Original Investigation / *Özgün Araştırma*

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Complications of Acute Bacterial Rhinosinusitis in Children: A Single Tertiary Care Center

Çocuklarda Akut Bakteriyel Rinosinüzit Komplikasyonları: Üçüncü Basamak Tek Merkez Deneyimi

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Abstract

Objective: Acute bacterial rhinosinusitis (ABRS) can lead to serious complications, especially when treated inadequately. In this study, we evaluated pediatric patients treated for sinusitis complications by the Pediatric Infectious Diseases Department at Dokuz Eylül University Faculty of Medicine.

Material and Methods: Patients who were consulted with a preliminary diagnosis of sinusitis complication and hospitalized between January 2014 and March 2021 were retrospectively analyzed. Patients who developed complications due to causes other than ABRS were excluded. Those with isolated orbital complications and those with intracranial complications were compared.

Results: Seventeen patients who were hospitalized for ABRS were included in the study. Median age was 13 (min 3-max 17) years, the majority were (14, 82.4%) males. There were isolated orbital complications in 11 (64.7%), intracranial complications in 4 (23.5%), and both orbital and intracranial complications in two (11.8%) patients. *S. pneumoniae*, *Streptococcus* spp. and *S. constellatus* grew in cultures obtained intraoperatively from three patients. Age (median 16 and 12, p= 0.048), number of surgeries (median 2 and 0, p= 0.027), length of stay (median 44 and 8, p< 0.001), total follow-up time (median 110 and 30, p= 0.015), absolute neutrophil count (median 16700/mm^3 and 7000/mm^3, p= 0.020) and C-reactive protein (229.0 ± 62.9 and 65.7 ± 57.4, p< 0.001) were found to be higher in patients with intracranial complications. Endoscopic sinus surgery was performed in one patient. Three patients were operated by neurosurgery, and one patient by the ophthalmology department. A sequela of drop foot was observed in a patient with subdural empyema and meningitis. Only one patient died after discharge due to her underlying disease.

Öz

Giriş: Akut bakteriyel rinosinüzit (ABRS) özellikle yeterli tedavi edilmediğinde ciddi komplikasyonlara yol açabilir. Bu araştırma ile Dokuz Eylül Üniversitesi Tıp Fakültesi Çocuk Enfeksiyon Hastalıkları tarafından sinüzit komplikasyonu nedeniyle tedavi edilen hastaların demografik, klinik özelliklerini, tedavi ve sonuçlarını değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Ocak 2014 ile Mart 2021 tarihleri arasında sinüzit komplikasyonu ön tanısı ile danışılan ve yatarak tedavi gören hastalar retrospektif olarak incelendi. ABRS dışındaki nedenlere bağlı olarak komplikasyon geliştiği düşünülen hastalar dışlandı. Yalnızca orbital komplikasyonu olanlar ile intrakranyal komplikasyonu bulunanlar karşılaştırıldı.

Bulgular: ABRS komplikasyonu nedeniyle yatarak tedavi edilen 17 hasta çalışmaya dahil edildi. Yaş medyanı 13 (3-17)'tü, çoğunluğu (14, %82.4) erkekti. Hastaların 11 (%64.7)'inde yalnızca orbital, dördünde (%23.5) yalnızca intrakranyal, ikisinde (%11.8) hem orbital hem intrakranyal komplikasyon mevcuttu. Üç hastanın intraoperatif elde edilen kültürlerinde *S. pneumoniae*, *Streptococcus* spp. ve *S. constellatus* üredi. İntrakranyal komplikasyonu bulunan hastaların yaşının daha büyük (medyan 16 ve 12, p= 0.048), cerrahi sayısı (medyan 2 ve 0, p= 0.027), yatış süresi (medyan 44 ve 8, p< 0.001) ve toplam izlem sürelerinin (medyan 110 ve 30, p= 0.015) daha fazla olduğu, başvuruda mutlak nötrofil sayılarının (medyan 16700/mm^3 ve 7000/mm^3, p= 0.020) ve C-reaktif protein (229.0 ± 62.9 ve 65.7 ± 57.4, p< 0.001) değerlerinin daha yüksek olduğu saptanmıştır. Yalnız bir hastaya endoskopik sinüs cerrahisi (ESC) uygulanmıştır. Üç hasta beyin cerrahisi, bir hasta göz hastalıkları bölümü tarafından opere edilmiştir. Takipte subdural ampiyem ve menenjit komplikasyonu olan bir hastada düşük ayak sekeli gözlenmiştir. Yalnızca

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Conclusion: Age, length of hospital stay, and surgical requirement in patients with intracranial complications are higher than those with only orbital complications. There may be sequelae in patients whose surgical needs are not met. However, there are cases in whom only conservative medical therapies were adequate. Randomized studies with larger numbers of patients are needed to obtain definitive data on optimal treatment methods and surgical indications for sinusitis complications in children.

Keywords: Acute bacterial rhinosinusitis, intracranial complications, orbital complications, pediatrics

bir hasta altta yatan hastalığı nedeniyle taburculuk sonrasında kaybedilmiştir.

Sonuç: İntrakranyal komplikasyonu bulunanların yaş, yatış süresi ve cerrahi gereksinimi yalnızca orbital komplikasyonu olanlardan daha fazladır. Cerrahi gereksinimi karşılanmayan hastalarda sekel kalabileceği gibi, yalnızca medikal tedavi ile kür sağlanan olgular da mevcuttur. Sinüzit komplikasyonlarının ideal tedavi yöntemi ve cerrahi endikasyonları konusunda kesin verilere ulaşılabilmesi için daha fazla hasta sayısıyla randomize çalışmalara ihtiyaç bulunmaktadır.

Anahtar Kelimeler: Akut bakteriyel rinosinüzit, intrakranyal komplikasyonlar, orbital komplikasyonlar, pediyatri

Introduction

Acute bacterial rhinosinusitis (ABRS) is a frequently observed condition in children. Five to ten percent of all viral upper respiratory tract infections result in ABRS (1-3). Despite the decrease in ABRS cases in recent years, there is an increase observed in the rate of orbital and intracranial complications (4).

If treated insufficiently, ABRS can lead to meningitis, osteomyelit, cavernous sinus thrombosis, epidural abscess, subdural empyema, intraparenchymal brain abscess or orbital abscess. These are often grouped as orbital complications (OC) and intracranial complications (IC) (5).

Orbital complications frequently occur as a result of the spread of ipsilateral acute ethmoiditis through lamina papyracea or hematogenous way (6). OCs have been defined under five categories by Chandler and are ranked as periorbital or preseptal cellulitis, orbital cellulitis, subperiosteal abscess, orbital abscess, and cavernous sinus thrombosis (7). In general, OCs do not result in death; however, they may lead to vision loss or ICs. Correct diagnosis and treatment are vital due to probable morbidities. Surgical approaches are gradually replaced by conservative treatment approaches in treatment (8). Presence of acute frontal sinusitis significantly raises the risk of intracranial complication. The infection may spread to the intracranial region directly through the frontal sinus posterior table, valveless diploic veins or septic embolism. High suspicion and quick treatment are of vital importance in order to prevent long-term complications.

Treatment management requires the participation of both ear-nose-throat and neurosurgery specialist and long-term intravenous antimicrobial treatment (6). Although rare, intracranial complications are important causes of morbidity and mortality in ABRS (5).

The most commonly known bacterial pathogens of acute rhinosinusitis are *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* (9). Pneumococci have decreased as agents subsequent to the extensive use of 7 and then 13-valent pneumococcus vaccines in ARBS and acute otitis media, and *H. influenzae* and *S. aureus* have become more widespread (4). However, microbiology of ABRS complications is different compared to that of uncomplicated ABRS. In retrospective studies conducted on children regarding the microbiology of complicated ABRS, polymicrobial infections are frequently seen. Non-pneumococci *Streptococcus* species (i.e., *Streptococcus milleri* group), other anaerobes and *Staphylococcus* species have been more frequently isolated than classic agents of ABRS. It is not known whether there is a difference between microbiological agents in patients with intracranial spread and in those with intraorbital or other types of complications (10,11).

In this study, it was aimed to evaluate the demographic and clinical characteristics of the patients and the treatments applied and their outcomes in those treated for sinusitis complications in our tertiary hospital.

Materials and Methods

A retrospective evaluation was made regarding patients aged 0-18 years treated as inpatients with a preliminary diagnosis of ABRS complication in Dokuz Eylül University, Pediatric Infectious Diseases Department between January 2014 and March 2021. Patients detected to have developed complications for reasons other than ABRS were excluded from the study. Data on age, sex, underlying disease, diagnosis related to sinusitis and complications, presenting symptoms and their durations, examination findings, laboratory values on presentation, radiological findings, antibiotic used before and after presentation, the ward where the patient was followed, surgical interventions, culture results, length of stay, length of follow-up, sequela, and mortality were retrieved from patient files and hospital information system. Patient groups of only those with OC and those with IC were compared.

Approval was received from the Ethics Board of Dokuz Eylül University, Medical Faculty (Decision no: 2021/20-06, Date: 30.06.21).

All data were statistically analyzed on "IBM Statistical Social Sciences SPSS 22.0" package program. Categorical variables were expressed with percentages, normally distributed continuous variables with mean ± standard deviation, and those with non-normal distribution with median and minimum and maximum (min-max) values. Chi-square test was used for the relation between categorical variables and dependent variables. Fisher's exact test was used when Chi-square test assumptions were not met. In independent groups, t-test was used for the relation between normally-distributed continuous variables and dependent variable. If non-normal distribution was present, then Mann-Whitney U test was used. Statistical significance was accepted when P value was under 0.05.

Results

The study included 30 patients presenting to our ward with a preliminary diagnosis of sinusitis complications, and all were treated as inpatients. Thirteen patients who were considered to have developed complications for reasons other than ABRS were excluded from the study. Of these patients, the complications were secondary to otitis media in four, infections other than sinusitis in three (cellulitis, dental infection Epstein-Barr virus infection) and trauma in two patients. One case was associated with malignancy and one with fungal agents (*Aspergillus* spp). Even though the etiology of one case with spinal epidural abscess and another one with isolated intracranial abscess was not determined, it was not assessed as sinusitis complication. The remaining 17 patients were included into the study as complication of acute bacterial rhinosinusitis.

OC alone was present in 11 of the patients (64.7%), IC alone in 4 (23.5%) and both orbital and intracranial complications in 2 (11.8%). Table 1 summarizes the distribution of IC and OC. Additionally, one of the cases had skull base osteomyelitis, another had superior sagittal sinus and necrotizing pneumonia with sinus rectus thrombosis, and another case had subperiosteal abscess anterior to the maxilla and dacryocystitis.

Median age was 13 years (min-max= 3-17 years), and majority of the patients were boys (14, 82.4%) (Table 2). There were two cases followed for thalassemia major and terminal phase cancer (giant cell glioblastoma), each in one. Other 15 patients did not have any underlying diseases.

Of the patients, 88% were assed using computed tomography and 58.8% with magnetic resonance imaging. In the images, maxillary and ethmoidal sinusitis could be detected in all patients. Frontal sinusitis and sphenoid sinusitis were present at a rate of 82.4% and 64.7%, respectively. Frontal sinusitis was found in all patients with IC (Table 2).

Duration of symptoms on presentation was nine days (2-30 days), number of surgical interventions was 0 (0-2), and length of stay was 12 days (3-60 days). Fever after admission during follow-up lasted median seven days (3-9 days) in the IC group. Fever after admission was not observed in the OC group. Follow-up of the patients continued for median 47 days (7-324 days) after presentation (Table 2).

It was detected that patients with intracranial complication were older (median 16 and 12 years, p= 0.048) and had a higher number of surgeries (median 2 and 0, p= 0.027), longer length of stay (median 44 and eight days, p< 0.001) higher duration of follow-up (median 110 and 30 days, p= 0.015). Again, patients with IC had higher values of absolute neutrophil count (median 16700/mm^3 and 7000/mm^3, p= 0.020), C-reactive protein (229.0 ± 62.9 and 65.7 ± 57.4 mg/L, p< 0.001), urea (mean 8.8 and 12.7 mg/dL, p< 0.001) and creatinine (mean 0.42 and 0.61 mg/dL, p= 0.035), and lower values of absolute lymphocyte count (median 2463/mm^3 and 1367/mm^3, p= 0.009) and sodium (mean 137.7 and 134.2 mmol/L, p= 0.005) on presentation. Table 2 summarizes the comparison of IC and OC and their data on laboratory findings.

The most frequently observed symptoms were fever (76%), runny nose (58.8%), swelling on the eyes (58.8%), and headache (58.8%). The most frequent examination findings were swelling on the eyes (64%), limitation in eye movements (35.3%) and postnasal discharge (17.6%). Table 3 demonstrated demographic data, diagnoses, symptoms, examination findings, and laboratory results of all patients.

Table 1. Intracranial and orbital complications

Intracranial complications n= 6	Epidural abscess	4	%66.7
	Subdural empyema	4	%66.7
	Meningitis	2	%33.3
	Intraparenchymal abscess	2	%33.3
Orbital complications (according to Chandler classification) n= 13	1 (Preseptal cellulitis)	4	%30.8
	2 (Orbital cellulitis)	5	%38.5
	3 (Subperiosteal abscess)	3	%23.1
	4 (Orbital abscess)	1	% 7.7
	5 (Cavernous sinus thrombosis)	0	%0

Table 2. Demographic and clinical characteristics with laboratory findings*

		Total n= 17 (%100)	Onlyorbital n= 11 (64.7%)	Intracranial n= 6 (35.3%)	p
Age (years)		13 (3-17)	12 (3-17)	16 (9-17)	**0.048**
Sex	Female	3 (17.6%)	1 (9.1%)	2 (33.3%)	0.515
	Male	14 (82.4%)	10 (90.9%)	4 (66.7%)	
Imaging	CT	15 (88.2%)	9 (81.8%)	6 (100%)	-
	MRI	10 (58.8%)	5 (45.5%)	5 (83.3%)	0.304
Paranasal sinuses	Frontal	14 (82.4%)	8 (72.7%)	6 (100%)	-
	Sphenoid	11 (64.7%)	6 (54.5%)	5 (83.3%)	0.333
	Maxillary	17 (100%)	11 (100%)	6 (100%)	-
	Ethmoid	17 (100%)	11 (100%)	6 (100%)	-
	Pansinusitis	10 (58.8%)	5 (45.5%)	5 (83.3%)	0.304
Symptom duration on presentation (day)		9 (2-30)	7 (2-18)	12 (7-30)	0.098
Number of surgeries		0 (0-2)	0 (0-0)	2 (0-2)	**0.027**
Length of stay (day)		12 (3-60)	8 (3-35)	44 (22-60)	**<0.001**
Length of follow-up (day)		47 (7-324)	30 (7-182)	110 (47-324)	**0.015**
Duration of fever during hospitalization (day)		5 (0-9)	0 (0-0)	7 (3-9)	0.133
Laboratory values	White blood cell (/mm^3)	10900 (6200-29900)	10100 (6500-22700)	18950 (6200-29900)	0.098
	ANC (/mm^3)	8100 (3100-27300)	7000 (3100-18800)	16700 (4400-27300)	**0.020**
	ALC (/mm^3)	2076 ± 887	2463 ± 742	1367 ± 695	**0.009**
	Hb (g/dL)	12.2 ± 1.6	12.1 ± 1.5	12.3 ±1.9	0.823
	Plt (10^3/mm^3)	309 (215-636)	303 (251-636)	424 (218-555)	0.350
	BUN (mg/dL)	10.3 ± 2.5	8.8 ± 2.0	12.7 ± 0.7	**<0.001**
	Cr (mg/dL)	0.5 ± 0.2	0.42 ± 0.14	0.61 ± 0.17	**0.035**
	AST (U/L)	22.5 (15-67)	24 (16-67)	19 (15-53)	0.606
	ALT (U/L)	18 (7-86)	18 (8-65)	23.5 (7-86)	0.776
	Alb (g/dL)	3.7 ± 0.6	3.95 ± 0.48	3.48 ± 0.74	0.211
	Na (mmol/L)	136.3 ± 2.57	137.7 ± 2.1	134.2 ± 1.6	**0.005**
	CRP (mg/L)	123.3 ± 98.8	65.7 ± 57.4	229.0 ± 62.9	**<0.001**
	Sedimentation	53.3 ± 19.3	48.7 ± 16.8	69.0 ± 22.3	0.113

*Data are given as median (min-max), mean ± standard deviation or number (%).
CT: Computed tomography, MRI: Magnetic resonance imaging, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, Hb: Hemoglobin, Plt: Platelet, BUN: Urea, Cr: Creatinine, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, Alb: Albumin, Na: Sodium, CRP: C-reactive protein.

A great majority of the patients had used peroral (7, 41.2%) or parenteral (6, 35.3%) antibiotics prior to presenting to our institution. In our hospital, 13 of the patients were started on third generation cephalosporin and/or cephalosporin with vancomycin or linezolid combination as empirical treatment. Metronidazole was added to 10 patients suspected or diagnosed to have intracranial extension. Treatments and their outcomes are given in Table 4.

Agents in cultures could only be demonstrated in three patients, and all of them were aspiration or tissue materials obtained through neurosurgical intervention. The agents were *S. pneumoniae, Streptococcus sppe* and *S. constellatus* (Table 4).

Endoscopic sinus surgery (ESS) was only performed on one patient. Three patients were operated on by neurosurgery, of whom two required recurring surgical interventions. Debridement was performed in one patient with bilateral preseptal abscess by ophthalmology.

Drop foot sequela occurred in a 17-year-old male patient with subdural empyema and meningitis complications. Only antibiotic, antiedema, and antiepileptic treatments were applied to this patient. Sequela was not observed in three patients who have undergone neurosurgery. The only patient in whom ESS was performed died after being discharged due to brain tumor. There was no other mortality in the study.

Table 3. Demographic data, diagnoses and findings of the patients

No	Age, sex, comorbidity or predisposing condition	Diagnoses of sinusitis/ complications	Symptoms/duration (day)	Examination findings	Laboratory
1	16 years, F, giant cell glioblastoma	Pansinusitis/Potts puffy tumor, frontal subperiosteal abscess, epidural abscess, preseptal cellulitis	Fever, runny nose, headache, nausea, vomiting, swelling on the forehead/10 days	Swelling on the left Sol frontal and left eyelid, postnasal discharge	WBC= 6.200 CRP= 278
2	12 years, F	Pansinusitis/Orbital subperiosteal abscess, osteomyelitis of the skull base (sphenoid)	Fever, swelling in the eye and pain/15 days	Swelling on the left half of the face, protrusion and limited movement of the left eye, periorbital edema on the right eye, free movement, oropharynx hyperemic	WBC= 10.100 CRP= 142 Sedimentation= 79 Pro= 8.5
3	14 years, M A ball hit his head 7 days ago	Pansinusitis/Preseptal cellulitis, preseptal abscess, epidural abscess, sinus vein thrombosis, necrotizing pneumonia	Redness and swelling in the eye, fever, runny nose, headache cough/6 days	Neck rigidity, both eyes swollen and edematous, limitation in looking upward	WBS= 29.900 CRP= 171 Sedimentation= 73 LP= glu 62, pro 72, leucocyte 10, erythrocyte 2.880, na 145, K 3, Cl 128.
4	16 years, M	Pansinusitis/Epidural abscess, subdural empyema, intraparenchymal abscess, meningoencephalitis	Fever, runny nose, headache, vomiting, fullness sensation on the face/14 days	Neurological examination: usual. Seromucoid drainage in bilateral nasal passages	WBC= 12.900 ANC= 9.000 ALC= 2.400 CRP= 228 Sedimentation= 45
5	17 years, M	Frontal, ethmoid and maxillary sinusitis/subdural empyema, meningitis	Headache, cough, runny nose, nasal blockage, GTC seizure/14 days	Purulent postnasal discharge, sensitivity on the left sinus with palpation	WBS= 25.700 CRP= 137 LP= glu 81, prot 49, leucocyte 15, erythrocyte 5, na 151, k 3, Cl 135.
6	14 years, M	Pansinusitis/Orbital cellulitis	Headache, fever, redness and ptosis of the left eye/4 days	Ptosis of the left eye	WBC= 10.300 CRP= 100.5 Sedimentation= 50
7	12 years, E	Frontal, ethmoid and maxillary sinusitis/Preseptal cellulitis	Fever, headache, runny nose, vomiting/10 days	Swelling on the left eyelid	WBC= 7.600 CRP= 55 Sedimentation= 40
8	16 years, M, Thalassemia major	Pansinusitis/Orbital cellulitis	Runny nose, headache, swelling on the right eye/7 days	Pain in the right frontal region with percussion and palpation, both eyes swollen, limited eye movement on the right, postnasal discharge	WBC= 6.500 CRP= 62 Sedimentation: 32
9	8 years, M	Ethmoid and maxillary sinusitis/ Orbital cellulitis	Redness on the right eye, swelling, diplopia/7 days	Edematous right eyelid	WBC= 7.400 CRP= 4.4 Sedimentation= 48
10	3 years, M	Frontal, ethmoid and maxillary sinusitis/Orbital subperiosteal abscess	Nasal congestion, fever, swelling on the right eye/6 days	Right eye swollen and hyperemic	WBC= 11.600 CRP= 4.3
11	5 years, M	Sphenoid, ethmoid and maxillary sinusitis/Orbital cellulitis	Fever, swelling on the left eye/5 days	Hypertrophic tonsils	WBC= 8.200 CRP= 12.3 Sedimentation: 48 Pro= 0.04

Table 3. Demographic data, diagnoses and findings of the patients (continue)

No	Age, sex, comorbidity or predisposing condition	Diagnoses of sinusitis/ complications	Symptoms/duration (day)	Examination findings	Laboratory
12	17 years, M	Pansinusitis/Epidural abscess, subdural empyema, intraparenchymal abscess, meningoencephalitis	Headache, cough, fever, runny nose, GTC seizure, vomiting, weakness on the left arm and leg/7 days	Left side 4/5 hemiparetic	WBC= 22.100 CRP= 293 Sedimentation= 89
13	9 years, E	Pansinusitis/Preseptal cellulitis, maxillary subperiosteal abscess. (Dacryocystitis on follow-up	Headache, fullness of the face, runny nose, fever, swelling on the left eye and cheek, 14-21 days	Bilateral nasal mucoid discharge, swelling on the left eye and cheek, sensitivity and redness on the malar region	WBC= 22.700 CRP= 175 Sedimentation= 40
14	9 years, F	Pansinusitis/Subdural empyema, meningitis	Cough, fever, weakness on the right arm and leg, difficulty in speaking, mental fog/9 days	Weakness on the right arm and leg, right fascial paralysis, neck rigidity, OF hyperemic	WBS= 15.800 CRP= 267 Pro= 0.95 LP= glu 49, prot 61, leucocyte 260, erythrocyte 0, na 140, k 2, cl 127.
15	13 years, M	Frontal, ethmoid and maxillary sinusitis/Orbital cellulitis	URTI 7 days prior, pain on the right eye, blurred vision/3 days	Right eye edematous and exophthalmic. Painful eyelid movements, no limitation, no diplopia.	WBC= 10.900 CRP= 26.7 Sedimentation= 22
16	3 years, M	Pansinusitis/Orbital cellulitis	Cough, fever, swelling on the right eye/10 days	Right periorbital advanced edema and hyperemia. Upward looking of the right eye slightly limited.	WBC= 18.600 CRP= 101.5 Sedimentation= 64
17	17 years, M	Frontal, ethmoid and maxillary sinusitis/Orbital abscess, subgaleal collection	Runny nose, headache, fever, redness on the left eye/7 days	Left eye periorbital hyperemic, edematous, proptotic. Swelling from the frontal area to the hairy skin.	WBC= 9.200 CRP= 39 Sedimentation= 64

WBC: White blood cell (/mm^3), CRP: C-reactive protein (mg/L), LP: Lumbar puncture, Pro: Procalcitonin, glu: Glucose (mg/dL), pro: Total protein (mg/dL), Na: Sodium (mmol/L), K: Potassium (mmol/L), Cl: Clor (mmol/L), ANC: Absolute neutrophil count (/mm^3), ALC: Absolute lymphocyte count (/mm3), GTC: Generalized tonic clonic, URTI: Upper respiratory tract infection.

Table 4. Treatments and outcomes

No	Antibiotic before presentation	Medical treatment during hospitalization	Ward that followed the patient and follow-up note	Surgery (Number)	Culture	Length of stay (day)	Last evaluation day/Sequela
1	1 dose ceftriaxone, 3 days PO cefuroxime	mero, vanco, metro, LAmB	Pediatric oncology – Weakness on the left arm due to tumor progression on the 18th day. Pyelonephritis (yeast) and cholelithiasis	Endoscopic sinus surgery (1)	1 colony CNS in sinus aspirate culture. Not considered significant	22	47/Weakness on the left arm (related to the mass). Exitus due to primary disease one month after discharge.
2	-	Ceft/cepho + vanco + metro	Eye	-	-	30	30/Sensitivity on the left zygoma continues.
3	PO amox-clav	Ceft/mero + vanco + metro	Neurosurgery	Neurosurgery (1), EYE (1)	Intraoperative tissue culture revealing *S. constellatus*	43	108/no sequela
4	PO cephaclor	Ceft/cefta+ vanco + metro	Neurosurgery – Abscess formation in the frontal lobe and subfascial herniation observed.	Neurosurgery (2)	Aspirate culture revealing *S. pneumoniae*	42	73/no sequela
5	PO amox-clav 4 days	Ceftr + vanco + metro	Pediatric Diseases – Subdural empyema progressed on the 12th day, 5 mm shift and edema developed on the left cerebral hemisphere, shifted to meropenem on the 25th day.	-	-	58	112/Drop foot, clonus on the right foot, and increase in DTRs of the right extremity
6	PO amok-clav 3 days	Ceft + vanco	Pediatric diseases	-	-	7	44/no sequela
7	-	Ceft+ vanco	E-N-T	-	-	3	124/no sequela
8	7 g IV	Cefur	E-N-T	-	-	12	18/no sequela
9	4 g IV	ceft+ vanco + metro	Eye	-	-	7	28/no sequela
10	2 g IV	ceft + vanco	E-N-T	-	-	9	19/proptosis of the right eye
11	5 g PO amox-clav, 2 g IV ertap + clin	Cipro + linez	Eye	-	-	8	34/no sequela
12	-	(cefo + metro)/mero + vanco	Neurosurgery	NRŞ (2)	Tissue culture revealing *Streptococcus* spp.	60	216/no sequela
13	7 g PO	Cefur + metro	ENT	-	-	7	7/3 days after discharge, abscess on the left eye due to dacryocystitis enlarged and spontaneously fistulized.
14	9 g PO	Ceft+ vanco + metro	Pediatric diseases -Thrombophlebitis and cholelithiasis observed	-	-	45	324/no sequela
15	amox-clav	ceft + vanco	Pediatric diseases	-	-	8	24/no sequela
16	-	ceft+ vanco + metro	Eye	-	-	12	182/no sequela
17	Cefo+ clin/vanco/ teiko	ceft + linez + metro	Eye – Two times drainage from the frontal subgaleal collection by ENT	-	-	35	52/Minimal double vision and proptosis of the left eye

PO: Peroral, mero: Meropenem, vanco: Vancomycin, metro: Metronidazole, LAmB: Liposomal amphotericin B, CNS: Coagulase negative staphylococcus, ceft: Ceftriaxone, cefo: Cefotaxime, amox-clav: Amoxycillin clavulonic acid amoksisilin klavulonik asit, cefta: Ceftazidime, DTR: Deep tendon reflex, ENT: Ear, nose, throat, ertap: Ertapenem, clin: Clindamycin, linez: Linezolid, sefur: Seforoxime, teiko: Teikoplanin.

Discussion

With this study, we presented the demographic and clinical characteristics of pediatric patients treated as inpatients due to ABRS complications in a tertiary university hospital and the treatments applied and their outcomes in a seven-year study period.

It was observed that majority of our cases were adolescent males with no underlying disease, and orbital complications were more frequently encountered. Age of the patients with IC were higher than those of OC (median the in the OC group was 12 years and 16 years in the IC group, p= 0.048). In a review of 16 studies examining pediatric patients with IC, adolescent males have been found to be the majority of the cases. In that review, it has been found that 50-100% of the cases were males and mean age varied between 10-15.8 years (12). In a study from the USA including inpatients due to ABRS complication, mean age of the patients under the age of 20 years has been found to be 8.6 years in the OC group and 12.4 years in the IC group. Age difference between these two groups has been found to be significant. Moreover, being male (OR= 1.69, CI 1.55-1.84, p< 0.001) an being aged 9-15 years have been found to be risk factors for OC development (4). As it is known, frontal sinusitis and ICs are frequently associated, and frontal sinuses do not complete their development until the adolescent period. This situation partly explains the older age found in IC groups. The predisposition of the adolescent age group and male sex to sinusitis complications can also be explained by the increased vascularization and width of the diploic system (4,13,14). Our findings are in concordance with the literature.

Median age of our patients with OC (12 years, min 3-max 17 years) was detected to be higher than previous studies. A clear reason cannot be given since our study did not search for the answer to this situation. Younger children may have presented to the doctor at an earlier period and received appropriate treatment sooner. As a result, they may have not developed complications or developed milder ones like preseptal cellulitis and been treated as outpatients.

The most frequent OCs in the literature are in Chandler II (orbital cellulitis) class (30.3%). Throughout the years, the prevalence of orbital abscess has decreased. Since preseptal cellulitis is a mild complication that could be treated in outpatient clinics, it is relatively less observed in research and case series (8). The most frequent ICs are subdural empyema (49%) and epidural abscesses (36%) (12). Distribution of complications in our patient population was found compatible with previous data.

Similar to our study, duration of symptoms on presentation has been reported as mean 10 days in a study including 202 cases (13). Although symptom duration was longer in the IC group of our study, the difference was not statistically significant [7 (2-18) days and 12 (7-30) days, p= 0.098]. In a systematic analysis of pediatric patients with IC, symptom duration has been found as mean 13.4 days, similar to our study (12).

Absolute neutrophil count and CRP values were found higher and absolute lymphocyte count and sodium values were found lower in the IC group. In a retrospective cohort study, higher CRP (mean 18.1 mg/dL) and sedimentation (mean 82 mm/h) values were found in those with intracranial empyema when compared to children with ABRS but without complication (15). Elevated CRP, high neutrophil count, low lymphocyte count, and sodium values can be alarming for the physician in terms of IC presence.

All of our culture growths were samples obtained from patients having undergone neurosurgical intervention, and all contained streptococci species. Two patients were types as *S. pneumoniae* and *S. constellatus,* each, but the last patient could not be types. ESS was performed in only one patient, and growth was not detected in sinus aspirate. In a case series of 25 pediatric patients, more than one organism has grown in 54% of abscess, sinus and peripheral blood cultures. Streptococci species have been isolated in 53% and staphylococci species in 24% of the cultures. In our study, similar to the above-mentioned one, *Streptococcus milleri* group (*S. anginosus, S. constellatus* and *S. intermedius*) and coagulase negative staphylococci were detected the most frequently (16).

Our case in whom *S. constellatus* growth was detected was a 14-year-old male patient that presented with neck rigidity, swelling on both eyes and limitation of looking upward. The patient in question was diagnosed with epidural abscess, preseptal cellulitis, sinus vein thrombosis, and necrotizing pneumonia. *Streptococcus milleri* group bacteria may cause disseminated infections, multiple abscesses, long hospitalization, and recurring surgical interventions (17).

Since culture could be performed in a handful of patients surgically in our study, treatment was started empirically and changes were made according to clinical course. Sinus aspirate cultures or intraoperative cultures can make it possible to detect the agent and plan treatment according to the agent.

In a current systematic review, it has been expressed that rate of surgical intervention dropped from 45% to 22% in pediatric patients with ophthalmologic complications (8). In our case series, none of the 11 patients with only orbital complication had a surgical intervention. Sequela was not observed in seven patients who were followed for an appropriate amount of time. Three patients did not come to follow-up visits. One of the cases who was not followed (patient number 10) was evaluated on day 10, and proptosis of the right eye still continues. In another patient, minimal

double vision and proptosis of the left eye continue but follow-up is still not terminated. Mortality was not observed in the OC patient group.

In a review examining 16 studies published between 1983 and 2011 including 179 pediatric cases with intracranial sinusitis complication, it has been detected that nearly all patients with subdural, epidural and intracerebral abscess underwent a neurosurgical intervention and most of them underwent ESS. Of the patients, 73% recovered fully. Complications in those who did not fully recover have been found as neurological alterations (ongoing seizures, hemiparesis, loss of hearing, aphasia), postoperative hydrocephaly, recurrent empyema development and recurring surgical requirement. Only six deaths have been reported in the review. Total morbidity and mortality have been reported as 27% and 3.3%, respectively (12). Mortality has been reported as 20.7% in a case series of 82 IC patients, mostly aged under 18 years, treated in Northern Africa between 2006 and 2009 (13). Among the six patients belonging to our IC group, one underwent only ESS, three underwent neurosurgery, but two did not undergo any surgical interventions. Patients that did not undergo any surgical interventions had meningitis and subdural empyema. While foot sequela still continues in one of these patients two month after discharge, the other one is sequela-free. All of the patients operated on by neurosurgery are sequela-free. The patient having undergone ESS was an oncology patient diagnosed with giant cell glioblastoma and died one month after being discharged. Rate of sequela in the IC group was 16.6%. Rate of surgical intervention was relatively lower than those of previous studies, and low rate of mortality and morbidity also caught attention. We can say that close monitoring of the patients and appropriate and long term parenteral antimicrobial treatment have an important role here.

Limitations of our study include lack of data due to its retrospective design, differences in practices and differences in follow-up. These limitations were tired to be avoided by meticulously scanning data from patient files, hospital information system, and epi-crisis reports. Low number of patients also lowers the power of statistical analysis. However, we believe that our study presented important outcomes since it focused on only pediatric patients in a tertiary hospital that serves both adults and children.

To conclude, age, length of stay, and need for surgery are higher in the intracranial complication group due to acute bacterial rhinosinusitis when compared to those with orbital complications. Cases with IC were less in number but received treatment longer as inpatients. The patient with sequela development was again in the IC group. This situation, once again, underlines the importance of IC, despite being rare. Just as sequela may be seen in patients whose surgical needs are not met, there are cases that are cured with only medical treatment. Today, when surgical treatments are decreasing gradually, it is seen that prospective studies, where the patients are thoroughly followed in the long-term, are needed to choose the most appropriate surgical approaches, empirical antibiotics and treatment durations. Until ideal approaches have been clarified, close follow-up of the patients after discharge for clinical worsening and sequela and early intervention are of grate importance.

Ethics Committe Approval: This study was approved by Dokuz Eylül University Non-Invasive Research Ethics Committee (Decision no: 2021/20-06, Date: 30.06.2021).

Informed Consent: Patient consent was obtained.

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