

# Clinical features and outcome of preseptal and orbital cellulitis in hospitalized children: Four years experience

## Hastanede yatan çocuklarda preseptal ve orbital selülitin klinik özellikleri ve seyri: Dört yıllık tecrübe

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### ABSTRACT

Preseptal and orbital cellulitis are relatively more common in children than adults. If left untreated orbital cellulitis is more serious, and can cause vision loss and life-threatening conditions. Thus, it's early differentiation from preseptal cellulitis is critical for initiating prompt treatment. In this study, contrasting features of preseptal and orbital cellulitis are highlighted to aid physicians in the management of these infections. Medical records of 62 children admitted to hospital with the diagnosis of preseptal or orbital cellulitis between January 2011 to July 2015 were retrospectively evaluated. In this series, preseptal cellulitis (81%) was observed more commonly than orbital cellulitis (19%). The average age of the patients with orbital cellulitis was higher than that of the cases with preseptal cellulitis ( $8.1 \pm 4$  v.s  $4.8 \pm 3$  years,  $p=0.009$ ). Ophthalmoplegia and proptosis were observed in the 58% of the patients with orbital cellulitis. Sinusitis was the most common predisposing factor. Orbital magnetic resonance imaging (MRI) revealed subperiosteal abscesses in three cases who were previously diagnosed as preseptal cellulitis by orbital computerized tomography (CT). Antibiotherapy with ampicillin-sulbactam with or without ceftriaxone was successful in 95.2% of the patients. The longer treatment period was required for orbital cellulitis when compared to preseptal cellulitis (median duration of 14 vs 29 total antibiotic days, respectively,  $p<0.001$ ). Sinus abscess drainage was needed in two cases of orbital cellulitis and abscess drainage in one case of preseptal cellulitis. During follow-up, any serious complications were not observed. Accurate diagnosis and prompt treatment of orbital cellulitis can prevent its serious complications, MRI can aid in difficult cases so as to differentiate orbital cellulitis from preseptal cellulitis.

**Keywords:** Orbital, preseptal, cellulitis, imaging

### INTRODUCTION

Preseptal and orbital cellulitis are much more com-

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### ÖZ

Preseptal ve orbital selülit çocuklarda erişkinlere kıyasla sık görülmektedir. Orbital selülit tedavisiz bırakıldığında görme kaybı veya yaşamı tehdit eden durumlarla sonuçlanabilen daha ciddi bir enfeksiyondur, preseptal selülitten erken ayırt edilmesi doğru yaklaşım ve tedavinin bir an önce başlatılması açısından kritiktir. Bu çalışmada, preseptal ve orbital selülitin ayırt edici özellikleri vurgulanarak hekimin ayırıcı tanıyı erken yapmasına yardımcı olmak amaçlandı. Ocak 2011 ve Haziran 2015 tarihleri arasında hastaneye preseptal veya orbital selülit tanısı ile yatırılan 62 çocuğun tıbbi kayıtları retrospektif olarak incelendi. Bu seride preseptal selülit (%81) orbital selülitte (%19) kıyasla daha sıklıkla görüldü. Orbital selülitli olgularda ortalama yaş preseptal selülitli olgulara göre daha büyüktü ( $8,1 \pm 4$ 'e karşın  $4,8 \pm 3$  yıl,  $p=0,009$ ). Orbital selülitli olguların %58'inde oftalmopleji ve proptozis görüldü. En sık predispozan faktör sinüzitti. Daha önce bilgisayarlı tomografi ile preseptal selülit tanısı alan üç olguda manyetik rezonans görüntüleme subperiosteal apseler olduğunu gösterdi. Ampisilinsulbaktam tek başına veya seftriakson ile beraber verildi, hastaların %95,2'sinde başarılı oldu. Orbital selülitte daha uzun süreli tedavi gerekti (ortalama 14 güne karşın, 29 toplam antibiyotik günü  $p<0,001$ ). İki orbital selülit olgusunda sinüs drenajı, bir preseptal selülit olgusunda apse drenajı gerekti. Hastaların ayaktan takibinde herhangi bir komplikasyon gözlenmedi. Orbital selülitin erken tanısı ve doğru tedavisi ağır komplikasyonların gelişmesini önler, orbital selülitin preseptal selülitte ayırt edilmesinde klinik bulgular yetersiz olduğunda kontrastlı orbital MRI yardımcı olabilir.

**Anahtar kelimeler:** Orbital, preseptal, görüntüleme, selülit

mon in young children than older ones and adults. In addition, preseptal cellulitis is more frequent than orbital cellulitis<sup>1,2</sup>. Preseptal cellulitis is an infection

involving anterior portion of the orbital septum, whereas orbital cellulitis involves ocular adnexal structures posterior to the orbital septum. Orbital cellulitis is more serious. It can lead to blindness by causing occlusion of central retinal artery or vein, or by damaging the optic nerve. Other serious complications of orbital cellulitis are endophthalmitis, cavernous sinus thrombosis, meningitis, intracranial abscesses, and even death that generally results from the delay in the diagnosis and initiation of appropriate treatment<sup>3</sup>.

Although preseptal and orbital cellulitis yield different clinical outcomes, initial symptoms such as pain, eyelid swelling and erythema are the mutual presenting symptoms. For this reason, the clinical differentiation of these two conditions can be initially difficult. If thorough history taking and physical examination including an ophthalmological evaluation could not help to differentiate difficult cases from advanced disease, contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) scanning can aid in differential diagnosis.

Here we used our experiences to characterize features of orbital and preseptal cellulitis in order to make a differentiation between them, and aimed to highlight importance of early diagnosis and treatment of orbital cellulitis.

## **MATERIAL and METHODS**

The study was performed in Marmara University Training and Research Hospital in Istanbul, Turkey. In this retrospective study, data were collected by reviewing medical records of all admissions for preseptal and orbital cellulitis in children below 18 years of age who were referred to us between January 2011 and July 2015. Data regarding clinical diagnosis, age, gender, predisposing factors, clinical manifestations, laboratory and radiological data, antibiotic treatment, surgical procedure, length of hospital stay and complications were recorded. Local Ethics Committee approval was obtained for this study.

Diagnosis of preseptal and orbital cellulitis was made according to recorded clinical findings. Hyperemia, tenderness and swelling of periorbital tissues were accepted as undifferentiating features, whereas chemosis, proptosis, limitation of extraocular movements of eyes, pain with eye movement are accepted as peculiar signs of orbital cellulitis. Radiological investigation was performed for the diagnosis of 60 cases with contrast-enhanced orbital MRI and/or CT. Daily ophthalmological examination had been made for patients with orbital cellulitis until regression of abscesses was demonstrated on control orbital MRI. Laboratory investigations including complete blood count (CBC), C-reactive protein (CRP) levels, blood cultures were assessed, and antibiotherapy regimens were also noted.

Statistical analyses were performed with NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA). When data were analyzed beside descriptive statistical methods (mean, standard deviation, median, frequency, rate, minimum, maximum), for the comparison of two groups of parameters that are not normally distributed, Mann-Whitney U test was used. For the comparison of qualitative data Fisher-Freeman-Halton test, Fisher's exact test, and Yates' Correction Continuity test (Yates' corrected chi-square) was used. Levels of significance were set at  $p < 0.01$  and  $p < 0.05$ .

## **RESULTS**

A total of 62 children with preseptal cellulitis (n=50; 81%) or orbital cellulitis (n=12; 19%) were identified and included in this study. Mean ages (mean±standard deviation [SD]) of the patients with orbital and preseptal cellulitis were  $8.1 \pm 4$  and  $4.8 \pm 3$  years, respectively ( $p=0.009$ ). Presentation of orbital cellulitis was in the fall or winter for six cases (n=6; 50%), in the spring or summer for other six cases (n=6; 50%), whereas the most of cases with preseptal cellulitis were seen in the spring or summer (70%). Eye involvement was seen in 59 cases (95.2%). Bilateral involvement was noted only in three cases with preseptal cellulitis and conjunctivitis. Baseline symptoms of all

cases were hyperemia, tenderness and swelling of periorbital tissues. In the orbital cellulitis group seven cases (58.3%) had ophthalmoplegia ( $p=0.001$ ), three of them also had proptosis ( $p=0.035$ ) (Figure 1). Sinusitis effected ten cases (83.3%) with orbital cellulitis, and nine cases (18%) with preseptal cellulitis

( $p<0.001$ ). Other predisposing factors include conjunctivitis, dental abscesses, varicella zoster infection, herpes simplex virus infection of adjacent skin, insect bite were recorded only in the preseptal cellulitis group (Figure 2). Demographic characteristics of the patients were summarized in Table 1.



Figure 1. A case of orbital cellulitis with proptosis.



Figure 2. A case of preseptal cellulitis with herpetic lesion.

Table 1. Demographic characteristics of preseptal and orbital cellulitis.

Cellulitis		Total	Orbital	Preseptal	P
Gender n (%)	Male n (%)	32 (51.6)	8 (66.7)	24 (48)	<sup>a</sup> 0.401
	Female n(%)	30 (48.4)	4 (33.3)	26(52)	
Age (median, years)	mean±SD	5.43±3.59	8.13±4.26	4.79±3.13	<sup>d</sup> 0.009**
	Min-Max	0.25-16 (5)	3-15 (7.75)	0.25-16 (4.25)	
	(Median)				
<b>Predisposing factors</b>	Sinusitis n (%)	19 (30.6)	10 (83.3)	9 (18.0)	<sup>b</sup> 0.001**
	Conjunctivitis n (%)	8 (12.9)	1 (8.3)	7 (14.0)	<sup>b</sup> 1.000
	Dental abscesses n (%)	5 (8.1)	-	5 (10.0)	<sup>b</sup> 0.573
	Herpes simplex virus infection n (%)	2 (3.2)	-	2 (4.0)	<sup>b</sup> 1.000
	Varicella zoster infection n (%)	2 (3.2)	-	2 (4.0)	<sup>b</sup> 1.000
	Insect-bite n (%)	1 (1.6)	-	1 (2.0)	<sup>b</sup> 1.000
<b>Laboratory findings</b>	White blood count (WBC)				<sup>d</sup> 0.084
	mean±SD	12761.13±4867.46	14483.33±5816.25	12347.80±4582.52	
	Min-Max (Median)	800-23400 (12300)	800-22800 (13550)	3900-23400 (11000)	
Absolute neutrophil count (ANC)	mean±SD	8080.65±4776.85	11183.33±5058.90	7336.00±4442.73	<sup>d</sup> 0.006**
	Min-Max	100-21400	200-17900	100-21400	
	(Median)	(6950)	(10500)	(6600)	
C-reactive protein (CRP)	mean±SD	39.79±66.22	69.99±78.18	32.54±61.72	<sup>d</sup> 0.020*
	Min-Max	0,4-393	1-247	0.4-393	
	(Median)	(17.45)	(37)	(13.5)	
Surgical therapy n (%)		3 (4.8)	2 (16.7)	1 (2.0)	<sup>b</sup> 0.093
Total antibiotic days	mean±SD	17.82±9.82	30.08±12.74	14.88±6.16	<sup>d</sup> 0.001**
	Min-Max	6-49	10-49	6-35	
	(Median)	(15)	(28.5)	(14)	
Hospitalization days	mean±SD	9.31±6.14	19.42±6.44	6.88±2.55	<sup>d</sup> 0.001**
	Min-Max	3-35	10-35	3-14	
	(Median)	(7)	(20.5)	(7)	

<sup>a</sup>Yates' Continuity Correction, <sup>b</sup>Fisher Exact Test, <sup>c</sup>Fisher Freeman Halton Test, <sup>d</sup>Mann Whitney U Test, \*\* $p<0.01$ , \* $p<0.05$

Mean white blood cell counts of the patients with orbital cellulitis and preseptal cellulitis were  $14483 \pm 5816/\text{mm}^3$  and  $12347 \pm 4582/\text{mm}^3$ , respectively ( $p=0.084$ ). On the other hand, mean absolute neutrophil count was significantly higher in the orbital cellulitis group, than in the preseptal group [ $11183 \pm 5058/\text{mm}^3$  and  $7336 \pm 4442/\text{mm}^3$  respectively, ( $p=0.006$ )]. Similarly, median CRP value was significantly higher in the orbital cellulitis group than preseptal cellulitis group [37 mg/L (range:1-247 mg/L) v.s. 13.5 mg/L (range: 0,4-393 mg/L), respectively ( $p=0.020$ )] (Table 1).

For diagnosis beside clinical assessment, contrast enhanced orbital MRI and/or CT were used in 60 cases. In 13 cases with preseptal cellulitis, because of inadequate response to treatment, or if their cranial CT obtained without contrast or with low quality, contrast enhanced orbital MRI was performed. Of those orbital cellulitis with subperiosteal abscess were detected in three patients (Figure 3).

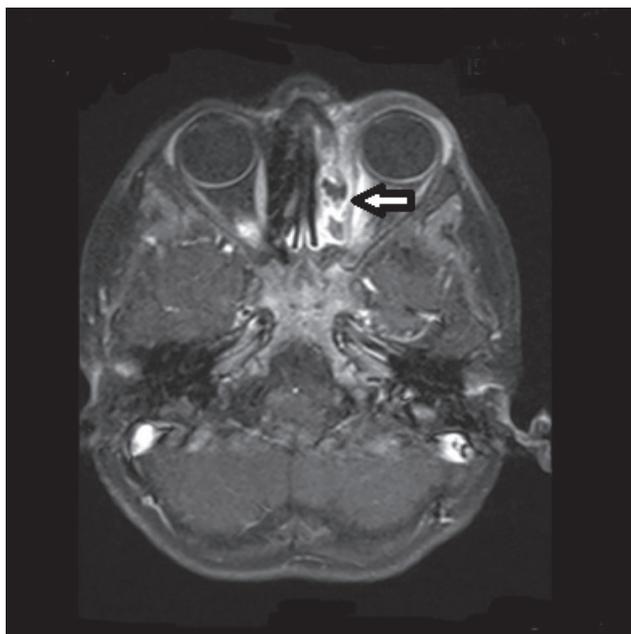


Figure 3. Orbital MR of same case in figure 1, arrow show subperiosteal abscesses.

Blood cultures were taken from 36 of 62 cases, and only 4 (%11) of them were positive. Methicillin-sensitive *Staphylococcus aureus* (MSSA) was isolated in 2, *Streptococcus pyogenes* in one, methicillin-

resistant *Staphylococcus epidermidis* (MRSE) in one patient. Three of four positive cultures were obtained from the patients in the orbital cellulitis group. The cultures of sinus drainage material remained sterile, all three cases had previously used antibiotherapy.

Ampicillin-sulbactam ( $n=35$ ) and ampicillin-sulbactam plus ceftriaxone ( $n=27$ ) were the most preferred treatment options. In three cases with orbital cellulitis; clinical response to treatment was deemed to be insufficient since high fever, elevated acute phase reactants and widening of peri-orbital tissue swelling persisted over three days of treatment. So antibiotherapy regimens were revised for each patient. Vancomycin+cefoperazone-sulbactam ( $n=1$ ), vancomycin+meropenem ( $n=1$ ) and vancomycin+piperacillin-tazobactam ( $n=1$ ) were used, so cure achieved. In four cases, acyclovir was added to antibacterial treatment for infection of adjacent skin with varicella zoster or herpes simplex virus. In three cases, surgical intervention, abscess drainage was required. Median duration of oral plus intravenous antibiotic use for orbital cellulitis and preseptal cellulitis were 28.5 days (range: 10-49 days) and 14 days (range: 6-35 days), respectively ( $p<0.001$ ). Median length of hospital stay was 20.5 days (range: 10-35 days) for orbital cellulitis and 7 days (range: 3-14 days) for preseptal cellulitis ( $p<0.001$ ). No serious complication was observed during the hospital stay and six months after discharge.

## DISCUSSION

Soft tissue infections around the eye globe are common and usually benign in nature. However, orbital cellulitis which may be missed during the initial evaluation of the patients can be severe and complicated. Despite the fact that our study included limited number of children, evaluation of these cases are important to stress major differences between milder (preseptal) and the more serious form of the disease (orbital cellulitis). By this way, the consequences of late diagnosis can be prevented and the proper treatment can be initiated.

In this study relative frequency of orbital cellulitis among infections involving in and around eye globe was similar to those reported in previous studies (4% to 28%)<sup>4-6</sup>. Mean age of the children with orbital and preseptal cellulitis in our study was compatible to the literature data, that the mean age of children with orbital cellulitis is greater than that of children with preseptal cellulitis<sup>7</sup>. This finding may reflect the sequential maturation of the sinuses, since infection of sinuses is the major predisposing factor for orbital cellulitis. Ethmoid sinus, the most involved sinus in orbital cellulitis, is present at birth and has a rapid growth phase between 3 and 8 years of age while maxillary sinus has rapid growth between 7 and 12 years of age<sup>8</sup>.

As well-known, sinusitis is the most important predisposing factor for preseptal and orbital cellulitis. Orbital cellulitis almost always occurs as a complication of sinusitis with extension of the infection into the orbit. In the study of Botting et al, 91% of 35 cases of orbital cellulitis had acute sinusitis at diagnosis<sup>1</sup>. Ethmoid sinus was demonstrated as the main source of the orbital infections in other reports<sup>2,9</sup>. In our study, sinusitis was associated with 83.3%, and 18% of the patients with orbital, and preseptal cellulitis, respectively. Dental abscesses, conjunctivitis, varicella zoster and herpes simplex virus infection of the adjacent skin, and insect-bite were other predisposing factors for preseptal cellulitis which may be associated with broken skin barrier. Similar to other series, the number of our patients with preseptal cellulitis reached the peak incidence during spring and summer<sup>6,10</sup>. This is assumed to be due to predisposing factors such as insect bite and conjunctivitis which are common in these seasons.

Hyperemia, tenderness and swelling of periorbital tissues are symptoms of preseptal cellulitis. But when the treatment is delayed, infection can spread to the posterior part of the orbital septum. Chemosis, proptosis, pain with eye movement, decreased visual acuity, and limitation of eye movements are known as predictors for orbital cellulitis although these symptoms are not seen uniformly in all

cases. Rudloe et al reported that 50.5% of 35 cases with orbital cellulitis did not experience these symptoms<sup>11</sup>. Similarly, our seven (58.3%) cases with orbital cellulitis had ophthalmoplegia, and three of them (25%) also had proptosis. In the remaining 5 patients, diagnoses were actually based on radiological appearance. Since our patients were children, the expression of painful eye movements may be underestimated. Daily ophthalmological examination was made for patients with orbital cellulitis during hospitalization but none of them had problems with vision acuity.

Similar to previous data, though not statistically significant, mean white blood cell count was higher in the orbital cellulitis group which did not aid in the diagnosis<sup>9</sup>. However, the absolute neutrophil count and median CRP level were statistically significantly elevated in orbital cellulitis .

In our study, contrast-enhanced orbital MRI was found to be more sensitive than CT to make a differentiation between orbital and preseptal cellulitis. However, since these two methods were not compared with controlled studies, clinical experience of our radiologists established the diagnoses of orbital and preseptal cellulitis. Magnetic resonance imaging is especially recommended for tracking the progression of soft tissue disease and it is also preferred to save pediatric patients from the side effects of radiation exposure<sup>12</sup>. But in young children it may require sedation. Guidelines from United Kingdom describe indications for radiologic imaging with CT as follows: inability to evaluate vision; ophthalmoplegia, proptosis, bilateral edema or worsening visual acuity; no improvement after 24 hours of administration of intravenous antibiotics; fever not resolved within 36 hours; or evidence of central nervous system involvement<sup>13</sup>.

Blood cultures were positive in four cases for MSSA, *S. pyogenes*, and MRSE. According to the reports of previous studies *Staphylococcus aureus*, *Haemophilus influenzae* type b (Hib), and *Streptococcus* species are the most common organisms in preseptal and

orbital cellulitis<sup>14</sup>. Because of widespread vaccination against Hib; *Staphylococcus aureus* and *Streptococcus* species account for 75% of etiologic agents of periorbital infections<sup>15</sup>. On the other hand, MSSA, MRSA and even some streptococcus species constitute the skin flora which can not be differentiated from contaminants. Despite the low rate of positivity, obtaining blood culture is recommended before antibiotic treatment.

As is known, the main indications for surgical intervention are poor response to antibiotic treatment, evidence of an abscess >10 mm in diameter, visual impairment and to intracranial spread of the infection<sup>17,18</sup>. Because of the effectiveness of antibacterial therapy, only three cases required surgical intervention. Mortality rate of orbital cellulitis was reported as 17% which was associated with blindness before the antibiotic era<sup>19</sup>. Nowadays, orbital cellulitis results in loss of vision, and death in 3-11, and 1-2 % of the patients, respectively<sup>20</sup>.

As expected, median duration of antibiotic use and length of hospital stay for orbital cellulitis were longer than preseptal cellulitis. This is because of clinical and laboratory response were slow in orbital cellulitis. We also preferred of intravenous treatment and close follow-up in hospital with daily ophthalmological examination for orbital cellulitis. Sinus drainage was performed in two patients with orbital cellulitis and they treated with vancomycin+meropenem and vancomycin+piperacillin-tazobactam. Drainage of the abscesses was required in one patient with preseptal cellulitis. No other serious complication was observed during the hospital stay and outpatient control.

## CONCLUSION

Major limitations of our study is its the retrospective design and relatively small number of cases. Nevertheless, we can conclude that both preseptal and orbital cellulitis can be prevented by timely treatment of sinusitis with appropriate antibiotic. In cases where clinical differentiation of orbital and

preseptal cellulitis is difficult, or in condition of delayed response to treatment in complicated cases, radiologic imaging with contrast induced MRI can be good choice.

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