Surgical Treatment of Rhinosinusitis-Related Orbital Complications: Factors Affecting Irreversible Blindness

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Abstract: If left untreated, rhinosinusitis can rarely cause a devastating complication irreversible blindness (IB). Despite new technologies in endoscopic sinus surgery and use of new broad-spectrum antibiotics, IB outcome is still a problem for surgically treated orbital complication of paranasal sinus infection (OCPSI) patients, and factors leading to IB outcome are not actually known. The aim of this study was to assess the factors leading to the IB outcome for surgically treated OCPSI patients. Results of 25 surgically treated OCPSI patients in our clinic were combined with surgically treated OCPSI patients reported through the PubMed database search from the year 2007. Patients were divided into 2 groups: IB group and recovery group. Patients having at least 1 immune status-related additional risk factor (ARF) were more common in the IB group, having an at least 1 ARF had 1.683 risk value of IB outcome (RR: 1.683, $P = 0.006$). IB patients had statistically significant higher mean (21.87 ± 40.35, $P = 0.005$) time interval (days) (TI) between onset of ophthalmological symptoms and surgical intervention compared to recovery group patients (2.92 ± 2.53). ROC curve analysis for an estimation of IB outcome according to the TI value demonstrated that a cut-off value of $\geq$2.5 days had the ideal sensitivity (87.5%) and specificity (71.9%) that resulted in IB outcome. (80.5% power, $P = 0.008$) IB and recovery group patients did not differ according to orbital complication type according to Chandler's classification ($P = 0.492$) and white blood cell count status ($P = 0.584$). In conclusion, OCPSI patients with ARFs and delayed admission after onset of orbital symptoms have a higher risk of IB outcome. These patients deserve prompt evaluation and early surgical intervention to prevent blindness. With future studies, new surgical criteria, including the ARF status and onset of ophthalmological symptoms ($\geq$2.5 days) may be added to classical surgical criteria to prevent IB for OCPSI cases.

Key Words: Blindness, orbital abscess, orbital cellulitis, rhinosinusitis, subperiosteal abscess

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Rhinosinusitis is a common disease that mostly recovers without sequela. If left untreated, this benign condition can cause irreversible blindness (IB) with affecting the orbital tissues and even can cause mortality with intracranial complications. Orbital complications of paranasal sinus infections (OCPSI) can be divided into 5 classes according to Chandler's classification[1]:

(1) Inflammatory edema (preseptal cellulitis)
(2) Orbital cellulitis (OC)
(3) Subperiosteal abscess (SPA)
(4) Orbital abscess (OA)
(5) Cavernous sinus thrombosis (CST): In fact, this complication can be classified in the same group with intracranial complications.[2,3]

IB is a catastrophic complication of OCPSIs. Before the antibiotic era, 20% of OCPSI cases had developed permanent visual loss. At the beginning of the 21st century, a 3% to 11% risk of this devastating outcome was published.[4] In the last 5 years, despite suitable use of new broad-spectrum antibiotics and early surgical interventions, still a 5.5% to 10% incidence of IB for OCPSI cases was published.[2,5,6]

The implication of delayed surgery on IB outcome has been mentioned by several authors,[7–9] but in fact factors affecting the final visual acuity for surgically treated OCPSI cases have not been evolved, yet.

In this study, we investigated the preoperative measures (presence of the additional health conditions, time interval (TI) between onset of the ophthalmological symptoms and surgical intervention, white blood cell count status and type of the orbital complication according to Chandler's classification) that led to the IB outcome for surgically treated OCPSI cases.

METHODS

Local ethical committee approval was acquired for the current study. Surgically treated sinogenic orbital complication cases between December 2013 and December 2017 in our tertiary center Otorhinolaryngology Department were taken to the current study. Exclusion criteria were:

(1) Patients having orbital complications due to the causes other than rhinosinusitis such as insect bites or trauma.
(2) Patients with orbital apex syndrome without inflammatory orbital signs or with few inflammatory signs such as limited eyelid swelling.
(3) Cases with pure odontogenic rhinosinusitis (clear history of dental pain before the onset of ophthalmic symptoms with a clear physical finding of dental origin such as dental caries).

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(4) Cases with invasive fungal infections.
(5) Cases with no involvement of the paranasal sinuses in the computerized tomography (CT) or magnetic resonance imaging (MRI) findings despite a history of upper respiratory tract infection.
(6) Patients who were treated by only medical treatment options without a surgical intervention.
(7) Patients with sinogenic intracranial complications.

CST cases were also excluded, since this type of complication can also be regarded as an intracranial complication.[2,3]

Retrospective medical chart review was done for surgically treated OCPSI cases without any exclusion criteria. Every patient was consulted with the ophthalmology and radiology departments. Adult patients were hospitalized in our otorhinolaryngology department, whereas pediatric cases were hospitalized in the pediatric infectious disease unit. Intravenous antibiotics were started according to the recommendations of the infectious disease department. Cultures from the pus or tissue specimens were taken from all patients and the antibiotic regimen could be changed according to the results.

Indications for surgical intervention were:

(1) Failure of clinical improvement in 24 to 48 hours of duration despite suitable antibiotic regimen,
(2) Subperiosteal ($>500-1250\,mm^3$, with ophtalmoplegia or decreased visual acuity) or OA formation,
(3) Initial visual acuity of less than 20/60.[5,9,10]

All patients were operated under general anesthesia. Functional endoscopic sinus surgery for drainage of the involved sinuses was done for all patients. Lamina papyracea (LP) was broken anteriorly just behind the uncinate process and elevated through the space between LP and orbital periosteum to drain the abscess for SPA cases. After excision of the LP, incision to the orbital periosteum was also done to drain the intraorbital abscess for OA cases. For cases with OC, LP excision was done without orbital periosteum incision and abscess drainage. External incision with the combination of the transnasal approach was performed for eyelid abscess or superior SPA cases. The diagnosis of type of the orbital complication according to Chandler's classification was done according to CT and/or MRI findings consulted with the radiologists as well as with physical and intraoperative findings.

Review of the medical charts focused on the following parameters:

(1) Additional risk factor (ARF): Health conditions affecting the immunological status, such as immunosuppression, diabetes mellitus, chronic renal failure, cancer, and others were investigated. Pregnancy was also regarded as an ARF since this situation can worsen an underlying sinonasal disease by vascular engorgement and increased glandular activity by hormonal effect.[9]
(2) TI between onset of ophthalmological symptoms and surgical intervention: According to the history of the patient, timing of the surgery after the beginning of the eye symptoms such as periorbital hyperemia, eyelid swelling, impairment of eye movements, diplopia, retroorbital or orbital pain and decreased vision apart from the sinogenic symptoms (nasal discharge, nasal obstruction, headache and facial pain) was investigated.
(3) White blood cell count status (WBCS): Laboratory findings for all patients were reviewed and initial white blood cell count statuses (increased vs normal) were obtained.
(4) Type of the orbital complication: Chandler's classification[1] was used to classify the type of the orbital complication.
(5) Final visual acuity status: Final visual acuity status was assessed before discharge from the hospital and 1 month after discharge by the ophthalmologist. IB was regarded as only light perception or no light perception in the affected eye.

To increase the patient number and make a powerful statistical analysis, our results were combined with the results of the related articles explored through a PubMed database search using the keywords of orbital complication and sinusitis, orbital cellulitis and sinusitis, subperiosteal abscess and sinusitis and orbital abscess and sinusitis starting from the year 2007.

Patients were separated into IB group and Recovery group (cases with full recovery regarding the final visual acuity).

Patients with decreased final visual acuity w/o IB were taken to the neither groups. These 2 groups were compared regarding the parameters mentioned above.

Statistical Analysis

Statistical analysis was performed using SPSS version 23 (SPSS Inc, IBM, Armonk, NY). Data were shown as mean ± SD for continuous variables and the number of cases was used for categorical ones. Data were controlled for normal distribution using the Shapiro-Wilk test. Chi-square test was used to compare the number of cases with ARFs and increased white blood cell count between IB and Recovery groups. Chi-square test was also used to compare the frequencies of the type of orbital complications between these 2 groups. Relative risk value was used to estimate the risk value between groups according to having ARFs. The Mann-Whitney *U* was used to compare the TI values between IB and Recovery groups. Receiver operating characteristic (ROC) analysis was used to evaluate the timing of surgery as a predictor of IB outcome and estimating a cut-off value for the timing of the surgery resulting in IB.

RESULTS

There were 25 patients who were undergone surgical intervention due to OCPSI. The mean age was 24.6 ± 19.94 (min: 2, max: 92). There were 13 (52%) pediatric (≤16 years old) and 12 (48%) adult patients. 14 (56%) patients were females and 11 (44%) were males. Functional endoscopic sinus surgery was performed for all patients. External approach combined with transnasal approach was performed for 3 (2 with upper eyelid abscess and 1 with superior SPA) cases. Three (12%) patients had IB sequela (Table 1). Other 22 (88%) patients recovered completely.

TABLE 1. Clinical and Demographic Characteristic of 3 Patients With Irreversible Blindness Outcome

Case No	Age-sex	Orbital Complication Type	ARF	TI (Days)	White Blood Cell Count Status
1	28-female	OC	Pregnancy	4	Increased
2	92-female	OA	Chronic renal failure, old age	5	Normal
3	15-male	OC	Immunosuppressive medication due to Crohn disease	3	Normal

ARF, additional risk factor; OA, Orbital abscess; OC, Orbital cellulitis; TI, time interval between onset of ophthalmological symptoms and surgical intervention.

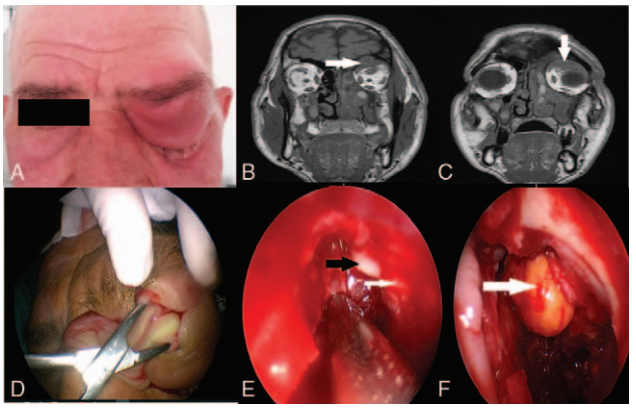


FIGURE 1. (A) Clinical appearance of the patient (case 2) was presented. (B) White arrow shows the upper eyelid abscess in T1 weighted MRI scan. (C) White arrow demonstrates the left orbital abscess in T1 weighted MRI scan. (D) External incision and drainage of the upper eyelid abscess was presented. (E) Black arrow demonstrates the endoscopic transnasal drainage of the left orbital abscess after incision to the orbital periosteum, white arrow shows the left orbital fat tissue. (F) White arrow presents the left orbital fat tissue after incision to the orbital periosteum and drainage of the abscess.

Selected Case Presentations

Case 1

Pregnant patient with OC and IB was presented before.[9]

Case 2

Fifty-nine years old otherwise healthy male patient admitted with severe left eyelid edema. He had an upper respiratory tract infection 5 days before treated with intramuscular ampicillin-sulbactam 1 g twice a day. Swelling of his left eyelid had started 2 days before and on admission his left eye was totally closed (Fig. 1A). Visual acuity and extraocular muscle movements could not be assessed. On the T1-weighted MRI, he had upper eyelid abscess (Fig. 1B) and superior OA (Fig. 1C) as well as inflammation of left-sided maxillary, ethmoid and frontal sinuses. His white blood cell count was 12400/mL. An urgent surgery was planned. External incision was performed to drain the upper eyelid abscess (Fig. 1D) and functional endoscopic sinus surgery was performed for drainage of the left-sided maxillary, ethmoid and frontal sinuses. Orbital decompression with drainage of the intraorbital abscess was also performed endoscopically (Fig. 1E and F). Piperacillin-tazobactam 4500 mg 3 times a day by intravenous route was started according to the suggestion of infectious disease department. There was no microorganism isolation in the culture specimens. Three days after the operation, his eyelid swelling recovered. On the 14th day of the treatment, he recovered totally without any visual sequela.

Case 3

Ninety-two-year-old female patient admitted with right-sided eyelid edema, diplopia and blindness in the right eye. In her previous medical history, she was learned to have chronic renal failure for 15 years treated with routine hemodialysis. She had an upper respiratory tract infection history 2 weeks ago treated with an unknown antibiotic by oral route. Five days before admission, right periorbital swelling had started and in the morning before admission diplopia with right-sided blindness had occurred. In her physical examination, there was ophthalmoplegia to all directions (Fig. 2A-D), visual acuity of the right eye was only light perception. She had 10.860/mL white blood cell count. CT of the paranasal sinuses presented right-sided maxillary sinusitis (Fig. 2E) and T1-weighted contrast-enhanced MRI demonstrated the right-sided OA (Fig. 2F). Under general anesthesia,

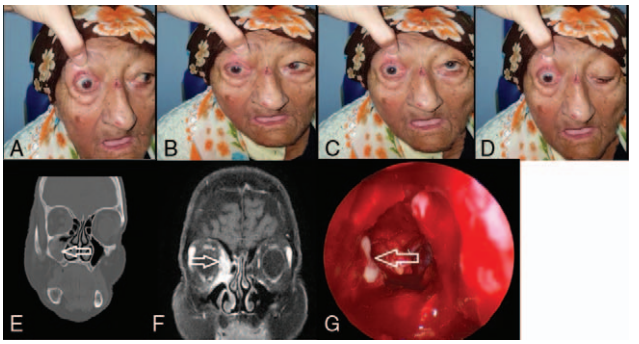


FIGURE 2. (A-D) Total ophthalmoplegia of the patient (Case 3) in all directions was presented. € White arrow demonstrates the right sided maxillary rhinosinusitis on coronal computerized tomography scan. (F) White arrow show the right sided orbital abscess in contrast enhanced T1 weighted MRI scan. (G) White arrow shows the endoscopic transnasal drainage of the orbital abscess.

functional endoscopic sinus surgery was performed to drain the right maxillary sinus. After excision of the LP and incision to the orbital periosteum right-sided OA was drained (Fig. 2G). Piperacillin-tazobactam 2250 mg 3 times a day (renal dose) was started by infectious disease department. There was no microorganism isolation in the culture specimens. One month after the surgery, visual acuity was still light perception without any improvement.

Additional Risk Factors

Study Results

In the recovery group (22 patients), 6 (27.2%) patients had diabetes mellitus (DM) as ARF. In the IB group, all 3 patients had ARFs (Table 1).

Combination With the Literature

14 articles[5–8,11–20] presented the results of surgically treated OCPSI cases with ARF status. Among them, 10 patients had ARFs: 6 DM,[5–7] 1 chronic lymphocytic leukemia,[11] 1 neonatal asphyxia,[15] 1 DM and immunocompromised due to renal transplantation,[17] 1 chemotherapy due to stage IV colon cancer.[6] From these, 6 cases[5–7] had IB, 4 cases[5,11,15,17] recovered without sequela. Combined with our results; IB group had statistically significant higher number of cases with ARFs ($P = 0.006$). Surgically treated patient with OCPSI and at least 1 ARF had a 1.683 risk value to have IB outcome compared to patients without any ARF (RR = 1.683, $P = 0.006$) (Table 2).

Time Interval Between Onset of Ophthalmological Symptoms and Surgical Intervention

Study Results

TI was 4 ± 1 in the IB group, and 1.86 ± 0.46 in the recovery group.

Combination With the Literature

10 articles[7,11,12,14–16,18,21–23] presented the results of surgically treated OCPSI cases with mentioned TI. Five cases[7,23] had IB. Joining with our results, IB group patients had statistically significant higher (mean ± SD = 21.87 ± 40.35, $P = 0.005$) TI compared to Recovery group patients (mean ± SD = 2.92 ± 2.53) (Fig. 3).

ROC curve analysis demonstrated that according to the area under curve values (AUC: 0.805, lower bound = 0.593, upper bound = 1.000, $P = 0.008$), TI had 80.5% power for differentiating irreversible blind and recovery cases. For an estimation of IB outcome, according to the TI; a cut-off value of equal to or greater

TABLE 2. Comparison of the Parameters Between Irreversible Blindness and Recovery Group Patients

	Irreversible Blindness Group n (%)	Recovery Group n (%)	*P*
ARF			
Positive N (%)	9 (69.3)	10 (24.3)	0.006* (RR = 1.683)
Negative N (%)	4 (30.7)	31 (75.6)	
TI (mean ± SD)	21.87 ± 40.35	2.92 ± 2.53	0.005*
Orbital Complication Type			
OC	4 (30.7)	71 (21.1)	0.492
SPA	7 (53.8)	233 (69.3)	
OA	2 (15.3)	32 (9.5)	
White blood cell count status			
Increased n (%)	1 (33.3)	19 (55.9)	0.584
Normal n (%)	2 (66.6)	15 (44.1)	

ARF, additional risk factor; OA, Orbital abscess; OC, Orbital cellulitis; RR, Relative risk value; SPA, Subperiosteal abscess; TI, time interval between onset of ophthalmological symptoms and surgical intervention.
*Statistically significant.

than 2.5 days had the ideal sensitivity (87.5%) and specificity (71.9%) results (Fig. 4).

Orbital Complication Type

Study Results

There were 11 (44%) patients with OC, 11 (44%) patients with SPA and 3 (12%) patients with OA. 2 of the OC (18.1%) and 1 (33.3%) of the OA patients had IB, others recovered without sequela.

Combination With the Literature

Thirty eight articles[2,3,5,6,8,10–42] demonstrated the results of surgically treated OCPSI cases according to the orbital complication type. There were 10 patients with IB. Among them, 7 had SPA, 2 had OC and 1 had OA. Combined with our results, there was no statistically significant difference between IB and recovery group patients regarding OC, SPA and OA type orbital complication frequencies ($P = 0.492$) (Table 2).

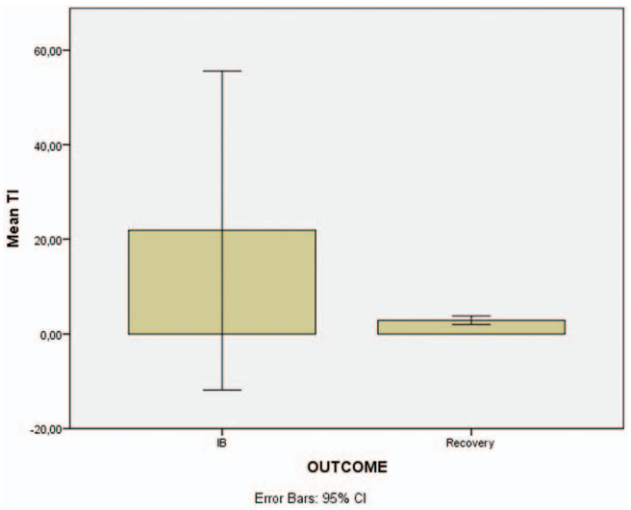


FIGURE 3. Comparison of mean TI between onset of orbital symptoms and surgical intervention between groups by error-bar chart (IB, irreversible blindness; TI, time interval (days); CI, confidence interval).

White Blood Cell Count Status

Study Results

A total of 14 (56%) patients had normal, whereas 11 (44%) patients had increased WBCS. Two patients (14.2%) with normal WBCS and 1 (9.1%) patient with increased WBCS had IB outcome.

Combination With the Literature

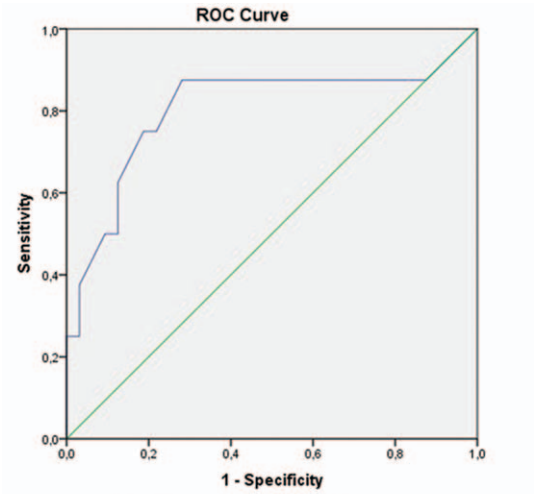
Eight articles[11,13,15,28,30,35,39,43] presented the visual acuity results of surgically treated patients with OCPSI according to WBCS. Summation with our results demonstrated that there was no statistically significant difference between IB and recovery group patients regarding increased WBCS patient numbers ($P = 0.584$) (Table 2).

DISCUSSION

IB is a rare outcome of paranasal sinus infection-related orbital complications, but if occurs, it can cause great morbidity with impairment of binocular vision and visual field. In the last 5 years, the incidence of IB outcome for OCPSI cases was published to be 0 to 10%[2,5,6,43] A slightly higher (12%) IB outcome in our study can be due to our study populations including only surgically treated cases. The pathogenesis of visual loss for OCPSI patients is thrombophlebitis of valveless orbital veins causing retinal ischemia or optic neuropathy as a reaction to the neighboring infection.[9]

Generally, indications of surgical intervention for OCPSI can be regarded as: failure of clinical improvement in 24 to 48 hours of antibiotic treatment, abscess formation and decrement in visual acuity to less than 20/60.[9] Whereas, small (<500–1250 mm^3) and medially located SPA cases without ophtalmoplegia or visual loss can also be cured medically without surgical intervention.[6,10,41,44,45] In our study, surgically treated SPA cases were also larger ones or smaller ones without clinical improvement despite 24–48 hours of medical treatment.

Timing of surgery for OCPSI cases is mentioned to be critical to prevent IB outcome by various authors,[7–9] but a statistical comparison was not performed before. OC patients with lesser duration of orbital symptoms before admission were shown to have lesser orbital complications including keratopathy, endophthalmitis, panophthamitis and SPA formation.[46] Chaudhry et al[7] presented 4 cases with OCPSI and IB outcome. The common characteristics of the patients were delayed admission after onset of ophthalmological symptoms, and the authors attributed the IB outcome to delayed diagnosis and intervention. Teinzer et al[47] postulated that delayed



Area Under the Curve

Test Result Variable(s): TI

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
,885	,108	,008	,593	1,000

The test result variable(s): TI has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Coordinates of the Curve

Test Result Variable(s): TI

Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
,0000	1,000	1,000
1,5000	,875	,875
2,5000	,875	,281
3,2500	,750	,219
3,7500	,750	,188
4,5000	,625	,125
5,5000	,500	,125
6,5000	,500	,094
8,5000	,375	,031
12,0000	,250	,031
19,5000	,250	,000
72,5000	,125	,000
121,0000	,000	,000

The test result variable(s): TI has at least one tie between the positive actual state group and the negative actual state group.

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

FIGURE 4. ROC curve analysis for estimating the cut-off TI value that resulted in IB outcome (IB: irreversible blindness, TI: time interval (days) between onset of orbital symptoms and surgical intervention).

surgery is a risk factor for recurrent surgery for OCPSI cases. Cheng et al[48] proposed delayed surgical intervention $\geq$ 48 hours after admission as a predisposing factor for longer hospital stay but not IB outcome, so they emphasized that delayed surgical intervention still appears to be a safe option. In fact, this finding may be spurious, because they did not have any case of surgically treated OCPSI with IB outcome to make a comparison. According to our results, timing of surgery after onset of orbital symptoms for OCPSI cases is very crucial to prevent visual loss; surgically treated OCPSI patients with IB outcome had a statistically significant higher mean TI compared the recovery group, and patients having ophthalmological symptoms $\geq$ 2.5 days are at risk of IB outcome (sensitivity = 87.5% and specificity = 71.9).

Having an ARF is another important issue that can affect the surgical success rate for patients with OCPSI. In the study of Erickson et al[6] 71.4% patients with OC or SPA had predisposing factors and 2 of the 3 patients with IB had comorbidities including stage IV colon cancer and DM. DM was also demonstrated to be seen more common in increasing OCPSI stage according to Chandler's classification,[2] and it was presented as a predisposing factor for IB in patients with SPA.[5] In our study, 24% patients had DM and all 3 patients with IB outcome had additional comorbidities. According to our results, surgically treated patients with OCPSI and ARF possess 1.683 times risk of IB outcome compared to patients without any comorbidities. OCPSI patients having immune state comorbidities merit prompt evaluation and early surgical intervention to prevent IB.[5]

The effect of WBCS on the formation or outcome of OCPSI is controversial. Ketenci et al[5] reported leukocytosis in a few (36%) patients with SPA, whereas Chang et al[2] found 68.7% patients with OCPSI had leukocytosis, but they could not find any relationship between WBCS and disease severity according to Chandler's classification. WBC count was stated to be both usable[49,50] and unusable[6] marker for distinguishing cellulitis and abscess cases by different authors. Regarding determination of OCPSI cases needing surgical intervention; Nation et al[44] and Ryan et al[51] stated that mean WBC count could not to be a predictor of decision to drain SPA surgically, whereas Beech et al[43] reported WBCS as a useful marker for choosing pediatric OCPSI patients deserving surgical intervention. According to our study results, WBCS was not a predictor of IB outcome for surgically treated OCPSI cases.

The severity of orbital complication may be thought to have an impact on visual acuity results for OCPSI cases. In fact the pathogenesis of blindness in OCPSI is thrombophlebitis of valveless orbital veins and optic neuritis as a reaction to nearby infection[9] which can be seen in OC, SPA, OA, and CST cases according to Chandler's classification. According to our results, IB outcome was not related to the type of the orbital complication. In our study, CST cases were excluded, since this complication can be classified as an intracranial complication.[2,3] It is important to mention that this type of complication can be a risk factor for IB.[2]

In conclusion, surgically treated OCPSI patients with additional immune status related co-morbidities and delayed admission after onset of orbital symptoms have a higher risk of IB outcome. These patients deserve prompt evaluation and early surgical intervention to prevent blindness. With future studies, new surgical criteria including the ARF status and onset of ophthalmological symptoms ($\geq$2.5 days) may be added to classical surgical criteria to prevent IB for OCPSI cases.

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