1064-nm Nd:YAG laser (Spectra VRM; Lutronic, Ilsan, Gyenonggi, South Korea). Anesthetic

cream (EMLA, Astra-Zeneca, Lund, Sweden) was used to provide cutaneous anesthesia. Initially, a 2-cm-diameter area at the left temporal region was treated as a trial area. The laser was applied at a fluence of 1 J/cm^2 with a pulse duration of 5 ns and using an 8-mm spot size with only a single pass. This low-fluence parameter produced mild erythema and edema without petechiae and tissue splatter. The blue-grey discoloration also gradually fainted just a few minutes after the treatment. No special wound care was needed and no adverse effect was found except a rather severe pain during the procedure which could be relieved by oral analgesic agents. She was also advised to apply sunscreen and avoid sun exposure as much as possible.

In summary, our case highlights the diagnostic challenge in generalized cutaneous argyria associated with breath freshener "Jintan™ silver pellet pills" and demonstrates the role of SEM/EDS analysis which characterized the dermal deposit and identified the elements in the tissue. Q-switched 1064-nm Nd:YAG laser was used and showed the satisfactory result after only one session.

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