Research Article

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Analytical investigation of demographic, laboratory, and clinical characteristics of patients with microbial keratitis

Mikrobiyal keratitli hastaların demografik, laboratuvar ve klinik özelliklerinin analitik olarak incelenmesi

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Abstract

Purpose: In this study, we investigated epidemiological properties, clinical findings, risk factors, direct microscopy, and culture results in patients diagnosed with microbial keratitis.

Materials and methods: We examined the hospital records of patients with microbial keratitis between March 2016 and March 2021, retrospectively. Also, clinical findings, risk factors, microbiological results, empirical treatment and, treatment responses were evaluated.

Results: 42 eyes of 42 patients whose mean age was 57.8 (range 18-70 years) were included in the study. Gram-positive and gram-negative bacteria were found on stained microscopic examination in 12 patients (28.5%). In total, microbial growth was detected in the culture of 7 patients (16.6%), while growth was not detected in 35 patients (83.4%). No etiological factor was detected in 27 patients (64.4%). The complaints at admission were pain in 24 patients (57.6%), redness in 12 patients (28.8%), and both redness and pain in 6 patients (14.1%). While the visual acuity of 18 cases was preserved after the treatment, 24 cases (88.8%) achieved 1 or more line with the treatment. While the mean visual acuity was 0.79±1.1 (0-3.1) logMAR before treatment, it increased to 0.69±1.1 (0-3.1) logMAR after treatment (p=0.006).

Conclusion: The keratitis is a common cause of unilateral blindness. Early diagnosis and treatment of keratitis is a significant role in the prognosis. The success of the therapy can be provided by starting empirical antimicrobial therapy by taking into consideration of the regional risk factors and common pathogens.

Keywords: Etiology, keratitis, treatment.

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Öz

Amaç: Bu çalışmada mikrobiyal keratit tanısı alan hastalarda epidemiyolojik özellikler, klinik bulgular, risk faktörleri, direkt mikroskopi ve kültür sonuçlarını inceledik.

Gereç ve yöntem: Mart 2016-Mart 2021 tarihleri arasında mikrobiyal keratit tanısı alan hastaların hastane kayıtları retrospektif olarak incelendi. Ayrıca klinik bulgular, risk faktörleri, mikrobiyolojik sonuçlar, ampirik tedavi ve tedaviye yanıt değerlendirildi.

Bulgular: Yaş ortalaması 57,8 (dağılım 18-70) olan 42 hastanın 42 gözü çalışmaya dahil edildi. Boyalı mikroskopik incelemede 12 hastada (%28,5) gram-pozitif ve gram-negatif bakteriler saptandı. Toplamda 7 hastada kültürde üreme saptandı (%16,6), 35 hastada (%83,4) büyüme saptanmazken, 27 hastada (%64,4) etyolojik özellik saptanmadı, 24 hastada (%57,6) başvuru yakınmaları ağrı, 12 hastada (%28,8) kızarıklık şeklindeydi ve 6 hastada (%14,1) kızarıklık ve ağrı şikayetleri vardı. 18 olgunun tedavi sonrası görme düzeyleri korunurken, olguların 24'ünde (%88,8) tedavi ile 1 sıra ve üzeri görme artışı sağlandı. Tedavi öncesi ortalama görme keskinliği 0,79±1,1 (0-3,1) logMAR iken tedavi sonrası 0,69±1,1 (0-3,1) logMAR'a yükseldi (p=0,006).

Sonuç: Keratit, tek taraflı körlüğün yaygın bir nedenidir. Keratitte erken tanı ve tedavi prognoz üzerinde önemli rol oynar. Bölgesel risk faktörleri ve sık görülen patojenler dikkate alınarak ampirik antimikrobiyal tedaviye başlanması tedavinin başarısı sağlayabilir.

Anahtar kelimeler: Etiyoloji, keratit, tedavi.

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Introduction

Microbial keratitis, (MK) characterized by infiltration in the epithelial and stromal layers of the cornea, is one of the leading causes of unilateral blindness all over the world [1]. Contact lens wear, surgical or nonsurgical trauma, previous corneal disease, and ocular surface problems are some of the predisposing risk factors for microbial keratitis, and the condition can be caused by a variety of bacteria [2]. The most common cause of microbial keratitis in developed countries is incorrect contact lens use, while ocular trauma takes the first place in the etiology in developing countries [3].

For efficient diagnosis, care, and prevention of microbial keratitis, it is vital to determine the incidence, microbiological agent diversity, and predisposing factors [4]. Before the culture and antibiotic sensitivity results are obtained, the clinician must decide on the antibiotic regimen and immediately start the treatment. While making this decision, the patient's demographics, risk factor profile, and local microbial distribution model are important. Geographic and climatic conditions generate regional variances in the pattern of microbiological isolates, necessitating local epidemiological research [5].

Our aim in this study is to determine the demographic characteristics of the patients we have followed up in our clinic for the last 5 years with the diagnosis of keratitis, to get an idea about the etiology of keratitis in our region, to evaluate the causative microorganisms, to present the empirical treatment protocols we have applied and the responses we have received to the treatment.

Materials and methods

Fourty-two eyes of 42 patients hospitalized in our ward with the diagnosis of keratitis from March 2016 and March 2021 were included in this retrospective study. The ethics committee approval of Recep Tayyip Erdogan University was obtained for the study and the Helsinki Declaration rules were followed. Patients who were hospitalized for less than 3 days in make microbiological evaluations were excluded from the study. The patient's age, gender, complaints, visual acuity before and after treatment, ocular examination findings including biomicroscopy, intraocular pressure measurement, fundoscopy and ocular ultrasonography, and treatment protocols were documented from their charts. After being admitted to our service, they were re-examined in our service and their consent was obtained for corneal scraping.

Before corneal scraping, one drop of topical anesthetic (0.5% proparacaine-Alcaine®) was instilled into the keratitis eye. Some irrigation was done with physiological saline. Scraping samples were taken from the edges of the lesion with the help of a sterile scalpel under the guidance of a slit lamp, and the slide was spread, then inoculated on blood agar, chocolate agar, thiogluconate medium and sabouraud agar. It was sent to the microbiology laboratory for stained microscopic examination and culture antibiogram. Empirical topical augmented treatments were started hourly, without waiting for the laboratory results, and changes were made in the treatment protocols according to the laboratory results. Dose adjustments were made according to the response to the treatment and the toxic reaction caused by the side effects of the treatment. Considering the clinical findings, subconjunctival treatment was also applied in some unresponsive cases with hypopyon. Topical steroid treatment was also added to the patients who had no epithelial defect and regression in their clinical findings in the post-discharge controls. Examination findings were noted every day. Reduction in the area and depth of infiltration, regularization of borders, and decrease in anterior chamber reaction, hypopyon, and pain were accepted as clinical improvement findings.

SPSS 20 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and numerical measurements were summarized as mean (median and minimum-maximum where necessary). The statistical significance level was accepted as $p \leq 0.05$.

Results

The mean age was 57.8 years (range 18-70), 50% were female and 50% were male. In 12 (28.5%) patients, a positive finding was found in the stained microscopic examination. In 9 of them, gr (+) cocci were detected and only leukocytes were found in 3 patients. While no factor could be seen in direct examination in three patients, growth was detected in the

culture. Pathogen was detected in both direct examination and culture in 3 patients. Pathogen was detected in direct examination in nine patients, but there was no growth in culture. In 71.5% of the patients, no findings were found in both the stained microscopic examination and the culture. Pseudomonas aeruginosa was grown in the culture of two of the 12 patients with Gram-positive cocci, and Streptococcus Pneumonia was grown in the others. In the cultures of 3 patients whose direct examination was negative, pseudomonas aeruginosa grew again. In total, growth was detected in culture in 7 patients (16.6%), while growth was not detected in 35 patients (83.4%). The results are shown in Table 1.

Table 1. Cases with microbiological findings

	Culture -	Culture +	Total
Direct view +	9	3	12
Direct view -	6	24	30
Total	15	27	42

There were predisposing factors that could cause keratitis in 15 patients (35.6%). Herbal trauma in 9 patients, no antibiotic use following foreign body removal in 4 patients, and unhygienic contact lens use in 2 patients were noted. No etiological feature was detected in 27 patients (64.4%). The complaints at admission were pain in 24 patients (57.6%), redness in 12 patients (28.8%), and both redness and pain in 6 patients (14.1%). At the first admission, the visual level was hand movements in 5 cases, finger counting from 1 meter (mps) – 5 mps in 6 cases, 0.1-0.5 in 16 cases, and full vision in 15 cases. While the visual levels 15 cases were preserved after the treatment, 24 cases (88.8%) achieved 1 or more line with the treatment. Visual acuity did not change in 3 cases (11.2%). While the mean visual acuity was 0.79±1.1 (0-3.1) logMAR before treatment, it increased to 0.69±1.1 (0-3.1) logMAR after treatment (p=0.006).

Vancomycin (50 mg/ml) and amikacin (50 mg/ml) combination were given to 57.14% of patients (28 patients), and 33.3% (8 patients) to vancomycin + amikacin + amphotericin B (0.15 mg/ml) combination, 4.76% (2 patients) fluconazole (0.04 mg/ml) + moxifloxacin; Topical fortified treatments were started empirically in 4.76% (2 patients) of amphotericin B + moxifloxacin + gentamicin (14 mg/ml) and 4.76% (2 patients) with vancomycin + ceftazidime (50 mg/ml). Systemic antibiotic therapy was not given because the ocular transmission was low. When the clinical response to the given treatment was evaluated, 80.9% of the patients (34 patients) benefited from the treatment. No clinical response was obtained in 8 patients (19.1%).

Discussion

Microbial keratitis is still one of the leading causes of unilateral blindness. Although there are predisposing factors such as ocular trauma and contact lens use, there are some microorganisms that can penetrate through the intact cornea [6]. Microorganisms and etiological factors causing keratitis may vary according to geographical regions [7]. Effective treatment of keratitis is possible by accurately determining the causative microorganism and initiating appropriate empirical treatment.

Rize; It is a province of the Eastern Black Sea Region, which has a climate with cool summers, mild winters, and rainy seasons. Tea production in the region is a source of livelihood. Our aim in this study; is to examine the keratitis patients in our region, to determine the epidemiological features and the factors that predispose to keratitis, to determine the importance of culture and gram staining in the detection of common microorganisms, and to examine the effectiveness of empirical treatment.

In our study, there were 42 patients and the mean age was 57.8. The numbers of men and women were equal. There is no clear distinction regarding gender in the literature. While the rate is in favor of women in Madurai, it is in favor of men in Praguay and Nepal [8, 9]. Although there was no gender difference in our study, it can be explained by the fact that males are more common in some publications, considering predisposing factors such as ocular trauma and that they take a more active role in activities such as agriculture and animal husbandry.

In the etiology of keratitis, contact lens use is the most common etiology in developed societies, while trauma is shown in developing countries [3]. Keratitis occurs due to contact lens misusage such as sleeping with the lens, taking a bath, swimming in the sea-pool, not changing

the lens on time and not renewing the solution in the lens case. In the study of Lam et al. [10], the use of contact lenses was determined as a risk factor in 26.4% of the patients. Culture positivity in patients using contact lenses was found to be 36%; P. aeruginosa grew in 20.3% of these [10]. P. aeruginosa overgrowth in our patients with a history of contact lens use.

Crosslinking treatment, which is one of the important causes of keratitis in developed countries, is a widely used treatment method recently to stop the progression of keratoconus. Crosslinking is a treatment method that stops the progression of keratoconus by activating riboflavin with UV-A, causing an increase in the collagen cross-links of the cornea, hardening and an increase in its biomechanical strength [11]. Common complications; It was reported as 7.6% sterile corneal infiltrates, 2.9% vision loss, 2.8% central corneal scar. A rare case of microbial keratitis has been reported [12] While the absence of epithelium is a ready-made risk factor for keratitis, the fact that topical antibiotic drops are not used regularly can be considered to predispose to the development of keratitis.

According to our results; in 12 (28.5%) patients, a finding was found in the stained microscopic examination. In 9 of them, gr (+) cocci and only leukocytes were found in 3 patients. While no factor could be seen in direct examination in three patients, growth was detected in the culture. Pathogen was detected in both direct examination and culture in six patients. Pathogen was detected in direct examination in six patients, but there was no growth in culture. In 71.5% of the patients, no findings were found in both the stained microscopic examination and the culture.

In the study of Tewari et al. [13], it was observed that 37% of the patients had direct examination (-) culture (-), and 4% had direct examination (+) culture (-). When we look at other studies in the literature, reproduction rates in culture are reported to be between 35% and 68% [14, 15].

Gram (+) cocci constitute the most common type of microorganism produced in keratitis [16]. The most common Gram-positive bacterium was reported as S epidermidis in some studies, S pneumonia in some, and S aureus in some [17]. In our study, Pseudomonas and S. pneumonia were the agents produced from those with growth.

Our culture reproduction rate was found to be lower than the literature data. The reason for the low growth rate in culture may be the treatments that the patients received in other centers before applying. Co-ordination with the microbiology department can also help to increase the growth rate from the culture.

Although our culture growth rate was low, it was observed that our success rate was high with empirical treatment and there was a significant increase in visual acuity after the treatment, in line with the studies in the literature. We attribute the high success rate in the treatment to the hospitalization of the patients, the rapid initiation of broad-spectrum antibiotic therapy, and close monitoring until clinical improvement is observed.

The limited number of our patients, the short follow-up period of the cases, and the lack of follow-up in all cases were the limitations of our study.

Early diagnosis and initiation of treatment for keratitis, which is one of the most serious diseases of the eye that can lead to blindness, are of great importance in terms of prognosis. Initiation of empirical treatment for microorganisms that may be causative without waiting for laboratory results will positively affect the visual prognosis. In case of unresponsiveness to empirical treatment, working in coordination with the laboratory unit and switching to treatment for the causative pathogen will both prevent antibiotic resistance and provide effective treatment.

In conclusion, the keratitis is a common cause of unilateral blindness. Early diagnosis and treatment of the keratitis is a significant role on the prognosis. The success of the therapy can be provided starting empirical antimicrobial therapy by taking into consideration of the regional risk factors and common pathogens. On the other hand, direct microscopy and culture-antibiogram provide serious support in cases where the treatment response is not available.

Conflict of interest: No conflicts of interest was declared by the authors.

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Authors' contributions to the article

I.B. constructed the main idea and hypothesis of the study. F.S. and IB and developed the theory and arranged/edited the material and method section. F.S. has evaluated the data in the results section. Discussion section of the article was written by F.S., F.U. and S.K. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.