Stenotrophomonas Maltophilia Keratitis and Scleritis

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Background: *Stenotrophomonas maltophilia* is a seldom-reported pathogen in ocular infections. The report describes six cases of *Stenotrophomonas maltophilia* (*S. maltophilia*) keratitis and scleritis. To our knowledge, this is the foremost report of *S. maltophilia* scleritis.

Methods: Laboratory reports of patients diagnosed with *S. maltophilia* ocular infections were collected from the ophthalmic department of Chang-Gung memorial hospital from January 1, 2000, through December 31, 2003. On evaluation of risk factors, isolates, antibiotic sensitivities, and response to the treatment ensued.

Results: Of the 6 reported cases, 5 related bacterial keratitis and 2 scleritis. (One case reported *S. maltophilia* keratitis and secondary scleritis.) The primary risk factor in such cases is ocular surgery. The organism cultured was the single isolate in three cases (50%). The susceptibility test showed that 50%, 83%, and 100% of the isolates were sensitive to ceftazidime, a combination of trimethoprim and sulfamethoxazole, and ciprofloxacin respectively.

Discussion: Ocular surface compromise such as penetrating keratoplasty was a primary risk factor of *S. maltophilia* keratitis in our study. The results of isolates and the antibiotic sensitivities were different from previously published results. Our cases responded well to antibiotic therapy and antibiotic therapy combined with conjunctival autografting. One case of *S. maltophilia* keratitis and secondary scleritis had a poor prognosis, arguably associated with a co-infection of *Mycobacteria chelonae*.

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Key words: *stenotrophomonas maltophilia,* keratitis, scleritis.

Stenotrophomonas maltophilia was previously termed as *Pseudomonas maltophilia.* In 1960 it was re-categorized and changed to *Xanthomonas maltophilia.*[1,2] It is a free-living, ubiquitous gram-negative bacillus with a wide geographic distribution, being isolated from water, soil, various plants and animals.[3,4] *S. maltophilia* is a seldom-reported pathogen in lens care systems or ocular infections.[5-11] However, there is an increasing frequency of post-operative and post-traumatic *S. maltophilia* ocular infection reports.

Snyder et al. reported a case of ciprofloxacin-resistant *S. maltophilia* keratitis in 1992.[12] Penland et al. retrospectively performed a series of studies that demonstrated eight cases of bacterial keratitis, two cases of acute conjunctivitis, two cases of infected scleral buckles, two cases of infantile dacryocystitis, and one case of preseptal cellulitis.[13] Cho et al.

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reported a case of co-infectious keratitis with *S. maltophilia* and *Aspergillus fumigatus* in 2002.[14]

To date, there is a 1992 report of *S. maltophilia* endophthalmitis after implantation of sustained-release ganciclovir in a case with acquired immunodeficiency syndrome.[15] Seven immunocompetent cases in 1997 and 2000 that followed from cataract surgery,[16-18] and three immunocompetent cases in 2001 and 2002 that followed from penetrating injury.[19-21]

We describe six additional cases with *S. maltophilia* keratitis and scleritis. To our knowledge, this is the foremost report of *S. maltophilia* scleritis. The purpose of our study is to survey the risk factors and the isolates, besides the antibiotic sensitivities,and evaluate the response to the treatment.

METHODS

Laboratory reports of patients diagnosed with *S. maltophilia* ocular infections were collected from the ophthalmic department of Chang-Gung memorial hospital from January 1, 2000, through December 31, 2003. All available medical records of these patients were reviewed. Isolates were identified by conventional biochemical methods or by commercial identification kits, ATB32GN (bioMerieux. Inc). The antibiotic sensitivities were tested by conventional disc diffusion method.

RESULTS

S. maltohilia was isolated from six cases of ocular infection (Table 1). Of the six cases, six related bacterial keratitis, two related scleritis. The fifth case related *S. maltophilia* keratitis and secondary scleritis. This case will be discussed subsequently.

The risk factors of corneal infections were corneal transplantation (three cases), ocular trauma (two cases), cataract surgery (one case), and herpes simplex keratitis (one case). The risk factor of the primary infectious scleritis is pterygium excision. But the cultures of scleral specimen were negative for *S. maltophilia* despite positive findings from the patient's eyedropper bottle.

The organism was cultured from the specimen and the eyedropper bottle. It was the single isolate in three cases, predominant isolate in one case. And partly responsible fora polybacterial infection in the remaining two cases.

The susceptibility test showed the isolates were resistant to aminoglycosides and cephalosporins, the exception ceftazidime. Three of six isolates (50%) were susceptible to ceftazidime. The combination of

Table 1. Stenotrophomonas Maltophilia Ocular Infections

No	Gender	Age	Diagnosis	Risk factor	Isolates
1	F	67	Keratitis	Trauma	*S. maltophilia* (moderate)
					Staphy. aureus (light)
2	M	41	Keratitis	HSV	*S. maltophilia* (heavy)
3	F	64	Scleritis	Pterygium excision	*S. maltophilia* (light)
				Normal saline bottle*	*Entero. cloacae* (light)
					Bacillus (light)
					Trichosporon sp. (moderate)
					Penicillium sp. (moderate)
					Phodotorula sp. (light)
4	F	68	Keratitis	PK + ECCE	*S. maltophilia* (rare)
				Trauma	
5	M	80	Keratitis	PK	*S. maltophilia* (rare)
			Scleritis		*Candida parapsilosis* (rare)
					Mycobacteria chelonae (light)
6	M	32	Keratitis	PK	*S. maltophilia* (moderate)

Abbreviations: *S. maltophilia: Stenotrophomonas maltophilia;* HSV: herpes simplex virus; PK: penetrating keratoplasty; ECCE: extracapsular cataract extraction

* The six species were cultured from the eyedropper bottle.

trimethoprim and sulfamethoxazole proved active in five isolates (83%). The isolates revealed the best susceptibility to ciprofloxacin (100%) (Table 2).

CASE REPORTS

Case 1

A 76-year-old male presented with a three-day history of right eye pain and decreased vision. On 30 January 2000, a bamboo splinter injured his right eye. He disaffirmed any systemic disease. He had undergone bilateral eyes cataract extraction with placement of posterior chamber intraocular lens three years earlier. Four days after the trauma, there was a central 3x3-mm corneal epithelial defect with an underlying stromal infiltrate on slit-lamp examination. Anterior chamber cells 3+ and ciliary injection were observed. Following corneal scrapings and cultures, topical amikin 25 mg/ml and cefazolin 25 mg/ml were administered hourly. Three days later, the culture results revealed a moderate growth of S. maltophilia and the slight growth of *Staphylococcus aureus. Stenotrophomonas maltophilia* was sensitive to ciprofloxacin and sulfamethoxazole-trimethoprim, but resistant to all aminoglycosides and ß-lactams. *Staphylococcus aureus* was resistant to penicillin and sensitive to chloramphenicol, clindamycin, erythromycin, oxacillin, sulfamethoxazole-trimethoprim, tetracycline, teicoplanin, and vancomycin. Topical amikin and cephazolin substituted topical ciprofloxacin 0.3% and vancomycin 50 mg/ml hourly. The patient's infiltrate cleared and the corneal epithelium healed within month.

Case 2

A 41-year-old male with recurrent episodes of right eye for approximately one year commencing April 1999. He complained of decreased right eye vision not right eye pain. He disaffirmed any systemic disease or previous ophthalmic surgery history. Slit-lamp examination disclosed a central corneal calcified plaque and 360 degree of limbal neovascular ingrowth. After the calcified plaque was removed, corneal infiltrate and deep stromal neovascularization with intrastromal hemorrhage were observed (Fig. 1A). Herpes simplex interstitial keratitis with bacterial superinfection was impressed. Herpes simplex virus DNA was detected. Scrapings and cultures of the ulcer was performed. The patient was treated with topical amikin 25 mg/ml every two hours and fluorometholone ophthalmic solution 0.1% four times daily. Four days later, the culture results showed a heavy growth of *Stenotrophomonas maltophilia*. It was sensitive to ceftazidime, ciprofloxacin, and sulfamethoxazole-trimethoprim. But it was resistant to amikin, cefazolin, gentamicin, and piperacillin. The patient's treatment was changed to topical ciprofloxacin 0.3% hourly. Six days later, the herpes simplex virus DNA report was negative. Due to the severity ofthe herpes simplex keratitis., acyclovir ophthalmic ointment, 3% five times daily and oral valaciclovir, 500 mg twice daily were added. The corneal epithelium healed rapidly and the infiltrate resolved within the next 2 weeks. However, the posterior stromal opacity developed gradually (Fig. 1B). Topical prednisolone acetate suspension 1% every two hours and balanced salt solution every hour were prescribed with a taper regimen of antibi-

Table 2. In Vitro Antibiotic Sensitivities of *S. Maltophilia* (outline)

Antibiotics / Patient No.	1	2	3	4	5	6
Amikin	R	R	R	R	I	R
Ceftazidime	R	S	S	R	S	R
Cefazolin	R	R	R	R	R	R
Ciprofloxacin	S	S	S	S	S	S
Gentamicin	R	R	R	R	R	R
Piperacillin	R	R	R	-	-	-
Sulfamethoxazole-Triamethoprim	S	S	S	S	R	S

Abbreviations: S: sensitive; I: intermediately sensitive; R: resistant; -: not tested

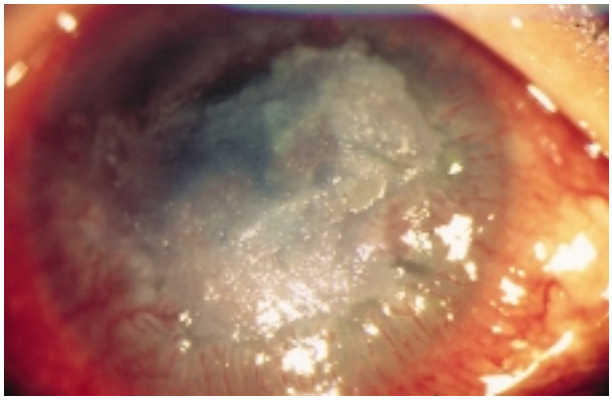

Fig. 1A After removing the calcified plaque, corneal infiltrate and deep stromal neovascularization with intrastromal hemorrhage were observed.

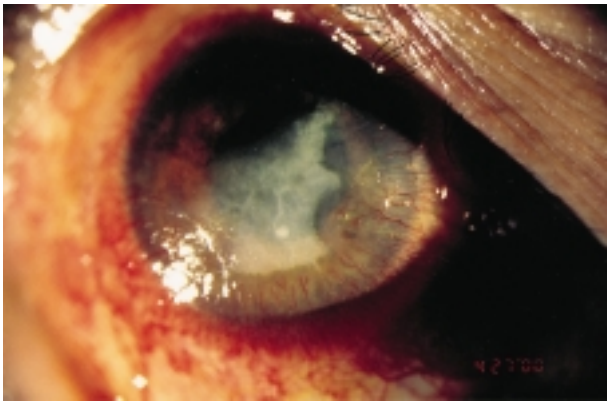

Fig. 1B The corneal epithelium healed and the infiltrate resolved. However, the posterior stromal opacity developed gradually.

otics and anti-viral agents. The infectious keratitis was controlled and did not recur in the one-year follow-up examination (Fig. 1C).

Case 3

A 64-year-old female manifested stinging right eye for several weeks. She was a long term victim of diabetes mellitus with oral anti-hyperglycemic agents control. She suffered from bilateral proliferative diabetic retinopathy and received panretinal photocoagulation several times since May 2000. Three years earlier, she had undergone right eye pterygium excision. Due to irritation, she prepared an eyedropper bottle filled with normal saline and sometimes applied it to her right eye. The examination disclosed scleral thinning and small abscess at 2 to 3 o'clock limbal area (Fig. 2A). An impression of infectious scleritis was made. Cultures from the necrotic sclera were performed and she was first treated with topical amikin 15 mg/ml every two hours. There was no definite finding from the culture result. However, the scleral lesion seemed uncontrolled and anterior chamber reaction 3+ was observed one month after the initiation of antibiotic therapy (Fig. 2B). A second set of cultures from the scleral lesion and the eyedropper bottle were taken. Ten days later, the cultures of the scleral lesion indicated no growth. However, the culture result from the eyedropper bottle demonstrated six species as follows: *S. maltophilia* (light), *Entero cloacae* (light), *Bacillus* (light), *Trichosporon sp.* (moderate), *Penicillium sp.* (moderate), and *Phodotorula sp.* (light). The *S. maltophilia* was sensitive to ceftazidime, ciprofloxacin, latamox-

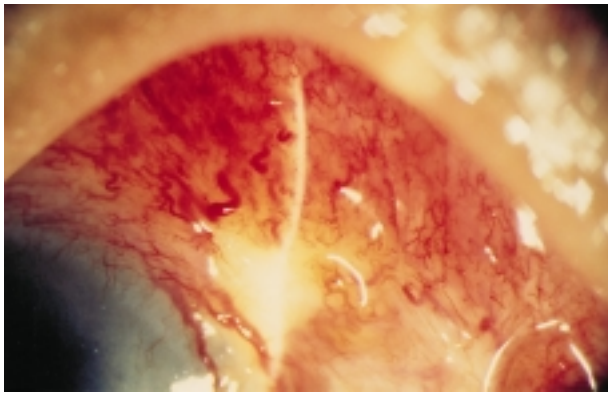

Fig. 2A Examination disclosed scleral thinning and small abscess at 2-3 o'clock limbal area.

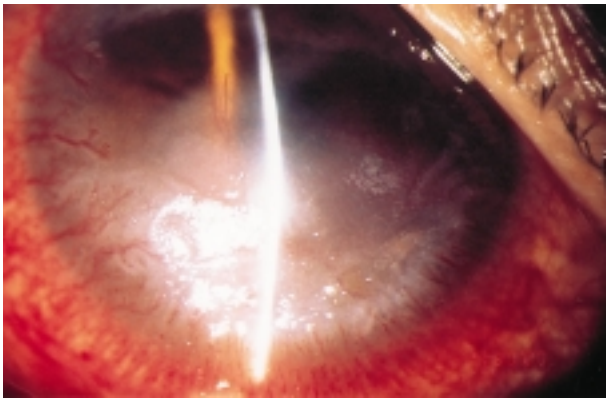

Fig. 1C The infectious keratitis was controlled and did not recur in the required one-year follow-up examination.

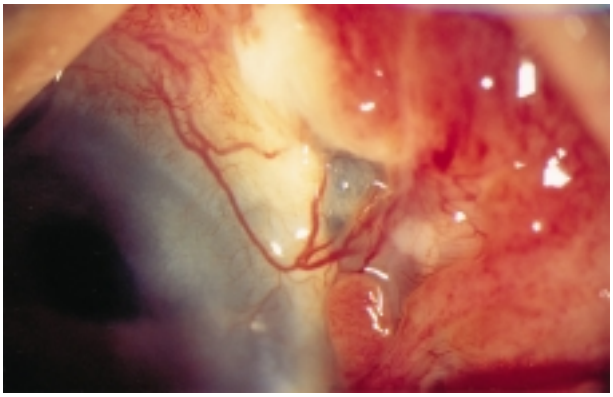

Fig. 2B The scleral lesion was not controlled by one month after the initiation of antibiotic therapy.

ef, and sulfamethoxazole-trimethoprim. However, it was resistant to amikin, cefazolin, gentamicin, and piperacillin. The *Entero cloacae* was sensitive to amikin, ceftazidime, ciprofloxacin, gentamicin, piperacillin, and sulfamethoxazole-trimethoprim. It was resistant to ampicillin and cefazolin.The *Bacillus* was sensitive to chloramphenicol, clindamycin, sulfamethoxazole-trimethoprim, teicoplanin, and vancomycin. It was resistant to erythromycin, oxacillin, and penicillin. According to the susceptibility result, topical ceftazidime 25 mg/ml and topical chloramphenicol 0.25% every four hours as well as oral cotrimoxazole 960 mg was prescribed twice daily. The scleral infectious lesion resolved and fibrosis occurred within the next 3 months (Fig. 2C).

Case 4

A 66-year-old female underwent left eye penetrating keratoplasty and extracapsular cataract extraction for leukoma cornea in September 2000. Four months after the surgery, she suffered from left ocular blunt injury by an elbow. The corneo-corneal wound was dehisced and the stitches untightened. She received further corneal wound repair. Six weeks later, she manifested a sudden onset of left eye pain. A small corneal epithelial defect with infiltrate was noted on slit-lamp examination. Bacterial corneal ulcer was impressed. Corneal scrapings were collected for smear and culture tests. Cefazolin 25 mg/ml and gentamicin 9 mg/ml were prescribed twice hourly. The lesion resolved about two months later when there was no specific finding from the culture. However, she had the second episode of left corneal ulcer approximately a year later. Examination of the left eye disclosed a heavily edematous cornea and a 6x6-mm dense central stromal infiltrate with an overlying epithelial defect. Corneal scrapings and cultures were performed and the patient was given cefazolin 25 mg/ml and gentamicin 9 mg/ml hourly. However, the infiltrate worsened despite of the treatment. Five days later, the cultures grew *S. maltophilia.* It was sensitive to ciprofloxacin and sulfamethoxazole-trimethoprim, but resistant to all aminoglycosides and ß-lactams. The patient's treatment was changed to topical ciprofloxacin 0.3% hourly and oral cotrimoxazole 960 mg twice daily. Her corneal infiltrate seemed to controlled in the following ten days. However, subsequently the epithelium failed to heal and the infiltrate exacerbated. The cornea finally progressed to melt (Fig. 3A). Conjunctival autografting was performed to cover the melting cornea and the patient was treated with the same fortified antibiotics. After surgery, clinical resolution was observed and the infectious keratitis did not recur in the required one-year follow-up examination (Fig. 3B).

Case 5

A 77-year-old male long term victim of diabetes mellitus with oral anti-hyperglycemic agents control. Four years earlier he had undergone left eye phacoemulsification with intraocular lens implantation for senile cataract. A trabeculectomy for chronic angle closure glaucoma was performed two years later. He received left eye penetrating keratoplasty for pseudophakic bullous keratopathy in March

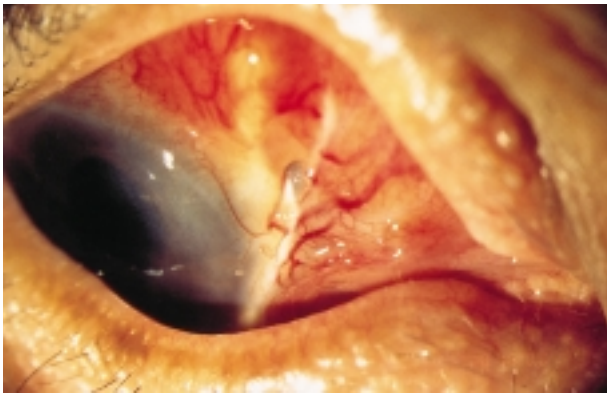

Fig. 2C The scleral infectious lesion resolved and fibrosis occurred.

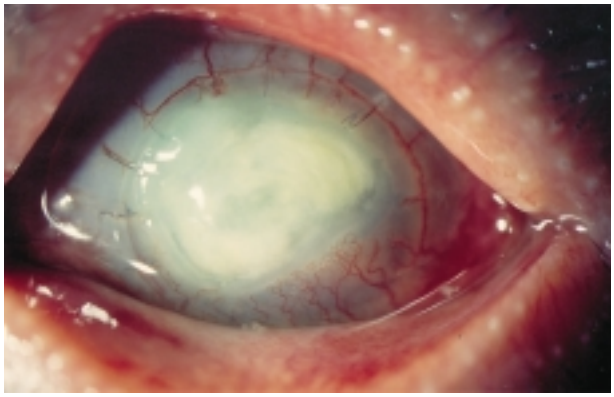

Fig. 3A The cornea progressed to melt.

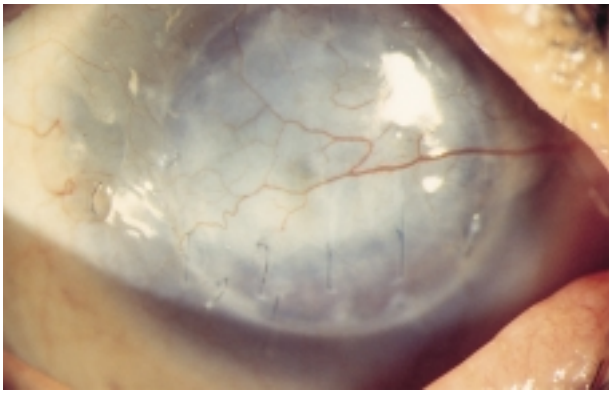

Fig. 3B Clinical resolution was observed after conjunctival autografting.

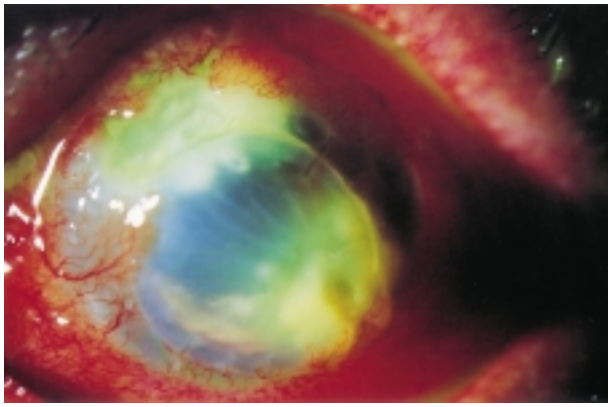

Fig. 4 The original infiltrate with the overlying epithelial defect enlarged to 2.7x3.0-mm and a new dense infiltrate with scleral extension at 11 o'clock peripheral cornea was noted.

2001. There were no complications noted in the follow-up examinations. Two years after the surgery, he manifested a two-week left eye pain. Examination disclosed a 1.2x1.2-mm corneal epithelial defect with a moderately dense corneal stromal infiltrate at 5 o'clock peripheral cornea. After scrapings were collected from the lesion for smear and culture, the patient was treated hourly with amikin 25 mg/ml and cefazolin 25 mg/ml. Five days later, the culture results showed *S. maltophilia.* It was sensitive to ceftazidime and ciprofloxacin, intermediately sensitive to amikin and resistant to sulfamethoxazole-trimethoprim. Topical ciprofloxacin 0.3% hourly and oral moxifloxacin 400 mg daily were administered in addition to topical amikin and cefazolin. However, the original infiltrate with the overlying epithelial defect enlarged to 2.7x3.0-mm and a new dense infiltrate with scleral extension at 11 o'clock peripheral cornea was noted (Fig. 4). Anterior chamber 4+ cellular reaction and 1.5 mm hypopyon were also observed. Corneal and scleral scrapings and cultures were performed again. Since the previous 12-day culture report revealed the alternate finding, *Candida parapsilosis*, topical natamycin 5% hourly and oral fluconazole 100 mg daily were added. Two days later, topical natamycin was changed to amphotericin-B 2.5 mg/ml hourly and oral erythromycin 250 mg six-hourly were prescribed. However the infectious keratitis and scleritis progressed rapidly to endophthalmitis and perforation. Left eye evisceration was performed finally and the eviscerated tissue was sent for culture. Four days after the surgery, the 25-day culture report showed another finding, Mycobacteria chelonae, sensitive to amikin and imipenem, resistant to ciprofloxacin, erythromycin, sulfamethoxazole-triamethoprim, and tetracycline. The second corneal and scleral culture report was the same as the first one. However only *Mycobacteria chelonae* was isolated from the culture of the eviscerated tissue.

Case 6

A 32-year-old male suffered from bilateral eyes alkaline chemical burn by ammonia at work on 21 May 1990. He had undergone five counts of bilateral eyes penetrating keratoplasty for initial macular cornea and subsequent corneal graft rejection between March 1991 and January 2001. There was no intra-operative or post-operative complication. Two years after the latest surgery, the patient presented with a four-day history of left eye pain and decreased vision. Slit-lamp examination disclosed a central corneal 2x3-mm epithelial defect with underlying infiltrate. The cornea was slightly steamy (Fig. 5). Anterior chamber reaction 3+ was noted. Corneal scrapings and cultures were performed. He was treated hourly with amikin 25 mg/ml and cefazolin 25 mg/ml. Seven days later, the cultures grew *Stenotrophomonas maltophilia*. It was sensitive to ciprofloxacin and sulfamethoxazole-trimethoprim, but resistant to all aminoglycosides and ß-lactams. The medication was changed to topical ciprofloxacin 0.3% hourly with a subsequent taper regimen. The patient's corneal infiltrate cleared and the epithelium healed within the following ten days.

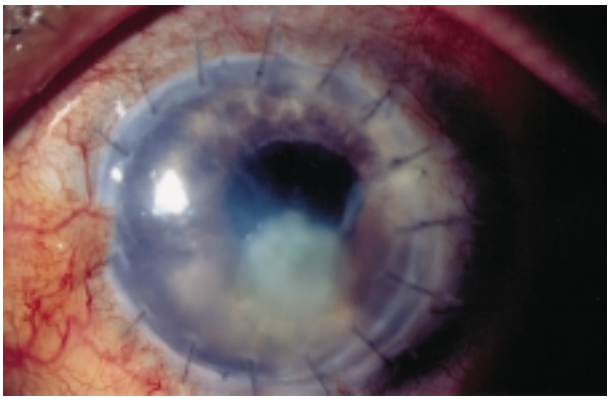

Fig. 5 Examination disclosed a central corneal 2x3-mm epithelial defect with underlying infiltrate.

DISCUSSION

Ocular surface compromise was considered an important predisposing factor of *S. maltophilia* ocular infections.[13] In our study, penetrating keratoplasty was a primary risk factor of *S. maltophilia* keratitis. There appears to be a relationship between immuno-compromised ocular surfaces. The use of the post-operative medications, such as topical or systemic steroid and immunosuppressive agents, was another factor.

S. maltophilia was reported as a part of the mixed flora of hospitalized patients.[4] In the study performed by Penland et al., *S. maltophilia* was isolated from polybacterial ocular infections in ten of fifteen cases. Only one case has single isolate.[13] However, the organism in our study was the single isolate in three cases, the predominant isolate in one case, and a part of polybacterial infections in the two remaining cases.

Previous reports about *S. maltophilia* ocular infections included keratitis, conjunctivitis, infected scleral buckles, infantile dacryocystitis, preseptal cellulites,[9-14] and endophthalmitis.[15-21] *S. maltophilia* scleritis was first mentioned so far. In the fifth, *S. maltophilia* scleritis was secondary to keratitis and progressed to endophthalmitis and evisceration. However, the poor outcome may also be associated with *Mycobacteria chelonae* infection.[22-24]

S. maltophilia keratitis that has proven resistant to Ciprofloxacin has been previously published.[12] It is believed that *S. maltophilia* has the ability to develop resistance to originally active agents such as Ciprofloxacin and the combination of trimethoprim and sulfamethoxazole.[25] However, the organism in our study showed the best susceptibility to ciprofloxacin (100%), and beter susceptibility to the combination of trimethoprim and sulfamethoxazole (83%) when compared with ceftazidime (50%).

Excluding the fifth case of co-infection with *S. maltophilia* and *Mycobacteria chelonae*, the organism was eradicated in the remaining 5 cases. The fourth case underwent conjunctival autografting after failure of conservative antibiotic therapy despite of the compatibility with the antibiotics sensitivities. The remaining four cases had good response to antibiotic therapy.

In summary, obtaining microbiologic confirmation and antibiotic sensitivities is crucial for treating *S. maltophilia* ocular infections. If *Stenotrophomonas maltophilia* keratitis takes a progressive course, persistent antibiotic therapy combined with conjunctival autografting may be considered as an alternative way to eradicate the infection.

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Stenotrophomonas maltophilia 引發角膜炎及鞏膜炎之報告

陳永豐 鐘珮禎 蕭靜熹

前 言： *Stenotrophomonas maltophilia* 是一種相當罕見於眼睛的細菌。我們研究並收集了六個由*Stenotrophomonas maltophilia* 所引發的角膜炎及鞏膜炎病例。其中的 *Stenotrophomonas maltophilia* 鞏膜炎，就我們所知，是截至目前爲止第一個病例報告。

方 法： 我們收集了自民國89年初至92年底，由林口長庚醫院眼科醫師診斷爲 *Stenotrophomonas maltophilia* 引發眼睛感染的病例。我們主要探討的目標是造成感染的危險因子，培養出的菌種，對抗生素的敏感性測試，及病人對藥物與手術治療的反應。

結 果： 這六個病例中有五個是角膜炎，兩個是鞏膜炎。(其中一個病例是角膜炎及次發性鞏膜感染。) 主要危險因子是眼部手術。培養出的菌種有一半的病例爲單一菌種。對 ceftazidime，trimethoprim-sulfamethoxazole，和 ciprofloxacin 的敏感性測試分別是 50%，83%，及100%。

討 論： 在我們的研究中，眼部表層的不健全，譬如接受過全角膜移植手術，是一個很重要的危險因子。這一點和之前的研究報告相去不遠，但就培養出的菌種及對抗生素的敏感性測試結果而言，就有很大的差別。我們培養出的菌種多數爲單一菌種，對抗生素的抗藥性也明顯比之前的報告低了許多。六個病例中，抗生素治療或加上自體結膜移植手術對其中五例有很好的成效。至於預後較差的那一病例，推測其可能原因是合併了 *Mycobacteria chelonae* 的感染。

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關鍵字： 嗜麥芽糖狹隘營養單胞菌 (*Stenotrophomonas maltophilia*)，角膜炎，鞏膜炎。

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