Foreign Body Reaction in the Conjunctiva and Ocular Surface Caused by Synthetic and Organic Fibers

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1 Introduction

Corneal and conjunctival foreign bodies generally fall under the category of minor ocular trauma. Small particles may become lodged in the corneal- or conjunctival epithelium or in the stroma, particularly when hitting the eye with considerable force.

The foreign object may set off an inflammatory cascade, resulting in dilation of the surrounding vessels and subsequent oedema of the lids, conjunctiva, and cornea. Inflammatory cells are also recruited, resulting in an anterior chamber reaction and/or corneal infiltration. If not removed, a foreign body can cause infection and/or tissue necrosis (Wilson et al., 2001).

The eye can be divided into different parts that are commonly involved in immunological reactions. In this review we will be focusing upon the anterior part of the eye, which consists of the tear fluid layer, conjunctiva and cornea – the anterior ocular barrier (AOB). AOB constitutes the primary barrier against environmental aeroallergens, infectious agents and foreign bodies.

Generally, the corneal ocular foreign bodies may be grouped into 3 main categories. 1) synthetic, 2) organic and 3) metallic. In more than 70 % of the cases foreign bodies originates from metal grinding or cutting activities (Nepp et al., 1999). These will just shortly be mentioned here. While the main focus of this review will be on the synthetic and organic foreign bodies. We herein describe the ocular surface defence and allergological mechanism when the AOB is exposed to foreign bodies.

2 Immunological Reaction to Foreign Body

Foreign bodies in the ocular tissue cause the formation of granuloma. Granulomas are focal, chronic, predominantly mononuclear cell driven inflammatory reactions evoked by persistent poorly biodegradable tissue irritants. The granuloma formation is either an immunological or a non-immunological (foreign body) granulomatous reaction.

Foreign body granuloma is induced by inert, non-biodegradable material. Although the cellular bulk of both types of granulomas are histiocytes and multinucleated giant cells (MGC) and their derivatives, the cell populations of granulomas differ with respect to several metabolic parameters. MGC are a common feature of both types of granuloma. MGC are highly stimulated cells of macrophage origin and are produced by cell-cell fusion induced by various cytokines, like interferon-c(IFN-c), interleukin (IL)-1, -3, -4 and -6, and granulocyte-macrophage colony stimulating factor (GM-CSF) (Hernandez et al., 2000).

Some experimental studies have shown that MGC represent an adaptation for enhanced phagocytic activity and serve a useful purpose in degrading or eliminating tissue irritants that are resistant to elimination by isolated macrophages. Macrophages are found to reside in the wound and to exert long term tissue reaction. They are actively involved in removing damaged tissue and foreign body debris via phagocytosis. They release a variety of chemokines, such as interferon-γ and tumor necrosis factor-α, resulting in an enhanced microbial or tumoricidal capacity and release of pro-inflammatory cytokines and cell mediators (Hernandez et al., 2000, Su et al., 2011).

The above mentioned granuloma formation is also taking place in the conjunctiva, that is a well vascularized tissue that contains large numbers of dendritic/Langerhans cells and macrophages (Kari & Saari, 2012). This is different in the cornea. The anatomy of the cornea is optimized for transparency in order to allow maximal light transmission. The cornea consists mainly of a relatively dense connective
tissue (stroma) built up by tightly arranged lamellae of collagen bundles. The cornea contains relatively few cells in the stroma, and these are so-called keratocytes (modified fibrocytes). There are no lymphoid cells or other apparent protective elements, apart from some dendritic cells and their precursors. For a number of functions such as moistening and nutrition, and also for the purpose of defence, the cornea therefore depends largely on its major support tissue – the conjunctiva (Knop & Knop, 2005). For this reason granuloma formation in the cornea only occurs after a prolonged period of untreated infection/inflammation, when there is vessel formation in the cornea (Papadopoulos et al., 1998).

3 Foreign Bodies

Superficial foreign bodies in the cornea cause discomfort rather than acute pain. When the deeper part of the cornea is involved pain is normally more intense, and the patient may not be able to cooperate until the pain is relieved. Establishing the velocity of the foreign body at the impact is essential. Low velocity foreign bodies will normally be found in the conjunctiva, the subtarsal plate or on the cornea. High velocity foreign bodies can enter the globe or the orbit (Jones, 1998).

Metallic foreign bodies account for the majority of foreign bodies found on the cornea and in the conjunctiva, but a wide variety of different aetiological foreign bodies have been described in the literature. These can generally be divided into synthetic and organic foreign bodies, ranging from pieces of wood or insect wings to synthetic fibers from a teddy bear or polyethylene foreign bodies (Covert et al., 2009, Fogla et al., 2001, Bansal et al., 2008).

3.1 Metallic

In more than 70 % of the cases foreign bodies originates from metal grinding or cutting activities. Superficial corneal foreign bodies are one of the leading causes of ocular trauma, affecting mainly young males who work with metal under strain, as locksmiths, mechanics and stoneworkers (Nepp et al., 1999, Koray et al., 2007). One of the most common reasons of metallic foreign bodies is welding-related injury. The welding process may expose workers to various sources of mechanical, radiant, thermal, or chemical energy (Pabley & Keeney, 1981). Often the foreign body is superficial but if introduced to the eye with considerable velocity it may cause more serious ocular complications, such as traumatic cataract, iris or pupillary deformities, and retinal detachment. Furthermore, posttraumatic endophthalmitis is one of the most severe complications of ocular trauma because of its poor prognosis. It is recommended to perform an orbital computed tomography, if an intra-ocular or -orbital foreign body is suspected (Davidson & Sivalingam, 2002).

3.2 Organic

Different types of organic corneal foreign bodies have been described in the literature. These may include wood and insect wing bodies (Covert et al., 2009, Fogla et al., 2001, Portero et al., 2013). We will focus on caterpillar hair and tarantula hair foreign bodies of the AOB in the following.
3.2.1 Caterpillar

Caterpillars are the larval form of members of the order *Lepidoptera* (the insect order comprising butterflies and moths). These insects fall victim to many larger predators, and have therefore developed irritating hairs, sharp spines, and various toxins as defense mechanisms (Hossler, 2010).

![Figure 1: Larva of pine processionary (*Thaumetopoea pityocampa*).](image)

Contact with the hairs can cause skin rashes. The caterpillar hairs can produce an acute IgE-mediated contact urticaria, especially on the body extremities. Moreover, the embedded hairs can induce delayed cutaneous reactions that produce small infiltrated papules, papulo-vesicles, or pustules due to a toxic irritant mechanism that is not mediated by IgE (Vega *et al.*, 2003, Vega *et al.*, 1999).

The ophthalmological symptoms can also be separated into immediate IgE-dependent and delayed hypersensitivity processes. The IgE-mediated process generally produces red eye, punctate keratitis, and itchiness of the ocular surface. The delayed corneal reactions are produced as a response to the embedded caterpillar hairs. The reaction appears as stromal granulomas around the hairs days after contact (Sengupta *et al.*, 2010, Portero *et al.*, 2013). The later reaction is known as “ophthalmia nodosa” and was first described by Saemisch in 1904 (Watson & Sevel, 1966). The term describes granulomatous nodules in the conjunctiva and iris due to caterpillar sensory setae. In 1966 one of the first case series was published in Europe and the different degrees of orbital involvement described (Watson & Sevel, 1966).

In 1984 Cadera *et al.* classified the ocular inflammatory manifestations in the following different clinical entities (Cadera *et al.*, 1984):

- **Type I**: An acute, anaphylactoid reaction to the hair, starting immediately and lasting a few days, causing chemosis and inflammation.
- Type II: Chronic mechanical keratoconjunctivitis caused by hair lodged in the bulbar or palpebral conjunctiva, leading to linear corneal abrasions.

- Type III: Formation of grayish-yellow granulomatous nodules in the conjunctiva. The hair may be subconjunctival or intracorneal and may be asymptomatic.

- Type IV: Iritis secondary to hair penetration into the anterior segment. The iritis may be very severe with iris nodule formation and even a hypopyon.

- Type V: Vitreoretinal involvement after hair penetration into the posterior segment.

The pathophysiologic mechanisms of these reactions are poorly understood but may involve irritant reactions, hypersensitivity reactions, and toxic envenomation (Hossler, 2010). An initially acute inflammation is followed by a granulomatous reaction around the hair. This is characterized by a lymphocytic infiltration, which is later followed by histiocytes presenting as epitheloid cells and giant cells. The lids, conjunctival fornices, subconjunctival space, cornea, and iris are most commonly involved. In the more severe reactions there is a perivascular infiltration of inflammatory cells in the retina, extending into the scleral channels and the episcleral tissues (Watson & Sevel, 1966).

From a larger subcontinental retrospective analysis, the majority of the cases were limited to manifestations of the above-mentioned type I to type III reactions (Sengupta et al., 2010). Recently a smaller European case series showed keratitis as the most common ocular presentation of embedded hairs from the caterpillar (Portero et al., 2013).

The prognosis is relatively good even with intraocular penetration of the hair. Despite the severe range of the manifestations, the outcome in most of the cases is satisfactory, if diagnosed early and treated appropriately. The superficially located hairs should be removed. The removal of the deeper located hairs could do more harm than good and should be clinically closely observed (Horng et al., 2000, Conrath et al., 2000, Corkey, 1955). The application of steroid ointments is recommended. Anti-allergic medication may provide relief from periocular edema or skin urticating lesions. The condition tends to be self-resolving over a period of weeks or months, with symptoms becoming reduced over time. The presence of intracorneal hair is a significant risk factor for intraocular penetration (Sengupta et al., 2010, Horng et al., 2000, Conrath et al., 2000).

### 3.2.2 Tarantula Hairs

Tarantulas are becoming an increasingly popular choice as pets. Some of them are relatively small, affordable and widely available at pet stores. While many of these pet tarantulas are considered relatively safe due to their lack of poison or fangs, they pose a non-realized danger from their defensive hairs (Rutzen et al., 1993, Battisti et al., 2011). These urticating hairs or setae are released easily from the abdomen with mechanical stimulation. If provoked, the tarantula will discharge a spray of setae by rapidly vibrating both hind legs as a defence mechanism (Battisti et al., 2011). Both caterpillar sensory setae and the urticating hairs of the tarantula are pointed and barbed and the tendency to cause ocular inflammation seems to be similar (Hered et al., 1988, Cadera et al., 1984).

Four types of hairs have been classified and range from 0.06 mm to 1.5 mm in size. Type 3 hairs, are supposed to penetrate the skin and ocular surface and cause irritation (Cooke et al., 1972). The irritant effect is thought to be primarily mechanical, while the role of a toxin or hypersensitivity reaction is not fully understood.
Tarantula hairs have been reported to cause a number of medical ocular conditions in humans (Mangat & Newman, 2012, Watts et al., 2000, Waggoner & Nishimoto, 1997, Hered et al., 1988). It has been shown that the hairs can penetrate the corneal tissue with either the barbed or the smooth end (Kaufman et al., 1994). Though it has been proposed that the hairs inflict injury initially through an acute inflammatory reaction followed by chronic granulomatous inflammation, there is also evidence that the hairs penetrate the ocular tissues apparently without inciting inflammation or causing fibrosis (Kaufman et al., 1994, Bansal et al., 2008). Specific lesions such as the focal damage and loss of corneal endothelial cells have also been visualized using the confocal microscope in rabbits (Kaufman et al., 1994).

The insect setae consist of a chitin skeleton with a matrix of proteins and covered by layers of lipoproteins, mucopolysaccharides and other constituents. These are foreign to mammals and may act as a strong inducer of inflammation and potentiator of mammals’ immune responses. Chitin particles can bind to receptors on macrophages and activate them to produce chitinases together with proinflammatory cytokines and other inflammatory and immune regulatory mediators (Battisti et al., 2011).

The initial symptom and clinical manifestations are skin urticarial or conjunctival hyperemia. This may be followed by a chronic granulomatous type reaction, resulting in nodular conjunctivitis, stromal keratitis, mutton-fat keratitic precipitates, iritis, vitritis, and multifocal punctate chorioretinal lesions (Mangat & Newman, 2012, Watts et al., 2000, Shrum et al., 1999).

Hered et al. recommends removal of offending hairs, or at least close observation of their movement to determine if surgical removal is necessary (Hered et al., 1988). Another study advocates the use of confocal microscopy for optimal diagnosis and follow up (Kaufman et al., 1994). Ocular injury from the barbed hairs of tarantulas is of particular concern due to the popularity of tarantulas as household.
3.3 Synthetic

Synthetic fibers from stuffed toy animals and blankets made of synthetic material may penetrate the conjunctiva or cornea. This may result from close exposure of stuffed toy animals to the eye (Weinberg et al., 1984, Schmack et al., 2005). Usually as mentioned earlier, the foreign bodies are removed from the ocular surface by the eye protective mechanisms such as blinking and tearing. However, foreign bodies may be retained and encapsulated by the mucous and initiate a local inflammatory response (Mantelli & Argüeso, 2008, Zierhut & Stiemer, 1997, Adams, 1976). This may, in the conjunctiva, give rise to granuloma formation, also known as “Teddy bear granuloma”, first described by Weinberg et al. in 1984.

We will be presenting two unique cases of synthetic foreign body granuloma formation in conjunctival epithelium and in cornea, respectively. These cases have been published formerly (Farooq et al., 2011).

3.3.1 Case 1

A 2-year-old girl presented with ocular irritation and corneal opacities of her left eye. Topical treatment with ciprofloxacin and chloramphenicol for suspected conjunctivitis had no improvement on the condition. No trauma or any foreign body complaints was observed or recalled according to the patient’s mother. Apart from mild asthma the patient was in a healthy medical condition.

Examination in general anaesthesia revealed a 4 x 5 mm oval ulceration infero-centrally of the left cornea with purulent exudate, stromal oedema and a couple of large “mutton fat” precipitates.

![Figure 3: Corneal ulceration measuring 4x5 mm](image)

No foreign bodies were detected. In addition a severe iritis with synechiae and a hypopyon less than one mm was found. Conjunctival and corneal swabs were sent for bacterial and fungal staining and culture. Due to a clinically suspected bacterial infection, topical treatment was changed to oxytetracyclin-
polymyxin-B ointment, ciprofloxacin and chloramphenicol eye drops six times daily and topical atropine once daily.

For the next two weeks there was a remarkable improvement of the corneal ulceration. However, suddenly a relapse with a new hypopyon and worsening of the corneal ulceration occurred. The treatment was supplemented with fortified gentamicin and fortified cefuroxin eye drops every hour. One week later the results of the staining and the cultures were proved negative for bacteria and fungi. The condition worsened and a spontaneous perforation occurred centrally in the ulceration. Furthermore, a new but smaller ulceration was observed more laterally. Corneal transplantation was performed and the corneal button was sent for microscopical examination. The results from the light microscopy showed a heavily inflamed and ulcerated cornea.

**Figure 4:** Haematoxylin-eosin (HE) staining of the inflamed corneal biopsy. The stroma contains multiple histiocytes and neutrophils and is embedded with bluish brown synthetic fibers (arrows) exhibiting central black granular spots. Bars: 150 µm (A), 50 µm (B).

Bowman’s layer was missing and the ulceration occupied most of the stroma reaching Descemet’s membrane. The stroma contained a granulomatous lesion with multiple histiocytes and neutrophils. Numerous rounds to oval shaped blue and brown fibers with black granular spots were seen centrally in the lesion. The diameter of the fibers ranged from 20-30 µm and showed strong birefringence in polarized light (figure 4).

To verify whether the synthetic fibers belonged to a toy teddy bear, we performed microscopical examination of two different types of synthetic fibers (whiskers and face hair) from the girl’s toy teddy bear (figure 5). Hairs from the face were morphologically and microscopically identical with the fibers causing the severe corneal ulceration in the two-year-old girl.

Investigation of the teddy bear fur demonstrated that the fiber was made of 100% polyethylene (Dacron, Terylene). The azo-dye (Faron Dark Blue, Clariant), applied to the fibers is not restricted by EU and is not known to cause inflammation.
3.3.2 Case 2

A five-year-old girl was admitted to the eye department because of irritation and foreign body sensation in her left eye for two days. She was otherwise in a good general health.

Slit lamp examination showed a 7 x 5 mm granuloma in the left inferior conjunctival fornix embedded with hairs and synthetic fibers. The lesion prolapsed easily with gentle pressure on the left lower lid. The examination was otherwise normal. The lesion was excised under general anaesthesia and sent for microscopical examination. Postoperatively, the eye was treated with chloramphenicol three times daily for five days. The wound healed within two weeks and the postoperative course was uneventful.

Microscopical examination of the conjunctiva revealed a normal differentiated conjunctival epithelium with goblet cells. The subepithelial stroma contained a granuloma with inflammatory cells, mostly eosinophils, histiocytes and foreign body giant cells. Synthetic fibers, identified by their strong birefringence in polarized light were found within the lesion (Figure 6). The diameter of the fibers ranged from 20-30 µm. We could not identify the chemical composition of these fibers.

3.3.3 Comments

Increased tear flow, redness, foreign body sensation, pain and photophobia are the symptoms associated with foreign body in the eye. Signs of possible deeper ocular penetration include decreased vision and clouding of the cornea (Lueder, 1999). However, the symptoms expressed by children or the toddler may be nonspecific, as they might be unable to communicate properly.

The majority of the previously described patients with conjunctival granuloma (caused by synthetic foreign bodies) were referred to an eye department after the granuloma was visible (Schmack et al., 2005). This may in children take weeks since children may neglect the symptoms until the granuloma has developed, or because the symptoms communicated to the parents are misunderstood (Schmack et al., 2005, McGrath, 1990). However, in the present case of conjunctival granuloma signs were seen early and the child was referred after two days.
Figure 6: HE stained conjunctival biopsy. The connective tissue is infiltrated with inflammatory cells mostly eosinophils, and synthetic fibers (black arrows) surrounded by foreign body giant cell (asterisk). Bars: 200 µm (A), 50 µm (B).

Even though the patient with the corneal ulceration was examined with slit lamp, the examiner was unable to identify the corneal foreign body. A main reason might be that the synthetic fibers were bluish brown, similar to the colour of hypopyon and the iris. Thus causing difficulties identifying the foreign body. However, a careful slit lamp examination combined with a negative bacterial and fungal staining and culturing should lead to the proper diagnosis.

Tarantula hairs and caterpillar setae foreign bodies in the eye are well documented (Watson, 1966, Cadera et al., 1984, Hered et al., 1988). However, so far only this present case of synthetic fiber causing severe ocular complications is reported in the literature (Farooq et al., 2011). The lesions are considered partly due to penetration and partly to the inflammatory/toxic reaction, in the same way as hairs from the tarantula back are supposed to cause irritation to the skin (Cooke et al., 1973). Whether the same mechanisms are responsible for the severe case of keratitis in our case is unclear. However, it is plausible that the synthetic fibers may cause an allergic and toxic reaction in the cornea. The synthetic fibers in case one were made of polyethylene. When used in joint arthroplasty, polyethylene may cause an osteolytic reaction when small particles are engulfed by macrophages in granulomatous reactions (Heisel et al., 2004). The azo dye applied in the fibers may also have had an influence; however, it has not been documented to have any adverse effect.

In 2005 Schmack et al. demonstrated the histopathological and ultrastructural features of conjunctival granulomas caused by synthetic fibers. The diagnosis is easily confirmed by the microscopical features of the conjunctival granuloma showing granulomatous inflammatory tissue with lymphocytes, plasma cells, eosinophils and usually foreign-body giant cells surrounding the synthetic fibers. The simplest method to confirm the diagnosis is excision of the conjunctival granuloma and microscopical examination demonstrating marked birefringence of the synthetic fiber when examined in polarized light (Enzenauer & Speers, 2002, Resnick et al., 1991). The synthetic fibers are fairly uniform in diameter and generally round to oval in configuration. The diameter of synthetic fibers in the cases published by Schmack et al. and Weinberg et al. ranged from 17-29 µm and 21-27 µm, respectively, which is also
suggested in our case (Schmack et al., 2005, Weinberg et al., 1984). The localization of the granuloma in the previously published 15 cases was unilateral and mainly in the inferior fornix, except in one case in the superior fornix (Schmack et al., 2005).

The ocular surface epithelium not only acts as a physical and mechanical barrier against harmful substances, but also participates actively during allergic inflammatory processes (Calonge et al., 2005). Patients with asthma might react with a profound ocular hypersensitivity (Hesselmar et al., 2010). Thus, the formation of a corneal granuloma, in the patient with known asthma (case 1) could have been potentiated by local ocular allergic reactions.

Surgical removal of the conjunctival granuloma and postoperative treatment with antibiotics is recommended and has shown to be successful (Enzenauer & Speers, 2002, Lueder et al, 1996). The crucial element in the treatment of keratitis is the identification of the cause of the keratitis. In young children rare causes such as synthetic fibers should always be kept in mind, especially in children who are attached to their toy teddy bears. Identification and removal of the corneal and conjunctival foreign body granuloma followed by antibiotic administration are the treatment of choice.

References


Figure 1: http://commons.wikimedia.org/wiki/File:Thaumetopoea_pityocampa_larva.jpg
Figure 2: http://commons.wikimedia.org/wiki/File:Grammostola_rosea_Chilian_Rose_Hair_Tarantula.jpg


