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Therapeutic difficulties in vegetative epileptic seizures as a sign of acute viral encephalitis: case presentation

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Abstract

Acute encephalitis is a severe pathology represented by the inflammation of the brain parenchyma associated with neurological dysfunction. The etiology is predominantly viral or autoimmune, with different therapeutic approach. The typical manifestations include fever, epileptic seizures and neurological focal signs. The treatment consists in specific drug therapies regarding the etiology and rehabilitation therapies in case of incomplete recovery.

We present a case of a 43-year-old woman with occipital cephalalgia and dizziness, associated with vesperal high blood pressure levels at the same hour daily. The brain MRI described possible acute encephalitis, with FLAIR and T2 hypersignal area on right parietal region and diffusion restriction. The lumbar puncture revealed no modifications and the EEG recordings showed irritative patterns. The acyclovir intravenous treatment and an antiepileptic drug were initiated. The repeated MRI revealed laminar necrosis which explained the vegetative epileptic seizures manifested with high blood pressure. The clinical status of the patient majorly improved due to specific treatment including rehabilitation interventions.

Key words: *acute viral encephalitis, vegetative epileptic seizures, laminar necrosis, cephalalgia, rehabilitation,*

1. Introduction

Encephalitis represents the inflammation of the cerebral parenchyma associated with a neurological dysfunction, caused by the infection of the central nervous system or by an immune-mediated mechanism (1).

Clinical manifestations of encephalitis include fever, epileptic crisis, focal neurologic signs, pleocytosis in CSF, neuroimages and EEG manifestations (2, 3).

The most common cause of encephalitis is the viral infection. In many cases, it can be difficult to determine the etiology considering that are over 100 pathogens which can be involved, most common being herpes simplex virus 1 and 2 (HSV).Almost 50% of encephalitis cases remain undiagnosed (4).

The diagnostic approach includes lumbar puncture, the analysis of the cerebrospinal fluid (CSF) and MRI (5). On the MRI, the main abnormalities include the presence of hypersignal in the temporal and frontal lobe and in the insular cortex, diffusion restriction and contrast enhancement (4). If the etiology is not determined the empiric treatment is with intravenous Acyclovir for 10-14 days. Following the above-mentioned treatment, the mortality in these cases decreases from 70% to just 8%. (4).

Some patients remain with neurological sequelae that can be partially diminished by specific rehabilitation therapy. The recovery from encephalitis is variable according to the patient predisposition and the severity of the case, from a complete and fast recovery to an incomplete or prolonged recovery that might last several months. Some of the chronic deficits that the patient may experience include neurological impairments, movement disorders, aphasia, behavioral abnormalities, and intellectual deficit. The general outcome can be improved by rehabilitation methods which can be applied according to each case particularity (6).

Cognitive therapy interventions, measuring for example memory and language processing, have a positive change in neuropsychological tests from baseline to follow-up, but with no complete recovery for the majority of patients. Behavioral therapy methods following infectious encephalitis also show an improved result. Physical therapy interventions are very important in improving motor and sensory deficits, with lower need of assistance for daily life activities (6).

The combination of physical, psychological, occupational and speech therapy plays a major role in the rehabilitation of these patients, and studies reveal a significant improvement in scores, but with incomplete recovery for some patients (6).

2. Case presentation

The patient, a 43-year-old woman with no pathological history, presented to the Neurology Department for pulsating occipital headache, dizziness and drowsiness. These symptoms suddenly started 5 days prior to the admission and at the beginning they included tremor, parenthesis in the upper and lower limbs, giddiness and headache.

At the general examination, there were no signs of pathological modifications.

When the neurological assessment was performed, the patient was conscious, spatially and temporally oriented, without any signs of meningeal irritation or intracranial hypertension, not showing any involuntary movements, without any pathological modifications on cranial nerves, except from a slightly positive unsystemised Romberg, independent walking, with no motor deficit, motor strength=5/5, normotonia, without dysmetria, deep tendon reflexes and abdominal cutaneous reflexes present bilaterally, plantar cutaneous reflex in flexion, without pathological reflexes, pain when palpating the bilateral Arnold points, sharp pain when palpating the occipital region, without subjective or objective sensibility disorders, continent sphincters.

Biologic: VEM 99,8fl slightly raised (VN 90-95fl), Vitamin B12 deficiency (150 pg/ml, VN=180-914pg/ml), microscopic hematuria.

Taking into consideration the uncharacteristic pathology and the multitude of differential diagnosis, an emergency native cerebral CT scan was performed with no pathological findings.

The investigations were continued with radiography of the cervical spine, but no degenerative or static changes were noticed. The ENT assessment found normal hearing and vertiginous syndrome of neurologic cause.

As the patient displayed persistent high blood pressure (of 145/90mmHg-180/90mmHg) which did not improve when given IECA and indapamide, a cardiologic examination was made, with normal EKG and echocardiography.

As the patient showed anxiety and panic attacks, a psychological assessment was completed and it revealed only signs of anxiety caused by the sudden appearance of the symptoms, with no suspicion of depression or somatization.

During this time, the patient followed a symptomatic treatment which showed a slight improvement, although the low intensity vertigo and the headache persisted. During the day, the patient presented normal-high blood pressure with a maximal value of 130/90mmHg, measured in the morning. In the evening, after 7pm, her general mood would worsen, with accentuated occipital headache and her blood pressure would be as high as 190/100mmHg. These symptoms would persist through the night until early morning, at around 4am. A chronic treatment with enalapril and indapamide was administrated with no success, followed by angiotensin-II-receptor antagonists and calcium channel blockers as a possible resistivity to IECA was taken into consideration, also unsuccessfully. During the moments of elevated blood pressure, numerous hypertensive medications were administrated, such as IECA, angiotensin II receptor blockers, beta blockers, furosemide, calcium channel blockers and anxiolytics when the patient presented panic attacks, but blood pressure continued to follow the same daily pattern: in the evening, blood pressure would suddenly increase over the values she presented during the day, the headache would aggravate along with anxiety. These symptoms would go for hours, only fade away back to normal in the morning with or without the medication.

A native cerebral MRI is performed and described a discrete FLAIR and T2 hypersignal coming from the right parietal region, as seen in Figure 1, and moderate diffusion restriction, as showed in Figure 2. The cortical distribution affected two gyri near a sulcus, with no SWI and T1 expression. The aspect of the MRI indicated a possible focal encephalitis.

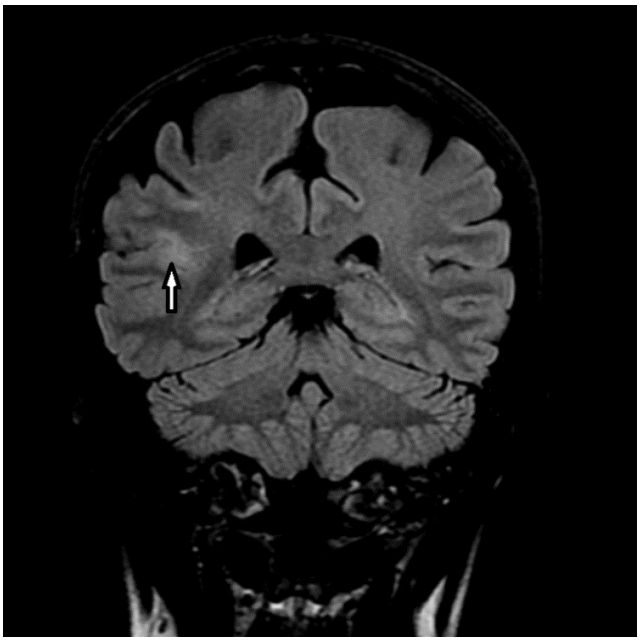

Fig. 1: *Native cerebral MRI, T2 FAIR, coronal section, hypersignal in the right parietal area*

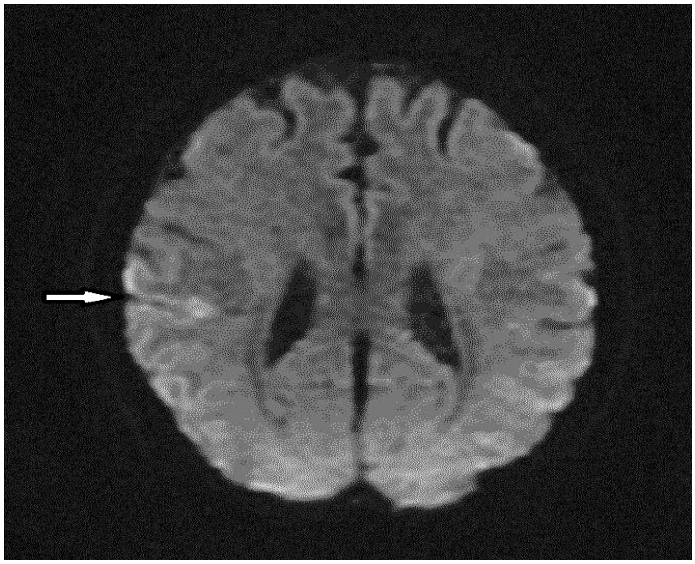

Fig. 2: *Native cerebral MRI, DWI, axial section, moderate diffusion restriction area*

As the suspicion of viral encephalitis arose, the Infectious Diseases clinic was contacted and recommended an emergency lumbar puncture and an intravenous treatment with Acyclovir 1500mg a day for 7 days, Mannitol 20% for 3 days and Dexamethasone.

The CSF analysis revealed no pathological modifications in biochemistry (normal amylase, chlorides, glucose, LDH, total proteins), normal leukocyte count, CSF bacteriologic exam (absent Streptococcus pneumoniae, Streptococcus beta hemolytic, Staphylococcus aureus, Enterobacteriaceae, Enterococcus spp, Pseudomonas spp, Acinetobacter spp.). The multiplex PCR Panel was undetectable for Escherichia coli K1, Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae, Cytomegalovirus, Enterovirus, Herpes simplex virus 1,2,6, Human Parechovirus, Varicella zoster virus, Cryptococcus neoformans/gattii.

The immunologic analysis from serum did not reveal any IgM anti-Herpes type 1,2, CMV reactivity, but there was IgG reactivity for HSV, VVZ, CMV and an uncertain result for EBV. Although the blood and CSF analysis did not reveal the encephalitis etiology, the clinical status and the imagistic aspects indicate viral encephalitis from the Herpesviridae category. From this reason, the Infectious Diseases specialists recommended that the empiric treatment with Acyclovir should continue.

During the treatment, the clinical state of the patient has considerably improved: the headache reduced in frequency, appearing only occasionally, the dizziness got better, the drowsiness and the high blood pressure which were present during hospitalization disappeared. Although the injectable treatment with Acyclovir usually is administrated for 10-14 days, the patient followed it only for 7 days because of the hepatic cytolysis syndrome which appeared. After that, the treatment was discharged with oral treatment of Acyclovir 400mg 2 pills 4 times a day for 14 days, while the hepatic and renal functions were monitored.

EEG: alpha rhythm 11 cycles/sec in posterior progressing towards the anterior area, with rare pathological irritative elements at the C4-P4 (right parietal and central) level (Figure 3). Taking into consideration the cortical damage showed on the cerebral MRI and the irritative changes in the right parietal region which correspond to the focal lesion, a prophylactic antiepileptic treatment was recommended: Levetiracetam 500mg one pill two times a day.

After three weeks from onset, a follow up cerebral MRI with contrast was performed and it revealed two areas of hypersignal T1, T2 and FLAIR, without a diffusion restriction, at frontal parietal level and right parietal with cortical distribution and a reduction of the hypersignal T2 zone in the right parietal region compared to the preceding examination (Figure 4). There was a suspicion for a possible cortical laminar necrosis in the right frontal parietal region.

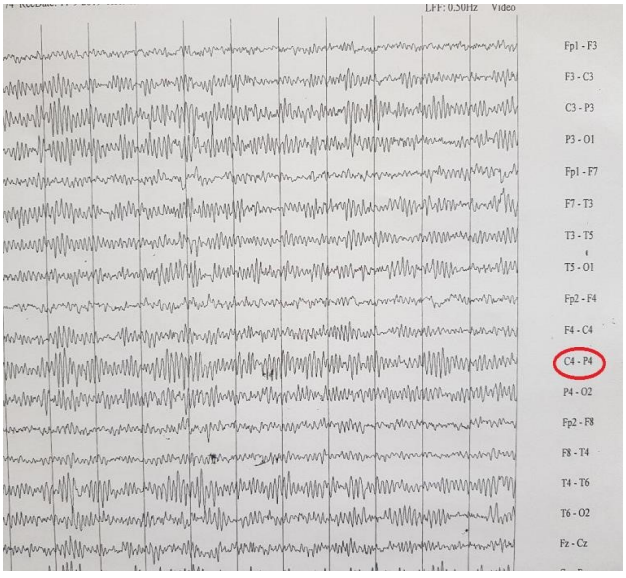

Fig. 3: EEG- *pathological elements of irritative type at C4-P4 (right parieto-central) level.*

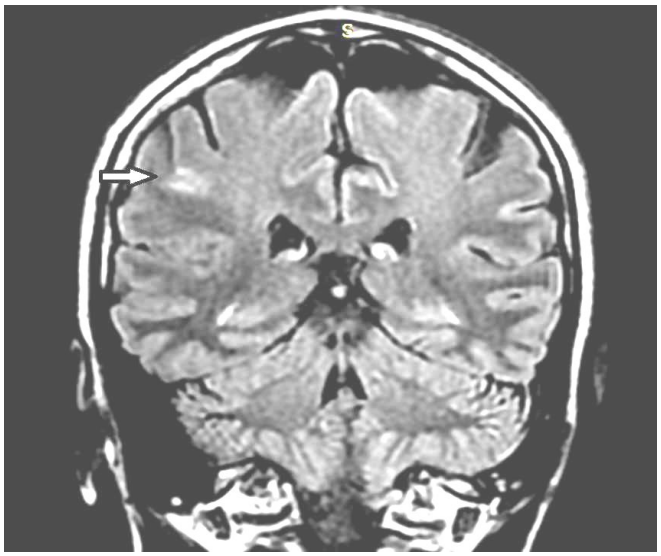

Fig. 4: *Cerebral MRI with contrast, T2 FLAIR, coronal section, hypersignal area in the right parietal level.*

At the release from hospital, the outcome was favorable, with an improved general condition under the medication mentioned above.

At a few weeks follow-up examination, the patient still complained about a remaining dizziness sensation, although majorly improved compared to the acute phase and a low intensity headache. Also, she developed general anxiety due to the medical condition, for which she refused to practice any psychotherapy or any other activity that will diminish it.

3. Discussions

Encephalitis represents a pathology with significant mortality and morbidity, which, if detected early on, can change the outcome for the patient.

The etiology can be infectious (viruses, bacteria, parasites, fungi), post infectious (Acute disseminated encephalomyelitis), non-infectious (autoimmune, paraneoplastic). Its frequency varies dependent on the geographical region and age, from 0.7 to 13.8 in 100,000 people (2).

The Herpes virus encephalitis caused is the most frequent in developed countries, with a predominance of 90% for HSV type1, not being favored by immunosuppressant. The HSV 1 affects especially the temporal and orbital and frontal lobe. A third of the cases are attributed to the primary infection which spreads through the olfactory nerves by nasopharyngeal and two thirds are caused by the viral reactivation and its spreading in the intracranial portion of the trigeminal nerve (1). Clinically, it manifests itself through fever, headache, personality disorders and epileptic seizures (4). The CSF exam discovers pleocytosis, normal glucose levels, and possible xanthochromia. The PCR test is an elective test with 98% sensibility and 94% specificity but can be negative initially (4). The cerebral CT in the case of the herpetic virus can show no visible changes, sometimes a hypo intensity at temporal level (7). The cerebral MRI T1 sequence shows an edema and sometimes, a hyper signal in the regions with hemorrhage and delayed enhancement under different shapes: gyrus, leptomeningeal, diffuse and annular. On the T2 sequences there can be noticed a hypersignal at the level of white substance of the cortex and hypo signal at the levels of hemorrhages. On the DWI and ADC sequences, a diffusion restriction is seen due to the cytotoxic edema, which is less intense compared to the one from a stroke (8,9).

The EEG is modified in 80% of the cases of viral acute encephalitis. It can be useful to make the differential diagnosis between an organic pathology and a psychiatric one, and also to identify the non-motor crisis. The changes are unspecific and include slow, high amplitude waves, with activity in the temporal lobe and periodic epileptiform discharges. There are no pathognomonic elements for the herpetic encephalitis (2).

The criteria for diagnosing encephalitis include:

- Major criteria: the alteration of the consciousness and the personality for over 24 hours, without any other possible alternative cause
- Minor criteria: documented fever, epileptic seizures present in the case of a patient not registered with epilepsy, focal neurologic signs which appear suddenly, the presence of leucocytes in CSF, suggestive neuroimages, EEG abnormalities.

The diagnosis of suspecting encephalitis is attributed when a major criteria is present along with two minor criteria, while the diagnosis of probable or definite encephalitis needs three minor criteria (1).

Acyclovir is an antiviral medication utilized for many species from the Herpesviridae category. The treatment should be initiated even in the cases which are not confirmed, even before the lumbar puncture or if this is delayed, and can be stopped in the case that another diagnosis is discovered to be more probable. This treatment implies a dose of 10 mg per body kilogram three times a day for approximately 14 days (2).

Because the herpetic encephalitis has also a necrotic effect, with a possible epileptogenic effect, the patients can be recommended a prophylactic antiepileptic treatment. A controversial treatment is the one with corticosteroids in the case of viral infection, as it is proven to be beneficial in certain bacterial infections, but there aren't enough clinical proofs to sustain its administration in the cases of viral infections as well (1).

The cortical laminar necrosis represents the lesions of neurons from the cerebral cortex when the oxygen and glucoses contribution cannot meet the necessities in the local tissue. The cause can be ischemia, hypoglycemia, hypoperfusion, epileptic crisis especially in epileptic status. The pathogenesis of this dysfunction which is predominant at the cortex level consists of the fact that these neurons are much more metabolically active compared to the white substance or to the glial cells around them, necessitating much more energy (10).

The changes seen on the cerebral MRI in the case of laminar cortical necrosis include in the beginning the diffusion restriction on DWI, after two weeks, the T1 hypersignal with a peak at week 4 and progressive disappearance for a few months. The T1 hypersignal shows that the denatured proteins accumulate in the damaged and macrophage cells and excludes the presence of hemorrhage or of calcium deposits. T2 Sequence presents a hypersignal (11).

The epileptic seizures are generally associated with high blood pressure because of the stimulation of the sympathetic nervous system and the secretion of catecholamine (12). Some patients can have vegetative epileptic seizures manifested only through dysfunctions of the autonomic nervous system and clinically through sudden and periodic increases in blood pressure which don't respond to usual antihypertensive medication (13).

In the case of our patient, we discovered a cortical laminar necrosis on the cerebral MRI, which was associated with the vegetative epileptic crisis from the encephalitis foci. The crises manifested through high blood pressure can be explained through rhythmicity, as these increases manifested at the same time every day, uninfluenced by numerous antihypertensive medications, through the irritative changes on the EEG and their disappearance after the antiepileptic treatment with levetiracetam has been initiated.

Regarding the long term rehabilitation, our patient experienced severe fatigue for several weeks, thus we created a lifestyle changes plan. We advised her to maintain a reasonable activity schedule, reduction of work hours, moderate and regular exercise such as walking, no intake of stimulant substances or alcohol and a healthy diet. The fatigue was significantly improved after a few days. For the persisted headache we recommend to the patient to keep a cephalalgia journal to monitor the frequency and intensity of the headache. We also encouraged psychotherapy combined with cognitive therapy to manage stress and anxiety, since the emotional component was an important reaction for our patient, but she was no compliant to this treatment and the anxiety syndrome still persisted. In our case, patient's behavior status, anxiety and cephalalgy are mandatory to be monitor in the future visits.

The quality of the rehabilitation care is not dependent of age, sex, type of infectious agent or intervention type, but is related more to establishing the correct diagnosis, the initial clinical picture, as well as the unique central nervous system characteristics of each individual (6).

The particularities of this case lay in the atypical symptomatology of encephalitis manifested through headache, without the alteration of the conscious state or other neurological signs, vegetative epileptic crisis manifested through high blood pressure, associated with cortical laminar necrosis and in the fact that the pathogen agent wasn't detected through the currently available methods.

4. Conclusions

Viral acute encephalitis is a serious pathology which can have long term consequences if it is not properly identified. The clinical manifestations can be atypical or unspecific. The treatment should be recommended to every patient with this possible diagnosis and not be delayed by the investigation process. General rehabilitation interventions can lead to a better outcome for the patient.

Informed consent

An informed consent was obtained from the patient participating in the study.

Declaration of conflict of interests

The authors declare that there was no conflict of interest regarding the publication of this paper.

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