Case Report

Chloramphenicol and acute esophagitis in the emergency department

Chad T. Andicochea, Steven J. Portouw, Melissa M. Bokan

Department of Emergency Medicine, Naval Medical Center San Diego, California, USA

ABSTRACT

Even with its broad spectrum and low cost, concern over chloramphenicol’s adverse effects limited its use in the United States during the 1980s. Reports from the United Kingdom and China in the 1990s demonstrated a low incidence of blood dyscrasias with the topical preparation of chloramphenicol, and showed continued good efficacy and low cost. Today, topical chloramphenicol is being used by some groups within otorhinolaryngology and ophthalmology in the United States. As a result, emergency physicians are once again considering chloramphenicol-induced side effects in patients presenting to the emergency department. To date, there have been no published reports associating chest pain, dyspnea with chloramphenicol use, and there has only been one report of fungal esophagitis associated with topical chloramphenicol. We present a 31-year-old woman, 4 months status post tympanoplasty with a modified radical canal wall down mastoidectomy due to a cholesteatoma involving the epitympanum who had a residual tympanic membrane defect. She presented to the emergency department with chest “burning”, with no other symptoms shortly after starting treatment with an insufflated combination antibiotic containing chloramphenicol. After ruling out cardiopulmonary or vascular etiology, she was treated successfully with a gastrointestinal cocktail cocktail for presumed esophagitis secondary to newly prescribed chloramphenicol.

Key Words: Chloramphenicol, chest pain, esophagitis, emergency department, tympanectomy

INTRODUCTION

Chloramphenicol is a broad spectrum antibiotic that gained popularity in the late 1940s for ophthalmic and systemic infections including upper respiratory infections, acne, and bronchitis. Beginning in the 1950s, landmark case reports demonstrated a possible relationship between chloramphenicol and aplastic anemia, bone marrow suppression, and blood dyscrasias, which lead to a drop in use by as much as 80% in the United States. Comparing data in the United Kingdom during the 1990’s, incidence of topical chloramphenicol was shown to have a low incidence of adverse events, while maintaining good efficacy against most pathogens at a low cost, making it a preferred first-line antibiotic among some ophthalmologist and otolaryngologists. Additionally, in the United States, case reports are surfacing showing chloramphenicol use for otitis media, meningitis, brain abscess treatment, and multiple accounts of vancomycin resistant infections. As such, emergency physicians are again considering chloramphenicol adverse effects as a differential diagnoses in some of the patient populations.

Although Candida esophagitis was diagnosed in a child taking multiple antibiotics in 1989, association of acute, nonfungal, esophagitis after initial use of topical chloramphenicol has not been reported. We report a case of a woman who presented to the emergency department with chest pain 2 weeks after initiating topical chloramphenicol applied to an ear canal that was status post tympanoplasty.

CASE REPORT

A 31-year-old Caucasian, military dependent, female presented to the Naval Medical Center Emergency Department with a chief complaint of “chest discomfort”, further described as a “burning sensation that started in (her) throat and migrated down to (her) chest”. This symptom occurred once before, 3 days prior to this presentation. She denied radiation of symptoms, dyspnea, or
any other associated symptoms. She had not experienced these symptoms in the past. Her past medical history was significant for being 4 months status post, uncomplicated, right tympanoplasty as treatment for a middle ear cholesteatoma, irritable bowel syndrome, and adenoid cyst carcinoma 5 years past. Review of her current, active medications includes a chloramphenicol, sulfanilamide, fungizone, and hydrocortisone otic insufflation combination (CSF + HC) for an oitis of her right ear. The medication was started approximately 2 weeks prior to her presentation. She noted burn-like throat pain that migrated down to her chest occurring twice after starting this treatment. Review of her social and family history revealed no risk factors for cardiopulmonary disease and was otherwise noncontributory. She was a nonsmoker and marginal alcohol consumer.

On physical exam, the patient was comfortable, pleasant, in no acute distress and breathing with normal oxygen saturation at a regular rate. Her vitals were within normal limits and stable. Heart, lungs, and vascular exam were normal. On head, ears, eyes, nose, and throat (HEENT) examination; the right tympanic membrane appeared to have postsurgical changes with a noted defect; otherwise the ear canal was clean without discharge or erythema. Oropharyngeal exam was unremarkable. The remainder of her exam was unremarkable. An electrocardiogram (ECG) was obtained which demonstrated a normal sinus rhythm. Her symptoms resolved completely after consuming a gastrointestinal cocktail. She was monitored for 2 h with no change in status and continued resolution of symptoms. She was discharged with an H2 blocker and referred to her otolaryngologist for evaluation.

**DISCUSSION**

Discovered in 1947 as a product of *Streptomyces venezuelae*, chloramphenicol acts by inhibiting protein synthesis via the 50S ribosomal subunit.[1] It is largely bacteriostatic, but also shows bactericidal activity against common pathogens of eyes, ears, nose, and throat infections as well as meningal pathogens, namely *Hemophilus influenzae*, *Streptococcus pneumoniae*, and *N. meningitidis*. Shortly after chloramphenicol's discovery, it rapidly gained popularity owing to its broad spectrum coverage, good tissue penetration, and low cost. In the 1950s; however, two landmark case reports presented a possible correlation of a lethal blood dyscrasias and bone marrow suppression due to topical and systemic chloramphenicol[2–8] with an incidence believed to be in the order of one in 24,000-40,000. [1] Two mechanisms of such an adverse effect originally included dose-dependent and reversible bone marrow suppression secondary to mitochondrial protein synthesis inhibition, as well as an idiosyncratic reaction resulting from deoxyribonucleic acid (DNA) damage.[1]

This conclusion has been called into question. Case reports and editorials have surfaced in the past 2 decades that argue in favor of chloramphenicol's low resistant patterns, low cost, and high efficacy as a topical[9] and systemic antibiotic.[1] Correlation between eye drops and bone marrow suppression seemed to be weaker than originally thought.[5] Lancaster and colleagues retrospectively reviewed medical charts and found an incidence of aplastic anemia amongst patients on chloramphenicol eye drops to be three per 442,543 over 7 years, enhancing the argument that chloramphenicol-induced aplastic anemia is exceedingly rare.[8]

Dr. Sherwin Isenberg pointed out that outside of North America chloramphenicol is one of the more popular first-line antibiotics.[10] In the US, the use is comparatively less common. However, individual US case reports have surfaced as well as multicenter studies looking at antibiotic use showing chloramphenicol is still a medication prescribed within the US. Additionally, the US Food and Drug Administration points out the growing issue of medications smuggled from Mexico and Canada for personal use as well as for retail.[12] Given the popularity of this medication internationally, it is important to have a growing knowledge of chloramphenicol's side effects for potential presentations in US emergency departments.

Such side effects include ototoxicity,[13] metabolic acidosis, encephalopathy, and neurotoxicity.[11] Thapa and Kumar reported two pediatric cases of *Candida* esophagitis in 2- and 9-year-old boys.[10] Both of which were on an oral chloramphenicol dose for *Salmonella* and fever, respectively. These cases demonstrate an association of esophagitis with symptoms of pain and dysphagia with an oral chloramphenicol. Outside of *Candida* esophagitis, there appears to be no other reported association to date of esophageal irritation/injury secondary to chloramphenicol. However, contact dermatitis with symptoms of erythema, edema, pruritus, and hyperemia of the face as well as arms have been seen with topical chloramphenicol.[14] Furthermore, Collins et al., described 16 cases of drug associated esophageal injury, seven of which were antibiotics including doxycycline and clindamycin.[15]

Ototopic chloramphenicol in patients with tympanic membrane perforation show a low, but increased risk of ototoxicity compared to nonperforated membrane[18–3] arguably due to loss of a barrier. In the case presented, the patient used an otic insufflation for her right ear after a recent tympanoplasty, likely allowing ototopic chloramphenicol to come in contact with the esophagus leading to symptoms reported upon presentation. Limitations of the described case report include the lack of supporting evidence for the proposed mechanism in the literature as well as clinical diagnostic studies at the time of evaluation. However, this case presents an interesting presentation of a patient taking a medication not commonly seen in the US. This patient had no prior history of gastrointestinal reflux disease, and this patient's symptom began within days of starting the chloramphenicol. It is reasonable to consider chloramphenicol in the differential as a causative agent for this presentation after ruling out other urgent etiology.

**CONCLUSION**

Chloramphenicol has gained popularity for its efficacy, low resistance, and very low cost. Its use was markedly reduced.
in the developed world due to presumed lethal bone marrow suppression and aplastic anemia. New insight has shown association of aplastic anemia and bone marrow suppression with topical chloramphenicol to be far less common than originally thought. However, other adverse effects of this medication should be highlighted given the upward trend of its use in the US. This case report presents a 31-year-old female with very limited risk factors for cardiopulmonary or vascular disease who presented with chest discomfort. Detailed history revealed she was approximately 4 months status post tympanoplasty and currently on chloramphenicol otic insufflator. Given documented evidence of antibiotic induced esophageal injury and esophagitis, and the loss of a barrier preventing an otherwise ototopical agent from being ingested, the patient was treated for presumed chloramphenicol-induced esophagitis.

REFERENCES

1. Wiest DB, Cochran JB, Tecklenburg FW. Chloramphenicol toxicity revisited: A 12-year-old patient with a brain abscess. J Pediatr Pharmacol Ther 2012;17:182-8.
2. Rich ML, Ritterhoff RJ, Hoffmann RJ. A fatal case of aplastic anemia following chloramphenicol (chloromycetin) therapy. Ann Intern Med 1959;33:1459-67.
3. Rosenthal RL, Blackman A. Bone-marrow hypoplasia following use of chloramphenicol eye drops. JAMA 1965;191:136-7.
4. Doona M, Walsh JB. Use of chloramphenicol as topical eye medication: Time to cry halt? BMJ 1995;310:1217-8.
5. Lancaster T, Swart AM, Jick H. Risk of serious haematological toxicity with use of chloramphenicol eyedrops in acute bacterial conjunctivitis. A comparison of 2 dosage regimes in general practice. Tidsskr Nor Laegeforen 1998;118:671-3.
6. Tan LK. Chloramphenicol-induced aplastic anemia—should its topical use be abandoned? Singapore Med J 1999;40:445-6.
7. Dohar JE, Kenna MA, Wadowsky RM. Therapeutic implications in the treatment of aural pseudomonas infections based on in vitro susceptibility patterns. Arch Otolaryngol Head Neck Surg 1995;121:1022-5.
8. Hofinger DM, Cardona L, Mertz GJ, Davis LE. Tularemic meningitis in the United States. Arch Neurol 2009;66:523-7.
9. Lautenbach E, Gould CV, LaRosa LA, Marr AM, Nachamkin I, Bilker WB, Fishman NO. Emergence of resistance to chloramphenicol among vancomycin-resistant enterococcal (VRE) bloodstream isolates. Int J Antimicrob Agents 2004;23:200-3.
10. Thapa BR, Kumar L. Candida esophagitis after antibiotic use. Indian J Pediatr 1989;56:296-9.
11. Isenberg SJ. The fall and rise of chloramphenicol. J AAPOS. 2003 Oct;7(Suppl):307-8.
12. US Food and Drug Administration. Imported Drugs Raise Safety Concerns. U.S. Department of Health & Human Services. [Internet]. 2011 Aug 24 [cited 2013 Aug 8]. Available from: http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143561.htm
13. Macfadyen CA, Acuin JM, Gamble C. Systemic antibiotics versus topical treatments for chronically discharging ears with underlying eardrum perforations. Cochrane Database Syst Rev. 2006. 25;1:CD005608.
14. Moyano JC, Alvarez M, Fonseca JL, Bellido J, Munoz Bellido FJ. Allergic contact dermatitis to chloramphenicol. Allergy 1996;51:67-9.
15. Collins FJ, Matthews HR, Baker SE, Strakova JM. Drug-induced oesophageal injury. British Medical J. 1979;1:1673-1676.

How to cite this article: Andicochea CT, Portouw SJ, Bokan MM. Chloramphenicol and acute esophagitis in the emergency department. J Emerg Trauma Shock 2015;8:65-7.

Received: 01.07.13. Accepted: 01.08.13.

Source of Support: Nil. Conflict of Interest: None declared.