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## Case Report

# Local Allergic Reaction to Ocular Chloramphenicol Ointment: A Diagnosis by High Index of Clinical Suspicion

### Abstract

Chloramphenicol is a widely used topical ointment applied routinely for ocular and periorbital infections due to its wide spectrum of anti-bacterial activity. Local delayed hypersensitivity reaction to chloramphenicol is a well reported but uncommon adverse effect, and has been reported to mismanaged initially as an infective cellulitis. The confirmatory tests for drug allergy are often not possible in developing countries and hence, the diagnosis is usually made with high index of clinical suspicion. Hereby, we are reporting a case of local hypersensitivity reaction to chloramphenicol after ocular use for adenexal infection, which was diagnosed with high index of suspicion without any clinical test, and was managed timely and successfully.

## Introduction

Chloramphenicol is a widely used topical ointment applied routinely for ocular and periorbital infections due to its wide spectrum of anti-bacterial activity. Local delayed hypersensitivity reaction to chloramphenicol is a well reported but uncommon adverse effect, and has been reported to be mismanaged initially as an infective cellulitis [1]. Hereby, we are reporting a case of local hypersensitivity reaction to chloramphenicol after ocular use for adenexal infection, which was diagnosed with high index of suspicion without any clinical test, and was managed timely and successfully.

## Case History

A 38-year-old man presented to out-patient department with painless swelling around both eyes of 24 hours duration. Onset of swelling was sudden, and started around 48 hours after application of chloramphenicol ointment for sty. There was no history of fever and any drug allergy. Patient also gave the history of recurrent sty in both eyes and the chloramphenicol ointment was prescribed for the same by a general physician in a government hospital about two months back. Patient used the same ointment pack, which was opened about two months back.

On systemic examination, vital parameters were within normal limits. On ocular examination the patient's both eyes had visual acuity of 6/6 by Snellen's chart. Erythema and non-tender oedematous swelling of the periorbital area including eyelids were noted in both eyes. The patient also had a sty in upper eyelid of both eyes. Anterior as well as posterior segments were quiet and normal (Figures 1 and 2).

With a high index of clinical suspicion due to absence of pain, tenderness and pyrexia, a diagnosis of chloramphenicol allergy was preferred over infective pathology. The chloramphenicol use was withheld and the patient was advised cold compression. The following day his periorbital erythema and swelling improved markedly, and complete resolution was noted on third day. For sty, patient was



**Figure 1:** Erythematous and oedematous non-tender periorbital swelling in both eyes.



**Figure 2:** Enlarged view showing sty in upper eyelid of left eye.

advised oral ciprofloxacin 500mg twice a day and ofloxacin ointment locally for 5 days, which responded well.

## Discussion

Topical ocular chloramphenicol is relatively inexpensive and have broad-spectrum coverage of most gram-positive, gram-negative, and anaerobic bacteria [2]. The topical ocular form of chloramphenicol became available in 1948, and since then it has become the most popular antibiotic prescribed topically by general practitioners for all red eyes and periocular infections [3,4]. In a study chloramphenicol was found as the most commonly prescribed treatment by general

practitioners for red eyes, accounting for 55% of consultations [3]. There was a time when chloramphenicol was considered as the gold-standard ocular antibiotic against which other antibiotics were used to be compared [5]. In our case also, chloramphenicol was prescribed to the patient by general practitioner for lid infection on the first occasion.

Topical chloramphenicol is generally very well tolerated with side effects ranging from uncommon local adverse effects of hypersensitivity and transient burning/stinging sensations to potentially lethal effects of bone marrow toxicity and anaphylactic reaction [5,6]. Systemic chloramphenicol is clearly associated with bone marrow toxicity, which can be dose related marrow suppression involving one or more cell lines, or the much more rare idiosyncratic aplastic anaemia [5]. Some patients are genetically predisposed to develop blood dyscrasias when they are prescribed chloramphenicol systemically, and it stands to reason that this would hold true for topical administration as well. However, only 45 cases of blood dyscrasia or aplastic anaemia from topical ocular chloramphenicol have been reported in the literature and the spontaneous reporting databases in last 20 years (1993-2013) [2]. Based on the known published case reports and the spontaneous reports submitted to the National Registry of Drug-Induced Ocular Side Effects, chloramphenicol eye drops' relation to aplastic anaemia and blood dyscrasias was classified as probable according to World Health Organisation (WHO) criteria [2]. On the other hand, chloramphenicol hypersensitivity is uncommon, but well-known local adverse effect of topical preparation. In a study, about half of the patients presenting to the eye casualty with reactions to the drops prescribed for their original complaint by general practitioners were using chloramphenicol [4]. Similarly in this case when patient presented, he was suffering from local hypersensitive reaction to topical chloramphenicol.

Systemic as well as local allergic reactions of eye ointments result from absorption through conjunctival membranes, or from drainage down the lacrimal duct and absorption through nasopharyngeal mucosal membranes. The systemic allergic reaction such as anaphylactic reaction is caused by systemic circulation of the antigen [6]. The mechanism of reactions to chloramphenicol are unknown, however, it is likely that the dichloroacetamide ring is the major antigenic determinant [7]. Local delayed type hypersensitivity to chloramphenicol manifests as localised erythema and swelling within first 24-72 hours of chloramphenicol application, not responding to antibiotics [1]. To confirm the allergy to chloramphenicol, skin prick tests and patch tests (chloramphenicol 1% in petrolatum) have been proposed, however serum IgE is not clinically relevant. Avoidance of chloramphenicol and cross-reacting synthetic derivatives should be recommended in a case with confirmed allergy or high degree of suspicion [7].

However, differential diagnosis for our case included more serious conditions like preseptal cellulitis and orbital cellulitis. These conditions of infective origin, which may result from spread of local infection such as acute hordeolum, are usually unilateral in presentation. Preseptal cellulitis usually present with unilateral, tender and erythematous periorbital oedema. Orbital cellulitis is a more

serious condition in which unilateral tender erythematous periorbital oedema is associated with fever, proptosis, visual impairment and painful ophthalmoplegia [8]. In our case, bilateral periorbital oedematous swelling with absence of fever, pain and tenderness following 48 hours of chloramphenicol ointment application in the setting of previously uncomplicated chloramphenicol use suggested to make a preferential diagnosis of chloramphenicol allergy.

There are some limitations for this case report. The re-challenge test, skin prick test or patch test could not be performed as patient did not consent for the same. Another possible mechanism for this presentation may be the allergic or toxic reaction induced by preservatives or stabilizing agents used for the preparation of ocular form of chloramphenicol ointment. Role of preservatives for allergic or toxic reactions induced by topical antibiotic eyedrops have been implicated in various clinical as well as experimental studies [9].

Due to resistance and safety concerns, chloramphenicol is no longer a first-line topical agent for ocular infection in developed nations. However, in low-income countries, it is still widely used because of low cost, easy availability and broad-spectrum activity. A delayed type hypersensitivity reaction is surely well known but uncommon adverse effect following use of chloramphenicol ointment, and must be kept in mind as a prominent differential diagnosis if patient presents with erythematous swelling of eyelids and periorbital area. Ophthalmologists as well as general practitioners must maintain a high index of clinical suspicion for the same particularly in those patients who present within the first 24-72 hours of chloramphenicol application, and without tenderness or pyrexia as diagnostic allergy tests such as skin prick test and patch test are not often possible.

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