Case Report

Journal of Pharmaceutics and Therapeutics

Toxic Optic Neuropathy secondary to Systemic Chloramphenicol for Septic Arthritis: Case Report

Okonkwo ACO*, Rostron E and Burnett C

Hull Eye Hospital, Hull Royal Infirmary, Hull and East Yorkshire Trust, England,

***Correspondence:** Arthur CO Okonkwo, Hull Eye Hospital, Hull Royal Infirmary, Hull and East Yorkshire Trust, England, E-mail: Arthur.okonkwo@doctors.org.uk

Rec date: May 22, 2018; Acc date: June 10, 2018; Pub date: June 18, 2018

Abstract

Introduction: Chloramphenicol is a broad-spectrum antibiotic with excellent tissue penetration. Systemic use was popularised in the 1950s due to its affordability and ease of preparation. It is now rarely used in developed countries due to its significant side effect profile including toxic optic neuropathy.

Case Description: A 68-year-old female presented to a neighbouring eye department with a 2-month history of bilateral visual deterioration, initially thought to be due to cataracts. However, due to the moderate cataract density and visual acuities of 6/60 and hand movements a medical history revealed that she had been taking systemic chloramphenicol for 6 months for chronic septic arthritis following a complicated total knee replacement. Following a normal ophthalmic examination besides reduced colour vision and constricted visual fields a diagnosis of toxic optic neuropathy secondary to chloramphenicol was made. Once systemic Chloramphenicol was stopped, her vision improved to 6/24 bilaterally although subjectively did not return to baseline.

Conclusion: Cataracts are a common cause of visual reduction, however, if the amount of cataract does not correlate with the extent of loss of visual acuity then an alternative cause must be considered. Early recognition of toxic neuropathy is key, as withdrawal of Chloramphenicol often results in improvement of visual symptoms.

Keywords: Optic neuropathy; Drug toxicity; Septic arthritis; Total knee replacement

Abbreviations: BD: Twice Daily; HM: Hand Movements; ICU: Intensive Care Unit; LE: Left Eye; MRI: Magnetic Resonance Imaging; RAPD: Relative Afferent Pupillary Defect; RE: Right Eye; TON: Toxic Optic Neuropathy

Introduction

Chloramphenicol is a broad-spectrum antibiotic with excellent tissue and fluid penetration, which can be administered orally, parenterally and topically. Topical chloramphenicol remains the most commonly prescribed antimicrobial for ocular infections. Systemic Chloramphenicol however, used widely in the 1950's owing to its broad antimicrobial cover coupled with affordability and easy preparation, has fallen out of favour, at least in the developed countries, due to serious

systemic adverse reactions [1,2]. The most significant of these were blood dyscrasias, namely bone marrow suppression and idiosyncratic aplastic anaemia. Other systemic reactions include cardiac toxicity, neuropathy, deafness and metabolic acidosis [3,4,5]. Toxic optic neuropathy (TON) secondary to systemic Chloramphenicol was first reported in 1950's [4,5]. Toxicity is thought to be treatment duration and dose dependant [6].

TON is a serious and potentially blinding condition where the anterior visual pathway is affected by means

of systemic exposure to environmental, nutritional or medicinal toxins [7]. The exact pathogenesis is not fully understood, but it is thought to be related to mitochondrial damage [8]. Neuropupillary bundle is particularly susceptible to systemic insults from systemic toxins. TON is often characterised by painless, progressive, bilateral visual decline. In patients with Chloramphenicol related toxicity, limb paraesthesia has been described as a preceding symptom [9]. Dyschromatopsia, or colour deficit, may be noted before the decline in central acuity and may be out of proportion to the acuity drop recorded on the Snellen chart. Isolated centrocecal scotomas are often associated and progressive. Pupils will largely be normal, particularly during the initial stages. As visual loss progresses the responses may become more sluggish. No relative afferent pupil defect (RAPD) is usually present due to bilateral nature of the condition. Optic nerve can appear normal, or hyperaemic, with optic nerve haemorrhages sometimes seen. In later stages the optic nerve often becomes pale and atrophic [5,6,8].

Diagnosis lies in careful history taking, which is the key when forming a differential diagnosis. It is important to bear in mind alternative systemic causes of optic neuropathy, such as Leber's hereditary optic neuropathy. Electro diagnostics can be helpful and an increase in the latency of the visual evoked potentials has been reported in Chloramphenicol related toxicity [5]. Nutritional deficiencies can cause a similar clinical picture and often play a synergistic role in development of optic neuropathy. Patients with chronic tobacco and alcohol misuse are often deficient in vitamin B12 or folate and susceptible to TON. Other causes of include methanol, ethambutol, amiodarone, and linezolid [10].

Case Description

A 68-year-old female was first seen by her optician who referred the patient to a nearby Eye Department. The patient was put on a waiting list for cataract surgery, but she grew impatient and sought a private ophthalmic appointment to expedite her surgery.

She gave a two months' history of progressive visual deterioration bilaterally. Upon taking a detailed medical history it was found that the patient was on long term systemic Chloramphenicol, 750mg BD, which have been started 6 months prior for a chronic left prosthetic knee infection. Her past medical history also included previous mitral valve replacement and atrial fibrillation, for which she was on warfarin for, as well as hypertension and ischaemic heart disease. She was a non-smoker and did

not drink alcohol.

Figure 1: Full field 81 point screening test

Her visual acuity was recorded as 6/60 in her right eye (RE) and hand movements (HM) in her left eye (LE). Pupil examination was unremarkable. She was noted to have 1+ nuclear sclerotic cataract in both eyes, however the amount of cataract did not correlate with her visual acuity at presentation. Her colour vision was reduced to 1/13 RE and 0/13 LE when tested by Ishihara. She had markedly constricted visual fields (Figure 1). Both optic nerves appeared grossly normal (Figure 2). Urgent diffusion weighted Magnetic Resonance Imaging (MRI) of the brain and optic nerve pathway was performed to investigate a central cause, this was found to be normal. Bloods were taken for inflammatory markers, full blood count, folate, vitamin B12 and Leber's optic neuropathy, the only abnormalities found were longstanding anaemia with Hb of 103g/L, and chronically elevated inflammatory markers in keeping with her history.

It was suspected that the cause of visual decline was Chloramphenicol related optic nerve toxicity, and therefore her systemic Chloramphenicol was discontinued, after a consultation with her Infectious Diseases clinicians.

Figure 2: Wide field optos fundus photographs

The patient had a complicated journey since post left total knee replacement in 2015. This required a revision of the total knee replacement following which she developed knee joint infection with sinus formation. Washout and debridement was performed, cultures at the time grew coagulase negative *Staphylococcus*, sensitive to Teicoplanin, Peptomycin, Linezolid, Chloramphenicol, Rifampicin and Tigecyclin. She was initially started on intravenous Teicoplanin followed by oral Linezolid monotherapy. The patient then underwent further debridement and a fasciocutaneous flap. Unfortunately she then developed sepsis secondary to severe pyelonephritis and required an admission to the intensive care unit (ICU) for inotropic support whilst she was treated with Piperacillin and Tazobactam. She was then started on Tidezolid treatment for her chronic knee infection, which was then switched to systemic Chloramphenicol. She had been on high dose systemic Chloramphenicol for 6 months prior to her being seen in the eye clinic. She declined any further surgical options for her knee including above knee amputation and remained immobile in a wheelchair. As well as visual decline, she also reported worsening deafness.

Once systemic Chloramphenicol was stopped, her vision has improved to 6/24 RE and 6/24 LE by snellen. Colour vision has improved to 3/13 RE and 5/13 LE. Initial improvement was noted within a week of stopping the antibiotics, and continued over subsequent two months, although vision never returned to normal.

Conclusion

Cataracts are a common cause of visual reduction, however, if the amount of cataract does not correlate with the extent of loss of visual acuity then an alternative cause must be considered.

Antibiotic resistance is a growing worldwide phenomenon. With increasing resistance a broader repertoire of antimicrobials is being used, some older agents with a potentially more severe side effect profile are now being used more frequently. Modern day physicians may not be as aware of some of the systemic side effects of older antimicrobials. Then again, risk of sight loss needs to be balanced against risk to life, particularly if the patient is suffering a serious multi drug resistant infection. In these cases the patient needs to be counselled appropriately. Early recognition of toxic neuropathy is key, as withdrawal of Chloramphenicol often results in improvement of visual symptoms [3,4,7].

Acknowledgements

The authors disclose no acknowledgements and no conflicts of interest. No Patient identifiable information was included in this case report and as such consent was not deemed necessary for its publication.

References

1. Best WR. Chloramphenicol-Associated Blood Dyscrasias: A Review of Cases Submitted to the American Medical Association Registry. *JAMA*. 1967; 201(3):181–8. <https://jamanetwork.com/journals/jama/article-abstract/334053>
2. YunisAA. Chloramphenicol-induced bone marrow suppression. *Semin Hematol*. 1973; 10(3):225–34. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/4577646>
3. Suarez CR, Ow EP. Chloramphenicol toxicity associated with severe cardiac dysfunction. *Pediatr Cardiol*. 1992; 13(1):48–51. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/1736269>
4. Lasky MA, Pincus MH, Katlan NR. Bilateral Optic Neuritis following Chloramphenicol Therapy. *Journal of the American Medical Association*. 1953; 151(16):1403–4. <https://www.cabdirect.org/cabdirect/abstract/19532702664>
5. Godel V, Nemet P, Lazar M. Chloramphenicol optic neuropathy. *Arch Ophthalmol*. 1980; 98(8):1417–21. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/7417077>

6. Wong S, Silva F, Acheson J, Plant G. An old friend revisited: chloramphenicol optic neuropathy. *JRSM Short Rep* [Internet]. 2013; 4(3). PMID: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3616301/>
7. Sharma P, Sharma R. Toxic optic neuropathy. *Indian Journal of Ophthalmology*. 2011; 59(2):137. <http://www.ijo.in/article.asp?issn=0301-4738;year=2011;volume=59;issue=2;spage=137;epage=141;aulast=Sharma>
8. Wiest DB, Cochran JB, Tecklenburg FW. Chloramphenicol Toxicity Revisited: A 12-Year-Old Patient With a Brain Abscess. *J Pediatr Pharmacol Ther*. 2012; 17(2):182–8. PMID: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3470440/>
9. Harley RD, Huang NN, Macri CH, Green WR. Optic neuritis and optic atrophy following chloramphenicol in cystic fibrosis patients. *Transactions -- American Academy of Ophthalmology and Otolaryngology*. 1970; 74(5):1011–31. [https://www.aaojournal.org/article/S0002-7154\(70\)30305-3/abstract?code=ophtha-site](https://www.aaojournal.org/article/S0002-7154(70)30305-3/abstract?code=ophtha-site)
10. Wasinska-Borowiec W, Aghdam KA, Saari JM, Grzybowski A. An Updated Review on the Most Common Agents Causing Toxic Optic Neuropathies. *Curr Pharm Des*. 2017; 23(4):586–95. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/28120722>

Copyright: © **Okonkwo et al.** This is an Open Access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.