ENCEPHALITIS WITH PROLONGED BUT REVERSIBLE SPLENIAL LESION

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Summary: Introduction: The splenium of the corpus callosum has a specific structure of blood supply with a tendency towards blood-brain barrier breakdown, intramyelinic edema, and damage due to hypoxia or toxins. Signs and symptoms of reversible syndrome of the splenium of the corpus callosum typically include disorientation, confusion, impaired consciousness, and epileptic seizures. Case report: A previously healthy 32-year-old man suffered from weakness, headache, and fever. Subsequently, he developed apathy, ataxia, and inability to walk, and therefore was admitted to the hospital. Cerebrospinal fluid showed protein elevation (0.9 g/l) and pleocytosis (232/1 ul). A brain MRI showed hyperintense lesions in the middle of the corpus callosum. The patient was treated with antibiotics, and subsequently, in combination with steroids. Two months later, the hyperintense lesions in the splenium and the basal ganglia had disappeared. Almost seven months since his hospitalization in the Department of Neurology, the patient has returned to his previous employment. He now does not exhibit any mental changes, an optic edema and urological problems have improved. In addition, he is now actively engaged in sports. Conclusion: We have described a case of a 32-year-old man with confusion, ataxia, and inability to stand and walk. The man developed a febrile meningeal syndrome and a hyperintense lesion of the splenium, which lasted for two months. Neurological changes, optic nerve edema, and urinary retention have resolved over the course of seven months. We think that the prolonged but transient lesion of the splenium may have been caused by encephalitis of viral origin.

Keywords: Splenium of the corpus callosum; T2-weighted lesion; Optic nerve edema; Confusion; Encephalitis

Introduction

Corpus callosum is the largest commissural pathway consisting of myelinated axons that cross the midline and connect homologous regions of both hemispheres. Magnetic resonance imaging (MRI) may commonly and unexpectedly display abnormalities of the splenium of the corpus callosum (SCC). Typically, such SCC lesions are reversible and are associated with various clinical symptoms (confusion, delirium, epileptic seizures) and etiologies (ischemic infarction, trauma, tumors, alcohol abuse, intoxication, and hypopituitarism) (7). Numerous studies have been conducted and case reports have been published; nonetheless, the body of knowledge concerning the SCC remains sketchy (2). A reversible lesion with transiently reduced diffusion in the SCC has been reported in patients with clinically mild encephalitis/encephalopathy, leading to a new clinical-radiological syndrome – mild encephalitis/encephalopathy with a reversible splenial lesion (MERS). Lesions in the middle of the SCC or MERS have been described in various infectious diseases (herpes, rickettsia, and influenza) and also after vaccination (11). We describe a case of a previously healthy man, who presented with a two-week history of fever and who developed meningeal syndrome, confusion, urinary retention, and other, mild signs of brain dysfunction. An MRI scan revealed hyperintense lesions in the middle of the SCC, lasting for more than two months.

Case report

A previously healthy 32-year-old man suffered from flu-like symptoms in July 2014 along with fever and weakness. He was treated by antibiotics and recovered. His condition improved for three weeks. Subsequently, the patient developed a fever, headache, a generalized body ache, and psychomotor decline. He was admitted to the urology department of a regional hospital with urinary retention and was treated with antibiotics (trimethoprim + sulfamethoxazole) for suspected urinary infection.

As the patient’s condition was not improving, he was examined by a neurologist. A lumbar puncture was performed, and proteinocytologic dissociation was found: proteins
1.2 g/l (0.20–0.40); leukocytes 3.7 × 10^6/l (0.0–5.0); glucose 2.4 mmol/l (2.50–4.50); lactate 2.9 mmol/l (1.20–2.10).

With suspected meningoencephalitis he was transferred to our hospital, Department of Infectious Diseases. The patient’s condition deteriorated rapidly. The examination revealed meningeal and cerebellar syndrome and another lumbar puncture (LP) was performed with a corresponding finding: a protein level of 0.9 g/l; a leukocyte count 232.0 × 10^6/l, only 3 days after the first lumbar puncture! He was treated by acyclovir and ceftriaxone. A brain MRI was performed, which showed T2 hyperintense lesions in the central part of the splenium of the corpus callosum. Similar, smaller lesions were identified in the area of the left thalamus, the basal ganglia, and the brainstem.

Since the patient’s condition was not improving, he was transferred to the Neurological Intensive Care Unit (ICU). His neurological examination revealed cognitive and behavioral deficiency, meningeal syndrome, and minor multifocal symptoms originating in the right hemisphere, the cerebellum, and the extrapyramidal system. Urological examination showed persistent urinary retention, and ophthalmic examination led to the diagnosis of papillary congestion.

The patient was hospitalized in the Department of Neurology for a total of two months. A total of seven LPs were performed. Most of them to relieve the fluid pressure. The cytologic findings of the cerebrospinal fluid (CSF) revealed uniform population of lymphocytes but the immune pheno- typing was normal, so the lymphoma was not proved. The laboratory findings of the CSF gradually improved: in a week – proteins 0.88 g/l; leukocytes 209.0 × 10^6/l, in two weeks – proteins 0.51 g/l; leukocytes 116.0 × 10^6/l. And so the CSF opening pressure, from 575 mm H_2O to 425 mm H_2O (200–300 mm H_2O) with a patient sitting up. The last CSF finding was: proteins 0.4 g/l; leukocytes 36.0 × 10^6/l.

A repeat MRI scan of the brain, performed approximately one month later, showed regression of the most extensive lesion in the splenium of the corpus callosum and also of the minor multifocal lesions in the basal ganglia and the thalamus bilaterally. Two months later, complete regression was present.

Fig. 1: MRI of the brain, axial FLAIR – hyperintense lesions of the splenium of the corpus callosum and the left thalamus.

Fig. 2: MRI of the brain, ADC/DWI – hyperintense lesions of the splenium of the corpus callosum: a) MRI of the brain, DWI; b) MRI of the brain, ADC.
Treatment of the patient proved to be very difficult. The origin of the meningoencephalitis was not found. The patient was treated with acyclovir and ceftriaxone. After three weeks, the patient was started on meropenem. Subsequently, methylprednisolone pulse therapy (a total amount of 3 grams) was given for a period of 11 days.

Urinary retention was present during almost the entire hospitalization period; therefore, an indwelling urinary catheter was used. Furthermore, the patient was treated with tamsulosin and distigmine bromide and was followed-up in an outpatient clinic in regular intervals over a period of six months. Nowadays he is treated only with tamsulosine.

In the Ophthalmology Department, regular follow-up assessments of the papillary congestion were performed, using optical coherence tomography (OCT). The patient was taking acetazolamide and the papillary edema had regressed after the period of six months.

The patient’s neurological examinations have revealed continuing improvement of his condition. Gradual verticalization was started, first using a stand tall walker, and later the forearm crutches. Finally, the patient’s gait became stable even without any assistive aids.

The patient was unfit for work for a total period of seven months. Nowadays, the patient is without any subjective problems. He is feeling well, and has started doing sports – running. The patient’s memory and cognitive function have returned to baseline.

Discussion

We have described a case of a 32-year-old man with confusion, meningeal syndrome, and a hyperintense lesion on MRI (T2-weighted images) in the middle of the corpus callosum. This is unique due to the duration of the T2 lesion (a period of 2 months) and the associated urinary retention and edema of the optic nerve, which completely resolved over a period of seven months. In our patient, we think that the reversible SCC lesion was caused by viral encephalitis. The laboratory findings did not detect any autoimmune parainfectious process.

The corpus callosum is the largest commissural pathway consisting of the cross-sectional area representing twice the magnitude of the sum of all other commissural structures.
in the brain of an adult. It consists of myelinated axons that cross the midline in the developing brain in order to connect homologous regions of both hemispheres (5). The splenium receives its arterial supply from the vertebrobasilar system. The exact mechanism of the development of transient splenial hyperintensity is not known. Some of the proposed mechanisms are blood-brain barrier breakdown, intramyelinic edema due to inflammation and migration of inflammatory cells, extrapontine osmotic myelinolysis due to sodium and glucose imbalance, and direct viral invasion or hypersensitivity to antiepileptic drugs. Studies about posttraumatic lesions in the corpus callosum generally explain the prevalence of callosal injury by its vulnerability to shearing forces (8). In our patient, we presume the presence of an inflammatory mechanism, with intramyelinic edema lasting for more than one month.

Clinical manifestations of reversible syndrome of the splenium of the corpus callosum include disorientation, confusion, epileptic seizures, headache, ataxia, symptoms of hemispheric disconnection, dysarthria, hallucinations, and impaired consciousness progressing to coma (2). Confusion was the most common clinical finding in 50% of cases. Cerebral infarction was the most common etiology (50%). The most consistent SCC changes on MRI were low signal on T1WI (T1-weighted images), high signal on T2WI and FLAIR, and high signal on DWI. SCC lesions are classified into in situ SCC lesions (SCC only) and multiple (SCC plus) lesions for patients with multiple lesions (7). In our patient, the T2 hyperintense lesion was in the middle of the SCC; furthermore, a small lesion was present in the left thalamus.

Shankar et al. presented a case of mild encephalitis with a reversible splenial lesion (MERS), evaluated with diffusion-weighted and diffusion tensor imaging along with various conventional sequences of MRI (10). At the time of presentation, the lesions in the splenium of the corpus callosum and bilateral cerebral white matter showed diffusion restriction with reduced apparent diffusion coefficient and no reduction in fractional anisotropy (FA) values on diffusion tensor imaging (10). On follow-up, diffusion restriction completely resolved with normalization of the apparent diffusion coefficient (10). The normal to slightly increased FA values in the lesions may indicate that MERS is a non-degenerative disorder (10). The reversible lesion was present for 5–7 days. Our patient suffered from MERS, but the T2 hyperintense lesion was present for 2 months, moreover not only SCC was affected.

Reversible splenial syndrome of the corpus callosum (RESLES) belongs to a new clinico-radiological diagnosis. Its development is attributed to antiepileptic drugs, alcohol abuse, hypernatremia, altitude sickness, radiation therapy, various toxic exposures, and infectious agents (2, 3). The etiology of MERS is infectious (1, 12), which was present also in our patient.

Reversible lesions in the splenium of the corpus callosum (SCC), caused by various infective agents such as influenza, rotavirus, mumps, Escherichia coli, and adenoviruses, have been documented in the literature. The changes

<table>
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<td>Miscellaneous</td>
<td>Drug toxicity (cyclosporine, fluorouracil), High-altitude cerebral edema, Trauma – diffuse axonal injury, Malnutrition – Vitamin B12 deficiency</td>
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Tab. 1: Clinical conditions associated with splenial hyperintensity.

AED antiepileptic drugs
ADEM acute disseminated encephalomyelitis
NMO neuromyelitis optica
PRES posterior reversible encephalopathy syndrome

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become apparent on MRI as early as the second day of onset of symptoms, and CSF findings are usually normal or non-specific (4). Many hypotheses have been suggested to explain such transient lesions of the SCC. Reversible demyelination due to antiepileptic drugs like primidone or carbamazepine may reduce arginine vasopressin levels, with changes of osmolality. According to another hypothesis, viral antigens or antibodies have an increased affinity for the receptors on splenial axons, resulting in inflammatory infiltrates. In 2003, Oster et al. reported reduced apparent diffuse coefficient (ADC) values in a reversible splenial lesion, seen on MRI (6). They suggested that repeated and excessive electrical discharges along the commissural fibers during seizures had caused transient changes in energy metabolism and ionic transport, resulting in rapidly resolving intramyelinic edema. We agree that the SCC is a specific anatomical structure with predisposition to edema, toxic changes of myelin, and vascular changes with hypoxia and ischemia. Differential diagnosis associated with splenial abnormalities includes: Marchiafava-Bignami Syndrome, renal failure, metabolic abnormalities (mainly sodium and glucose level disturbances), encephalitis from influenza or rotavirus infection, altitude sickness, intoxication, antiepileptic drug treatment, thiamin deficiency, and alcoholism. Presumably, all of these conditions can disturb cellular fluid regulation and lead to a cellular lesion (9).

Conclusion

Transient hyperintense T2 MRI lesion in the middle of the splenium of the corpus callosum is associated with confusion, epileptic seizures, and mental changes. The etiology of the lesion is varied – toxic, hypoxic, and inflammatory – and its duration is 1–2 weeks. We have described a case of a young man with fever, meningeal syndrome, and confusion. We think the cause was viral encephalitis. It is unique because the clinical findings and the MRI lesion were present for two months. In addition, they were associated with optic nerve edema and urinary retention. Over a period of seven months, all the findings have improved, and the patient is now able to work full-time and engage in sports again.

References


Received: 14/05/2015
Accepted in revised form: 10/09/2015

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