J Occup Health 2008; 50: 521–524

Case Study

Ocular Argyrosis in a Silver Craftsman

Gianni PALA[1], Aldo FRONTERRÉ[2], Fabrizio SCAFA[1], Mario SCELSI[3], Roberto CECCUZZI[4], Elisabetta GENTILE[1] and Stefano M. CANDURA[1]

[1]Occupational Medicine Unit, University of Pavia and Salvatore Maugeri Foundation, Work and Rehabilitation, IRCCS, Scientific Institute of Pavia, [2]Studio Oculistico Fronterré Milan, [3]Department of Pathology, Salvatore Maugeri Foundation, Work and Rehabilitation, IRCCS, Scientific Institute of Pavia and [4]Ophthalmic Department, University of Pavia and Policlinico S. Matteo Foundation, IRCCS, Italy

Key words: Silver, Conjunctive, Cornea, Histopathology, Confocal microscopy

Silver (Ag) is a rare, naturally occurring element. Because of its physical properties (hardness, ductility, malleability, high thermal and electrical conductivity) and antimicrobial activity, Ag has been extensively mined and utilized since antiquity in a wide variety of applications, including metallurgy, soldering, electroplating, photography, medicine and dentistry (wound and burn care, surgical devices, dental amalgams), water sanitation, cosmetics, electronics, production of coins, medals, jewellery, silverware and mirrors[1, 2].

Small Ag quantities are absorbed by humans through diet, even though the element fulfils no physiological role in any human tissue. In the case of occupational or iatrogenic exposure, Ag is less toxic than other xenobiotic metals (such as lead and mercury) and the most common clinical presentations are argyria (slate gray discoloration of the skin and other soft tissues, due to generalized accumulation of the metal) and argyrosis (discoloration of the eye, skin and/or external mucous membranes, caused by local Ag absorption and deposition). Additionally, soluble Ag compounds may cause liver and kidney damage, irritation of the eyes, skin, respiratory and intestinal tract, and haematological changes[2, 3].

Thanks to the improvement of hygiene in the workplace, and to the restrictive use of Ag-containing medications, Ag-related disorders are uncommon in current clinical practice. We describe here the clinical and pathological findings of an exceptional (nowadays) case of occupational argyrosis diagnosed in advanced age.

Received Apr 4, 2008; Accepted Aug 7, 2008
Published online in J-STAGE Oct 30, 2008
Correspondence to: S.M. Candura, Occupational Medicine Unit, University of Pavia and Salvatore Maugeri Foundation, Work and Rehabilitation, IRCCS, Scientific Institute of Pavia, Via Maugeri 10, I-27100 Pavia, Italy (e-mail: stefano.candura@fsm.it)

Case Presentation

The subject was a 71-yr-old man, working from the age of 17 as a craftsman producing a variety of Ag articles, including vases, plates, trays and frames. These articles were created by cutting, welding and hammering Ag sheets and leaves into the desired shapes. Subsequently, they were polished and re-silvered in a galvanic bath. The working bench was situated approximately 30–40 cm from the subject's face, who never wore any ocular or respiratory protective devices. No aspiration systems were present in the workplace. The patient used to work up to 8 h daily, alternating crafting with the selling of the articles. His producing activity had gradually diminished during the last few years. He never used Ag-containing medications.

When the worker first came to our observation, his urinary Ag concentration was 0.10 μg/*l* (0.15 μg/24 h), *i.e.* within the reference range (0.04–0.88 μg/*l*) for the general Italian population[4]. No previous environmental or biological monitoring data were available.

The patient reported that his vision (both proximal and remote) had worsened during the last few months. He did not complain of nyctalopia or other subjective visual symptoms. General medical history and physical examination, routine blood/urine analysis, electrocardiography, and chest radioimaging were unremarkable. Ocular examination revealed a bilateral, marked blue-gray discoloration of the tarsal and bulbar conjunctive (Fig. 1), and of the cornea (Fig. 2). No abnormal pigmentation of the skin or other external mucous membranes was noted. Natural visual acuity (not susceptible to improvement with lenses) was 5/10 in the right eye and 4/10 in the left. Besides corneal discoloration, slit-lamp examination of the anterior segment disclosed bilateral, nuclear sclerotic cataract, without pigment deposition. *In vivo* confocal microscopy showed highly reflective material with a granular pattern in the deep layers of both corneae, anterior to the endothelium (Fig. 3). Because of this diffuse structural alteration, endothelial cell count was impossible. The corneal thicknesses (measured by ultrasound pachymetry), intraocular pressures, visual fields (evaluated by Humphrey computed perimetry), and retinal appearances at fundoscopic examination were normal.

A biopsy was obtained from the bulbar conjunctive of the right eye. Histopathological examination revealed a normal non-keratinizing squamous epithelium and deposits of a dark granular pigment in the submucosa (Fig. 4). No atypia or inflammation were observed.

The study was conducted with the patient's informed consent. Both the University of Pavia and the Salvatore Maugeri Foundation follow the Declaration of Helsinki in conducting medical research involving human subjects.

Final diagnosis was occupational, bilateral

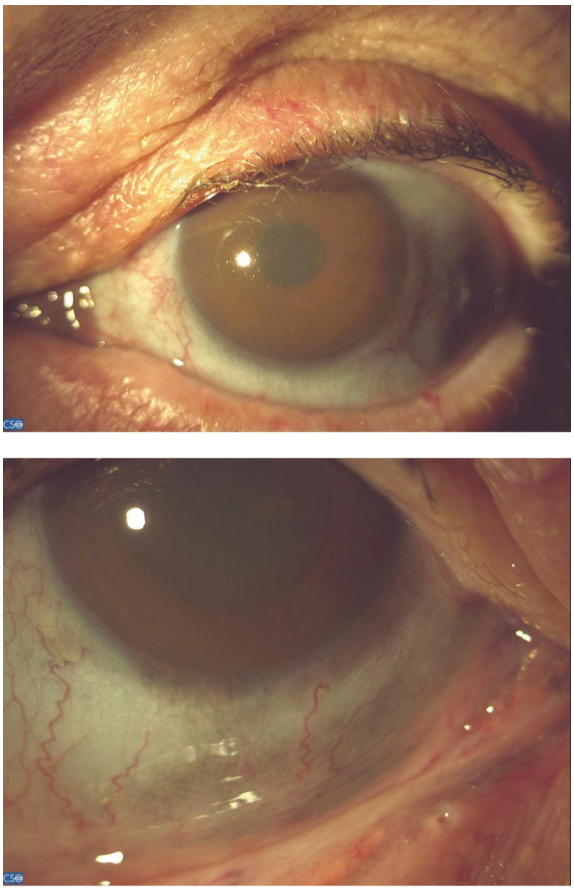

Fig. 1. Ocular argyrosis (top: external photograph of the left eye; bottom: detail of the right eye). The conjunctival pigmentation is most prominent on the temporal side, around the cornea, at the inferior fornix, and over the lachrymal caruncle.

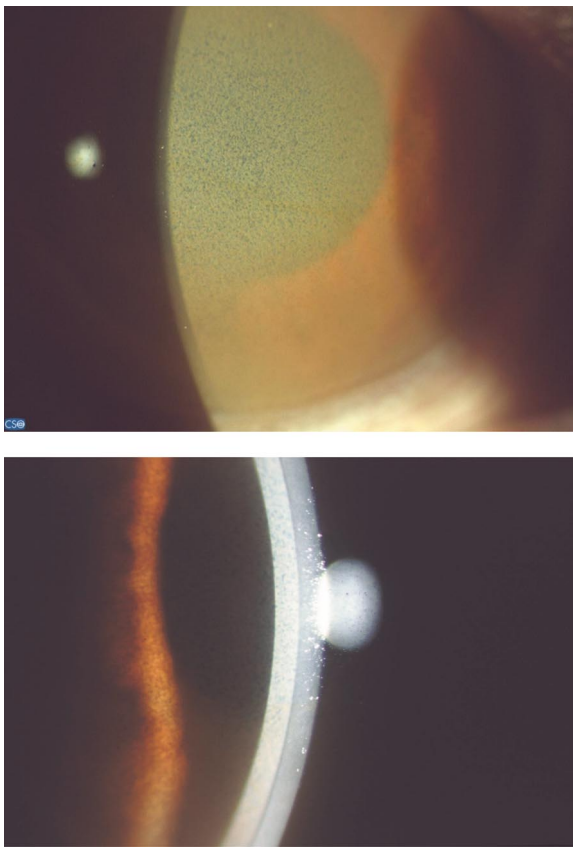

Fig. 2. Slit-lamp images of cornea. Frontal view (top): diffuse and punctiform blu-gray discoloration. Lateral view (bottom): stromal and Descemet's membrane localization of the deposits.

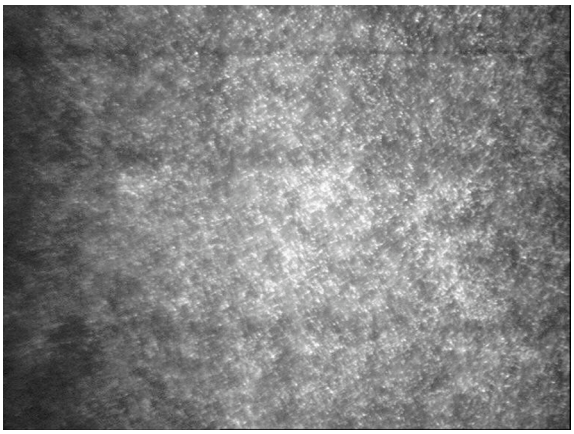

Fig. 3. Confocal biomicroscopic corneal image (left eye) showing diffuse hyperreflective granules.

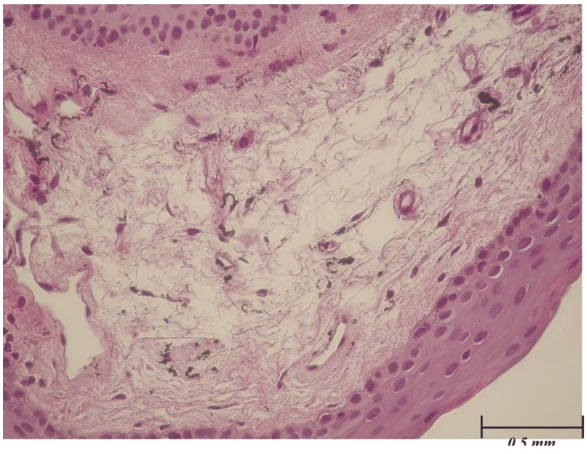

Fig. 4. Section of the bulbar conjunctive showing brown-blackish granular deposits in the submucous tissue, mainly along the endothelial basal membranes (haematoxylin-eosin stain; original magnification × 100).

conjunctival-corneal argyrosis without systemic intoxication. Ag exposure was stopped. No specific treatment was proposed. The case was referred to the Italian Workers' Compensation Authority.

Discussion

Ocular argyrosis used to be caused mainly by prolonged application of colloidal Ag eye drop preparations (*e.g.*, argyrol, protrargol), utilized as disinfectants[5, 6]. Since these eye drops are no longer used, argyrosis is now a rare occupational disease, essentially caused by inadequate ocular protection in the workplace. Systemic Ag absorption through the lungs has also been suggested to play a role[7]. Ag accumulation in eye tissues has been described in engravers and polishers[7], solderers[8, 9], photographers and photochemists[10], and in industrial workers producing Ag-containing compounds[11]. In exposed workers, the amount of Ag deposits, and the degree of ocular discoloration, correlate with the length of employment[8, 9].

No information was available on the Ag concentration, size and form in the working environment of our patient. During the 1970s, Italian Ag polishers working in comparable conditions were found to be exposed to 0.31 mg/m^3 of Ag metal dust. As in our case, their urinary Ag excretion was the same as that of the general population, and they presented deposits on the conjunctiva and/or the cornea, without generalized argyria[7]. This is not surprising since metallic Ag and insoluble Ag compounds are not readily taken up by the body, and are less toxic than soluble Ag compounds. Accordingly, the American Conference of Governmental Industrial Hygienists (ACGIH) has established separate threshold limit values for metallic (0.1 mg/m^3) and soluble (0.01 mg/m^3) Ag[2, 12].

Occupational argyrosis usually involves both eyes. An exceptional unilateral case was described in a photographic laboratory technician, suffering from epiphora of the right eye, who had the habit of wiping his eye with the same piece of cloth that he used to wipe developer and fixer solutions from his hands[10].

In both iatrogenic and occupational argyrosis, the conjunctive and the cornea are the ocular tissues most frequently affected (as reported here), whereas the eyelids[13, 14], the crystalline lens[15, 16] and the lachrymal sac[5, 17] are rarely involved. Conjunctival Ag deposits are mainly formed in the inferior fornix and lachrymal caruncle[11, 14]. In the lower portions of the mucous membrane, the deeper coloration is due to the metal being washed, by the tears, into the lower retrotarsal fold, where it can be absorbed over a long period of time[18]. Additionally, in our patient, a marked discoloration was present at the temporal side of the eye and around the cornea. Histopathologic examination of the conjunctiva with haematoxylin-eosin staining revealed brown-blackish granular deposits in the submucous tissue, mainly along the endothelial basal membranes. The epithelium was unaffected, and no phlogistic reaction was present. These findings are in agreement with previous reports[10, 14]. Former histochemical and ultrastructural studies have demonstrated that the observed granules are precipitates of Ag salts[6, 18, 19].

Microscopic analysis of corneal tissue sections from patients with corneal argyrosis demonstrated that Ag is most frequently deposited in Descemet's membrane, while the Bowman membrane is usually spared[6, 8]. At slit-lamp examination, two patterns of pigmentation have been described. In some cases, the Ag deposits predominate peripherally, whereas in others the central cornea is most affected[9, 11]. The central involvement is usually associated with longer Ag exposures[9]. Accordingly, our patient who had been occupationally exposed for a lifetime, presented diffuse deposits in the whole stroma and in the Descemet's membrane.

In clinical practice, the recognition of ocular argyrosis may not be immediate due to the rarity of the disease. Differential diagnosis should include other keratopathies (*e.g.*, pre-Descemet dystrophy, X-linked ichthyosis), as well as other causes of abnormal eye pigmentation, such as malignant melanoma and deposition of heavy metals (iron, copper) or drugs (ciprofloxacin, amiodarone)[9, 10]. In this regard, confocal microscopy is valuable for real-time, non-invasive observations of the cornea in various pathologic conditions. Several reports exist on its use for the evaluation of corneal deposits, as recently reviewed by Sánchez-Huerta *et al.*, who firstly utilized this diagnostic tool in four cases of occupational argyrosis[9]. Both in Sánchez-Huerta's study and in the present case, Ag deposits appeared as diffuse hyperreflective dots in the posterior stroma (with no endothelial involvement), suggesting that confocal biomicroscopy may provide important information for the diagnosis of corneal argyrosis.

It is controversial whether ocular argyrosis is associated with nyctalopia and a decrease of visual acuity[6, 8, 11, 20]. We believe that the vision impairment in our patient is mainly due to concurrent, bilateral opacification of the crystalline lens. Whatever the causes, the diffuse structural alteration of the cornea caused by Ag deposition would certainly be a considerable risk factor in case of cataract surgery.

Argyrosis does not progress if Ag exposure is interrupted or consistently reduced[21], but the discoloration is permanent, and chelation therapy is ineffective at removing Ag deposits from the body[2]. Back in the 1930s, a decrease of conjunctival pigmentation was obtained by local injections of a reducing ferricyanide-thiosulphate solution, with a suitable cosmetic effect[18]. More recently, clearing of corneal argyrosis by YAG laser has been reported[22]. The efficacy of these techniques awaits to be confirmed on a larger number of patients.

In conclusion, this case report highlights the hazard of Ag crafting without adequate eye protection, and indicates that occupational ocular argyrosis may still be observed in clinical practice today. In such cases, occupational anamnesis, ophthalmologic examination, confocal corneal biomicroscopy, and histopathology will allow the correct diagnosis that, in turn, is important for work-related medico-legal issues.

Acknowledgments: We thank Dr. Anna Maria Ronchi for urinary Ag analysis, and Ms. Christin Broughton for linguistic revision. The microphotography shown in Fig. 4 is by Dr. Luca Semeraro.

References

1) Candura F, Candura SM. Principles of Industrial Technology for Occupational Medicine Scholars' Use. Piacenza, Italy: Casa Editrice La Tribuna, 2002 (in Italian).
2) Drake PL and Hazelwood KJ: Exposure-related health effects of silver and silver compounds: a review. Ann Occup Hyg 49, 575–585 (2005)
3) Lansdown ABG: Critical observations on the neurotoxicity of silver. CRC Crit Rev Toxicol 37, 237–250 (2007)
4) Minoia C, Sabbioni E, Apostoli P, Pietra R, Pozzoli L, Gallorini M, Nicolau G, Alessio L and Capodaglio E: Trace element reference values in tissues from inhabitants of the European Community. I. A study of 46 elements in urine, blood and serum of Italian subjects. Sci Total Environ 95, 89–105 (1990)
5) De Schweinitz GE: Argyrosis of the conjunctiva and lachrymal sac following the prolonged instillation of a five per cent solution of protargol—microscopic examination of the excised sac. Trans Am Ophtalmol Soc 10(Pt 1), 161–164 (1903)
6) Hanna C, Fraunfelder FT and Sanchez J: Ultrastructural study of argyrosis of the cornea and conjunctiva. Arch Opthalmol 92, 18–22 (1974)
7) Perrone S, Clonfero E, Gori G and Simonato L: Observations on four cases of occupational argyrosis. Med Lav 68, 178–186 (1977) (in Italian)
8) Scroggs MW, Lewis JS and Proia AD: Corneal argyrosis associated with silver soldering. Cornea 11, 264–269 (1992)
9) Sánchez-Huerta V, De Wit-Carter G, Hernández-Quintela E and Naranjo-Tackman R: Occupational corneal argyrosis in art silver solderers. Cornea 22, 604–611 (2003)
10) Zografos L, Uffer S and Chamot L: Unilateral conjunctival-corneal argyrosis simulating conjunctival melanoma. Arch Ophtalmol 121, 1483–1487 (2003)
11) Moss AP, Sugar A, Hargett NA, Atkin A, Wolkstein M and Rosenman KD: The ocular manifestations and functional effects of occupational argyrosis. Arch Opthalmol 97, 906–908 (1979)
12) American Conference of Governmental Industrial Hygienists. 2008 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati: ACGIH Publication, 2008.
13) Goldstein JH: Effects of drugs on cornea, conjunctiva, and lids. Int Ophtalmol Clin 11, 13–34 (1971)
14) Gallardo MJ, Randleman JB, Price KM, Johnson DA, Acosta S, Grossniklaus HE and Stulting RD: Ocular argyrosis after long-term self-application of eyelash tint. Am J Ophtalmol 141, 198–200 (2006)
15) Rosen E: Argyrolentis. Am J Ophtalmol 33, 797–800 (1950)
16) Bartlett RE: Generalized argyrosis with lens involvement; report of unusual case. Am J Ophtalmol 38, 402–403 (1954)
17) Loeffler KU and Lee WR: Argyrosis of the lacrimal sac. Graefes Arch Clin Exp Ophtalmol 225, 146–150 (1987)
18) Weymann MF: Argyrosis of the conjunctiva. Trans Am Opthalmol Soc 30, 538–547 (1932)
19) Pariser RJ: Generalized argyria. Clinicopathologic features and histochemical studies. Arch Dermatol 114, 373–377 (1978)
20) Pifer JW, Friedlander BR, Kintz RT and Stockdale DK: Absence of toxic effects in silver reclamation workers. Scand J Work Environ Health 15, 210–221 (1989)
21) Williams N: Longitudinal medical surveillance showing lack of progression of argyrosis in a silver refiner. Occup Med (Lond) 49, 397–399 (1999)
22) Geyer O, Rothkoff L and Lazar M: Clearing of corneal argyrosis by YAG laser. Br J Ophtalmol 73, 1009–1010 (1989)