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Encephalopathy with a reversible lesion in the splenium of the corpus callosum in adults

Gokhan OZDEMIR *MD*, Fettah EREN *MD*

Selcuk University Medical Faculty, Department of Neurology, Konya, Turkey

Abstract

Background & Objectives: Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a clinical and radiological syndrome with a lesion in splenium of the corpus callosum. This lesion is typically detected in the corpus callosum with magnetic resonance imaging (MRI) and usually disappears within a few weeks. The clinical and radiological features of MERS were evaluated for this study. *Methods:* Twelve patients were included in the study. They were treated between 2018 and 2021 years. The patients' demographic and clinical features, laboratory data, treatment and prognoses were documented. *Results:* There were 7 male and 5 female patients in the series. The mean age was 37.92 ± 15.32 (19–62) years. There was history of upper respiratory tract infection in 7 patients, visual loss episodes in 3 patients, epileptic seizure in 2 patients, arthroplasty in 1 patient, cardiac arrhythmia in 1 patient, and COVID-19 (SARS-CoV-2) infection in 2 patients. Focal lesion was detected in the splenium of the corpus callosum with diffusion-weighted MRI which resolved with repeat diffusion MRI and clinical symptoms improved.
Conclusions: Axial diffusion-weighted MRI images show typical splenium ovoid lesion of corpus callosum in patients with MERS. Patients with MERS have a good prognosis. It is important to consider MERS as one of the differential diagnoses in adult patients with fever and cognitive impairment.

Keywords: Corpus callosum, splenium, transient lesion, encephalopathy, fever, cognitive impairment

INTRODUCTION

Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a new clinical and radiological syndrome that involves lesions in the splenium of the corpus callosum. The pathophysiology of this syndrome is unclear. There are several potential etiologies of MERS; seizures, antiepileptic drugs, hypoglycemia, hemolytic uremic syndrome, Wernicke's encephalopathy, Marchiafava-Bignami disease and acute axonal injury. However, its association with infection is frequently emphasized.[1] The reversible isolated lesion is typically detected in the corpus callosum with magnetic resonance imaging (MRI) and usually disappears within a few weeks. In addition, clinical symptoms completely resolved within one month.[2-6] The MERS cases in the literature are usually pediatric patients, and only ~ 60 cases have been reported in adults.[3] These are usually single case reports associated with MERS in the literature. We reported 12 patients of MERS presented with encephalopathy and their evaluated clinical and radiological characteristics.

METHODS

Ethics approval was obtained from Selcuk University Clinical Research Ethics Committee. Twelve patients with MERS in the Selcuk University Neurology Clinic and Emergency Department were included in this study from 2018 to 2021 years. The patients were 19-61 years old; 5 female and 7 males.

The patients were included in the study according to clinical symptoms with encephalopathy and reversible lesion in the splenium of corpus callosum. All patients were transferred from emergency department to neurology clinic after MRI scanning for treatment and etiology of encephalopathy. Neurological examination of all patients was performed in emergency room and neurology clinic. Routine hematological and biochemical tests, control MRI scanning and neurological examination were performed. However; cerebrospinal fluid (CSF) analysis was

Address correspondence to: Fettah EREN, Selcuk University Medical Faculty, Department of Neurology, Konya, Turkey. Tel: +90 5058604146, e-mail: dreren42@hotmail.com

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performed only in two patients.

Information about the patients' ages, genders, clinical features, laboratory data, treatment options and prognoses are summarized in Table 1 and Table 2. All patients were discharged when their clinical status and MRI lesion improved (5-16 days after hospitalization). All patients had different degrees of cognitive impairment.

RESULTS

There were twelve patients in this case series, 5 (41.7%) female and 7 (58.3%) males. The mean age was 37.92 ± 15.32 (19–62) years old. All of the patients had a history of the respiratory, gastrointestinal, or postoperative infection. The most common clinical symptoms were fever in 6 (50%) patients, vomiting and throat pain in 4 (33.3%) patients each, episodes of visual loss in 3 (25%) and epileptic seizure (secondary generalized and generalized tonic-clonic) in 2 (16.6%) patients. The duration of symptoms was 2.83 ± 1.52 (1–6) days. Four (33.3%) patients were treated with antibiotics and 1 (8.3%) with antiepileptic drug before hospitalization. On neurological examination, only one of the patients had dysmetria on the left arm and ataxia, though most of the patients had some degrees of confusion. The patients' clinical details are in the Appendix.

Focal diffusion restriction was detected in the splenium of the corpus callosum in the diffusion-weighted MRI images in all patients with hypo-intensity on apparent diffusion coefficient (ADC) mapping (Figure 1) and hyper-intensity on T2 sequence. No contrast enhancement was found on T1 sequences. A diffusion-weighted MRI before discharge showed resolution of the lesion on ADC mapping (Figure 1, 2).

On blood tests, 4 patients (33.3%) had leukocytosis (10.3 x 10^3/uL, 13.4 x 10^3/uL 11.8 x 10^3/uL, and 16.9 x 10^3/uL). The C-reactive protein level (mean ± standard deviation) was 21.99 ± 22.71 mg/dL in total patient. The blood, urine and throat cultures and viral serological tests were negative. Lumbar punctures were performed for two patients; CSF protein, immunoglobulin G index and PCR were normal. CSF microscopy showed 143 cells/mm^3 only one patient and other was acellular. COVID-19 (SARS-CoV-2)

Table 1: Demographic and clinical features in patients with mild encephalitis/encephalopathy with a reversible splenial lesion

	Age/ year	Gender	Clinical symptoms	Symptom time/days	Disease history	Body temperature
Patint-1	27	Female	Throat pain and vision loss attacks	3	Cryptic tonsillitis	36.7 ^{0}C
Patint-2	51	Male	Throat pain, fever, speech disorder and numbness in the four extremities	2	Acute pharyngitis	38.2^{0}C
Patint-3	19	Male	Headache, vomiting, fever, confusion and amnesia	6	Acute sinusitis	38.0 ^{0}C
Patint-4	34	Female	Secondary generalized epileptic seizure 3 times, confusion and sedation	1	Epilepsy	37.6 ^{0}C
Patint-5	22	Female	Vomiting and vision loss attacks	4	None	36.9 ^{0}C
Patint-6	21	Male	Generalized tonic-clonic epileptic seizure 2 times	1	None	37.3 ^{0}C
Patint-7	27	Male	Vomiting and vision loss attacks	2	None	37.2 ^{0}C
Patint-8	48	Male	Vomiting, fever, throat pain, syncope attack, confusion	5	None	37.6 ^{0}C
Patint-9	61	Female	Confusion	3	Arthroplasty	37.3 ^{0}C
Patint-10	46	Male	Fever, confusion, cough, dyspnea	2	Arthroplasty	38.1 ^{0}C
Patint-11	62	Female	Syncope, fever, confusion, dyspnea	2	Atrial fibrillation	38.0 ^{0}C
Patint-12	36	Male	Headache, confusion and cough	3	None	36.7 ^{0}C

Table 2: Laboratory parameters, treatment strategies and prognoses in patients with mild encephalitis/ encephalopathy with a reversible splenial lesion

	C-reactive protein (mg/dL)	White blood cell (K/Ul)	Cerebrospinal fluid	In-hospital period/days	Treatment in hospital	Clinical process
Patint-1	14.7	13.4	Normal	9	Symptomatic treatment and antibiotic	Symptoms regressed after 1 week
Patint-2	8.32	4.8	None	5	Symptomatic treatment and antibiotic	Symptoms regressed after 4 days
Patint-3	11.9	9.3	None	5	Symptomatic treatment and antibiotic	Symptoms regressed after 3 days
Patint-4	8.9	7.81	None	8	Levetiracetam 1000 mg/day	Seizure activity was controlled. Symptoms regressed after 10 days
Patint-5	5.27	8.71	Normal	9	Symptomatic treatment	She had transient visual symptoms. There were no recurrent symptoms.
Patint-6	15.6	11.8	None	6	Levetiracetam 1000 mg/day	No seizure recurrence was observed in hospital-period.
Patint-7	3.11	8.25	None	7	Symptomatic treatment	He presented with transient nausea, vomiting and visual defect. There were no recurrent symptoms.
Patint-8	12.69	10.3	None	8	Symptomatic treatment and antibiotic	His symptoms associated with respiratory infection were regressed after 5 days
Patint-9	53.4	16.9	None	12	Symptomatic treatment and antibiotic	Symptoms regressed after 7 days
Patint-10	78.8	9.3	None	16	Hydroxychloro-quine 200 mg (BID)	Symptoms regressed after 5 days
Patint-11	16.7	5.15	None	10	Symptomatic treatment, antibiotic and anticoagulation	Symptoms regressed after 7 days
Patint-12	34.5	8.1	None	13	Symptomatic treatment, antibiotic and steroid	Symptoms regressed after 8 days

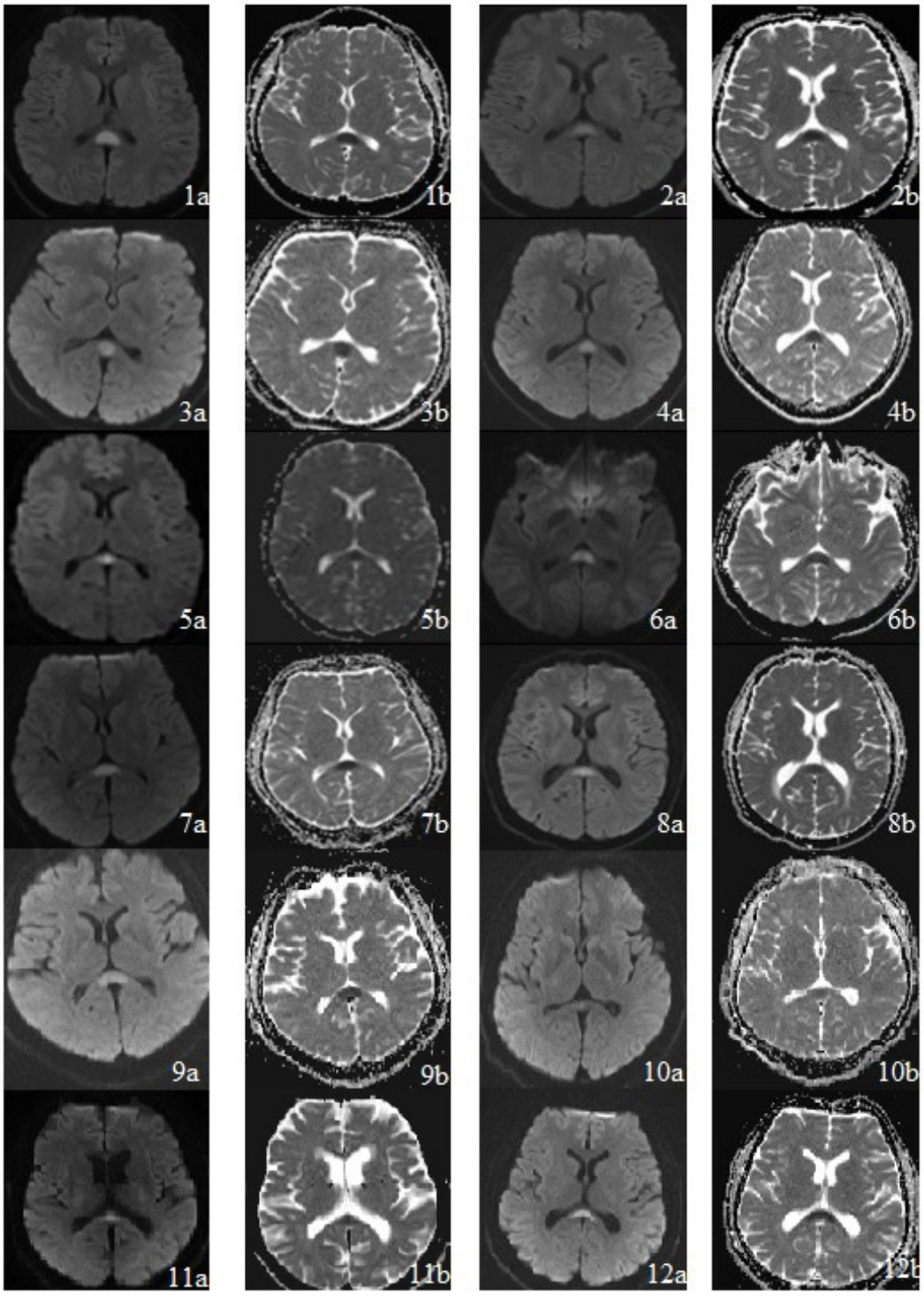

Figure 1. Brain diffusion-weighted magnetic resonance imaging and apparent diffusion coefficient (ADC) map in cases 1-12.

Patient 1-12, a: Diffusion-weighted magnetic resonance imaging, b: Apparent diffusion coefficient (ADC) map

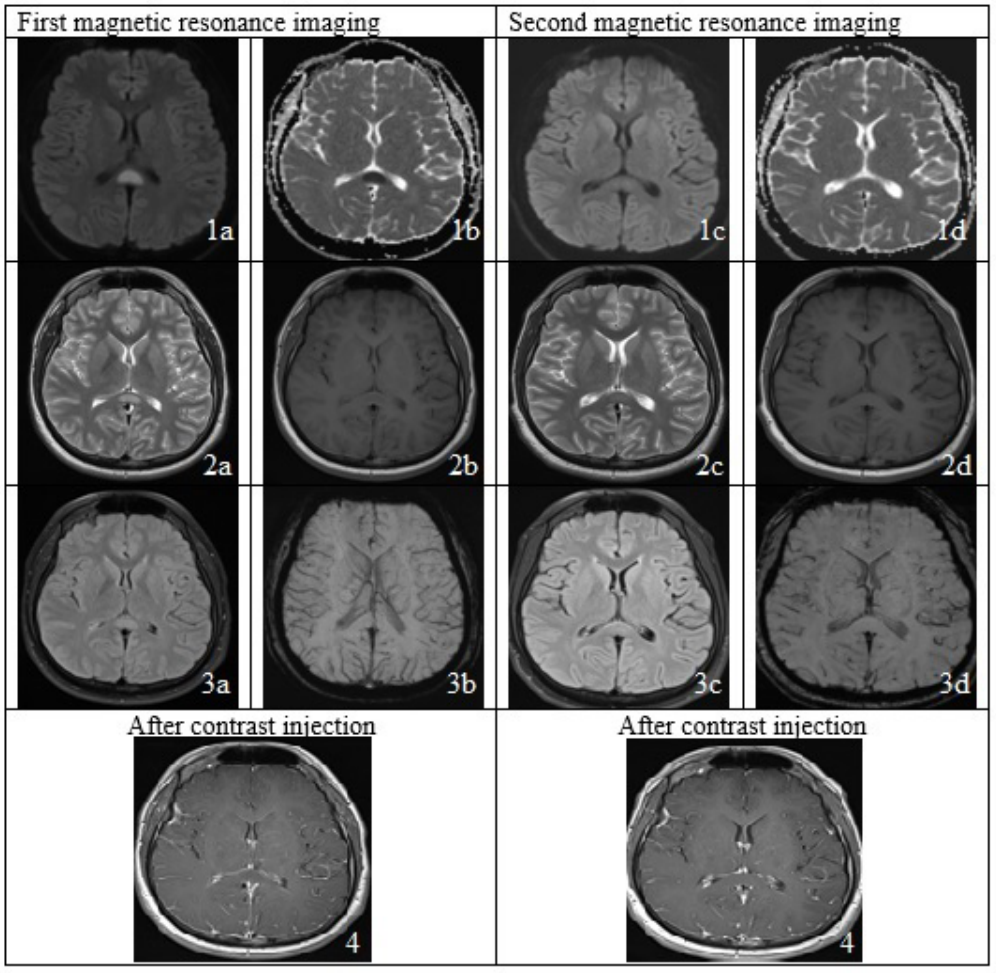

Figure 2. Brain magnetic resonance imaging for first patient (first images: initial time, second images: 10 days later) **Magnetic resonance imaging, 1a-1c:** Diffusion-weighted, **1b-1d:** Apparent diffusion coefficient (ADC) map, **2a-2c:** T2 sequence, **2b-2d:** T1 sequence, **3a-3c:** Flair sequence, **3b-3d:** Gradient echo sequence, **4:** T1 sequence after contrast (1a, 1b: Acute time- 1c, 1d: 10 days later)

infection was detected in two patients. Antibiotic and intravenous hydration treatments were continued in patients with acute infections. Clinical and radiological findings improved after treatment. One patient was vaccinated with second dose of SARS-CoV-2 vaccine (Pfizer-BioNTech) 12 days prior. On follow-up, the corpus callosum lesion resolved in the diffusion MRI and clinical symptoms resolved.

DISCUSSION

MERS is a disease associated with many clinical symptoms and a lesion in the splenium of the corpus callosum. In the literature, MERS is reported to cause encephalopathy. However, some MERS patients presented with epileptic seizures or focal neurological deficits without encephalopathy.[3] In our study, most of patients had different degrees of confusion. Two of our patients had epileptic seizures, and 1 had focal neurological deficits. MERS has usually benign clinical symptoms and the splenial lesions on the MRI were reversible. Our patients were discharged with no clinical symptoms and lesion disappeared in the splenium on diffusion-weighted MRI.

There are various hypotheses on the pathophysiology of the lesion in the splenium of the corpus callosum. The splenium has a relatively high-water component compared to other brain areas making it more susceptible to cytotoxic edema. An influx of biomolecules and inflammatory cells, possibly combined with related cytotoxic edema, might have decreased

diffusion-weighted signal on MRIs. Others have postulated that viral antigens or antibodies induced by the antigens could have an increased affinity for the receptors on splenium axons.[7-9]

Most patients with MERS have an upper respiratory tract and diarrhea infection prior to the disease. The different viruses, e.g. Epstein-Barr, herpes, rotavirus, Hantaan and influenza, have been associated with this condition.[10,11] In our series, 7 patients had respiratory infection, 4 had diarrhea, nausea and vomiting, and 2 had COVID-19 (SARS-CoV-2) infection though the microbiological examination of CSF, blood and urinary tract were normal.

Splenium-specific involvement is more common in some chronic diseases and associated with some drugs. It is also detected in epilepsy and antiepileptic drug therapy. This is thought to be due to a fluid–electrolyte imbalance caused by antiepileptic drugs. Specifically, carbamazepine has strong diuretic activity associated with the arginine-vasopressin system. As a result, cytotoxic oedema may occur and causes lesion in corpus callosum splenium.[12,13] Two of our patients had epileptic seizures (Patient 4-secondary generalized epileptic seizure 3 times in 24 hours, Patient 6-generalized tonic-clonic epileptic seizure twice in 24 hours). One patient had epilepsy for 10 years and a history of carbamazepine treatment. It was thought that the involvement of the corpus callosum in these patients may be associated with epilepsy and carbamazepine treatment.

Liu *et al*. examined the radiological features of twelve patients with MERS. They claimed that corpus callosum is not the predilection site for viral encephalitis, which is mostly in grey matter, so acute disseminated encephalomyelitis (ADEM) may be a more appropriate diagnosis for these cases.[14] In our patients, there was only involvement in the splenium of the corpus callosum. The grey matter was normal in the brain MRI. Patients with MERS may develop encephalopathy but it is not appropriate to use the term 'encephalitis'. It is more appropriate to use encephalopathy instead. The literature suggested that the immune system plays an important role in the pathogenesis.[15] Our view is that the lesion developed as a result of the immune cross-reaction associated with infection. Following the impairment of self-tolerance, immune activity against the pathogen creates immune disorder in normal neuronal structures.

Fever originating from the hypothalamus is termed 'central fever'. However, recent studies indicate that the corpus callosum has thermoregulatory functions in the brain. Impaired consciousness in central fever is common.[16] There are some cases with hypothermia associated with callosal agenesis in the literature.[17] It is not clear the pathogenesis of MERS, but fever and infection are thought to be risk factors in the etiology of the disease.[10,18] In general, MERS does not progress to other regions and the patients recover in a few days. This is thought to occur as a result of secondary reactions mediated by immunity.[19,20]

In the literature, 3 cases of MERS were associated with COVID-19 (SARS-CoV-2) infection. Bektaş *et al*. reported two pediatric patients with encephalopathy and both children showed rapid recovery, with the splenial lesion completely resolved within 1 week on brain MRI.[21] Elkhaled *et al*. described a 23-year-old male MERS patient associated with COVID-19 (SARS-CoV-2). However, they reported that on day 15 of his hospitalization, the patient died from multiple organ dysfunction syndrome (MODS) and severe intra-abdominal and cerebral hemorrhage.[22] Our 2 patients also presented with COVID-19 (SARS-CoV-2) associated encephalopathy. With the diagnosis of MERS, they were discharged with clinical improvement on the 16th and 10th day. However, no COVID-19 vaccine-associated MERS case was reported on literature review. The 12th patient is the first case on this association.

The strengths of this report is the substantial number of patients on an uncommon condition and adequate laboratory/MRI characterization. The weakness of the manuscript is inadequate detail on consciousness assessment. The main reasons being that, the patients were admitted to the neurology clinic from the emergency service and the focus was on the treatment and cause of the illness.

In conclusion, MERS is a rare cause of encephalopathy with a transient lesion in the corpus callosum. A good understanding of the transient nature may allow avoidance from unnecessary invasive diagnostic and therapeutic intervention. In addition, it is important to consider MERS as one of the differential diagnoses in adult patients admitted to the emergency department with fever and cognitive impairment.

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DISCLOSURES

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APPENDIX: The patients' clinical details

Patient 1

A 28-year-old, right-handed female primary school teacher whose family history was negative for neurological disorders. The patient's husband reported that she had cough, weakness and fever for the last 4 days. She was treated with cefaclor with the diagnosis of cryptic tonsillitis for 3 days (May 03, 2018). She presented to the emergency room because of visual loss episodes in both eyes for 30 seconds, several times within 2 hours. In the emergency room, an emergency specialist and the neurologists conducted a standard neurologic examination, including cognitive, motor and sensorial assessment. Her cerebellar tests were impaired and her gait was ataxic. On systemic examination, the pharyngeal tonsils were hyperemic. She scored 29 out of 30 on the Mini-Mental State Examination losing 1 point on attention and calculation on the Mini-Mental State Examination. Her brain MRI showed a focal hyper-intense lesion in the splenium of corpus callosum (SCC) (18x15 mm) on diffusion weighted sequence which was hypo-intense on ADC mapping (Figure 1a, b and Figure 2). She was hospitalized in the neurology service. Both personality (apathy, disinhibition, affective flattening, obsessive thinking, irritability) and behavior (motor stereotypies, a finalistic motor activity, aggressiveness, eating disorders) test scores were normal with neuropsychiatric inventory. Her electroencephalography (EEG) showed slow waves in left hemisphere; her C-reactive was 14.7 mg/L (0-5) and white blood cell (WBC) = 13.4 K/uL (3.5-10.5) were high. Her CSF proteins, albumin, the cell count, and IgG (Immunoglobulin G) index were normal. The patient's antibiotic therapy was continued. In addition, paracetamol (twice a day) and 1000 cc isotonic/daily were given. After 10 days, there was no lesion in SCC in the repeat MRI (Figure 2).

Patient 2

A 51-year-old, right-handed, male judge was brought to the emergency room by his wife who reported that he had a few minutes of speech disorder and numbness in his limbs (September 8, 2018). His family history was negative for neurological disorders. He had throat pain and fever for 2 days. He was not taking medication for these complaints. His neurological examination was normal and on systemic examination, the pharyngeal area was hyperemic. His brain MRI diffusion weighted sequence showed a focal hyper-intense lesion of 16x8 mm in the SCC and corresponding anatomical parts was hypointense in ADC mapping (Figure 1.2a, 1.2b). His EEG was normal. His other laboratory tests results showed platelets of 125 K/uL (150-450) with normal hemoglobin, WBC, folic acid, vitamin B12, procalcitonin and erythrocyte sedimentation rate (ESR). The patient was given 1 gr ampicillin (twice a day), paracetamol and 1000 cc isotonic daily. His cognitive and neurological examination was normal during hospitalization. After 10 days, there was no lesion in SCC in the repeat MRI.

Patient 3

A 19-year-old, mix-handed, male student presented with headache, vomiting and fever for 6 days (December 1, 2018). He was examined by an otolaryngologist 3 days prior and was diagnosed with sinusitis and treated with moxifloxacin for 3. He was transferred to our emergency service with unconsciousness and amnesia lasting a few minutes. His neurological examination, hematological, biochemical analyzes and Mini-Mental State Examination were normal. His diffusion weighted MRI showed a focal hyper-intense lesion of 8x10 mm in the SCC and on ADC mapping (Figure 1.3a, 1.3b). His EEG was normal; his CSF protein was 75 mg/dl (15-85), glucose 55 mg/dL (blood glucose 104 mg/dL) and polymerase chain reaction (PCR) = negative (for adenovirus, cytomegalovirus, enteroviruses, Epstein Barr virus, herpes simplex virus, human herpesvirus 6 and 7, parvovirus B19 and varicella-zoster virus). CSF microscopy showed 143 cells/mm^3 (46% atypical lymphocyte, 24% lymphocyte, 30% neutrophil). He was treated with ceftriaxone 1gr (twice a day), dexamethasone 8 mg (three times a day) paracetamol and 1000 cc isotonic daily. His cognitive and neurological examination is normal as long as the patient was hospitalized. After 14 days, there was no lesion in SCC in the repeat MRI.

Patient 4

A 34-year-old, right-handed, female housewife who had epilepsy (two seizures episodes last month) for 10 years and treated with carbamazepine for 4 years. She was brought to the emergency department with complaints of fever and recurrent partial seizures. On examination she was lethargic. She was treated with phenytoin infusion at a dose of 18 mg/kg in the emergency room. Her brain diffusion weighted MRI sequence showed a focal hyper-intense lesion

of 12x10 mm in the SCC and which on ADC mapping was hypointense (Figure 1.4a, 1.4b). Her hemoglobin, PLT, WBC, folic acid, vitamin B12 and biochemistry analyses were normal. She was treated with mannitol 500 cc/day, dexamethasone 8 mg (three times a day) and paracetamol. After the seizures were controlled, the patient was transferred to the neurology service one day later. Her EEG was normal. Levetiracetam 1000 mg/day was added and her seizure activity was controlled. Mannitol and dexamethasone were reduced and then stopped. A diffusion weighed MRI after 10 days showed resolution of the lesion. Her cognitive and neurological examination were normal in the neurology service. She was discharged 10 days later. The clinical situation was considered as MERS associated with epilepsy.

Patient 5

A 22-year-old, right-handed female was brought to the emergency department by her parents with the complaints of nausea, vomiting and temporary vision loss in both eyes (February 19, 2019) for 2 days. She did not use any medication and she had no chronic medical history and her neurological examination was normal in the emergency department. The diffusion weighted MRI showed a 9x11 mm focal, hyper-intense lesion in the SCC and on ADC mapping hypo-intensity in the same area (Figure 1.5a, 1.5b). Her EEG, hemoglobin, ESR, PLT, WBC, folic acid, vitamin B12, biochemistry, immunoglobulin (Ig) G and M, visual evoked potential (VEP), CSF protein, IgG, IgG Index, PCR (for adenovirus, cytomegalovirus, enteroviruses, Epstein Barr virus, herpes simplex virus, human herpesvirus 6 and 7, parvovirus B19 and varicella-zoster virus) and cultures were normal or negative. Her anti CCP, anti-ds DNA, anti-neutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA), rheumatoid factor (RF) and anti-cardiolipin IGM/IGG were negative. Her C-reactive protein was 5.27 mg/L (0-5). Her vomiting and vision loss improved with only intravenous hydration for 5 days. Her cognitive and neurological examination is normal as long as the patient is hospitalized. After 12 days, there were no lesion in SCC in MRI.

Patient 6

A 21-year-old, right-handed, male cashier who had no history of chronic illness was brought directly to the emergency department after 2 tonic and clonic seizures. He had fever and fatigue on the same day. (March 28, 2019). The patient's cognition was mildly impaired during his examination in the emergency room. There was no motor deficit. In his systemic examination, the pharyngeal area was hyperemic. His brain MRI diffusion weighted sequence showed a focal hyper-intense lesion of 13x7 mm in the SCC and hypo-intense on ADC mapping in the same area (Figure 1.6a, 1.6b). His EEG, CSF and blood tests results were normal. Levetiracetam 1000 mg/day and dexketoprofen 25 mg (twice a day) were started. His seizures did not recur after levetiracetam. Dexketoprofen was stopped after 3 days. After 6 days, there were no lesion in SCC with repeat MRI. The clinical symptoms were considered as MERS associated with epilepsy.

Patient 7

A 27-year-old, left-handed, male construction worker presented with nausea and vomiting with visual loss in both eyes lasting for a few seconds and was brought to the emergency department by his wife (July 13, 2019). He had no chronic diseases history. His cognition, neurological and systemic examination were normal. The diffusion weighted brain MRI showed a focal hyper-intense lesion of 15x8 mm in the SCC which on ADC mapping was hypointense (Figure 1.7a, 1.7b). His blood count, biochemistry and visual evoked potential (VEP) were normal. Only 1000 cc isotonic/daily was given in the treatment. He did not have any additional complaints during his stay in the service. After 14 days, there were no lesion in SCC on the repeat MRI.

Patient 8

A 48-year-old, right-handed, male truck driver was brought to the emergency service with short-term consciousness (disorientation about the time of day, where he was and even who he was) and syncope attack (November 26, 2019). The patient's wife reported that he had throat pain, fever, nausea and vomiting for 3 days. His physician prescribed analgesic anti-inflammatory and ampicillin-sulbactam 1 gr (twice a day). The patient's consciousness was mildly impaired in the emergency department though he was oriented and cooperative (he occasionally said unmeaning sentences). His motor and cerebellar tests were normal though his axillary temperature was 37.8 °C. His throat was slightly hyperemic and he had a nasal discharge. The brain MRI diffusion weighted sequence showed a focal hyper-intense lesion of 16x9 mm within SCC and hypo-intense on ADC mapping in the same area (Figure 1.8a, 1.8b). His C-reactive protein of 12.69 mg/L (0-5) was high. His other blood tests results and EEG

were normal. His treatment was moxifloxacin 400 mg/250 ml, paracetamol and 1000 cc isotonic/ daily. He did not have any additional complaints or fever on follow-up. After 10 days, there were no lesion in SCC his repeat MRI.

Patient 9

A 61-year-old, right-handed female housewife who had an arthroscopic operation 3 days prior in the orthopedics department. She had moxifloxacin for 3 days post-operatively (February 17, 2020). She had intermittent fever and her highest temperature was 38.2 °C. She was referred for impairment of consciousness on the same day. In our neurological examination, the patient's oriented and cooperation were mildly impaired (oriented about the time of day, where she was and even who she was; however, she occasionally said inappropriate words and sentences). Since the patient was not cooperative her motor, sensory and coordination examinations were not performed. There was hyperemia in the left hip (arthroplasty area). Her routine hemogram and biochemical values were normal. The diffusion weighted MRI showed a focal hyper-intense lesion of 19x16 mm within SCC which was hypo-intense on ADC mapping (Figure 1.9a, 1.9b). Her C-reactive protein was 53.4 mg/L (0-5) and WBC of 16.9 K/uL (3.5-10.5) were high. Her urine culture was normal. The moxifloxacin was continued and paracetamol was added. She was orientated and cooperative the next days. Her neurological examination was normal. Her symptoms, C-reactive protein and WBC level resolved after 7 days. After 12 days, there were no lesion in SCC in her repeat MRI.

Patient 10

A 46-year-old, right-handed male office worker presented with fever, cough, and dyspnea for 2 days. He was referred to the emergency service with transient impairment of consciousness on the same day (October 03, 2020). His wife gave the history of loss of consciousness for 2-3 minutes. His neurological examination, orientation and cooperation were normal and he was afebrile. Rhonchus were detected in the left lower lung zones on auscultation. The diffusion brain MRI showed a focal lesion of 16x8 mm within SCC and on ADC mapping (Figure 1.10a, 1.10b). His EEG was normal. Pneumonic infiltrates were detected in the lower left lung on thorax computed tomography. His blood count test was normal, C-reactive protein was 78.8 mg/L (0-5 and Covid-19 (SARS-CoV-2) PCR test result was positive. He was treated with hydroxychloroquine 200 mg (BID) and prednisone (1 mg / kg / day for 1 week) for 5 days. There was no neurological complaint during follow-up. After the 10 days, his symptoms regressed and there was no lesion in SCC in his control MRI after 16 days.

Patient 11

A 62-year-old, right-handed, female housewife presented with fatigue, loss of appetite, fever and dyspnea for 2 days with an episode of unconsciousness and dyspnea. She was brought to the emergency department by her son (March 08, 2021), who said that she was using painkillers, the name of which he does not know. The patient was treated with amlodipine 5 mg/daily. Her axillary temperature was 39.4 °C. She was oriented and cooperative. Her diffusion weighted MRI showed a focal lesion of 13.0x9.0 mm within SCC and on ADC mapping (Figure 1.11a, 1.11b). Pneumonic infiltrates were detected in the lower of the bilateral lung on thorax computed tomography. Her blood count was normal, C-reactive protein was 16.7 mg/L (0-5) and Covid-19 (SARS-CoV-2) PCR test was positive. She was treated with low molecular weight heparin 6000 unit (two times in a day), prednisone (1 mg/kg/day for 1 week), vitamin C, moxifloxacin (400mg/day) and oxygen. After 7 days, her symptoms regressed and there was no lesion in SCC in her repeat MRI after 21 days.

Patient 12

A 36-year-old, right-handed male government officer had fever, headache and cough for 3 days. Due to a change in consciousness that lasted for a few minutes today, he was brought to the Emergency Department by his wife (November 17, 2021). He was taking 650 mg of paracetamol and 4 mg of chlorpheniramine maleate for 2 days. The second dose of SARS-CoV-2 vaccine (Pfizer-BioNTech) was received 12 days ago. His cognitive, motor and sensorial, cerebellar, and gait examination were normal. The diffusion weighed MRI showed a focal hyper-intense lesion of 24.0x11.0 mm within SCC and hyper-intense lesion in the same are on ADC mapping (Figure 1.12a, 1.12b). His blood count, vitamin B12 and ferritin were normal, though his C-reactive protein was 34.5 mg/L (0-5), and his Covid-19 (SARS-CoV-2) PCR test result was negative. He was treated with prednisone (1 mg/kg/day) and moxifloxacin (400mg/day). After 8 days, his symptoms regressed and there was no lesion in SCC in his repeat MRI after 30 days.