Argyrosis of the lacrimal sac

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Abstract. Silver deposition in the wall of the lacrimal sac after prolonged application of mild silver protein (Argyrol) eye drops is documented at the light and electron microscopic level. Silver granules were found in the extracellular matrix predominantly on elastic fibres and within cells forming conglomerates in secondary lysosomes. Most of the silver-containing cells showed a prominent rough endoplasmic reticulum, suggesting their fibroblastic origin. Investigation by energy-dispersive analysis of X-rays (EDAX) indicated the precipitation of silver as selenide.

Introduction

Ocular argyrosis is well documented and can arise not only as an occupational disease (Subal 1922; Metzger 1926; Moss et al. 1979), but also after topical application of silver-containing solutions (salts and proteinates) within and around the eye. Silver has been used for various reasons, e.g. corneal tattooing and dyeing of eyelashes, but mainly for its antiseptic properties (Godman and Gilman 1980) in the treatment of infectious diseases, particularly the prevention of ophthalmia neonatorum as recommended by Credé (Duke-Elder 1977). The histopathological appearances of silver deposits have been described in the conjunctiva (Loewenstein 1941), the cornea (Hanna et al. 1974; Karciglu and Caldwell 1985), and on rare occasions also in the lacrimal sac (Loewenstein 1941; Yanoff and Scheie 1964). After ingestion of silver, the lens capsule and Bruch’s membrane may be the site of deposition (Spencer et al. 1980).

Relatively few ultrastructural studies have been performed on ocular tissues in local argyria, and the tissue effects of this metallotoxin, the exact location, and the cellular response are still controversial.

To our knowledge, silver deposition in the mucosa of the lacrimal sac has not been studied at the electron microscopic level. We present this case to document and discuss the ultrastructural features of argyrosis after long-standing exposure to a colloidal silver preparation at this particular site.

Materials and methods

An 80-year-old female underwent excision of the right lacrimal sac because of corneal complications secondary to chronic dacryocystitis. Following the detection of silver deposits in the excised tissue, the patient admitted that she had used silver-containing eye drops (Argyrol) routinely for many years to prevent soreness of the eyes while she was gardening. The conjunctiva, however, showed no evidence of silver staining on external examination.

The excised lacrimal sac was fixed immediately in cacodylate-buffered glutaraldehyde (2%). Most of the specimen was processed routinely for paraffin histology and stained with haematoxylin and eosin, periodic acid-Schiff (PAS), Gram-Weigert, Gram-Jensen, Perls’ Prussian blue for iron and Orcein for elastic tissue. Some sections were also bleached with potassium permanganate. Residual tissue was cut into five small blocks for electron microscopic investigation, post-fixed in osmium tetroxide (1%), dehydrated through graded alcohols and embedded in Araldite. Ultrathin sections were cut with an LKB ultrotome III, stained with uranyl acetate and lead citrate and examined with a Philips 301 transmission electron microscope. Araldite-embedded tissue also underwent energy-dispersive analysis of X-rays (EDAX).

Results

Light microscopy showed a markedly inflamed wall of the lacrimal sac with focal ulceration of the epithelium (Fig. 1a), some haemorrhage and reactive stromal fibrosis. Neither bacteria nor fungi were demonstrated. However, numerous conspicuous deposits of uniform, fine brown-black granules were found in the submucosa. Sometimes these deposits were present as granular accumulations within cells (Fig. 1b), but predominantly they were arranged as thin bands in the connective tissue (Fig. 1c). Deposits within the epithelium were not seen. Only occasionally did the silver-containing cells show the morphological appearance of macrophages. The granules did not stain for iron, but with the Orcein stain their tendency to coat elastic fibres could be demonstrated, and the deposits were still visible after bleaching of the sections.

At the ultrastructural level the granular deposits were spherical, very electron dense structures. They were located
predominantly within the extracellular tissue (Fig. 2a) and were often associated with remnants of cellular organelles and condensations of amorphous extracellular material (Fig. 2b, c). Sometimes coating of elastic fibres was also observed (Fig. 2d, e). Intracellular granules were arrayed in clusters within secondary lysosomes (Fig. 3). In many of the silver-containing cells, rough endoplasmic reticulum was a prominent feature and these cells were thought to be most probably fibroblastic in type.

Subsequent EDAX investigation of these particles confirmed their metallic origin: the majority of corpuscles caused a peak characteristic for silver. In addition, a fraction of selenium was also demonstrated (Fig. 4), localised at the same site as silver.

Discussion

Argyrol is a mild silver protein solution, containing silver, gelatin and calcium disodium edetate (Smith 1976), which has been used in ophthalmology for its antiseptic properties. Due to its large carrier protein it penetrates poorly, but there are several reports in the literature demonstrating ocular argyrosis after various Argyrol application times (Karcioglu and Caldwell 1985; Gutman and Crosswell 1968; Hanna and Fraunfelder 1974; Yanoff and Scheie 1964). The deposition of silver within the ocular tissues has been studied predominantly in the conjunctiva as the most commonly exposed and easily accessible tissue, and previous light microscopic findings in the lacrimal sac revealed a similar appearance of the affected tissue (see Yanoff and Scheie 1964). There are, however, different opinions as to the specific localisation of the silver granules. By light microscopy they appear to be deposited along elastic fibres (Loewenstein 1941; Yanoff and Scheie 1964), not causing any significant inflammatory response (Spencer et al. 1980), and are only occasionally found intracellularly (Loewenstein 1941). In contrast, Hanna et al. (1974) in their ultrastructural study localised the silver granules within the connective tissue cells of the submucosa.

In the present case there was definite evidence of both extracellular and intracellular silver deposition (see Figs. 2 and 3), and in both instances the silver was of similar appearance. The affinity of silver for elastic fibres was confirmed by light and electron microscopy. The cells that were observed to contain silver granules exhibited morphological features characteristic for active fibroblast with a prominent rough endoplasmic reticulum and numerous polyribosomes. Secondary lysosomes within these cells were limited to silver-containing globules, indicating their non-macrophagic origin. There was only little evidence to suggest phagocytosis by macrophages. The toxic influence of metallic deposits in lysosomes has been suggested to result in enzyme activity inhibition, impaired function and rupture of lysosomes with subsequent cell damage and necrosis (Ghadially 1982). Our finding of silver aggregates associated with free cell organelles would support this assumption, although toxic effects due to the existing inflammation cannot be excluded.

As described by Loewenstein in his study (1941), the epithelium was free of silver, indicating that no storage of the metal occurred in this cell layer. Endothelial cells of blood vessels within the wall of the lacrimal sac were also free of silver deposits in this case.

Silver ions have been used as a marker for basement