RESEARCH / ARAŞTIRMA
DOI: 10.26650/IUITFD.1162804
İst Tıp Fak Derg 2022 / J Ist Faculty Med 2022

CYTOTOXIC LESIONS OF THE CORPUS CALLOSUM: MAGNETIC RESONANCE IMAGING FINDINGS AND ETIOLOGIC FACTORS

KORPUS KALLOZUMUN SİTOTOKSİK LEZYONLARI: MANYETİK REZONANS GÖRÜNTÜLEME BULGULARI VE ETİYOLOJİK FAKTÖRLER

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Cite this article as: Barburoglu M, Gunoz Comert R, Huseynov H, Cobanoglu S, Ulukan C, Kipoglu O, et al. Cytotoxic lesions of the corpus callosum: magnetic resonance imaging findings and etiologic factors. J Ist Faculty Med 2022;85(4):447-55. doi: 10.26650/IUITFD.1162804

ABSTRACT

Objective: Cytotoxic lesions of the corpus callosum (CLOCCs) are usually detected as a diffusion restriction in the splenium of the corpus callosum. They are rare secondary radiological findings associated with various clinical entities. The aim of this study is to evaluate the magnetic resonance imaging (MRI) findings and underlying clinical factors of cases with CLOCCs.

Materials and Methods: The MRI images of 850 patients who were admitted to the emergency services between January 2017 and March 2021 with encephalopathy and epilepsy-like neurological complaints were scanned retrospectively. Twenty nine patients (20 men, 9 women) with CLOCCs were included in the study. Their radiological and clinical findings were evaluated.

Results: The mean age was calculated as 26.4 years (5-72 years). The patients had neurological symptoms such as dysarthria, confusion, ataxia, syncope, epileptic seizure, and headache. Lesions were developed secondary to various infections in 20 (68.9%) patients. Diabetic decompensation was found in three patients and uremic decompensation in one patient. In the remaining patients, subarachnoid hemorrhage, asthma attack, trauma, high-dose lithium-levetiracetam intake and anti-epileptic drug withdrawal were responsible. Twenty patients had MRI control. In 16 (80%) patients, MRI findings returned to normal between 6 days and 8 months (median 30, Mean 53.8 days). One of the

ÖZET

Amaç: Korpus kallozumun sitotoksik lezyonları (KKSL) genellikle korpus kallozum spleniumunda diffüzyon kısıtlılığı olarak saptanan farklı birçok klinik durum ile ilişkilendirilmiş nadir bir radyolojik bulgudur. Çalışmamızın amacı kliniğimizde manyetik rezonans görüntülemesinde (MRG) KKSL saptanan olguların radyolojik ve klinik bulgularını incelemek ve literatür eşliğinde değerlendirmektir.

Gereç ve Yöntem: Ocak 2017 – Mart 2021 tarihleri arasında erişkin ve pediatri acil servislerine ensefalopati ve epilepsi benzeri nörolojik şikayetler ile başvuran, diffüzyon veya kraniyal MRG çekilmiş yaklaşık 850 hastanın görüntülemeleri retrospektif olarak tarandı. KKSL saptanan 29 hasta (20 erkek, 9 kadın) çalışmaya dahil edilerek radyolojik ve klinik bulguları değerlendirildi.

Bulgular: Yaş ortalaması 26,4 yıl (5-72 yıl) olarak hesaplandı. Hastalarda dizartri, bilinç bulanıklığı, ataksi, senkop, epileptik nöbet, baş ağrısı gibi nörolojik semptomlar mevcuttu. Hastalardan 20 (%68,9) tanesinde çeşitli enfeksiyonların merkezi sinir sistemine direkt veya indirekt etkisi ile lezyonların geliştiği görüldü. Üç hastada diyabetik, bir hastada üremiye bağlı metabolik dekompansasyon saptanmıştır. Diğer 5 hastada; subaraknoid hemoraji, astım atağı, travma, yüksek doz lityum - levetirasetam alımı ve antiepileptik ilaç çekilmesi gibi etyolojik faktörlere bağlı geliştiği değerlendirildi. Yirmi hastada MR kontrolü bulunmaktaydı. 16

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Submitted/Başvuru: 16.08.2022 • **Revision Requested/Revizyon Talebi:** 17.08.2022 •
Last Revision Received/Son Revizyon: 29.08.2022 • **Accepted/Kabul:** 05.09.2022 • **Published Online/Online Yayın:** 17.10.2022

other 4 patients had partial regression, and 3 patients recovered with sequelae gliosis.

Conclusion: CLOCCs are nonspecific MRI findings associated with a broad underlying clinical spectrum. They are usually reversible. Determination of the underlying clinical etiology, avoidance of an ischemic stroke and tumor-like misdiagnoses are important for appropriate patient management.

Keywords: Cytotoxic callosal lesions, reversible splenial lesion, splenium, corpus callosum

(%80) hastada bulgular 6 gün ile 8 ay arasında normale dönmüştür (Median 30, Ortalama 53,8 gün). Diğer 4 hastadan birinde parsiyel regresyon olduğu, 3 hastada sekel gliozis ile iyileştiği izlendi.

Sonuç: Kallozal sitotoksik lezyonlar altta yatan geniş bir klinik spektrum ile ilişkili nonspesifik kranial MRG bulgularıdır. Genellikle geri dönüşümlüdür. Radyolojik olarak tanınmaları, altta yatan klinik etiyolojinin saptanması, iskemik inme ve tümör benzeri yanlış tanılardan kaçınılması, uygun hasta yönetimi için önemlidir.

Anahtar Kelimeler: Sitotoksik kallozal lezyonlar, reversibl splenial lezyon, splenium, korpus kallozum

INTRODUCTION

The corpus callosum is the largest white matter pathway that provides interhemispheric communication and coordination. Splenium is the part of the corpus callosum that remains in the posterior part and consists of thick fibers that connect both the temporal, posterior parietal and occipital cortices (1,2). In recent years, cytotoxic lesions observed in the splenium of the corpus callosum have been identified by Magnetic Resonance imaging (MRI). These lesions which are called cytotoxic lesions of the corpus callosum (CLOCCs), are rare radiological findings that can be seen secondary to a wide range of diseases (3,4). These lesions are usually ovoid, homogeneous, non-hemorrhagic lesions detected in the middle part of the splenium. Extracallosal involvement and irregular lateral extension have been described in some patients (4,5) . In MRI examinations, the signal features are usually mildly hyperintense on T2-weighted and FLAIR sequences, slightly hypointense on T1-weighted images, hyperintense in diffusion sequences and do not show contrast enhancement (3,4).

These lesions are usually detected incidentally when imaging for encephalopathy, encephalitis or epileptic seizures. Although the clinical prognosis is generally good in these patients, the clinical situation varies depending on the underlying etiology (5,6). The underlying pathogenesis of these lesions is still controversial. Currently, the most accepted hypothesis explains these lesions with cytotoxic edema and demyelination secondary to inflammatory cytokinopathy in the brain. Differential diagnoses include a wide range of etiological factors with varying clinical importance (7,8). Radiological identification of these lesions and knowing the associated clinical conditions are important for avoiding a misdiagnosis like an acute ischmeia or tumor -like lesions and to apply appropriate treatment to patients. In this study, 29 cases with CLOCCs detected on cranial MRI were included and these cases were evaluated in terms of MRI findings, clinical symptoms and underlying etiological factors. The similar features and differences of these cases were examined with the literature examples.

MATERIAL AND METHODS

After applying to the appropriate ethics committee, the MRI images of 850 patients who were admitted to the adult and pediatric emergency services between January 2017 and March 2021 with encephalopathy and epilepsy-like neurological complaints were scanned retrospectively. The review of our database records revealed 29 patients with CLOCCs who were included in the study. Their radiological and clinical findings were evaluated retrospectively through the image archive system and the hospital database records. MR images were evaluated by a neuroradiologist with 6 years of experience in neuroimaging. Patients with arterial territorial diffusion restriction due to acute ischemic stroke were not included in the study. Patients with a known diagnosis of demyelinating disease and presenting with callosal lesion due to an acute attack were excluded from the study.

Patients' age, initial complaints, clinical signs and symptoms, laboratory findings, chronic/previous disease parameters, initial and control MRI findings and final diagnosis were evaluated. MRI examinations of the patients were performed with 1.5 Tesla (T) or 3 Tesla devices, and the initial MRI examinations were made with or without contrast or just diffusion and T2, FLAIR sequences. The shape, localization, MR signal intensity, diffusion restriction, apparent diffusion coefficient (ADC) values, enhancement patterns, affected areas and extra callosal lesions were evaluated in MRI examinations. In addition, medical records of patients such as clinical symptoms, underlying diseases, clinical course, recurrence and post-treatment response were evaluated. All statistical analyses were calculated using Statistical Package for the Social Sciences (SPSS) for Windows version 20.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Demographic characteristics of the patients

In the study, 29 patients who were reported to have cytotoxic lesions of the corpus callosum according to the findings obtained in MRI examinations were included.

There were 20 female (68.9%) and 9 male patients, with a mean age of 26.4±19.6years (range, 5 -72 years). Eleven patients (37.9%) were aged 18 years or younger. Eighteen patients (62.1%) were older than 18 years. Patient gender, age, MRI findings and clinical characteristics are detailed in Table 1.

MRI findings

Corpus callosum splenium was involved in all cases. Splenial involvement was localized in the middle part in 20 patients (68.9%), in the middle and paramedian part in three patients (10.3%), in the middle and left lateral part in three patients (10.3%) and only in the lateral parts and paramedian parts of the splenium in three patients (10.3%). The lesions which were localized to the middle part of the splenium were oval, crescent-shaped and band-like morphological structures (Figure 1). All lesions restricted diffusion and ADC responses were monitored. In the additional T2 and FLAIR sequences taken in the diffusion examination, the lesions were evaluated as slightly hyperintense. It was observed that the lesions did not enhance contrast in 18 patients with contrast-enhanced examination.

As extracallosal involvement, one patient had acute diffusion restriction in the bilateral centrum semiovale simultaneously with the splenial lesion (Patient 19) due to disseminated intravascular coagulation (DIC), septicemia and acute respiratory distress syndrome (Figure 2). In a second patient, involvement of the corpus callosum genu and left centrum semiovale was observed as well as splenial lesion involvement (patient 20) due to meningitis and septicemia. One patient who presented with diabetic ketoacidosis had bilateral thalamic and left globus pallidus involvement concomitant in the splenial lesion (patient 26). In one patient with trauma, focal diffusion restriction was observed in the corpus callosum corpus and bilateral cerebral hemispheres other than the splenium (patient 28). One patient diagnosed with meningitis had concomitant leptomeningeal enhancement in post contrast MRI. In one of the patients, cerebellar meningitis findings were added in the MRI examination during the follow-up, and the findings were observed to regress after appropriate treatment (patient 8).

Control MRIs of 20 patients could be accessed. In 16 (80%) patients with MRI control, the imaging findings returned to normal between 6 days and 8 months (median 30, Mean 53.8 days). In the 2nd month follow-up MRI of one patient with meningitis, it was observed that the findings had partially regressed. In two patients who developed cytotoxic lesion due to diabetic ketoacidosis and one patient with post-traumatic lesion, the MRI findings healed with sequelae gliosis.

Clinical symptoms and findings

Patients often had neurological symptoms such as confusion, dysarthria, ataxia, dizziness, syncope, epileptic seizures, headache, meningeal irritation findings and visual complaints. Seven (24.1%) patients presented with upper respiratory tract infection (URTI) symptoms at the time of admission. Six patients (20.6%) had complaints related to the gastrointestinal system such as nausea, vomiting, abdominal pain and diarrhea. Two patients presented with epilepsy attacks. Other patients had complaints such as fatigue, tremor, hypertension at the time of admission.

In the follow-up and examinations, it was evaluated that callosal cytotoxic lesions developed in 20 (68.9%) patients due to the direct or indirect effects of various systemic or local infections. Influenza infection was diagnosed in three patients (one influenza pneumonia, two URTI), plasmodium falciparum malaria in one patient, Listeria monocytogenes meningitis in one patient, pneumonia in one patient, viral and bacterial serology negative cerebellitis in one patient, adenovirus enteritis in one patient, mastitis in one patient, otitis media in one patient, URTI in two patients, covid 19 in one patient, acinetobacter septicemia in one patient with a known diagnosis of methyl malonic acidemia, serology and culture negative meningitis in two patients and septicemia due to URTI in one patient. It was diagnosed after meningitis and septicemia in a patient who had been operated for subdural hematoma two months before the cytotoxic lesion. It was found that a patient diagnosed with familial Mediterranean fever (FMF) had delayed his treatment for the last seven months and a cytotoxic lesion developed after a mild respiratory infection. In addition, it developed secondary to metabolic decompensation after acute tonsillitis in a patient with a known diagnosis of Maple Syrup Disease.

Except for infection-related lesions, metabolic decompensation due to diabetes mellitus was found as an etiological factor in three patients (10.3%). Metabolic decompensation (osmotic demyelination) due to uremia was detected in one patient. Subarachnoid hemorrhage was determined as etiological factor in one patient and post-traumatic injury in one patient. Asthma attack, high-dose lithium-levetiracetam intake and discontinuation of anti-epileptic drug (drug withdrawal) were responsible for cytotoxic lesions in the remaining 3 patients.

DISCUSSION

Transient splenial lesions were first described by Chason et al. in 1996 in epilepsy patients (3). The actual mechanism in the formation of these lesions has not been fully elucidated. Some researchers have thought that it develops due to the involvement of crossing white matter fibers from the temporal lobes in the splenium. They suggested that this mechanism is caused by focal edema that develops due to the temporary deterioration of the blood-brain barrier in the splenium in the postictal period after epileptic seizures (3,9). Kim et al. attributed these lesions to transient demyelination induced by an-

Table 1: MRI findings, demographic and clinical characteristics of the patients

Patient No	Age	Gender	Pre-existing disease	Prodromal manifestations	Etiological factor-Diagnosis	Neurological manifestations	Splenial involvment	CSF examination	Extracallosal lesion, findings	Therapy for neurological symptoms	MRI normalization
1	22	M	No	Fever/URTI	Infection-associated (İnfluenza)	Dizziness	Middle	NE	No	Symptomatic treatment	1 month
2	5	M	MSUD	Fatigue	Infection-associated (Metabolic decompation due to tonsillitis)	Ataxia, increased deep tendon reflexes	Left paramedian	NE	No	Sodium phenylbutyrate, insülin, ceftriaxone	No control
3	63	M	No	URTI	Infection-associated (NBC, NVT)	syncope	Middle	NE	No	Oseltamivir, azithromycin	10 days later
4	25	M	No	Fever, vomiting	Infection-associated (Listeria Monocytogenes meningitis)	Headache, neck stiffness	Middle	Protein: 53.7 mg/dL, lymphocyte	leptomeningeal enhancement	Ampicillin-sulbactam	1 month
5	21	F	No	Sore throat, fever	Infection-associated (İnfluenza pneumonia)	Syncope	Middle	NE	No	Oseltamivir	No control
6	13	M	No	Fever, vomiting	Infection-associated (pneumonia)	Horizontal nystagmus	Middle	NE	No	Ceftriaxone	No control
7	20	M	No	Fever, fatigue	Infection-associated (malaria plasmodium falciparum)	Disturbance of consciousness	Middle	NE	No	Artemeter, lumefantrine	No control
8	21	F	No	Chills and shivering, fever	Infection-associated (NC, NVT cerebellitis)	Involuntary contraction of the body	Middle	Protein and lymphocyte	Cerebellitis (cerebellar enhancement, expansion)	Doxycycline, acyclovir, dexamethasone	6 days
9	19	F	No	URTI	Infection-associated (NBC,NVT)	Bilateral temporary loss of vision	Middle	NE	No	Symptomatic treatment	No control
10	9	M	No	Diarrhea, fever	Infection-associated (enteric adenovirus)	Hand spasms, meaningless speech, walking disorder	Middle	Normal	No	Ceftriaxone, acyclovir	8 days

Table 1: MRI findings, demographic and clinical characteristics of the patients (Continued)

Patient No	Age	Gender	Pre-existing disease	Prodromal manifestations	Etiological factor-Diagnosis	Neurological manifestations	Splenial involvment	CSF examination	Extracallosal lesion, findings	Therapy for neurological symptoms	MRI normalization
11	32	M	Hyperaldosteronism	Hypertension	Bilateral renal artery stenosis Chronic renal failure (metabolic decompensation due to uremia)	Dizziness, dysarthria	Right lateral	NE	No	Antihypertensive therapy, hemodialysis	No control
12	21	M	Methylmalonic acidemia, Chronic renal failure, epilepsy	Nausea, fever, fatigue	Infection-associated (acinetobacter septicemia)	headache	Middle	NE	No	Piperasiline, tazobactam	7 months
13	15	M	FMF	Stomach ache, fever	Infection-associated (oropharyngeal hyperemia)	Dizziness	Middle, left lateral	Normal	No	Ceftriaxone, acyclovir	1 month
14	11	M	No	Headache,	Infection-associated (otitis media)	Headache, otalgia	Middle, left lateral	NE	No	Ampicillin, sulbactam	1 month
15	18	M	Epilepsy	Epileptic seizure	Epileptic drug withdrawal (1 week after discontinuation of oxcarbazepine)	epileptic seizure	Middle	NE	No	Levesiteram, lacosamide	4 months
16	12	M	No	Sore throat, fever	Infection-associated (Covid 19 +)	Headache,	Middle	NE	No	Piperacillin, tazobactam	No control
17	18	M	Recurrent craniopharyngioma	Fever, vomiting	Infection-associated (NC,N-VT meningitis)	disturbance of consciousness, temporary loss of vision	Middle	Normal	Stable recurrent craniopharyngioma	Vancomycine, acyclovir	No control
18	15	M	Asthma	Stomach ache	Asthma attack	Headache,	Middle	NE	No	No	1 month
19	34	F	No	URTI	Infection-associated (DIC,ARDS, sepsis)	disturbance of consciousness	Middle, paramedian	NE	Diffusion restriction in bilateral sentrum semiovale	Intensive care hospitalization	20 days

Table 1: MRI findings, demographic and clinical characteristics of the patients (Continued)

Patient No	Age	Gender	Pre-existing disease	Prodromal manifestations	Etiological factor-Diagnosis	Neurological manifestations	Splenial involvment	CSF examination	Extracallosal lesion, findings	Therapy for neurological symptoms	MRI normalization
20	72	F	Operated for subdural hematoma 2 months ago	Epileptic seizure, confusion	Infection-associated (Sepsis, menengitis)	Epileptic seizure, confusion	Middle	Protein (164 mg/dl)	CC Genu involvement, left sentrum semiovale involvement	Vancomycine amphotericin b, meropenem	2 months later partial involution
21	65	F	No	SAH	Aneurysmal SAH	Headache, vomitting	Middle	NE	No	Endovascular embolization	8 months
22	22	F	Bipolar disorder		High-dose lithium and levetiracetam intake	Headache	Middle	Normal	No	Gastric lavage	1 month
23	60	M	Diabetes mellitus	Dizziness	Uncontrolled diabetes	Dizziness	Right and left lateral involvment	NE	No	Diabetes mellitus regulation	2 months control gliotic sequelae
24	68	F	Diabetes mellitus, hypertension	Disturbance of consciousness	Uncontrolled diabetes	Disturbance of consciousness	Middle	NE	No	Diabetes mellitus regulation	1 month
25	32	F	No	Headache, dizziness	Infection-associated (mastitis)	Headache, dizziness	Middle	Normal	No	Ampicillin-sulbactam for mastitis	No control
26	7	M	No	Abdominal pain, vomiting, confusion	Diabetic ketoacidosis	confusion	Middle, left paramedian	NE	Bilateral thalamic, left globus pallidus involvement	Diabetes mellitus regulation	9 months later control gliotic sequelae
27	22	M	No	Fever, vomiting	Infection-associated (NC, NVT meningitis)	Headache, Disturbance of consciousness	Middle	Protein:86 mg/dl, lymphocyte, (culture negative)	Bilateral globus pallidus calcification on CT	Ceftriaxone, acyclovir	Bilateral splenial paramedian extension on first week control MRI, 1 month control normal
28	20	M	No	Posttraumatic confusion	Posttraumatic	Confusion	Middle, left paramedian	NE	CC corpus involvement, bilateral DAI	Symptomatic treatment	1 month control gliotic sequelae
29	5	M	No	Sore throat, fever	Infection-associated (İnfluenza)	Headache	Middle	NE	No	Symptomatic treatment	8 days

CSF: Cerebrospinal fluid, MRI: Magnetic Resonance Imaging, M: Male, F: Female, URTI: Upper respiratory tract infection, NE: not examined, MSUD: Maple syrup urine disease, NBC: Negative blood cultere, NVT: Negative viral tests, mg: milligrams, dl: deciliter, NC: Negative culture, , FMF: Familial Mediterranean Fever, DIC: Disseminated Intravascular Coagulation, ARDS: Acute respiratory distress syndrome, CC: Corpus Callosum, SAH: Subarachnoid Haemorage, CT: Computed Tomography, DAI: Diffuse Axonal Injury

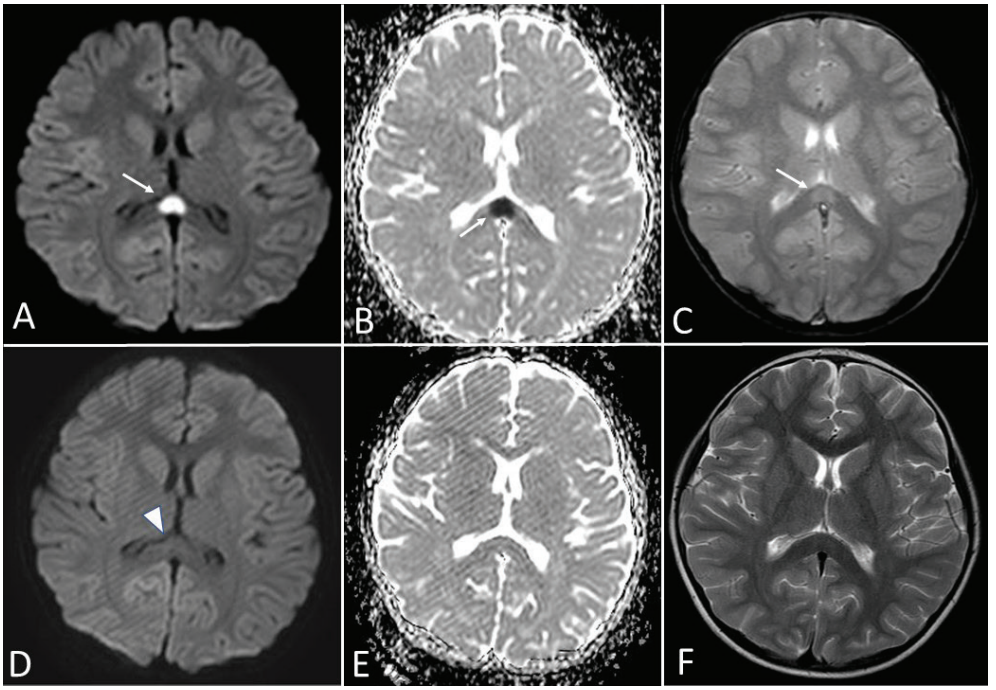

Figure 1: Cytotoxic splenial lesion. A) Increased signal intensity on axial plane Diffusion Weighted Image in the middle part of the splenium (arrow) B) ADC map shows low signal intensity on the same localization (arrow) C) T2 axial image show mildly hyperintensity (arrow) eight days control show normalization on DWI (arrow head) (D), ADC (E) and T2 (F) axial images

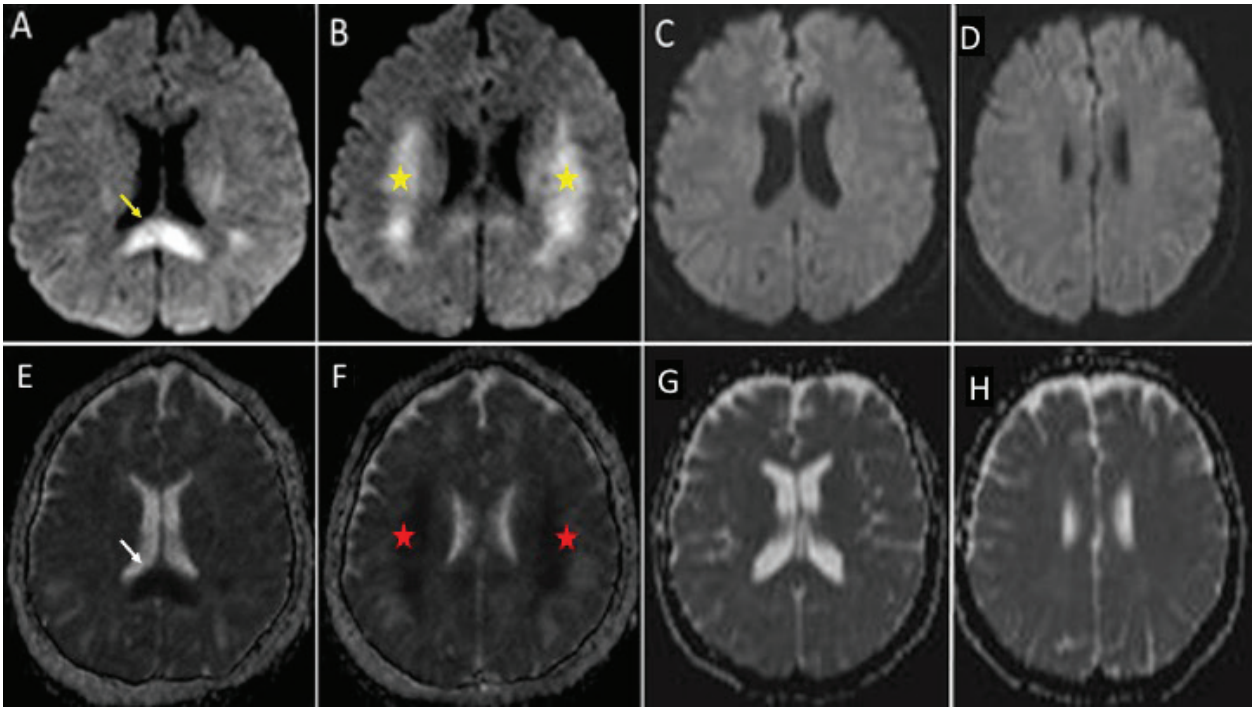

Figure 2: 34-year-old female images A) Acute diffusion restriction in the middle part of the splenium (yellow arrow), B) diffusion restriction in the bilateral centrum semiovale (yellow aterisks) C,D) Normalization is seen in the control diffusion images after 20 days, E) ADC map in the splenium (white arrow) indicates low signal intensity on her first MRI and F) indicates low signal intensity in bilateral centrum semiovale (red asterisks), G,H) after 20 days control ADC maps show normalization in splenium and bilateral centrum semiovale

ti-epileptic drug toxicity (4). As another possible putative mechanism, transient extrapontine osmotic myelinolysis caused by sodium and glucose imbalance due to toxicity, hypersensitivity or drug withdrawal of anti-epileptic drugs has been reported (10,11). Mild encephalopathy with transient splenial lesion (mild encephalitis/encephalopathy with reversible isolated splenial corpus callosum lesion (MERS)) is a clinical and neuroradiological syndrome with a good prognosis that has been used to describe a similar entity in the literature (5,7).

Nowadays, instead of the term transient splenial lesion, these lesions have started to be named cytotoxic lesions of the corpus callosum, which is a more inclusive term. Today, it is known that the splenium region of the corpus callosum has a higher density of cytokine, glutamate, drug and toxin receptors compared to other regions of the brain. For this reason, it has been reported in many studies that the splenium region of the corpus collosum is more sensitive to cytokineopathy (12). The widely accepted theory for CLOCC is that cytokine-mediated immunological reactions cause microvascular endothelial damage, causing perivascular-intramyelinic edema, inflammatory cell migration and associated cytotoxic edema (6). CLOCCs are nonspecific lesions that are usually centrally located in the splenium of the corpus callosum, oval, homogeneous, non-hemorrhagic, non-contrast, hyperintense on FLAIR and T2W images, slightly hypointense on T1W images, and with marked focal diffusion restriction on diffusion-weighted examination (8).

It is usually detected as an incidental finding in cranial MR imaging performed in patients presenting with encephalopathy, encephalitis or seizure complaints. Its etiology has been associated with a wide spectrum of diseases such as drug withdrawal of antiepileptic drug therapy, infection (influenza, EBV, adenovirus, varicella zoster, legionella pneumonia, rotavirus, HIV, tuberculous meningitis), malaria, malignancy, trauma, subaracnoid hemorrage, metabolic disorders (hypoglycemia, electrolyte imbalance) and hemolytic uremic syndrome (3-6).

Callosal cytotoxic lesions due to various infections developed in 20 (68.9%) of our patients. Meningitis was found as the etiological cause in four of our cases. Three of them were serology and culture negative meningitis and one was Listeria monocytogenes meningitis. One patient was diagnosed with cerebellitis of unknown etiology. Except these 5 patients, we did not detect direct central nervous system involvement in the other 15 patients which was associated with infection. Diabetic decompensation was found in three patients and uremic decompensation in one patient. Subarachnoid hemorrhage, asthma attack, trauma, high-dose lithium-levetiracetam intake and antiepileptic drug withdrawal were responsible for the remaining patients.

All patients included in the study showed clinical improvement without any deficits after appropriate treatments for the etiological factors. The clinic of the patients whose etiological factors were related to secondary infections returned to normal in a short time and no permanent deficits developed. In addition, radiological findings returned to normal in all patients except two who presented with diabetic ketoacidosis and one who presented with trauma. In these three patients, the splenial lesions healed with sequelae gliosis without any clinical deficit. We observed that many etiological factors played a role in our cases, as stated in different literatures. Trying to reveal the etiological cause with clinical and laboratory findings is important in terms of applying the appropriate treatment.

MR imaging findings of callosal cytotoxic lesions are from demyelinating diseases such as acute disseminated encephalomyelitis (ADEM) or multiple sclerosis (MS); it can be easily distinguished by the fact that generally it is a single lesion on the middle part of the splenium, and the absence of a prominent inflammatory margin. It has been described in the literature that in some cases, splenial lesions may extend to the lateral parts of the corpus callosum and lesions may occur in both frontoparietal regions (13). In this case, demyelinating diseases such as ADEM and pathologies such as progressive reversible encephalopathy should be excluded with clinical and laboratory findings in the differential diagnosis.

Involvement was observed only in the midline of the splenium in 16 patients (55.1%). Three patients had splenial involvement outside the splenium midline (left paramedian, right lateral part and bilateral lateral part involvement). Six patients had midline splenium and accompanying paramedian and/or lateral segment involvement. As extracallosal involvement, leptomeningeal enhancement in a patient with meningitis, cerebellum involvement in one patient in the following few days, bilateral centrum semiovale involvement in one patient, corpus callosum genu and centrum semiovale involvement in one patient, bilateral thalamus and globus pallidus involvement in one patient, corpus callosum corpus involvement and subcortical white matter involvement-compatible with axonal damage in one patient. Acute ischemic stroke should not be considered primarily in the differential diagnosis because of its incompatibility with the lesion localization, features, and vascularization territory. Recognition of the lesion radiologically and clinically is important for differential diagnosis. In the literature, it has been reported that MR findings quickly return to normal, but it is found in cases that last up to three months. In our patient group, it was observed that the lesions returned to normal between 6 days and 8 months in 16 of 20 patients who were under control. In three patients, the splenial lesions healed with sequelae

gliosis. In one patient, partial involution was observed in the 2nd month follow-up MRI.

Since it is a retrospective study, the inaccessibility of control MRI scans of all patients and the fact that the existing control images were not performed at regular intervals make it difficult to follow the true evolution of the lesions over time and make it difficult to predict the actual recovery time. This is one of the major weaknesses of the study. Prospective studies are needed to fully reveal the etiology of the indicated callosal cytotoxic lesions and to monitor the imaging findings in real time.

In conclusion, cytotoxic lesions of the corpus callosum are nonspecific MR imaging findings and they are associated with many underlying entities. The prognosis is generally good. It is important to be aware of the MRI findings of these lesions and to know that they are secondary lesions. The broad clinical spectrum associated with the lesion should be known for the identification and elimination of the underlying true etiology and for appropriate clinical management.

Ethics Committee Approval: This study was approved by Istanbul University Istanbul Faculty of Medicine Clinical Research Ethics Committee (Date: 21.05.2021, No: 204262).

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- M.B.; Data Acquisition- R.G.C., S.Ç., H.H., O.C., O.K., M.U., M.S., Ç.U.; Data Analysis/Interpretation- Ç.U., R.G.C., M.B., H.H.; Drafting Manuscript- M.B., H.H., R.G.C., S.Ç., M.U.; Critical Revision of Manuscript- M.B., M.U., O.C., O.K., Ç.U., M.S.; Final Approval and Accountability- M.B.; Material or Technical Support- M.B., M.U., O.C., O.K., R.G.C., H.H.; Supervision- M.B., M.U.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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