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The Etiology, Clinical Characteristics and Treatment Modalities in Children with Meningitis and Encephalitis: A Retrospective Single Center Study in Türkiye

Menenjit ve Ensefalitli Çocuklarda Etiyoloji, Klinik Özellikler ve Tedavi Yöntemleri: Türkiye'den Retrospektif Tek Merkezli Bir Çalışma

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Abstract

Objective: Central nervous system infections are diseases with high morbidity and mortality if not treated early and effectively in the childhood. In our study, it was aimed to evaluate the demographic and clinical characteristics, complications and treatment modalities and to determine short-term prognosis in pediatric patients with meningitis and encephalitis.

Material and Methods: In this retrospective cross-sectional study; patients aged between one month and 18 years, who were hospitalized in the Department of Pediatrics of Adana City Training and Research Hospital, between October 2017 and May 2021 were included.

Results: A total of 70 patients; 38.5% females, 61.5% males were included into the study. When grouped according to their diagnosis, 36 patients were diagnosed with meningitis, seven patients with meningoencephalitis and 27 patients with encephalitis. Mean age of the meningitis patients was 90.9 ± 74.1 months, that of meningoencephalitis patients was 115.4 ± 58.1 months, and that of encephalitis patients was 67.9 ± 54.3 months. Headache, neck pain and vomiting in meningitis patients; altered consciousness in patients with meningoencephalitis and encephalitis; convulsion in encephalitis patients were found to be significantly higher than in other diagnostic groups. CSF culture and multiplex PCR showed the causative agent in 44% (n= 16) of the patients. *S. pneumoniae* was detected in 43% (n= 7), *N. meningitidis* in 25% (n=

Öz

Giriş: Santral sinir sistemi enfeksiyonları, çocukluk çağında erken ve etkin bir şekilde tedavi edilmediği takdirde morbidite ve mortalitesi yüksek hastalıklardır. Çalışmamızda, menenjit ve ensefaliti olan pediyatrik hastalarda demografik ve klinik özelliklerin, komplikasyonların ve tedavi yöntemlerinin değerlendirilmesi ve kısa dönem prognozunun belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Retrospektif kesitsel çalışma olarak tasarlanan bu çalışmaya; Adana Şehir Eğitim ve Araştırma Hastanesi Çocuk Sağlığı ve Hastalıkları Anabilim Dalında Ekim 2017-Mayıs 2021 tarihleri arasında yatan bir ay-18 yaş arası hastalar dahil edildi.

Bulgular: Çalışmaya 70 hasta dahil edildi. Tanılarına göre gruplandırıldığında 36 hastaya menenjit, yedi hastaya meningoensefalit ve 27 hastaya ensefalit tanısı konuldu. Toplam hastaların 27 (%38.5)'si kadın, 43 (%61.5)'ü erkekti. Menenjit hastalarının ortalama yaşı 90.9 ± 74.1 ay, meningoensefalit hastalarının 115.4 ± 58.1 ay ve ensefalit hastalarının 67.9 ± 54.3 aydı. Menenjit hastalarında baş ağrısı, boyun ağrısı ve kusma; meningoensefalit ve ensefalit hastalarında bilinç değişikliği; ensefalit hastalarında konvülsiyon diğer tanı gruplarına göre anlamlı olarak yüksek bulundu. Kan nötrofil sayısı ve CRP değerleri menenjit hastalarında ensefalit hastalarına göre anlamlı olarak yüksek, BOS glukoz düzeyi ve BOS/serum glukoz oranı anlamlı olarak düşük bulundu. BOS protein düzeyleri menenjit hastalarında ensefalit hastalarına göre anlamlı olarak yüksekti (p< 0.05). BOS lökosit sa-

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4), *M. tuberculosis* in 19% (n= 3) of the patients with bacterial meningitis. Enterovirus was detected in 13% (n= 2) of patients. Brain MRI abnormalities were detected in 52% (n= 14) of encephalitis patients. EEG abnormality was detected in 63% (n= 17) of encephalitis patients. Antiepileptic use was also present in 81% (n= 22) of encephalitis patients. Complications developed in the acute phase during the course of treatment in 17% (n= 6) of meningitis patients. Fifty-two percent (n= 14) of encephalitis patients, 43% (n= 3) of meningoencephalitis patients, and 11% (n= 4) of meningitis patients were discharged with sequelae. Two patients with tuberculous meningitis/meningoencephalitis died. The risk of sequelae was found to be significantly higher in meningoencephalitis and encephalitis patients compared to meningitis patients (p< 0.05).

Conclusion: Central nervous system infections are a disease group presenting with fever, nausea and vomiting. In addition to these findings, the disease may progress with neurological findings and may require intensive care follow-up. With an early diagnosis and treatment, satisfactory results can be obtained, especially in patients with encephalitis with a high risk of sequelae.

Keywords: Meningitis, encephalitis, children

yısı ensefalit hastalarında menenjit ve meningoensefalit hastalarına göre anlamlı olarak düşüktü (p< 0.05). BOS kültürü ve multipleks PCR menenjit hastalarının %44 (n= 16)'ünde etkeni gösterdi. Bunların %43 (n= 7)'ünde *S. pneumoniae*, %25' (n= 4)'inde *N. meningitidis*, %19 (n= 3)'unda *M. tuberculosis* ve %13 (n= 2)'ünde enterovirüs saptandı. Ensefalit hastalarının %52 (n= 14)'sinde beyin MRG anormallikleri saptandı. Ensefalit hastalarının %63 (n= 17)'ünde EEG anormalliği saptandı. Ensefalit hastalarının %81 (n= 22)'inde antiepileptik kullanımı da mevcuttu. Menenjit hastalarının %17 (n= 6)'sinde tedavi süresince akut fazda komplikasyon gelişmiştir. Ensefalit hastalarının %52 (n= 14)'si, meningoensefalit hastalarının %43 (n= 3)'ü, menenjit hastalarının %11 (n= 4)'i sekel ile taburcu edildi. Tüberküloz menenjiti/meningoensefaliti olan iki hasta mortalite ile sonuçlandı. Meningoensefalit ve ensefalit hastalarında sekel riski menenjit hastalarına göre anlamlı olarak yüksek bulundu (p< 0.05).

Sonuç: Santral sinir sistemi enfeksiyonları ateş, bulantı ve kusma gibi belirtilerle karşımıza çıkan bir hastalık grubudur. Bu bulguların yanı sıra nörolojik bulgularla seyreder ve yoğun bakım takibi gerektirebilir. Erken tanı ve tedavi ile özellikle sekel riski yüksek olan ensefalitli hastalarda yüz güldürücü sonuçlar alınabilmektedir.

Anahtar Kelimeler: Menenjit, ensefalit, çocuk

Introduction

Central nervous system infections are named according to the involvement of anatomical regions as encephalitis, meningitis, rhomboncephalitis, myelitis and radiculitis. Encephalitis is the inflammation of the brain parenchyma and is characterized by impaired consciousness, behavioral and personality changes, speech and movement disorders, neurological dysfunctions such as convulsions and cerebrospinal fluid pleocytosis and/or findings suggestive of encephalitis on imaging or electroencephalography (1,2). The most commonly isolated agents are enteroviruses (echovirus, coxsackievirus A, B), parechoviruses, herpes simplex virus (HSV) type 1 and 2, other herpes viruses [Epstein-Barr virus (EBV), varicella-zoster virus (VZV), cytomegalovirus (CMV), human herpes virus 6 (HHV 6)], influenza and arboviruses (2). Nonpolioenteroviruses and parechoviruses are the most common agents of encephalitis in children and constitute 10-20% of all cases (3,4).

Meningitis is inflammation that occurs in the pia, arachnoid and subarachnoid spaces against infectious agents and their building blocks, which usually pass from the respiratory tract mucosa to the blood circulation and then to the meninges. It is one of the most common causes of death among infectious diseases (5). Although many bacterial agents have the potential to cause meningitis in children, *N. meningitidis, S. pneumoniae* and *H. influenzae* type b (Hib) are the most common causes of bacterial meningitis seen over three months of age. Group B streptococci*, E. coli* and *L. monocytogenes* are the most common pathogens in the etiology of bacterial meningitis in the age group below three months. Changes in the epidemiology of bacterial meningitis have been observed in countries where conjugated vaccines are included in the routine vaccination schedule (6).

Encephalitis may present with various findings, causing neurological dysfunction. Clinical findings vary depending on the agent, the affected brain region, the age group of the patient and immune status (2). Fever, nuchal rigidity and changes in consciousness, which are the classic findings of bacterial meningitis, may not be seen in all patients. In viral infections and meningococcemia, maculopapular rash can be seen in the early period (7,8).

In this study, it was aimed to evaluate demographic, clinical features, complications, treatment modalities and to determine their short-term prognosis in pediatric patients diagnosed with meningitis and encephalitis. It is considered worthy of presentation because there are limited studies in Türkiye, we do not have enough data in our region and etiological agents can change over time.

Materials and Methods

Ethics approval was obtained for the study from the Adana City Training and Research Hospital Clinical Research Ethics Committee (Date: 20.05.2021, Meeting no: 81, Decision no: 1418). In this study, the files of 70 patients diagnosed with meningitis, meningoencephalitis and encephalitis, who were hospitalized in Adana City Training and Research Hospital Pediatrics Clinics between October 2017 and May 2021, were retrospectively analyzed. Information on patients' demographic characteristics, diagnoses, clinical findings, pretreatment laboratory values, imaging methods and treatment modalities were retrospectively scanned from patient files and hospital electronic data system, and IBM SPSS Statistics Version 20.0 package program was used for statistical analysis of the data. Statistical significance level was taken as 0.05 in all tests.

Patients with ventriculoperitoneal shunt, 0-28-day newborn patients, patients who applied with varying degrees of newly developed neurological system problems but were diagnosed with demyelinating disease or acute inflammatory polyneuropathy in the follow-up, patients with encephalitis thought to be non-infectious were not included in the study.

Diagnostic criteria were determined according to clinical findings, laboratory findings and PCR results. Patients were accepted as meningitis if growth of the agent was seen in the CSF culture. Patients were accepted as meningitis if there was no growth in the CSF culture, detection of the agent with CSF multiplex PCR and/or if CSF biochemistry, cell count and Gram staining were compatible with meningitis in clinically compatible patients. Patients with poorly treated meningitis and patients with a history of recurrent meningitis were also included in the study. HSV PCR was studied in patients with clinically suspected and MR&EEG findings compatible with encephalitis. When determining encephalitis patients, encephalitis diagnostic criteria determined by the International Encephalitis Consortium in 2014 were taken as reference (9). Patients who had clinical and CSF examination compatible with meningitis and met encephalitis criteria were accepted as meningoencephalitis.

For the classic triad of tuberculous meningitis on CT, in cases where meningeal enhancement, obstructive hydrocephalus and cerebral infarction are seen mostly in the basal ganglia, primarily tuberculosis meningitis is considered. If tuberculoma, low-intensity or isodense lesions are seen on contrast-enhanced brain CT in the early stage and if edema and mild encapsulation, and prominently encapsulated, isodense or hyperdense lesions are seen in the late stage, tuberculosis meningoencephalitis is considered radiologically.

Results

Demographic and clinical characteristics of 70 patients included in our study are shown in Table 1. Laboratory examinations and microbiological examinations performed in the hospitalization of the patients are shown in Tables 2 and 3.

When CSF culture and multiplex PCR were evaluated together, the causative agent was shown in 44% (n= 16) of the meningitis patients. Of these, 43% (n= 7) were *S. pneumoniae,* 25% (n= 4) were *N. meningitidis*, 19% (n= 3) were *M. tuberculosis*, and 13% (n= 2) were enterovirus (Table 3).

Seventeen percent (n= 6) of meningitis patients and 29% (n= 2) of meningoencephalitis patients were followed up with the diagnosis of central nervous system tuberculosis. The presence of *M. tuberculosis* was shown in three patients by PCR and culture. Five patients were evaluated as CNS tuberculosis with clinical findings, positive family history, PPD positivity and neuroimaging methods.

Brain MRI was performed in 56% of meningitis patients and in all patients with meningoencephalitis and encephalitis. Brain MR abnormalities were detected in 31% of meningitis patients, 43% of meningoencephalitis and 52% of encephalitis patients. EEG was evaluated in 44% of meningitis patients, 72% of meningoencephalitis patients, and 93% of encephalitis patients, and abnormalities were detected in 8%, 43%, and 63%, respectively.

Dexamethasone, IVIG and dosage, high-dose corticosteroid and antiepileptic use vary according to the diagnoses of the patients. Accordingly, the rate of dexamethasone use was lower in encephalitis patients compared to meningitis patients, and the use of IVIG, high-dose corticosteroid and antiepileptic use was statistically significantly higher ($p= 0.002$; $p< 0.001$; $p< 0.001$; $p< 0.001$). In our study, IVIG was given to 29% of meningoencephalitis patients, 44% of encephalitis patients, and 20% of all patients. IVIG treatment was given to two patients with HSV-1, two patients with influenza, and one patient with SARS-CoV-2. High-dose corticosteroid was given to 29% of meningoencephalitis patients and 31% of encephalitis patients, for a total of 10 patients. High-dose corticosteroid therapy was given in one patient with HSV-1, three patients with influenza, and two patients with SARS-CoV-2. Plasmapheresis was applied to three patients, of which two were followed up with the diagnosis of encephalitis and one with the diagnosis of meningoencephalitis (Table 4).

Complications developed in 16.6% of meningitis patients. Subdural effusion developed in two patients, subdural empyema in one patient and hydrocephalus in three tuberculosis patients. At discharge, 48% of encephalitis patients have epileptic activity on EEG, 44% have motor deficits and 7% have neurocognitive effects. Two patients with tuberculosis died.

Discussion

Central nervous system infections are one of the leading diseases that cause severe morbidity and mortality in children if they are not recognized and treated early. Although vaccination programs have reduced the incidence of infection, especially in developed countries, CNS infections still continue to be an important cause of mortality and morbidity for children all over the world. Viruses, bacteria and parasitic agents constitute the majority of the etiology, but the incidence of the agents may vary according to regions (1,5).

In the majority of meningitis patients, CSF glucose level was found to be below 40 mg/dL at admission, and CSF glucose level was generally found to be less than 60% of the blood glucose level (8). In encephalitis, CSF glucose is usually normal, but CSF glucose may decrease in tuberculous meningoencephalitis, encephalitis due to HSV and mumps virus (1). Although the CSF glucose concentration in our study

Table 1. Demographic and clinical characteristics of the patients

	Hospitalization diagnosis			
	Meningitis	**Meningoencephalitis**	**Encephalitis**	**p**
Age (months), mean ± SD	90.9 ± 74.1	115.4 ± 58.1	67.9 ± 54.3	0.173
Age groups, n (%) 1-23 months 24-59 months 60 months and above	 11 (31%) 4 (11%) 21(58%)	 0 (0%) 2 (29%) 5 (71%)	 8 (30%) 3 (11%) 16 (59%)	0.436
Sex, n (%) Female Male	 17 (47%) 19 (53%)	 2 (29%) 5 (71%)	 8 (30%) 19 (70%)	0.304
Fever, n (%)	35 (97%)	7 (100%)	27 (100%)	0.999
Headache, n (%)	23 (64%)	3 (43%)	4 (15%)	**<0.001**
Neck pain, n (%)	22 (61%)	2 (29%)	2 (7%)	**<0.001**
Vomiting, n (%)	23 (64%)	3 (43%)	9 (33%)	**0.043**
Consciousness change, n (%)	16 (44%)	7 (100%)	25 (93%)	**<0.001**
Fatigue, n (%)	35 (97%)	6 (86%)	23 (85%)	0.169
Poor feeding, n (%)	34 (94%)	5 (71%)	15 (56%)	**0.001**
Restlessness, n (%)	14 (39%)	4 (57%)	13 (48%)	0.609
Convulsion, n (%)	9 (25%)	3 (43%)	19 (70%)	**0.001**
Rash, n (%)	4 (11%)	1 (14%)	0 (0%)	0.157
Diarrhea, n (%)	4 (11%)	0 (0%)	2 (7%)	0.841
Double vision, n (%)	3 (8%)	0 (0%)	0 (0%)	0.458
Weight loss, n (%)	5 (14%)	1 (14%)	0 (0%)	0.082
History of pre-illness infection, n (%)	6 (17%)	1 (14%)	14 (52%)	**0.008**
Use of antibiotics before admission, n (%)	8 (22%)	2 (29%)	7 (26%)	0.908
Comorbid disease, n (%)	7 (19%)	1 (14%)	3 (11%)	0.791
Risk factors*, n (%)	20 (56%)	1 (14%)	4 (15%)	**0.002**
Intensive care hospitalization, n (%)	16 (44%)	4 (57%)	24 (89%)	**0.001**
Intubated (MV), n (%)	1 (3%)	3 (43%)	5 (19%)	**0.010**
Mechanical ventilation day, mean ± SD Median (IQR)	32 ± UD 32 (32-32)	23.3 ± 19.1 26 (3-41)	7.4 ± 6.0 7 (2-13)	**0.200**
Intensive care hospital stay (days), mean ± SD Median (IQR)	7.5 ± 10.7 5 (2-5)	24.8 ± 13.0 23 (15.5-34)	8.6 ± 7.9 6.5 (3-11.5)	**0.015**
Length of hospital stay (days), mean ± SD Median (IQR)	19.4 ± 14 13.5 (12-19)	23.4 ± 11.7 20 (13-36)	20.7 ± 11.8 14 (12-29)	0.351

*Risk factors; Immunodeficiency, family history of tuberculosis disease, anatomical defect in the kranial base (history of post-traumatic skull base fracture, presence of dermal sinus), not initiating or incomplete vaccination schedule, and presence of comorbid disease.

was found to be lower in meningitis patients compared to the other groups, it was found to be higher than other studies in the literature (10,11). We associated this situation with 22% of meningitis patients using antibiotics before admission. In our study, sex distribution in meningitis patients was similar to the case series in the literature (12,13). Unlike the studies in the literature, meningitis patients were seen more frequently in the period above five years of age, when viral meningitis was most common before the age of one, after which it peaked for the second time (14,15). Fever, headache, vomiting, neck pain, fever, change in consciousness, convulsions, weakness and malnutrition in meningitis patients were common findings in patients with meningoencephalitis and encephalitis, and were consistent with studies in the literature (8,16,17). The presence of more than 1000 leukocytes in a cubic millimeter in which neutrophils predominate in the cell count in CSF often supports acute bacterial meningitis (ABM), but in the early stages of bacterial meningitis, fewer or no leukocytes can be seen in the CSF than is seen classically (8,17). CSF pleocytosis can also be seen in patients with encephalitis (16). However,

Table 2. Laboratory characteristics of the patients at diagnosis

	Hospitalization diagnosis			
	Meningitis	**Meningoencephalitis**	**Encephalitis**	**p**
Leukocytes (n/mm^3), mean ± SD	16197.2 ± 6894.1	11685.7 ± 5634	12588.9 ± 6908.3	0.070
Neutrophil (n/mm^3), mean ± SD	12486.1 ± 7284.6	8785.7 ± 4663.1	8440.7 ± 5161.3	**0.037**
CRP (mg/L), mean ± SD Median (IQR)	80 ± 92 40.7 (3.2-125)	25.2 ± 43.3 10.1 (0.4-23)	8.1 ± 12.9 4.5 (1.3-8.5)	**0.001**
Growth in blood culture, n (%) Yes No	 2 (6%) 34 (94%)	 0 (%0) 7 (%100)	 2 (%7) 25 (%93)	0.999
CSF glucose (mg/dL), mean ± SD Median (lower-upper)	48.1 ± 27.7 53 (0.3-112)	80.6 ± 67.3 60 (26.9-225)	65.9 ± 21.4 64 (30-143)	**0.016**
CSF/Serum glucose ratio, mean ± SD Median (lower-upper)	0.43 ± 0.22 0.47 (0.003-0.82)	0.42 ± 0.14 0.42 (0.15-0.57)	0.59 ± 0.14 0.60 (0.32-0.85)	**0.003**
CSF protein (mg/dL), mean ± SD Median (IQR)	191.4 ± 175.4 123 (83-249)	162.9 ± 201.3 87 (63-150)	126.1 ± 295.3 38 (28-75)	**<0.001**
CSF leukocytes (n/mm^3), mean ± SD Median (IQR)	1191.4 ± 1694.2 400 (90-1920)	177.1 ± 170.9 150 (20-240)	47 ± 174.4 0 (0-10)	**<0.001**
Microorganism in CSF Gram stain, n (%) Yes No Not studied	 2 (6%) 27 (75%) 7 (19%)	 0 (0%) 7 (100%) 0 (0%)	 0 (0%) 26 (96%) 1 (4%)	0.195
CSF culture growth, n (%)	11 (30%)	1 (14%)	0 (0%)	-
CSF multiplex PCR, n (%) Positive Negative Not studied	 8 (22%) 16 (44%) 12 (32%)	 0 2 5 (71%)	 0 15 (56%) 12 (44)	-
CSF HSV 1 PCR, n (%) Positive Negative Not studied	 0 (0%) 23 (64%) 12 (36%)	 0 (0%) 7 0 (0%)	 3 (11%) 21 (78%) 3 (11%)	-
CSF HSV 2 PCR, n (%) Positive Negative Not studied	 0 (0%) 23 (64%) 12 (36%)	 0 7 0 (0%)	 1 22 (81%) 4 (15%)	-
Central nervous system tuberculosis, n (%)	6 (17%)	2 (29%)	0 (0%)	-

the absence of pleocytosis does not exclude the diagnosis of encephalitis. Accordingly, results similar to those in the literature were obtained in our study (8,16,17).

In the multicenter study of Ceyhan et al. between 2005 and 2012, 476 of 645 patients with meningitis used antibiotics before LP, and the agent could be cultured in 16.2% of the patients (6). In our study, the microorganism, which we think is the causative agent, grew in 30% of meningitis patients and 14% of meningoencephalitis patients, including *S. pneumoniae* in seven patients, *M. tuberculosis* in three patients, and *N. meningitidis* in one patient in the CSF culture. In a multicenter study in which Ceyhan et al. evaluated 408 meningitis patients between 2005 and 2006, the causative agent was detected in 243 of the patients by CSF multiplex PCR (13). In a study of 186 patients by Törün et al., viral agents were detected in 26.8% of them by PCR (18). In our study, multiplex PCR was performed in 24 of the meningitis patients, *N. meningitidis* was found in four, *S. pneumoniae* in two, and enterovirus in two patients. In our study, CSF multiplex was studied in 15 of 27 encephalitis patients, and the agent could not be determined. HSV-1, HSV-2 specific PCR was studied in 24 of the encephalitis patients, and CSF HSV-1 specific PCR was positive in three patients and HSV-2 specific PCR was positive in one patient. In addition, we found influenza PCR positivity in nasal swab in four of the encephalitis patients and SARS-CoV-2 PCR positivity in nasal

Table 3. Number and percentage distribution of agents detected by CSF culture growth and CSF multiplex PCR

Causative microorganism	Count	Percent %
S. pneumoniae	7	43
N. menengitidis	4	25
M. tuberculosis	3	19
Enterovirus	2	13

Table 4. Treatments used in patients

	Hospitalization diagnosis			
	Meningitis	Meningoencephalitis	Encephalitis	p
Antiepileptic, n (%)	12 (33%)	5 (71%)	22 (81%)	**<0.001**
Dexamethasone, n (%)	25 (69%)	3 (43%)	7 (26%)	**0.002**
Antibiotic duration, mean ± SD Median (IQR)	16.7 ± 9 13.5 (12-15.5)	24.6 ± 11.1 24 (14-36)	17 ± 7.1 14 (12-23)	0.067
IVIG, n (%)	1 (3%)	2 (29%)	12 (44%)	**<0.001**
High dose corticosteroid, n (%)	0 (0%)	2 (29%)	8 (31%)	**<0.001**
Plasmapheresis, n (%)	0 (0%)	1 (14%)	2 (7%)	0.070
Treatment of cerebral edema, n (%)	12 (33%)	4 (57%)	17 (63%)	0.057
Mannitol, n (%)	0 (0%)	1 (14%)	3 (11%)	0.089
Hypertonic salin, n (%)	12 (33%)	3 (43%)	17 (63%)	0.057

swab in two of them. *M. tuberculosis* was found positive by PCR in CSF in one patient, and mumps virus serology was found in one patient. In our study, a lower rate of causative pathogen was detected compared to the literature. This is associated due to the fact that 22% of meningitis and 29% of meningoencephalitis used antibiotics before LP, our study was after Hib and 13-valent pneumococcal vaccines were included in the national vaccination schedule, the national vaccination program was successfully implemented, and our cases were concentrated over five years old when viral meningitis had its second peak.

Patients with CNS tuberculosis may present with meningitis, meningoencephalitis or encephalitis. In some patients, it may show an acute, rapidly progressive course. In some patients, they may present with an encephalitic course manifested by stupor, coma and convulsions without meningitis symptoms (19). The diagnosis of tuberculous meningitis can be made definitively with a positive smear for acid-fast bacilli in CSF, a positive CSF culture for *Mycobacterium tuberculosis*, or a positive nucleic acid amplification test (20). In our study, tuberculous meningitis was found in six patients, and tuberculous meningoencephalitis was found in two patients. CSF culture positivity is present in four patients. Two patients were intubated during follow-up, and hydrocephalus developed in three patients. Two patients were discharged with sequelae. Two patients died. Tuberculosis disease is still seen as an important problem for our country.

There are no systematically controlled studies on the use of immunomodulatory therapy in encephalitis. Due to the difference in the pathogenesis of etiologies, it should be carefully evaluated after starting appropriate antibiotic therapy for active infections before giving immunosuppressive treatments such as corticosteroids and plasmapheresis. In patients with suspected infectious encephalitis, modality with the lowest risk of immunosuppression at diagnosis is IVIG. IVIG, corticosteroid and plasmapheresis can be used in the treatment of autoimmune encephalitis (21). IVIG, corticosteroid and plasmapheresis treatments can also be used in the SARS-CoV-2 associated multisystem inflammatory syndrome and neurological involvement of SARS-CoV-2 in children (21,22). In our study, IVIG was given in 14 patients, high-dose corticosteroids were given in 10 patients, and plasmapheresis was performed in three patients. IVIG treatment was given in two patients diagnosed with HSV-1, two patients with influenza, and one patient with SARS-CoV-2. In addition, SARS-CoV-2 related multisystem inflammatory syndrome, which is seen in children, was considered in a patient who presented with the complaints of fever and rash during the pandemic period, and IVIG treatment was given, but LP was performed in the patient whose clinical findings

could not exclude meningitis, and *N. meningitidis* growth was detected in the CSF. High-dose corticosteroid was given to 29% of meningoencephalitis patients and 31% of encephalitis patients, for a total of 10 patients. High-dose corticosteroid therapy was given in one patient with HSV-1, three patients with influenza, and two patients with SARS-CoV-2. Plasmapheresis was applied to three patients, two of whom were followed up with the diagnosis of encephalitis, and one with the diagnosis of meningoencephalitis. Plasmapheresis was applied in one patient with HSV-1 and one patient with SARS-CoV-2.

In conclusion, central nervous system infections are a disease group presenting with fever, nausea and vomiting. In addition to these findings, progress with neurological findings and may require intensive care follow-up. With an early diagnosis and treatment, satisfactory results can be obtained, especially in patients with encephalitis with a high risk of sequelae.

Ethics Committe Approval: The approval for the study was received from the Turkish Republic Health Sciences University Adana City Training and Research Hospital Clinical Research Ethics Committee (Date: 20.05.2021, Decision no: 1418).

Informed Consent: Patient consent was obtained.

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Author Contributions: Concept - ÜÇ, EÇD, TÇ; Design - OT, CC; Supervision - ÜÇ, MKÇ; Resource - EÇD, MKÇ; Data Collection and/or Processing - EÇD, İA, OT; Analysis and/or Interpretation - CC, İA; Literature Search - OT, MKÇ; Writing - EÇD, ÜÇ, TÇ; Critical Review - TÇ, CC, İA.

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