Predictors of surgical intervention and visual outcome in bacterial orbital cellulitis
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Abstract
This study aims to identify predictive factors associated with surgical intervention and the visual outcome of orbital cellulitis and to evaluate the treatment outcomes.

A retrospective study involving 66 patients (68 eyes; 64 unilateral and 2 bilateral) diagnosed with bacterial orbital cellulitis was conducted between November 2005 and May 2019.

The mean (± standard deviation) age was 42.1 (± 25.8) years (range: 15 days–86 years). Sinusitis was the most frequent predisposing factor, occurring in 25 patients (37.9%), followed by skin infection in 10 patients (15.2%), and acute dacryocystitis in 9 patients (13.6%). Subperiosteal abscesses were found in 24 eyes and orbital abscesses in 19 eyes. Surgical drainage was performed in 31 eyes. Regarding the abscess volume for surgical drainage, a cut-off of 1514 mm³ showed 71% sensitivity and 80% specificity. There was significant improvement in visual acuity (VA) and decrease in proptosis after treatment (for both, \( P < .001 \)). Only pre-treatment VA \(< 20/200 \) was a significant predictor for post-treatment VA of 20/50 or worse (adjusted odds ratio: 12.0, \( P = .003 \)). The presence of a relative afferent pupillary defect was the main predictor of post-treatment VA of 20/200 or worse (adjusted odds ratio: 19.0, \( P = .003 \)).

The most common predisposing factor for orbital cellulitis in this study was sinusitis. VA and proptosis significantly improved after treatment. We found that the abscess volume was strongly predictive of surgical intervention. Pretreatment poor VA and the presence of relative afferent pupillary defect can predict the worst visual outcome. Hence, early detection of optic nerve dysfunction and prompt treatment could improve the visual prognosis.

Abbreviations: RAPD = relative afferent pupillary defect, ROC = receiver-operating characteristic, SD = standard deviation, VA = visual acuity.

Keywords: orbital abscess, orbital cellulitis, sinusitis, subperiosteal abscess

1. Introduction
Orbital cellulitis is an uncommon infection involving the ocular structures posterior to the orbital septum. In the pre-antibiotic era, orbital cellulitis was associated with serious complications, including decreased visual acuity (VA), cavernous sinus thrombosis, meningitis, intracranial abscess, and death.[12,13] Nowadays, due to the formulation of effective antibiotic treatments, these serious complications have become much less frequent.[13] Orbital cellulitis is more common in the pediatric group; however, it can affect all age groups.[4]

The clinical presentation of orbital cellulitis includes eyelid swelling, proptosis, pain, decreased VA, ptosis, headaches, diplopia, restriction of extraocular muscle movement, and optic nerve dysfunction.[1,6] The most common cause of orbital cellulitis is rhinosinusitis; other potential causes are ophthalmic surgery, including strabismus surgery, blepharoplasty, aqueous humor surgery, peribulbar anesthesia, orbital trauma with fracture, dacryocystitis, and infection of the teeth, middle ear, or face.[7–14] Various complications of orbital cellulitis, such as subperiosteal abscess, orbital abscess, epidural or subdural empyema, brain abscess, or cavernous sinus thrombosis, have been reported.[2,3,5]

Most patients with uncomplicated orbital cellulitis can be treated with a course of antibiotics alone. The antibiotics of choice are parenterally administered broad-spectrum regimens aimed toward targeting *Staphylococcus aureus* (including methicillin-resistant *S. aureus*),[13–17] *Streptococcus pneumoniae*, and other *streptococci.*[18–20]

The indications for surgery include evidence of an abscess (especially a large abscess >10 mm in diameter or with volume >1250 mm³)[21,22] and other factors considered needing surgical drainage, including no improvement or a worsened condition within 24 to 48 hours and/or intracranial extension of the infection.[23] Medical subperiosteal abscesses in children often
respond to medical treatment without surgery. However, it is difficult to determine the age group, abscess size, visual function, or referral pattern that relates to the decision making for surgical intervention, due to the limited number of oculoplastic surgeons. Elshafei et al reported that a patient’s age, relative afferent pupillary defect (RAPD), and subperiosteal abscess affect the final VA.

The purpose of this study was to identify indicators for surgical management of orbital cellulitis. The main outcome was a post-treatment vision that defined a VA of 20/50 or worse as visual impairment and 20/200 or worse as legal blindness. Hence, we were interested to determine the prognostic factors for post-treatment visual outcomes in cases of bacterial orbital cellulitis. This information may improve the effective management of the disease and support patient counseling. The study also aimed to determine the demographic data, predisposing factors, causative organisms, and treatment outcomes for this disease.

2. Methods

2.1. Study design

This retrospective study included all patients diagnosed with bacterial orbital cellulitis, admitted between November 2005 and May 2019 at Songklanagarind Hospital, which is a major tertiary care center in southern Thailand. The inclusion criteria for the diagnosis of orbital cellulitis were based on clinical diagnosis and/or radiologic evidence of posterior septal inflammation. We excluded patients presenting with preseptal cellulitis, noninfectious orbital inflammatory disease, or orbital malignancy. This study was approved by the Ethics Committee of Faculty of Medicine, Prince of Songkla University (REC number 59-386-02-4), and the study adhered to the tenets of the Declaration of Helsinki. Formal consent was waived due to the retrospective nature of the study.

2.2. Data collection

All patient records were reviewed for data including age, sex, affected eye, presenting signs and symptoms, predisposing factors, VA, degree of proptosis, presence or absence of RAPD, referral status, previous treatment before admission, and imaging studies. Abscess volume was calculated using the ellipsoid formula \( \frac{4}{3}\pi xyz \), where \( x, y, \) and \( z \) correspond to the radius of each dimension (Fig. 1). Microbiological reports from blood and pus (if surgical drainage was performed) were also reviewed.

2.3. Outcome measures

The primary outcome measure was an analysis of the optimal cutoff point of abscess volume, which is a predictor of surgical abscess drainage, using the receiver-operating characteristic (ROC) curve. The cutoff point with the highest sensitivity and specificity was identified. The secondary outcome was post-treatment VA.

2.4. Statistical analysis

Data were analyzed using Stata Statistical Software (Stata/MP 14.1, StataCorp LP, College Station, TX). Descriptive data were evaluated for the mean ± standard deviation (SD) and median. Quantitative analysis of continuous and categorical data was performed using Fisher exact test, paired \( t \) test, and \( \chi^2 \) test. An age \( \leq 18 \) years was defined as a pediatric patient, and age \( > 18 \) years was determined to be an adult patient. This age stratification was selected to calculate in multivariate analysis, which was performed based on stepwise regression models. A \( P \) value <.05 was considered statistically significant.

3. Results

3.1. Demographic and clinical characteristics of the study population

A total of 66 patients with bacterial orbital cellulitis were included in the study, among whom 28 (42.4%) were men and 38 (57.6%) were women. The mean (± SD) age of the patients was 42.1 (± 25.8) years (range: 15 days–86 years). The presenting signs and symptoms included eyelid swelling in 100.0%, followed by pain in 97.3% of the patients (Table 1). All patients presented with multiple signs and symptoms. Thirty-seven patients were referred to our center (34 patients by general ophthalmologists and 3 patients by general practitioners) and 29 (78.4%) of 37 referred patients had been already treated with systemic antibiotics. The mean (± SD) duration from presentation...
of symptoms to admission was 7.7 (±13.3) days, and the median was 4 days (range: 1–92 days). Age groups were stratified between 0 and 6 years, >6 to 12 years, >12 to 18 years, and >18 years, in which each age group was not associated significantly with preoperative VA and RAPD (P=.62 and P=.22, respectively).

Sinusitis was the most common predisposing factor in 25 patients (37.9%), followed by skin infection in 10 patients (15.2%), and acute dacryocystitis in 9 patients (13.6%) (Table 2). Blood culture was obtained in 45 cases, of which 2 (4.4%) were positive. The major complications were subperiosteal abscess in 24 of 68 eyes (35.3%), orbital abscess in 19 of 68 eyes (27.9%), intracranial extension in 6 of 66 cases (9.1%), and cavernous sinus thrombosis in 6 of 66 cases (9.1%).

### 3.2. Subperiosteal/orbital abscess

Contrast-enhanced computed tomography of the orbit was performed in 60 cases (90.9%), magnetic resonance imaging in 1 case (1.5%), and both imaging studies in 4 cases (6.1%). The mean volume of the abscesses was 2598.4 mm³ (range: 30.2–10,372.9 mm³). Thirty-one eyes (72.1%) of the 43 patients with abscesses required surgical abscess drainage, 11 of whom received abscess drainage combined with endoscopic sinus surgery. In an ROC curve analysis for abscess volume as a predictor of surgical abscess drainage, the optimal volume of abscess cutoff value was 1714 mm³ with a sensitivity of 71%, specificity of 80%, and area under the ROC curve of 0.79 (Fig. 2).

### 3.3. Antibiotic treatment

All patients were treated using intravenous broad-spectrum antibiotics. Antibiotic coverage was adjusted as bacterial culture results were obtained. The mean (± SD) duration of hospitalization was 11.0 (±10.9) days; median was 9 days (range: 2–77 days). The mean (± SD) duration of intravenous antibiotics was 15.4 (±10.9) days; median was 14 days (range: 2–76 days); 39 patients (59.1%) were switched from intravenous to oral antibiotic treatment when they were discharged to outpatient care. The mean (± SD) duration of oral antibiotics was 20.7 (±57.0) days; median was 10 days (range: 3–366 days).
3.4. Visual acuity outcomes

The mean (± SD) pre-treatment VA of the affected eye was 0.82 (± 0.77) logMAR. After treatment, the mean (± SD) VA at discharge significantly improved with a 0.5 (± 0.85) logMAR (P < .001), whereas post-treatment VA at the last follow-up did not, with a mean (± SD) VA of 0.48 (± 0.85) logMAR (P = .77). The improvement in the mean Hertel exophthalmometer values is shown in Table 5. The mean (± SD) duration of follow-up time was 13.0 (± 23.6) months; median was 4.4 months (range: 0.5–123.3 months).

Univariate analysis for predictors of post-treatment visual outcome is illustrated in Table 6. Multivariate analysis based on

Table 3
Organisms isolated from abscess (n=30).

| Organisms                                      | No. of isolates |
|-----------------------------------------------|-----------------|
| Single organism                               | 26              |
| Mixed organisms                               | 4               |
| Gram-positive                                 |                 |
| Staphylococcus aureus                         | 8               |
| Staphylococcus epidermidis                    | 4               |
| Streptococcus pneumoniae                     | 1               |
| Alpha-hemolytic streptococcus (group D)       | 1               |
| Gamma-hemolytic streptococcus (not group D)   | 1               |
| Beta-hemolytic streptococcus (not group A, B, D) | 1               |
| Gram-negative                                 |                 |
| Klebsiella pneumoniae                         | 4               |
| Pseudomonas aeruginosa                        | 2               |
| Burkholderia pseudomallei                    | 2               |
| Burkholderia cepacia                         | 2               |
| Klebsiella ozaenae                            | 1               |
| Haemophilus influenzae                        | 1               |
| Pseudomonas stutzeri                          | 1               |
| Citrobactor diversus                          | 1               |
| Anaerobes                                     | 2               |
| Propionibacterium spp.                        | 2               |
| Bacteroides fragilis                          | 1               |
| Bacteroides ovatus                            | 1               |
| Proteus mirabilis                             | 1               |

Table 4
Improvement in VA and decrease in proptosis after treatment.

| Variables                                      | Mean ± SD | Paired differences |
|------------------------------------------------|-----------|--------------------|
| VA at admission—at discharge                  | 0.27 ± 0.56 | < .001             |
| VA at discharge—at last follow-up             | 0.01 ± 0.43 | .77                |
| Decrease in proptosis (mm) at admission—at discharge | 2.00 ± 2.25 | < .001             |
| Decrease in proptosis (mm) at discharge—at last follow-up | 0.82 ± 1.17 | .04                |

VA = visual acuity, SD = standard deviation.
Table 5
Univariate analysis for surgical abscess drainage.

| Variables        | N | Nonabscess drainage | Abscess drainage | P     | cOR (95% CI) | P  |
|------------------|---|---------------------|------------------|-------|--------------|----|
| Age              |   |                     |                  |       |              |    |
| 0–6 y            | 1 | 8 (8.3)             | 7 (22.6)         | .38   | 1            |    |
| >6–12 y          | 1 | 8 (8.3)             | 5 (16.1)         | 0.71  | 0.04–14.35   | .83|
| >12–18 y         | 0 | 0 (0.0)             | 3 (9.7)          | 1     | (omitted)    |    |
| >18 y            | 10| 83.4                | 16 (51.6)        | 0.23  | 0.02–2.15    | .20|
| ≤18 y            | 2 | 16.7                | 15 (48.4)        | .09   | 1            |    |
| >18 y            | 10| 83.3                | 16 (51.6)        | 0.21  | 0.07–1.14    | .07|
| Proptosis        |   |                     |                  |       |              |    |
| No               | 4 | 33.3                | 5 (16.1)         | .24   | 1            |    |
| Yes              | 8 | 66.7                | 26 (83.9)        | 2.60  | 0.56–112.07  | .22|
| VA at admission  |   |                     |                  |       |              |    |
| 20/20–20/40      | 6 | 54.5                | 5 (18.5)         | .12   | 1            |    |
| <20/40–20/160    | 2 | 18.2                | 11 (40.7)        | 6.60  | 0.97–44.93   | .05|
| ≤20/200          | 3 | 27.3                | 11 (40.7)        | 4.4   | 0.77–25.15   | .16|
| RAPD at admission|   |                     |                  |       |              |    |
| Negative         | 8 | 60.0                | 15 (53.6)        | .26   | 1            |    |
| Positive         | 2 | 20.0                | 13 (46.4)        | 3.47  | 0.62–19.33   | .16|
| Predisposing factor |   |                     |                  |       |              |    |
| Sinusitis        | 4 | 33.3                | 17 (54.8)        | .31   | 1            |    |
| Non-sinusitis    | 8 | 66.7                | 14 (45.2)        | 0.41  | 0.10–1.66    | .21|
| Referral case    |   |                     |                  |       |              |    |
| No               | 6 | 50.0                | 8 (25.9)         | .16   | 1            |    |
| Yes              | 6 | 50.0                | 23 (71.1)        | 2.88  | 0.72–11.52   | .14|
| Leukocytosis     |   |                     |                  |       |              |    |
| No               | 4 | 33.3                | 10 (32.3)        | 1.00  | 1            |    |
| Yes              | 8 | 66.7                | 21 (67.7)        | 1.05  | 0.25–4.33    | .95|
| Thrombocytosis   |   |                     |                  |       |              |    |
| No               | 10| 83.3                | 16 (51.6)        | .09   | 1            |    |
| Yes              | 2 | 16.7                | 15 (48.4)        | 4.69  | 0.88–24.99   | .07|
| Volume of abscess|   |                     |                  |       |              |    |
| ≤1514 mm³        | 8 | 80.0                | 8 (28.6)         | .008  | 1            |    |
| ≥1514 mm³        | 2 | 20.0                | 20 (71.4)        | 10.0  | 1.73–57.72   | .01|

CI = confidence interval, cOR = crude odd ratio, RAPD = relative afferent pupillary defect, VA = visual acuity.

Table 6
Univariate analysis of predictors associated with post-treatment visual outcome.

| Variables        | N | VA ≤20/50 at discharge | VA ≤20/200 at discharge |
|------------------|---|------------------------|-------------------------|
|                  |   | cOR (95% CI)           | P                       | cOR (95% CI)           | P  |
| Age              |   |                       |                         |                        |    |
| 0–6 y            | 1 | 1.06 (0.37–3.07)       | .91                     | 1.17 (0.30–4.57)       | .82|
| >6–12 y          | 1 | 2.29 (0.67–7.75)       | .19                     | 7.88 (1.80–34.38)      | .006|
| >12–18 y         | 1 | 0.5 (0.12–2.10)        | .34                     | 0.80 (0.17–3.82)       | .78|
| >18 y            | 1 | 1.04 (0.33–2.93)       | .98                     | 1.09 (0.27–4.36)       | .91|
| Proptosis        |   |                       |                         |                        |    |
| No               | 1 | 1.06 (0.37–3.07)       | .91                     | 1.17 (0.30–4.57)       | .82|
| Yes              | 1 | 2.29 (0.67–7.75)       | .19                     | 7.88 (1.80–34.38)      | .006|
| VA at admission  |   |                       |                         |                        |    |
| 20/20–20/40      | 1 | 0.5 (0.12–2.10)        | .34                     | 0.80 (0.17–3.82)       | .78|
| <20/40–20/160    | 1 | 1.04 (0.33–2.93)       | .98                     | 1.09 (0.27–4.36)       | .91|
| RAPD at admission|   |                       |                         |                        |    |
| Negative         | 1 | 1.06 (0.37–3.07)       | .91                     | 1.17 (0.30–4.57)       | .82|
| Positive         | 1 | 2.29 (0.67–7.75)       | .19                     | 7.88 (1.80–34.38)      | .006|
| Degree of proptosis |   |                       |                         |                        |    |
| ≤2 mm            | 1 | 0.67 (0.22–1.98)       | .47                     | 0.84 (0.21–3.38)       | .81|
| >2 mm            | 1 | 1.88 (0.41–8.60)       | .41                     | 1.24 (0.20–7.74)       | .82|
| Predisposing factor |   |                       |                         |                        |    |
| Sinusitis        | 1 | 0.67 (0.22–1.98)       | .47                     | 0.84 (0.21–3.38)       | .81|
| Non-sinusitis    | 1 | 1.88 (0.41–8.60)       | .41                     | 1.24 (0.20–7.74)       | .82|
| Subperiosteal abscess |   |                       |                         |                        |    |
| No               | 1 | 0.67 (0.22–1.98)       | .47                     | 0.84 (0.21–3.38)       | .81|
| Yes              | 1 | 1.88 (0.41–8.60)       | .41                     | 1.24 (0.20–7.74)       | .82|
| Orbital abscess  |   |                       |                         |                        |    |
| No               | 1 | 0.67 (0.22–1.98)       | .47                     | 0.84 (0.21–3.38)       | .81|
| Yes              | 1 | 1.88 (0.41–8.60)       | .41                     | 1.24 (0.20–7.74)       | .82|
| Volume of abscess|   |                       |                         |                        |    |
| ≤1514 mm³        | 1 | 1.06 (0.37–3.07)       | .91                     | 1.17 (0.30–4.57)       | .82|
| ≥1514 mm³        | 1 | 2.29 (0.67–7.75)       | .19                     | 7.88 (1.80–34.38)      | .006|
| Previous treatment|   |                       |                         |                        |    |
| No               | 1 | 0.67 (0.22–1.98)       | .47                     | 0.84 (0.21–3.38)       | .81|
| Yes              | 1 | 1.88 (0.41–8.60)       | .41                     | 1.24 (0.20–7.74)       | .82|

CI = confidence interval, cOR = crude odd ratio, RAPD = relative afferent pupillary defect, VA = visual acuity.
the stepwise regression model revealed that only pre-treatment VA ≤ 20/200 was a predictor for the post-treatment VA of 20/50 or worse. Presence of pre-treatment RAPD was the only predictive factor for the post-treatment VA of 20/200 or worse.

4. Discussion

The most common predisposing factor of orbital cellulitis in this study was sinusitis, which was similar to that reported in previous studies. However, the proportion of patients with sinusitis in our study was lower than that in previous studies. The tertiary center in which this study was conducted considers sinusitis-related orbital cellulitis to be a complicated disease because patients with uncomplicated orbital cellulitis can be treated by an ophthalmologist in a primary or secondary center or by an otolaryngologist. The high proportion of skin infection and dacryocystitis may be the result of including older patients, with a mean age of 42.1 years, in our study. We found a high rate of complications, including orbital abscess, subperiosteal abscess, and intracranial extension, when compared with a previous study. An abscess volume of ≥ 1514 mm³ was the optimal cutoff point for surgical abscess drainage. There was significant improvement in VA and decrease in proptosis after treatment. Pre-treatment VA ≤ 20/200 was a significant predictor for post-treatment VA of 20/50 or worse. Presence of pre-treatment RAPD was a predictor for post-treatment VA of 20/200 or worse. Therefore, early recognition of VA and RAPD was beneficial for the detection of optic nerve dysfunction due to compression, optic nerve stretching, and severe inflammation.

The proper prescription of effective antibiotics is the mainstay of treatment for orbital cellulitis. Broad-spectrum antibiotics were administered to our patients before pathogen identification. Therefore, the majority of antibiotic regimens were chosen to cover a broad spectrum of bacteria, including aerobes and anaerobes. A third-generation cephalosporin combined with clindamycin was used most frequently with antibiotics adjusted according to bacterial susceptibility and/or the infectious disease consultant’s suggestion. The yield of pus cultures from surgical drainage was highly positive, although it was more invasive and performed only when there were indications for surgery. Likewise, pus culture results in this study more commonly revealed single organisms than mixed organisms, which differed from a previous study, thereby suggesting an ineffective anaerobic media culture collection process. The most common bacterial pathogens isolated were Staphylococcus species and Streptococcus species, which was similar to that in a previous study.

Haemophilus influenzae had been a major pathogen in the pediatric group in the previous studies. Nevertheless, in our study, there was a low rate of H influenzae infection because of regular H influenzae vaccine immunization over the past 10 years in our country. Although blood cultures showed a low yield in this study, which was similar to that in a previous study, most patients had received antibiotic drugs before their transfer to our tertiary care center. Additionally, all patients presenting with orbital cellulitis had localized infection within the orbit.

In our study, surgical intervention indicated worsening of the condition in patients who had subperiosteal or orbital abscesses 48 to 72 hours after medical treatment or large abscesses affecting visual function. Surgical drainage of subperiosteal abscesses was performed according to Garcia and Harris’s study, especially for large abscesses. The ROC curve showed that a cutoff abscess volume of ≥ 1514 mm³ was a predictor for surgical drainage, which was within the range of abscess volume cut-offs between 1250 and 3800 mm³ in previous studies. However, we also evaluated the patients’ pre-treatment vision and subsequent improvement after antibiotic administration before making the decision for surgical intervention. In our study, oculoplastic surgeons mostly performed traditional external subperiosteal abscess drainage as it offers adequate visibility and effective drainage despite leaving a visible scar.

Surprisingly, subperiosteal abscesses or orbital abscesses were not a poor prognostic factor for the inferior post-treatment visual outcome in this study because our center had 2 oculoplastic surgeons who could perform emergency surgical abscess drainage. In addition, prompt recognition and appropriate treatment of orbital cellulitis and abscesses are crucial. However, an orbital abscess, possibly affecting the optic nerve, is a poor prognostic factor.

Although bacterial orbital cellulitis is a serious disease affecting visual morbidity and is a leading cause of mortality, adequate treatment in terms of intravenous antibiotics and surgical intervention can significantly improve VA and decrease proptosis at discharge. Although VA was not significantly different between the day of discharge and a median 4.4-month follow-up, the degree of proptosis decreased significantly at the last follow-up. To our knowledge, patients could follow-up their vision at primary or secondary care centers.

The limitations of this study include its retrospective nature and selection bias which occurred because the study was conducted at a major tertiary care center and had missing data. Additionally, the VA measurement method was not accurate because of the patients’ illness status. Further studies with a larger number of pediatric patients or adult patients are warranted to determine the strong predictors for surgical intervention and treatment outcome in each age group. Prospective studies are required, involving participants who can inform their VA, in addition to a similar protocol of intravenous antibiotics and follow-up dates to eliminate the confounding factors.

In conclusion, the most common predisposing cause of orbital cellulitis in this study was sinusitis. We inferred that abscess volume was the only significant predictor of surgical drainage. Our study also provides evidence that pre-treatment VA and the status of RAPD are most predictive of the visual outcome. Therefore, clinicians should be aware that patients with orbital cellulitis can develop permanent vision loss. Close monitoring of their visual function, early detection of complications and disease progression, and prompt management are necessary.

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Author contributions

Study concept and design: OA and SA; Acquisition of data: OA, SA, and NS; Analysis and interpretation of data: OA, SA, and NS; Drafting the manuscript: OA, SA, and NS; Revising the manuscript critically for important intellectual content: OA, SA, and NS; Study supervision: OA, SA, and NS. All authors had full access to all of the data in this study and take responsibility for the integrity of the data and the accuracy of the data analysis.
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