Preseptal and orbital cellulitis: 15-year experience with sulbactam ampicillin treatment

İlker Devrim[1], Güler Kanra[1], Ateş Kara[1], A. Bülent Cengiz[1], Mehmet Orhan[2]
Mehmet Ceyhan[1], Gülten Seçmeer[1]
Departments of [1]Pediatrics, and [2]Ophthalmology, Hacettepe University Faculty of Medicine, Ankara, Turkey

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The infection of the orbita and ocular tissues can result in severe local and systemic complications. We aimed to determine the predisposing factors for preseptal and orbital cellulitis, the clinical and routine laboratory differences between orbital and preseptal cellulitis, and the change in the spectrum of the pathogens and the antibiotics used in the last 10 years.

One hundred thirty-nine patients, hospitalized in Hacettepe University Faculty of Medicine Children's Hospital between 1 January 1990 and 31 December 2003 with diagnosis of periorbital or orbital cellulitis, were reviewed retrospectively. Ten of the patients (7%) had orbital and 129 (93%) had preseptal cellulitis. The male/female ratio was 1.7:1. The average age (mean±standard deviation) was 5.7±4 years. The seasonal distribution was most marked in spring and fall periods.

When compared with preseptal cellulitis, the mean blood cell count, erythrocyte sedimentation rate and C-reactive protein levels were significantly higher in patients with orbital cellulitis. *Staphylococcus aureus* was isolated in 13 (41.9% of total microbiologically confirmed cases), coagulase-negative staphylococcus in 8 (25.8%), and *H. influenza* type b in 2 patients (6%). Thirty out of 77 clinical sample cultures (39%) were positive.

In clinical studies, etiological agents of orbital and preseptal cellulitis could be identified in only 20-30% of cases, so in clinical practice treatment is usually empiric. We observed that sulbactam-ampicillin was a safe and effective choice of treatment in orbital and preseptal cellulitis in our cases.

Key words: preseptal cellulitis, orbital cellulitis, ampicillin sulbactam.

The orbita is susceptible to infections because of the anatomic location and neighboring structures. Infection of the orbita and ocular tissues can result in severe ocular and systemic complications[1]. The orbital septum, which is formed by the extension of connective tissue of the periosteum to the upper and lower eyelids, acts as an anatomical barrier to the spread of preseptal infection to orbital tissue. Periorbital cellulitis is defined as the inflammation of the anterior parts of the orbital septum. The infection involves both the pre- and postseptal regions in case of orbital cellulitis[2-4]. The stages of orbital infection are divided into the following five groups: inflammatory edema, orbital cellulitis, subperiosteal abscess, orbital abscess, and cavernous sinus thrombosis[5].

Differentiation of orbital and preseptal cellulitis is not easy in every case, so our objective in this report was to point out some useful clinical features and laboratory findings. We also aimed to determine the predisposing factors for preseptal and orbital cellulitis, the clinical and laboratory differences between orbital and preseptal cellulitis, and change in the spectrum of the pathogens and antibiotics used in the last 10 years. In addition, we aimed to determine the effectiveness of sulbactam-ampicillin (SAM) as a first-line empiric therapy for these infections.

Material and Methods

One hundred thirty-nine patients, hospitalized at Hacettepe University Faculty of Medicine Children's Hospital between 1 January 1990 and 31 December 2003 with diagnosis of periorbital or orbital cellulitis, were reviewed retrospectively from their medical files.

Patients with periorbital edema, erythema, and increase in local hyperemia but without proptosis, ophthalmoplegia and visual impairment were defined as having preseptal cellulitis. The patients with proptosis, ophthalmoplegia and visual impairment were defined as having orbital cellulitis.

The demographic features of all patients, including age, gender, admission date (season, month, day, year) and possible risk factors such as conjunctivitis, upper respiratory tract infections, sinusitis, odontogenic infections and dental carries, history of trauma and allergy, and presence or absence of hordeolum, were recorded.

Results of routine laboratory tests including white blood cell count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were recorded.

Statistical data was analyzed with SPSS for Windows release 11.5 (SSPS Inc, USA) and the non-parametric data were analyzed with chi-square test.

Results

One hundred thirty-nine patients with diagnosis of periorbital or orbital cellulitis who were hospitalized and followed in Hacettepe University Faculty of Medicine Children's Hospital were reviewed. Ten of the patients (7%) had orbital and 129 (93%) preseptal cellulitis. Fifty-one of the 139 patients (36.7%) were female and 88 (63.3%) were male. The average age (mean±standard deviation) was 5.7±4 years.

When the seasons of admission were compared from 1990-2003, 31 (22.3%) patients were admitted to the hospital in winter, 40 (28.8%) in spring, 31 (22.3%) in summer, and 37 (26.6%) in fall (Fig. 1). The seasonal distribution was most striking in children under one year, in whom 60% of admissions were in winter. Beyond this period, hospitalization was higher in the fall and spring, probably due to the windier weather in these periods and the increased amount of circulating pollens.

When the risk factors for orbital infections were evaluated, conjunctivitis and upper respiratory tract infections were the most striking factors; local lesions that destroy intact skin and tooth abscess were the other risk factors (Table I).

Clinical sinusitis defined as patients with postnasal drainage with diurnal coughing and sensitivity (tenderness) over the maxillary area was present in 38 (29.5%) out of 129 patients

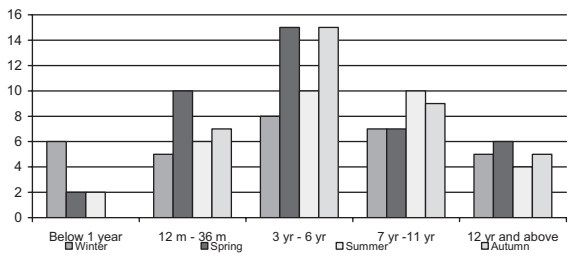

Fig. 1. Seasonal age distribution of cases.

Table I. Risk Factors and Associated Diseases in Orbital and Preseptal Cellulitis

Risk factors	Present	Absent	**Total**
Conjunctivitis	103 (74.1%)	36 (25.9%)	139 (100%)
Upper respiratory tract infections	52 (37.4%)	87 (62.6%)	139 (100%)
Focal lesions on the face or near the orbita*	35 (25.2%)	104 (74.8%)	139 (100%)
Sinusitis	34 (24.5%)	105 (75.5%)	139 (100%)
Odontogenic infections and dental caries**	27 (19.4%)	112 (80.6%)	139 (100%)
Trauma	15 (10.8%)	124 (89.2%)	139 (100%)
Similar history	9 (6.5%)	130 (93.5%)	139 (100%)
Allergy	5 (3.6%)	134 (96.4%)	139 (100%)
Hordeolum	5 (3.6%)	134 (96.4%)	139 (100%)

*35 cases in following groups: acne 8 (5.8%), insect bite 8 (5.8%), herpetic lesions 8 (5.8%), lesions secondary to the trauma 8 (5.8%), impetigo 8 (5%), and acute dacryocystitis 1 (0.7%).

**18 out of 27 patients had 18 dental caries and the remaining had dental abscess.

with preseptal and 3 (30%) out of 10 patients with orbital cellulitis. Radiologically defined sinusitis (as evidenced by fluid-air levels, hypertrophy of mucosa and decrease in the inflation of sinuses) was present in 48 (37.2%) patients with preseptal cellulitis and in 7 (70%) patients with orbital cellulitis.

The mean white blood cell count of patients with preseptal cellulitis was 12620±5919/mm^3 (mean±standard deviation [SD]). When compared with preseptal cellulitis, the mean blood cell count, ESR and CRP levels were significantly higher in patients with orbital cellulitis ($p<0.01$) (Table II).

Pus and swab cultures from secretion of conjunctiva were taken from 81 of 139 patients (58.3%). Thirty cultures (37%) yielded the following microorganisms: *Staphylococcus aureus* in 13 (43%) cases and coagulase-negative staphylococcus in 8 (26.5%) cases. Blood cultures were taken from 137 of 139 (98.6%) patients and only 9 of them (7%) were positive. In blood cultures, coagulase-negative staphylococcus was isolated in 8 (88.8%) patients, whose pus cultures also yielded coagulase-negative staphylococcus (Table III). Eight of 9 positive blood cultures were from orbital cellulitis cases.

Sulbactam–ampicillin (SAM), a beta-lactamase inhibitor combined amino-penicillin, was used as a first-line empiric antimicrobial drug for the treatment for preseptal and orbital cellulitis (in 89.9% of cases) at the dose of 100 mg/kg/day. All patients completely recovered without any severe side effects that resulted in drug discontinuation. A glycopeptide, vancomycin, was added in the starting regimens in 4 (3%) complicated cases, such as intracranial abscesses accompanying orbital cellulitis. Intravenous acyclovir was combined in the initial regimens for 7 (5%) patients with herpetic lesions.

Surgical procedures were applied in 2 (1.6%) patients with preseptal cellulitis (sinus surgery and sinus endoscopy), and in 5 (50%) patients with orbital cellulitis (intracranial abscess drainage, orbital surgery, and ethmoidectomy).

The duration of hospitalization of cases with orbital cellulitis was 16.6±9.03 days longer compared to patients with preseptal cellulitis (5.2±2.2 days).

Discussion

Periorbital and orbital cellulitis were seen more frequently in children than adults[6]. Unless appropriately treated, periorbital and orbital cellulitis can result in optic neuritis, optic

Table II. Laboratory Findings of the Study Groups

	Hemoglobin (g/dl)	White blood cell count (WBC/mm^3)	ESR (mm/hour)	CRP (mg/dl)
Total (mean±SD)	11.8±1.90	12620±5919	36.95±27.1	3.9±6.07
Preseptal cellulitis (mean±SD)	11.8±1.95	12322±5064	39.6±26.1	3.67±5.93
Orbital cellulitis (mean±SD)	11.7±1.14	17620±11945	67.22±29.4	7.78±7.73
		P<0.01	P<0.01	P<0.01

ESR: Erythrocyte sedimentation rate. CRP: C-reactive protein.

Table III. Isolated Agents in Periorbital and Orbital Cellulitis

	Pus cultures n (%)	Blood cultures n (%)	Total n (%)
Staphylococcus aureus	13 (43%)	–	13 (32.5%)
Coagulase–negative staphylococcus	8 (26.6%)	8 (88.8%)	8 (20%)
Streptococcus pneumoniae	3 (10%)	1 (11.2%)	4 (10%)
Haemophilus influenzae type b	2 (6.6%)	–	2 (5%)
Streptococcus (other than pneumococci)	2 (6.6%)	–	2 (5%)
Others*	2 (6.6%)	–	3 (2.5%)
Total	30 (77.5%)	9 (22.5%)	39 (100%)

*1 *Klebsiella pneumoniae* and 1 *Pseudomonas aeruginosa*.

atrophy, blindness, cavernous sinus thrombosis, superior orbital fissure syndrome, orbital apex syndrome, meningitis, brain abscess, subdural empyema and even death[7,8]. Before the antibiotic era, it was reported that orbital cellulitis had a fatality rate of 17% associated with blindness in one-quarter of the patients[9].

There is a close relationship between orbital infections and infections of the paranasal sinuses[10-12]. The ratio of sinusitis accompanying orbital infections was reported as ranging between 81%-91%[13,14]. In our study, clinically diagnosed sinusitis was seen in 34 patients (24.5%) and radiologically confirmed sinusitis in 48 patients (37.2%). Upper respiratory tract infections were seen in a higher proportion (52 patients, 37.4%). The rate of sinusitis may seem to be lower than expected, but it could be a result of the higher number of patients under six years old, in whom the development of the sinuses was not yet completed. It must be noted that even in patients with preseptal cellulitis, sinusitis must be ruled out radiologically.

The other important risk factors are trauma, odontogenic infections and skin lesions near the eye. Conjunctivitis was seen in 74.1% (103 patients) and was seen as the most prominent risk factor, but it could be only an early accompanying symptom of orbital/ preseptal cellulitis.

White blood cell count, ESR and CRP levels and the ratio of fever and presence of lymphadenopathy were higher in the orbital cellulitis group than in preseptal cellulitis. In addition to the symptoms of periorbital edema, erythema, increase in local hyperemia associated with proptosis, ophthalmoplegia and visual impairment, the presence of lymphadenopathy and fever and higher levels of the white blood cell count, ESR and CRP levels can help in the differentiation of preseptal and orbital cellulitis. However, it must be kept in mind that all of those high values of routine laboratory results can be seen in preseptal cellulitis. Blood cultures revealed positive results in only one case of preseptal cellulitis, which was correlated with pus results. It could be concluded that routine blood cultures had no effect on clinical follow-up of patients with preseptal cellulitis.

In our study, 30 (37%) of 81 pus cultures and 9 (7%) of 137 blood cultures were positive. Israele[7], Mills[15] and Kanra[3] found that cultures taken from 75%, 50% and 43% of patients, respectively, were found to be positive. Generally, the main isolated organism was *Haemophilus influenzae*[7,15-17] and *Streptococcus pneumoniae*[18]. With the introduction of the *H. influenzae* type B (Hib) vaccines in routine immunization schema, recent studies indicated a definite decline in Hib-related orbital and periorbital infection[14,19,20]. In our study from 1990-2003, *S. aureus* was the predominant etiologic agent (41%), followed by coagulase-negative *S. aureus* (25%), *S. pneumoniae* (9%) and *H. influenzae* (6%), which is consistent with the study made by Kanra[3] at the same hospital from 1983-1993. There was no methicillin-resistant staphylococcus isolate in this group. Although in recent years, increased community-acquired methicillin-resistant *S. aureus* (MRSA) infection has been reported, none was isolated in our series.

The major antimicrobial therapy was SAM. Patients were administered parenteral antibiotics for five days on average followed by seven additional days of oral antibiotics. The hospitalization duration was significantly longer in orbital cellulitis (16 days on average) than preseptal cellulitis (5 days on average), and this period was not affected by the etiologic agents.

In conclusion, we can say that orbital infections require urgent diagnosis and treatment. We conclude that SAM can be the first choice of antibiotics in orbital infections with good tissue penetration and spectrum. The major advantage of SAM is early discharge from hospital and the availability of an oral formulation of SAM, or amoxicillin-clavulanate as a concurrent treatment following intravenous SAM treatment. Secondly, Hib vaccination should be suggested to families to prevent not only the meningitis but also other potentially severe infections including preseptal cellulitis.

REFERENCES

1. Uzcategui N, Warman R, Smith A, Howard CW. Clinical practice guidelines for orbital cellulitis. J Pediatr Ophthalmol Strabismus 1998; 35: 73-79.
2. Lessner A, Stern AG. Preseptal and orbital cellulitis. Infectious Dis Clin North Am 1992; 6: 933-952.
3. Kanra G, Secmeer G, Gonc EN, Ceyhan M, Ecevit Z. Periorbital cellulitis: a comparison of different treatment regimens. Acta Paediatr Jpn 1996; 38: 339-342.
4. Mawn AL, Jordan RD, Donahue PS. Preseptal and orbital cellulitis. Ophthalmol Clin North Am 2000; 13: 324-335.

5. Chandler JR, Langenbrunner DJ, Stevens ER. The pathogenesis of orbital complications in acute sinusitis. Laryngoscope 1970; 80: 1414-1428.
6. Howe L, Jones NS. Guidelines for the management of periorbital cellulitis/abscess. Clin Otolaryngol Allied Sci 2004; 29: 725-728.
7. Israele V, Nelson JD. Periorbital and orbital cellulitis. Pediatr Infect Dis J 1987; 6: 404-410.
8. Jackson K, Bekar SR. Clinical implications of orbital cellulitis. Laryngoscope 1986; 96: 568-574.
9. Gamble RC. Acute inflammation of the orbit in children. Arch Ophthalmol 1993; 10: 483-497.
10. Curtin HD, Rabinov JD. Extension to the orbit from paraorbital disease. Radiol Clin North Am 1998; 36: 1201-1213.
11. Diaz I, Bamberger DM. Acute sinusitis. Semin Respir Infect 1995; 10: 14-20.
12. Gellady AM, Shulman ST, Ayoub EM. Periorbital and orbital cellulitis in children. Pediatrics 1978; 61: 272-277.
13. Weiss A, Friendly D, Elgin K, et al. Bacterial periorbital and orbital cellulitis in children. Ophthalmology 1983; 90: 195.
14. Barone SR, Aiuto LT. Periorbital and orbital cellulitis in the Haemophilus influenzae vaccine era. J Pediatr Ophthalmol Strabismus 1997; 34: 293-296.
15. Mills R. Orbital and periorbital sepsis. J Laryngol Otol 1987; 101: 1242-1247.
16. Antoine GA, Grundfast KM. Periorbital cellulitis. Int J Pediatr Otorhinolaryngol 1987; 13: 273-278.
17. Powell KR, Kaplan SB, HAll CB, Nasello MA, Roghmann KJ. Periorbital cellulitis. Am J Dis Child 1988; 142: 853-857.
18. Herbert L. Conjunctivitis, keratitis and infections of periorbital structures. In: Armstrong D, Cohen J (eds). The Infectious Diseases (1st ed). Philadelphia: Mosby Harcourt; 1999: 11.1-11.8.
19. Donahue SP, Schwartz G. Preseptal and orbital cellulitis in childhood. A changing microbiologic spectrum. Ophthalmology 1998; 105: 1902-1905; discussion 1905-1906.
20. Balamurali KA, Jayakrisha A, Nathalie A, Larry S. Periorbital and orbital cellulitis before and after the advent of Haemophilus influenzae type B vaccination. Ophthalmology 2000; 107: 1450-1453.
21. O'Brien TP, Green WR. Periocular infections. In: Feigin RD, Cherry JD (eds). Textbook of Pediatric Infectious Diseases (4th ed). Philadelphia: W.B. Saunders Company; 1998: 1273-1278.