PEER REVIEWED

Ocular Chrysiasis

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Abstract

Ocular chrysiasis is a deposition of gold in ocular structures secondary to gold salt therapy, which is primarily used in infectious, rheumatoid and psoriatic arthritis. Gold therapy has become an extremely rare treatment due to the advent of rheumatologic medications with better safety profiles. However, any patient who has undergone gold therapy could potentially have ocular chrysiasis. Therefore, it must be included as a differential in the presence of corneal or lenticular changes in these patients. Additionally, it is important to include ocular chrysiasis as a differential in the presence of crystalline keratopathies. A detailed medical history and thorough ocular examination can assist clinicians in making a correct diagnosis.

Key Words: *gold salts, ocular chrysiasis, autoimmune disease, cornea*

Background

The following case report is meant to be used as a guide in teaching optometry students and residents. It is relevant to all levels of training. Ocular chrysiasis is a deposition of gold in ocular structures following chrysotherapy, which is the medical use of gold salts. Chrysotherapy was primarily used to treat infectious, rheumatoid and psoriatic arthritis. This therapy has become an extremely rare treatment due to the advent of rheumatologic medications with better safety profiles. Any patient who has undergone gold therapy could potentially have ocular chrysiasis. Therefore, it must be included as a differential in the presence of corneal or lenticular changes in these patients. This case illustrates the importance of history-taking skills, examination and decision-making in effectively diagnosing this condition.

Case Description

A 54-year-old Caucasian female presented for an annual eye examination. She reported a haze to her vision in bright conditions, as if she were continually looking through “dirty glasses.” She was wearing progressive lenses, primarily for reading. Ocular history was positive for dryness, seasonal allergies, bilateral LASIK in 1999, and past bouts of iritis. The patient was using a fish oil supplement and artificial tears as needed for dry eye. Her allergies were being treated with olopatadine hydrochloride ophthalmic solution (Pataday) and prednisolone acetate (Pred Forte), as needed, as prescribed by her previous optometrist.

Family ocular history was positive for dry age-related macular degeneration on her mother’s side. Her medical history was significant for high blood pressure controlled with hydrochlorothiazide and triamterene, migraines controlled with rizatriptan, diastolic dysfunction and heart block controlled with a pacemaker, and occasional oral herpes simplex treated with valacyclovir. In addition, she had a history of psoriasis, psoriatic arthritis and iritis, currently treated with etanercept (Enbrel) injections and calcipotriene (Dovonex) ointment. She reported no recurrences of iritis since starting Enbrel injections in 2000. She was a non-smoker and had no drug allergies. She was oriented to person, place and time.

Figure 1. Image of the patient's cornea, showing gold deposits, captured at the slip lamp using an iPhone 5.
Click to enlarge

Best-corrected vision was 20/15 OD with +0.25-0.50×030 and 20/15 OS with +0.50-0.50×015 at distance and 20/20 OU at near with a 2.50 add. Cover test was measured to be orthophoria at distance and 4 exophoria at near. Extraocular motility was full with no pain or diplopia. Pupils were equal, round and reactive to light with no afferent defects. Visual field was full based on screening with frequency doubling perimetry. HRR (Hardy Rand and Rittler) color vision screening was normal in each eye. Slit lamp examination revealed yellow-brown glistening gold deposits in the stroma of each cornea. **(Figure 1)**. No discoloration of the skin of her face or elsewhere was noted. The anterior chamber was clear, without cells or flare. Goldmann applanation tonometry was 11 mmHg in each eye. Dilated fundus examination was performed using one drop of 1% tropicamide in each eye. Crystalline lenses of both eyes showed trace nuclear sclerosis. The vitreous humor was clear in each eye. Optic nerves were a healthy pink color, and cup/disc ratios were 0.30/0.30 in the right eye and 0.35/0.35 in the left eye with distinct margins. Maculae were normal without degenerative or pigmentary changes. Retinal blood vessels showed no hypertensive changes. Peripheral retinae were flat with no holes, breaks or tears.

Upon further questioning, the patient reported originally being diagnosed with rheumatoid arthritis in 1985. Treatment with the gold injection Solganol was initiated at that time. After a year of treatment, injections were switched to Myochrysine until therapy was discontinued in 1987 due to pregnancy. A short Myochrysine treatment course of a couple of months was administered after the conclusion of the pregnancy in 1988. The oral gold medication Ridaura was also tried during chrysotherapy but was immediately discontinued due to gastrointestinal intolerance.

In total, the patient had received 1935 mg of gold salt injections. However, the severity of the arthritis decreased drastically during a second pregnancy and never returned to its pre-pregnancy severity. In 1992, plaque-like seborrhea of the scalp developed and the diagnosis was changed to psoriasis with psoriatic arthritis.

Educators Guide

Key concepts

- Recognize clinical findings of ocular chrysiasis
- Differential diagnosis of ocular chrysiasis
- Treatment and management considerations in patients with ocular chrysiasis

Learning objectives

At the conclusion of the case, participants should be able to:

- Know the systemic conditions for which gold salt treatment may be used
- Know the typical cumulative dose of gold salts that may result in ocular chrysiasis
- Describe the signs of chrysiasis
- Understand the physiology behind gold deposition in ocular structures
- Provide proper patient education on management and long-term prognosis of ocular chrysiasis

Discussion questions/points

- What is the definition of chrysiasis vs. ocular chrysiasis?
- Describe the signs and symptoms of ocular chrysiasis
- What conditions have gold salts (chrysotherapy) been used to treat?

- How would you educate patients with chrysiasis about their condition and prognosis?
- Should a patient with ocular chrysiasis discontinue gold salt treatment?
- What is the natural course of ocular chrysiasis?
- Discuss the differential diagnoses of ocular chrysiasis
- How would you manage the ocular symptoms for the patient in the case report?
- What history questions should be asked of patients presenting with anterior segment crystalline deposits?

Learning assessment

- Incorporate the case into clinical or didactic discussion to achieve learning objectives
- Assess clinical skills using application of anterior segment photography and corneal topography
- Use photography and topography to facilitate understanding by identifying normal vs. abnormal findings
- Further assess knowledge by use of student-directed presentations to compare and contrast differential diagnoses

Discussion

Chrysiasis is derived from the Greek word chrysos, meaning “golden flower.”[1] It is due to the deposition of gold salts throughout tissue in the body, most noticeably on the skin.[1] The use of gold salts in medical therapy dates back thousands of years. In the late 19th and early 20th centuries, gold cyanide was used to treat tuberculosis. Physicians at that time believed that rheumatoid arthritis was a form of tuberculosis. Jacques Forestier, a French physician, was the first to find that gold salts improved the condition of patients with rheumatoid arthritis.[2-5] Gold salt administrations were common in the treatment of rheumatoid arthritis until the advent of alternative treatments with better safety profiles, such as methotrexate, in the 1990s. Chrysotherapy (gold salts) has also been used to treat Sjögren’s Syndrome and systemic lupus erythematosus.[6]

Gold salts were primarily given by intramuscular injection or orally. Doses started at 10 mg to determine patients’ ability to tolerate the therapy. Doses were slowly increased to 50 mg at weekly intervals until a total of 2000-3000 mg was given. The patient was reassessed at that time. If inflammation persisted, another course of treatment was started in 6-8 weeks. Patients were monitored closely for signs and symptoms of toxicity, which included itching, mouth ulcers, jaundice and digestive upset. Urinalysis was conducted at every visit to check for protein in the urine, the presence of which indicated kidney damage. If protein was found in a urine sample, gold salt administration was immediately paused until a subsequent urine sample was found to be free of protein. Blood sedimentation rates were performed approximately every six weeks during therapy to track inflammatory signs and treatment progress.[3,5]

The exact mechanism of action of gold salts is not entirely understood. Prevailing theories suggest that gold ions and their metabolites serve an inhibitory role in inflammation. This inhibition is believed to act on immune cells such as macrophages and T-lymphocytes, immunoglobulins and inflammatory cytokines as well as at other points along the inflammatory cascade. In addition, gold ions may interfere with antigen processing and recognition of T-cell receptors.[5]

Chrysiasis typically begins with a mauve discoloration of the skin around the eyes, which changes to a grayish/slate blue or gray and extends to other sun-exposed areas of the body.[1,7] Ocular chrysiasis can involve the cornea, conjunctiva and lens. Deposition of gold in the cornea has typically been seen in cumulative doses higher than 1-1.5 grams.[7,8]

Ocular chrysiasis is a common finding in patients undergoing chrysotherapy. One study found that 62% of chrysotherapy patients developed corneal chrysiasis during treatment.[8] Other studies have produced

estimates that between 45% and 97% of patients receiving a total of 1 gram of gold salts develop corneal chrysiasis.[9-11] Lenticular chrysiasis has also been reported with variability in the frequency of manifestation. Overall, lenticular chrysiasis is believed to be rare. One study found that 36% of gold salt-treated patients displayed lenticular chrysiasis.[11] Another suggested 55% of patients develop lenticular chrysiasis.[9]

The underlying mechanism of gold deposition is unknown. Gold is believed to circulate and be deposited by the aqueous humor because it is primarily found in the posterior half of the inferior cornea and often spares the superior and peripheral cornea.[9,12] Although some investigators have reported that most ocular gold salts deposit in the posterior stroma, a 2010 confocal microscopy study revealed gold deposits throughout all layers of the cornea, with the largest deposits in the anterior stroma. Histopathology and in vivo confocal microscopy showed no associated inflammation.[7,13] However, two variants of corneal chrysiasis have been described. Most commonly, it presents as asymptomatic deposition of fine brown or purple granules in the central posterior corneal stroma, sparing the periphery. Other patterns include peripheral deposition with extension toward the central cornea, superficial, and deep axial deposition. These findings are not an indication to stop gold therapy.[12] The second corneal variant is rare but may present with inflammatory signs and symptoms such as marginal interstitial keratitis that may ulcerate, with white subepithelial limbal infiltration and deep, brush-like stromal vascularization. Crescent-shaped marginal ulcers 2-3 mm in length may also be present. This variant is thought to be an idiosyncratic reaction. It may be unilateral or bilateral and is considered an indication to stop gold therapy.[12]

Overall, ocular chrysiasis after systemic gold administration is considered inert.[10] However, Raj et al. reported a case of a patient who received a chemical injury when a gold/amine compound exploded and caused gold particles to embed in the cornea bilaterally. After cataract extraction 40 years later, he developed a localized ulcerative keratitis adjacent to embedded gold in the cornea and recurrent bouts of stromal erosion.[12]

Lenticular chrysiasis appears as fine, dust-like, yellowish glistening deposits in the anterior capsule or in the anterior suture lines. Gold can collect in the conjunctiva as well, forming irregular brown deposits. However, conjunctival changes typically resolve after cessation of therapy.[10] A study published in the *Annals of the Rheumatic Diseases* by Prouse, Kanski and Gumpel explored ocular chrysiasis as a predictor for clinical improvement or systemic toxicity. However, the study found no such association.[8]

In the absence of inflammation, there is no necessary treatment or management for ocular chrysiasis as the deposits typically do not cause decreased visual acuity or other symptoms. UV protection may assist with reducing glare. However, it is necessary to monitor for changes and differentiate the condition from other corneal pathology. Although this condition can be noticed visually, it should not be detrimental to vision.

The key to diagnosis is thorough patient history to identify any autoimmune conditions or history of chrysotherapy. Location of the deposits is likewise important for ruling out other corneal pathologies. Ocular chrysiasis should be considered in any patient who has undergone chrysotherapy if abnormalities within the cornea or lens are noted.

Differential diagnosis

Several differential diagnoses should be considered if corneal deposits are observed. The appearance and location of the deposits will aid correct diagnosis.

Pigment dispersion syndrome is a condition that results from mechanical rubbing of the posterior iris epithelium on the lens zonules due to mid-peripheral bowing of the iris. This rubbing results in shedding

of the pigment into the posterior chamber. Following the aqueous currents, this pigment travels into the anterior chamber and is deposited on the corneal endothelium. Pigment deposits form a characteristic vertical line called Krukenberg spindle. In these cases, the anterior chamber is typically deep, and melanin may be floating within the chamber during active pigment dispersion. Anterior chamber angles are open, and the trabecular meshwork is hyperpigmented. Patients with pigment dispersion syndrome may develop elevated intraocular pressure leading to pigmentary glaucoma.[14]

Wilson's disease is a degenerative liver condition that causes copper to be deposited in tissues, including the cornea. Copper deposits in the cornea within Descemet's membrane in a peripheral ring, called a Kayser-Fleischer ring. The appearance of this ring can change color based on illumination type. Patients may present with corresponding liver disease, basal ganglia dysfunction and psychiatric disturbances.[14]

Bietti's corneoretinal crystalline dystrophy, an autosomal recessive condition primarily affecting those of East Asian ancestry, results in slow, progressive vision loss. Onset of this condition occurs in the third to fourth decade of life. Patients develop crystals in the superficial peripheral cornea as well as in all retinal layers of the posterior fundus. They also develop atrophy in the macular retinal pigment epithelium and choriocapillaris.[14]

Conclusion

Ocular chrysiasis is a condition associated only with use of gold salts for treating autoimmune conditions. It is becoming increasingly rare as newer and safer therapies for rheumatoid arthritis are developed. It is important to include ocular chrysiasis as a differential in the presence of crystalline keratopathies whenever gold therapy has been administered. A detailed medical history and thorough ocular examination can assist in arriving at the correct diagnosis.

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