Localized Chrysiasis Induced by Laser in a Patient with Rheumatoid Arthritis

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Chrysiasis is an uncommon permanent blue-gray discoloration occurring on the sun-exposed skin of the patients who have been exposed to gold salts. Light exposure and total amount of gold administered have been reported to play important roles in the development of chrysiasis. We herein report a case of localized chrysiasis in a patient with rheumatoid arthritis who had received long-term parenteral chrysotherapy. Blue-gray discoloration has developed after laser treatment for her freckling and lentigines over the treatment areas. Punch biopsy was obtained and the biopsy specimen showed light microscopic and ultrastructural characteristics of gold deposition. (Dermatol Sinica 23: 36-40, 2005)

Key words: Chrysiasis, Chrysotherapy, Rheumatoid arthritis

金沉著症是一發生於曾接受長期金製劑治療之病人，在光暴露皮膚處的現而永久的藍灰色色素斑。光暴露及所接受之金治療總劑量皆曾被報告與金沉著症的發生有關。我們在此報告一曾接受長期肌肉注射金製劑治療之類風濕性關節炎病例，因接受雷射治療而引發永久性之金沉著症色素斑。我們在色素斑沉著處取得之皮膚切片，在病理組織學及電子顯微鏡下顯示出金沉著症之代表性特徵。(中華皮誌 23: 36-40, 2005)
INTRODUCTION

Chrysiasis was first applied to describe the deposition of the gold in the dermis following long-term gold injections for the treatment of tuberculosis in 1928. The clinical manifestations of chrysiasis are displayed with permanent, blue-gray skin discoloration, which occurs mostly in sun-exposed areas of the body. Light exposure has been reported to play an important role in the pathogenesis of chrysiasis. The cutaneous discoloration in chrysiasis has been induced by UV irradiation and laser therapy. In addition to skin, gold pigment can also be deposited in the cornea, sclera, nails, hairs, kidney, liver, spleen and lymph nodes. Chrysiasis has been recognized as a complication of gold salts therapy in patients with rheumatoid arthritis when total gold administered exceeds a threshold level.

We herein report a case of laser-induced chrysiasis on the face of a patient who had received intramuscular gold salts treatment for her rheumatoid arthritis. The diagnosis of chrysiasis was confirmed on clinicopathological backgrounds as well as ultrastructural features. To our knowledge, this is the first reported case of localized chrysiasis induced by laser in Taiwan.

CASE REPORT

A 43-year-old female presented with the chief complaint of persistent discoloration over bilateral zygomatic areas and cheeks on her face. They have been present since 2 years ago, when she received Q-switched ruby laser treatment elsewhere for her previous facial freckles and lentigenes (Fig. 1). Blue-gray patches were noted immediately after laser treatment, and post-inflammatory hyperpigmentation was suspected initially. Half a year later, a second kind of laser, Q-switched Nd-YAG laser treatment was then performed for the discoloration by another dermatologist. Unfortunately, there is no obvious improvement and the blue-gray pigmented areas persisted over her face. She applied some blenching agents for several months, but the lesions did not lighten. Therefore came to us for the second opinion. Careful review of her medical history disclosed she has more than 20 years' history of rheumatoid arthritis and that she had received a 2-year course of gold salt therapy. Gold sodium thiomalate 50 mg per-week was given intramuscularly for about 2 years (1984-1986). The total administered dose exceeded 5 gm. There was no discoloration of the sclera, nails or hairs.

A punch biopsy of a representative area was performed. H&E stained sections of specimen demonstrated numerous fine black granular particles within the endothelial cells and, to a lesser amount, the histiocytes in the dermis. The amount varied from scattered fine particles to large collections within the cells (Fig. 2). Under the crossed polarized light, no orange-red birefringence were noted in the paraffin embedded sections. Electron microscopy showed ultrastructural characteristics of cutaneous gold deposits. Clusters of electron-dense particles within lysosomes of histiocytes were demonstrated (Fig. 3). According to the clinical presentation, the medical history of the patient, the pathologic pictures, and the striking ultrastructural characteristics of cutaneous gold deposits under the electron microscopy, the diagnosis of chrysiasis induced by laser therapy was made.

The patient is currently receiving long-pulsed ruby laser therapy (SINON) as well as...
Strict sun protection, according to Yun, et al. Initial round of treatment showed diminishing of coloration.

**DISCUSSION**

Chrysiasis refers to the deposition of gold in the systemic tissue, in particular the skin, in the patients who received long-term chrysotherapy. It was first described in 1928 in a patient of tuberculosis who received chrysotherapy and was later identified in the patients with rheumatoid arthritis receiving similar treatments.

Gold has been utilized clinically in the management of rheumatic diseases since Forestier in 1929. The two preparations commonly used are aurothioglucose and sodium aurothiomalate. Gold can strongly inhibit sulphhydril system, alter collagen by increasing cross-linkage, inhibit lysosomal hydrolase, suppress histamine release more effectively than do steroids, prevent prostaglandin synthesis, and moderately suppress cellular immunity. Therefore, organic gold compounds can alter the activity of macrophages and cells that play a central role in inflammation, especially that of arthritis. This agent has a very slow onset of anti-inflammatory action in patients with rheumatoid arthritis or other immune complexes in their serum. Benefits may require several months to become manifest, so that the agent is one kind of so-called disease modifying, slow acting antirheumatic drugs (DMARDs). The gold therapy is seldom being prescribed recently due to its high incidence of adverse effects and great advance of treatment modalities in rheumatoid arthritis. The adverse effects of chrysotherapy include severe gastrointestinal disturbance, nausea, vomiting, diarrhea, stomatitis, proteinuria, hematuria, nitritoid (nitrite-like) reaction, bone marrow suppression, and skin rashes. The most common cutaneous adverse effects of gold salt therapy are general pruritus, non-specific erythematous maculopapular eruption, lichen planus-like dermatitis, pityriasis rosea-like dermatitis, and oral ulcer. The pigmentaion change occurs very rarely as a complication of chrysotherapy. There are relative few cases of chrysiasis reported since the first case was described by Hansborg in 1928. Most cases were predominately female Caucasians receiving long-term gold salts therapy. The accumulative dosage of gold exceed 2.5 gm in the majority of reported cases. The extents of discoloration were widely distributed on the light-exposed areas of skin such as eyelids, face, neck, upper chest, hands, and forearms. There is no significant treatment modality proposed in these literatures.

![Fig. 2](image1.png)

A punch biopsy specimen demonstrated numerous black fine granular particles within the histiocytes in the dermis, especially around the perivascular areas (H & E stain, X 400)

![Fig. 3](image2.png)

Electron microscopy showed numerous electron-dense particles within cytoplasmic lysosomes near the nuleus in a dermal histocyte. The sizes range from 6.7 nm to 12 nm. (Electron microscopy, X12,000)
for discoloration of chrysiasis except reducing sunlight exposure and avoiding long-term chrysotherapy if unnecessary.

In 1995, Trotter et al. reported a unique case of localized chrysiasis developed immediately after Q-switched ruby laser irradiation for post-inflammatory hyperpigmentation secondary to granuloma faciale who has received long-term gold therapy. This is the first reported case of localized chrysiasis induced by laser exposure. In 2002, Yun et al. reported the second case of laser induced localized chrysiasis on cheek. To avoid the undesired surgery scars after surgical excision of the numerous discrete discolored lesions on face, Yun et al. chose to treat the patient with long-pulsed ruby laser and cleared the discoloration successfully without inducing new hyperpigmentation.

In general, the diagnosis of chrysiasis is usually suggested by the clinical history, and the confirmation is commonly achieved by skin biopsy with microscopic characteristics and electron microscopic features. X-ray probe microanalysis can also provide further confirmation of gold particles. However, it requires the special expertise and equipment and is also a time consuming and expensive method. On the other hand, the detection of the orange-red birefringence under the polarized light has been suggested by AL-Talib et al. as a simple and convenient way to confirm the gold pigment. In our patient the orange-red birefringence was not observed in paraffin wax embedded sections. This negative result could be due to size reduction of the gold particles after laser treatment. The Q-switched laser can significantly reduce the particle size of the gold deposit and led to loss of faceted appearance. Trotter et al. noted that the particles are 106 +/- 35 (mean+/− SD) nm in diameter and faceted before laser irradiation and 16 +/- 4nm after laser treatment. The sizes of the gold particles are reduced by laser treatment and therefore loss of their faceted appearance, which may lead to loss of their optical reflectance when examined under polarized microscope. The cases proposed by Al-Talib et al. didn't undergo laser treatments which explained the presence of birefringence under polarized microscopy. The gold particles in our patient are measured about 6.7-12 nm after laser treatments, consistent with the size of gold particles after laser therapy.

The important role of light exposure in pathogenesis of cutaneous discoloration in patients receiving parenteral gold therapy is widely recognized. Besides sun exposure, the pigmentation can be induced in sun-protected skin by UV irradiation. The mechanism of blue-black color as observed clinically is not fully understood. Benn et al. suggested that photoaging favors the conversion of the organometallic gold compounds to crystalline metallic gold, which result in the bluish skin discoloration in chrysiasis. However, Trotter et al. proposed that the Q-switched laser can produce the high peak power generated by a short pulse duration and develope a extremely high temperature which may be responsible for the changes in gold structure from crystalline to elemental gold, resembling colloidal gold. The color of the colloid gold in solutions is blue-purple and the pigment dispersion in dermis give rise to blue discoloration. Trotter et al. also found that the pulsed dye laser dose not induce the gold structural change. It is possible that the pulsed dye laser dose not induce photoacoustic shock waves which changed the gold structure. Yun et al. also observed that laser induced chrysiasis in patients treated with gold is primarily an irradiance-dependent phenomenon rather than fluence-dependent phenomenon. Therefore, clearing the discoloration of laser induced chrysiasis with long-pulsed laser can be achieved. Further investigation of the physiochemical properties of laser or UV-induced chrysiasis is needed.

The discoloration of chrysiasis induced by laser should be differentiated from pigment darkening of cosmetic tattoo after laser therapy. Cosmetic use of facial tattoos to simulate makeup application, such as tattoo of eyebrows, lip lines, midcheek rouge and eyeliner is widely accepted. However, a lot of tattooed people ask for tattoo removal due to the sequential compli-
cations, unsatisfied results or concepts of the fashion changed in the present time. Cases of cosmetic tattoo ink darkening after irradiating with Q-switched laser have been reported. The chemical mechanism of tattoo ink darkening may be associated with the conversion of ferric oxide (Fe₂O₃) to ferrous oxide (FeO), which is black in color. The diagnosis of cosmetic tattoo darkening can be clarified according to the history, clinical manifestations, and the pathologic findings. The pigment granules of tattoo are more coarse and heterogeneous in size and color which dispersed mostly in the upper dermis free or within macrophages. However, the gold granules located predominantly within endothelial cells or macrophages perivascularly in dermis. Laser treatments of unwanted facial tattoos should also be approached with caution as in cases of chrysiasis because of the potential irreversible pigment darkening induced by laser interaction with iron oxide pigments or titanium dioxide.

Patients receiving parenteral gold therapy are susceptible to chrysiasis induced by laser therapy. The blue-gray discoloration may be a potent complication of the Q-switched laser treatment in patients who had received chrysotherapy. Thorough review the medical history helps to make the diagnosis. Although gold therapy is very rarely used as a treatment modality for rheumatoid arthritis in the modern time, dermatologists still may have a chance to see it in rheumatoid arthritis patients, especially those who are over 40 years old. In view of the ubiquity of pigment problems, care must be taken before conducting a short-pulsed, Q-switched laser therapy in these patients. Long-pulsed ruby or Alexandrite laser might be useful to treat these discolorations on the skin.

REFERENCES