Vitreous Cultures and Antibiotic Analysis in Puerto Rican Endophthalmitis Patients

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Objective: To analyze positive vitreous cultures and their respective antibiotic sensitivities in patients with endophthalmitis in Puerto Rico.

Methods: We conducted a retrospective cohort study of vitreous cultures from all of the patients with a clinical diagnosis of endophthalmitis at the Puerto Rico Medical Service Administration Center in San Juan, Puerto Rico, from August 2009 to July 2010. Positive isolates were selected for analysis. A retrospective chart review was performed to establish the mechanism involved in the development of endophthalmitis.

Results: Forty-three patients underwent vitreous cultures for a diagnosis of endophthalmitis, of which 16 patients had positive cultures. Seventy-eight percent of the isolates were bacterial and 22% fungal. *Staphylococcus* genus was identified in 38% of patients. All of the *Staphylococcus epidermidis* and Streptococcus pneumonia isolates were resistant to oxacillin; 66% of the *Staphylococcus aureus* isolates were also resistant to oxacillin. All of the Gram-positive isolates in our study were sensitive to vancomycin. All of the gram-negative isolates were sensitive to ceftazidime. Twenty-nine percent of the post-traumatic endophthalmitis cases were fungal in origin.

Conclusion: The majority of endophthalmitis cases in our study were bacterial in origin, and the *Staphylococcus* genus was the most common type of organism identified. In our cohort, post-traumatic endophthalmitis was the most common mechanism leading to infection. Vancomycin in combination with ceftazidime appears to be adequate for the empiric treatment of all cases of bacterial endophthalmitis in our population. Anti-fungal agents should be considered as adjuvant empiric treatment in patients with post-traumatic endophthalmitis. [*P R Health Sci J 2011;30:198-202*]

Key words: Endophthalmitis, Ocular Trauma, Antibiotic resistance

Endophthalmitis refers to inflammation inside the eye. For over a decade, the Endophthalmitis Vitrectomy Study (EVS) has served as the main guideline for the treatment of post-operative endophthalmitis. Since delaying the treatment of endophthalmitis can lead to long-term visual impairment and even the loss of an eye, an initial, empirical treatment with broad spectrum intraocular antibiotics is imperative to assure the best possible prognosis for the patient being treated (1). The emergence of new antibiotics with higher degrees of penetration to the vitreous body, such as third-generation fluoroquinolones, has led some physicians to add these agents as oral or intravenous adjuvants for the treatment of endophthalmitis (2-4).

The main 3 mechanisms involved in the induction of endophthalmitis are post-surgical, post-traumatic, and endogenous infection. The most likely etiology of post-cataract surgery endophthalmitis is coagulase-negative staphylococci, which in some case series can represent up to 70% of the isolates (3-4). Chronic pseudophakic endophthalmitis is usually caused by *Propionibacterium acnes* (5). *Streptococcus viridans* and *Streptococcus pneumonia* are the most important pathogens in post-trabeculectomy–associated endophthalmitis (6-7). Post-traumatic endophthalmitis is mainly caused by *Bacillus cereus* and coagulase-negative staphylococci; however, Gram-negative infections and fungal infections can also be found in as many as 7% and 6% of patients, respectively (8-10). Thirty to fifty percent of endogenous endophthalmitis cases are caused by streptococci, while *Staphylococcus aureus* is responsible for 25% of cases and Gram-negative bacilli for 30% of cases (11-12).

It is common practice in our community to prescribe topical antibiotics to post-operative patients with the purpose

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of preventing endophthalmitis. The most commonly used agents are first- and third-generation quinolones as well as aminoglycosides, with the latter being used less commonly nowadays because of the availability of quinolones (which as a class have a higher rate of intraocular penetration and are less likely to provoke retinal toxicity) (13). In the last decade, the availability of third-generation quinolones, which are more effective against Gram-positive organisms, has led some surgeons to prefer these over the older quinolones such as ofloxacin (14). In addition, some surgeons in our community use subconjunctival injections of cefazolin or gentamicin at the end of surgery as endophthalmitis prophylaxis (15-17).

This study seeks to provide a better understanding of the organisms leading to endophthalmitis in Puerto Rico. We also recognize the fact that having an increased knowledge of the antibiotic sensitivity patterns of microorganisms in our community can lead to better institutional management protocols and antibiotic prophylaxis guidelines for ophthalmologists in our community.

Methods

We conducted a retrospective cohort study of vitreous cultures from all of the patients with a clinical diagnosis of endophthalmitis at the Puerto Rico Medical Service Administration Center (ASEM) in San Juan, Puerto Rico, from August 2009 to July 2010. To do so, we accessed the database at the microbiology laboratory at ASEM and requested the results of all of the patients who had microbiological cultures from which a diagnosis of endophthalmitis was made in the aforementioned time period. Patients with negative cultures were excluded from our analysis. The records of those patients with positive isolates were selected for careful retrospective chart review and in order to analyze the results from the antibiotic susceptibility tests. According to the institution's protocol, vitreous contents were cultured in blood agar, chocolate agar, Sabouraud's agar, and thioglycollate medium. Patients were stratified according to etiology, isolate, sex, and age at presentation. We also analyzed the results from the antibiotic susceptibility tests.

Results

Forty-three patients underwent vitreous cultures for a diagnosis of endophthalmitis at the ASEM in the 1-year period of our study. Sixteen patients (37%) had positive cultures and were included in our analysis (Table 1). There were 12 men and 4 women. The mean age was 57 years, ranging from 6 to 101 years.

Fourteen patients (88%) had a single organism, and 2 patients had 2 organisms isolated. Of the organisms isolated, 78% were bacterial and 22% fungal. *Staphylococcus* genus was identified in 38% of patients and was the most common type of organism identified. We were able to retrospectively establish the mechanism leading to endophthalmitis in 94% of patients; among these patients, post-traumatic endophthalmitis was identified in 47% of cases and was the most common mechanism leading to infection.

Table 1. Positive isolates by etiology, isolate, sex, and age

Patient	Etiology	Isolate	Sex	Age
1	endogenous	*Staphylococcus aureus* (BL+)	M	36
2	endogenous	*Staphylococcus aureus* (BL +)	M	46
3	endogenous	*Staphylococcus epidermidis* (BL+)	M	42
4	endogenous	*Staphylococcus epidermidis* (BL+)	M	70
5	endogenous	*Pseudomona aeruginosa*	M	73
6	post-cataract	*Streptococcus pneumoniae*	M	75
7	post-cataract	*Streptococcus mitis*	M	72
8	post-cataract	*Aspergillus fumigatus*	F	82
9	post-traumatic	*Staphylococcus epidermidis* (BL+)	F	57
10	post-traumatic	*Streptococcus pyogenes* (group A)	F	101
11	post-traumatic	Beta hemolytic non-group A/B/D	M	62
12	post-traumatic	Diphtheroids	M	6
13	post-traumatic	*Pseudomona aeruginosa*	M	71
14	post-traumatic	*Acremonium* species	M	10
15*	post-traumatic	*Scopulariopsis Penicillium* species	M	60
16*	undetermined	*Staphylococcus aureus* (BL+) *Streptococcus agalactiae*	F	52

*Patient had 2 isolated organisms

Five isolates were related to endogenous sources. The etiologic microorganisms and their respective frequencies in this group were *Staphylococcus aureus*, 40%, *Staphylococcus epidermidis*, 40%, and *Pseudomonas aeruginosa*, 20%.

Three isolates were related to post-cataract extraction. The etiologic microorganisms were *Streptococcus pneumoniae*, *Streptococcus mitis*, and *Aspergillus fumigates*.

Eight isolates were related to eye trauma. The etiologic microorganisms for this group were *Staphylococcus epidermidis*, *Streptococcus pyogenes*, diphtheroids, *Pseudomonas aeruginosa*, *Acremonium* species, *Scopulariopsis* and *Penicillium* species, and an unidentified b-hemolytic non-group A, B, or D.

There were 2 isolates from a single patient in which the etiology for the endophthalmitis was not established; these were *Staphylococcus aureus* and *Streptococcus agalactiae*.

There were 13 isolates from which antibiotic sensitivity data were obtained; all of these were bacterial in origin: 11 (85%) were Gram-positive and 2 (15%) were Gram-negative. The antibiotic sensitivity data for these patients are shown in tables 2 and 3, respectively.

Of all of the gram-positive isolates in which sensitivity data were obtained, 100% were sensitive to vancomycin and 36% were resistant to clindamycin. Isolates from the *Staphylococcus* genus and *Streptococcus pneumonia* species were tested for oxacillin sensitivity; the overall resistance to this antibiotic in all these isolates combined was 86%. All of the *Staphylococcus epidermidis* and *Streptococcus pneumonia* isolates were resistant

to oxacillin; 66% of *Staphylococcus aureus* isolates were also resistant to oxacillin. All of the staphylococci in our study were resistant to penicillin.

Staphylococci were also tested for fluoroquinolone (levofloxacin and gatifloxacin) antibiotic sensitivity. Overall, 33% of *Staphylococcus aureus* and 67% of *Staphylococcus epidermidis* were resistant to levofloxacin. Thirty-three percent of *Staphylococcus aureus* had intermediate resistance to levofloxacin. The resistance patterns to levofloxacin were identical to those of gatifloxacin across all the isolates that were tested for both of these antibiotics in our study.

All of the Gram-negative organisms in our study were sensitive to cefepime, amikacin, ceftazidime, ciprofloxacin, gentamicin, imipenem, levofloxacin, and tobramycin.

There were 4 fungal isolates in our study, representing 22% of the total isolates and being present in 19% of the endophthalmitis cases in our study. No sensitivities were established for these microorganisms.

Discussion

This is the first study in the literature that describes the etiology and antibiotic resistance of endophthalmitis in Puerto Rico. In our study, the most common mechanism involved in the development of endophthalmitis was ocular trauma. Previous studies have suggested cataract surgery as the primary mechanism leading to endophthalmitis in developed countries (3, 18-20, 22). It is possible that our data are biased towards traumatic endophthalmitis. ASEM is the only level 1 trauma center in Puerto Rico, and, while some of the post-operative and endogenous endophthalmitis cases in our island are managed in other hospitals or by retinologists in private practice, most of the ophthalmology trauma cases in the island are sent exclusively to our center for management. Furthermore, trauma cases might have a larger inoculum, which facilitates having a positive culture (22).

Table 2. Gram-positive isolates and antibiotic sensitivity

Organism	Chloramphenicol	Clindamycin	Cefotaxime	Erythromycin	Cefepime	Linezolid	Penicillin	Tetracycline
Staphylococcus aureus (BL+)		s		r		s	r	s
Staphylococcus aureus (BL+)		s		s		s	r	s
Staphylococcus aureus (BL+)		s		s		s	r	s
Staphylococcus epidermidis (BL+)		r		r		s	r	s
Staphylococcus epidermidis (BL+)		s		s			r	r
Staphylococcus epidermidis (BL+)		r		r			r	r
Streptococcus pneumoniae	s	r		r		s		r
Streptococcus pyogenes (group A)	s	s		s			s	
Streptococcus mitis	s	s	s	s		s		i
Streptococcus agalactiae		s		s		s		
Beta hemolytic non-group A/B/D	s	r	s	s	s	s	s	r

Organism	Vancomycin	Gentamycin	Levofloxacin	Gatifloxacin	Oxacillin	Quinupristin/ dalfopristin	Trimethoprim/ Sulfamethoxazole	Rifampin
Staphylococcus aureus (BL+)	s	s	i	i	r	s	s	
Staphylococcus aureus (BL+)	s	s	s	s	s	s	s	
Staphylococcus aureus (BL+)	s	s	s	s	r	s	s	s
Staphylococcus epidermidis (BL+)	s	r	r	r	r	s	r	
Staphylococcus epidermidis (BL+)	s	s	s	s	r		s	
Staphylococcus epidermidis (BL+)	s	r	r	r	r		r	
Streptococcus pneumoniae	s				r		r	
Streptococcus pyogenes (group A)	s							
Streptococcus mitis	s							
Streptococcus agalactiae	s		s	s		s		
Beta hemolytic non-group A/B/D	s							

Table 3. Gram-negative isolates and antibiotic sensitivity

Organism	Cefepime	Amikacin	Ceftazidime	Ciprofloxacin	Gentamycin	Imipenem	Levofloxacin	Tobramycin	Piperacillin/ Tazobactam
Pseudomona aeruginosa	s	s	s	s	s	s	s	s	s
Pseudomona aeruginosa	s	s	s	s	s	s	s	s	s

Gram-positive organisms were the most common form of isolate in our study. This finding is consistent with other studies that suggest that the most likely organisms leading to overall endophthalmitis are gram-positive microorganisms (1, 20, 22). Gram-negative organisms were the least common isolates. In the EVS, Gram-negative isolates accounted for 5.9% of cases. (22) It appears that the patients with endophthalmitis who visit our institution have a low incidence of gram-negative infections, a rate that is similar to what has been found by other research studies in the United States (22, 27).

The initial empirical antibiotic treatment regimen for endophthalmitis in our institution consists of intravitreal vancomycin (1mg/0.1cc) and ceftazidime (2.5mg/0.1cc), which, according to our results, appears to be adequate to treat bacterial infections from all of the mentioned mechanisms identified. Our data also suggest that these 2 agents may also be effective for the empirical systemic treatment of patients in whom an endogenous source is suspected.

A significant percentage of the Gram-positive isolates in our study were fluoroquinolone (27%) resistant. Miller and colleagues suggested that fourth-generation fluoroquinolones have an efficacy of less than 80% in staphylococcal infections. (21-22) Concern exists about the emerging resistance of gram-positive isolates to third- and fourth-generation fluoroquinolones because of their common prophylactic use before and after intraocular surgery (23-26). For these reasons, we advise against the adjuvant use of topical, oral, or intravitreal fluoroquinolones in patients with established post-operative endophthalmitis who have received proper intraocular broad-spectrum antibiotic coverage.

In our study 31% of the isolates were related to an endogenous source. In these patients, only infections by staphylococcal species and Pseudomonas species were isolated. Eighty percent of isolates were from the staphylococcal species. In the North American and European populations, streptococci account for 30-50% of endogenous endophthalmitis cases; *Staphylococcus aureus* causes 25% of cases and Gram-negative bacilli account for 30% of cases (11, 28). In Asia, Gram-negative bacilli, especially *Klebsiella* and *Escherichia coli*, cause the majority of cases of endogenous endophthalmitis (12, 29). Our study was too small to obtain a representative cohort of endogenous endophthalmitis cases in Puerto Rico.

Post-traumatic infection was the most common mechanism leading to endophthalmitis in our study. Results in our population are similar to the results of other studies done in the United States in which the organisms causing post-traumatic endophthalmitis include streptococci, Gram-negative bacilli such as *Klebsiella* and *Pseudomona*, molds, and coagulase-negative staphylococci (9-10). In our institution, because a significant proportion of cases with traumatic endophthalmitis appear to have fungal isolates, we recommend that patients in Puerto Rico with traumatic endophthalmitis be managed prophylactically with intravitreal and systemic antifungal therapy.

Fungal isolates in our study account for 17% of cases; of these, 66% were caused by post-traumatic endophthalmitis, and 33% were caused by post-cataract surgery endophthalmitis. In some countries with tropical climates such as ours, up to 50% of central corneal ulcers are caused by fungi (30-33). Exogenous fungal infections of the eye are of a particular concern mainly because of the increasing prevalence of contact-lens users (34). The tropical climate of our island also predisposes individuals to an increased annual incidence of fungal infection. Previous studies have revealed that when exogenous fungal endophthalmitis occurs, it is mostly caused by molds (mainly *Fusarium* and *Aspergillus* species) (34). Unsurprisingly then, in our study all of the fungal isolates were molds.

As in all retrospective studies, the data in this study must be interpreted with caution. A referral bias may exist because the cases forming the basis for our study came exclusively from the only trauma center in Puerto Rico. Infections caused by certain difficult-to-culture organisms (requiring methods, such as polymerase chain reaction, that were unavailable) may have gone unidentified, possibly leading to ascertainment bias. Other important limitations include the small sample size and the lack of historical population data. Further studies may allow us to obtain a broader picture of intraocular infections in Puerto Rico and help us detect changes in antibiotic resistance patterns over time.

Resumen

Objetivo: Analizar los cultivos positivos de humor vítreo y sus respectivas resistencias a antibióticos en pacientes con endoftalmitis en Puerto Rico. Métodos: Hicimos un estudio de corte retrospectivo de los cultivos del humor vítreo de todos los pacientes con un diagnóstico clínico de endoftalmitis en el Centro de Administración de Servicios Médicos de Puerto Rico desde agosto del 2008 hasta julio del 2010. Los cultivos positivos fueron seleccionados para el análisis. Los expedientes médicos fueron revisados retrospectivamente para establecer el mecanismo que condujo a la endoftalmitis. Resultados: A cuarenta y tres pacientes se les hizo un cultivo del humor vítreo. Dieciséis de estos tuvieron resultados positivos en el cultivo. De los organismos aislados, 78% fueron de origen bacteriano y 22% de origen fungal. *Staphylococcus* fue el género identificado en el 38% de los pacientes. Todos los *Staphylococcus epidermidis* y los *Streptococcus pneumoniae* fueron resistentes a oxacilina; 66% de los *Staphylococcus aureus* fueron resistentes a oxacilina. Todos los organismos Gram positivos aislados fueron sensitivos a vancomicina. Todos los organismos Gram negativos aislados fueron sensitivos a ceftazidima. Veintinueve por ciento de los casos de endoftalmitis post-traumática eran de origen fungal. Conclusión: La mayoría de los casos de endoftalmitis en nuestro

estudio eran de origen bacteriano, y estafilococo fue el género más común de organismo identificado. En nuestro corte, el mecanismo más común que llevo a infección fue endoftalmitis post-traumática. Vancomicina y ceftazidima aparenta ser una combinación adecuada para el tratamiento de todos los casos de endoftalmitis bacteriana en nuestra población. Agentes antifungales deberían ser considerados como tratamiento empírico adyuvante en pacientes con endoftalmitis post-traumática.

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