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Case Report

DIFFERENTIAL DIAGNOSIS OF ATYPICAL MODERN ENCEPHALOMYELITIS OF UNKNOWN CAUSE

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ABSTRACT

To this day, there are cases of neuro infections that cannot be etiologically specified and are cured empirically. Clinics are difficult, and the healing process is prolonged with risks of complications. It is not uncommon for diseases to remain unrecognized for a long time due to an atypical clinical picture. This leads to prolonged exposure of the patient to the harmful effects of infection and prolongation of the disease process. The result is many costly studies without results. It is necessary to revise the current course of neuro infections and their classification, as well as to share information in specially created platforms for searching for coincidence and exchange of experience. In this regard, we present one of our cases, which remained undiagnosed and we find it interesting. The presented clinical case is atypical and etiologically unproven. An example of a challenge in diagnosis and treatment, that bears no resemblance to the relatively rare neuro infections in our region. We have studied the current changes and course of some of the most common encephalitis and summarized them with an aim to do the differential diagnosis. We need a revision of the current course of neuroinfections and a new classification based on the clinical picture.

Key words: Encephalomyelitis, Differential diagnosis, Neuroinfection

INTRODUCTION

Depending on the affected area, inflammatory diseases of the CNS are divided into those affecting the meninges (meningitis), spinal cord (myelitis) and brain (encephalitis). Often these concepts overlap due to the anatomical relationship of these structures and get affected simultaneously: meningoencephalitis, encephalomyelitis, meningoencephalomyelitis or meningoencephalomyelopolyradiculoneuritis. Encephalitis is divided into acute, subacute and chronic; primary and secondary and poly- (affecting the gray matter) leuko- (affecting the white matter) and panencephalitis. Etiologically, encephalitis is autoimmune, infectious, as a result of systemic staining, metabolic and paraneoplastic. Clinically, encephalomyelitis presents with a significant variety of clinical symptoms and course of the disease, presented with focal, cerebral symptoms and toxic infectious syndrome; with a leading symptom of disorientation. Acuteness and severity correlate with prognosis. The clinical challenge is to distinguish encephalopathy (including septic, toxic, and metabolic) from infectious encephalitis.

CASE REPORT

This is a 33 years old woman from East Europe with diffuse headache, low-grade fever, myalgia, arthralgia and general fatigue, starting in the spring of 2018. There is no medical history of travelling around the world. Lives in a place with a rich distribution of mosquitoes. Also keeps a pet dog and cat. No data on registered diseases. In apparently good general health. Additionally, upper dyspeptic complaints are added to these symptoms. One week later, the symptom complex develops with the appearance of pseudo-peripheral paresis of the facial nerve on the right, impaired swallowing and speech. A maculopapular rash spread throughout the body, which lasted for 3 days. Treated for 4 days in the Neurological Clinic with a working diagnosis of Bell's palsy until the time of the lesion and the contralateral

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face nerve and coordination disorders. Neurological status revealed neck rigidity without other symptoms of meningeal syndrome. Bilateral pseudo peripheral paresis of the facial and glossopharyngeal cranial nerve. No pyramidal signs with symmetrical, living reflexes. Laboratory studies revealed mild thrombocytosis and hematuria. Erythrocytorachia and leukocytorachia (70 $x10^9$L), proteinorachia (6.31 mg/dL) and glucose (5.67 mmol/l) were found in the cerebrospinal fluid (CSF). From the sediment of CSF, it was found that the cells are mainly segmental and lymphocytes with a mass of erythrocytes. From the conducted microbiological investigations with cultural diagnostics, the results were negative for pathogenic and conditionally pathogenic bacterial flora, incl. Candida. Brain CT showed a hypoplasia of the right vertebral artery throughout its MRI angiogram. With a preliminary diagnosis of viral encephalitis, treatment was started with corticosteroids, antibiotics and immunoglobulins in combination with symptomatic agents to permanent improvement and reversal of symptoms. Virological and/or serological diagnostics were not carried out at this stage, because these methods are not funded when carried out in a neurological unit. Discharged with minimal improvement and prescribed treatment with galantamine, despite the persistent finding in the cerebrospinal fluid. A day later, her condition deteriorated sharply, the headache started again, trembling and severe weakness in all four limbs in the course of a pronounced toxic infectious syndrome. Rehospitalized for intensive care and resuscitation, due to the threatening respiratory disorders, which again directed the differential diagnostic plan to inflammatory polyradiculoneuropathy of Guillain Barre type Landry. The next day she showed improvement with the disappearance of tetra paretic symptoms due to facial diplegia. The fluctuation is then tripled and directed for treatment in a higher class facility.

DISCUSSION

Encephalitis is inflammation of the brain that occurs due to infectious processes, resulting from infection with viruses, bacteria, fungi, and parasites, in immunosuppression or autoimmune processes, as well as a consequence of iatrogenic and toxic agents. The disease is rarely clinically evident, but it is a serious medical problem that requires timely etiological diagnosis and treatment. The consequences for individuals who have had the disease can sometimes be permanently disabling and lifelong. Even with modern diagnostic possibilities in medicine, the etiology of encephalitis remains unknown in about 30% to 40% of cases (1). With increased migrant flows from conflict areas and following mass natural disasters, as well as the intensity of tourism with visits to new tourist destinations, along with the unpredictable consequences of global climate change and a number of other challenges of the present time, real conditions are created for the emergence of new diseases, expansion of the ranges of old ones, and typically progressing ones of already well-known diseases. The presented article discusses a clinical case characterized by atypical neurological and general symptoms. Despite microbiological, imaging-diagnostic, clinical-laboratory investigations, and pathogenetic and symptomatic treatment, the etiological diagnosis was not established. The patient's clinical condition episodically worsened, necessitating her transfer to a higher-level medical institution. There is no data on the progression of the clinical condition and the outcome of the disease. A brief literature review of the most common encephalitis cases diagnosed in humans is presented to shed light on the differential diagnostic aspect of the presented clinical case.

Herpes Simplex Encephalitis. An acute and subacute disease, that causes initiate general cerebral and focal neurological symptoms. The infection is transmitted through the trigeminal or olfactory nerve to the CNS. The disease progresses with fever, headache, vomiting, psychiatric disorders, seizures, paresis and amnesia. The onset is mild or atypically acute in immunocompromised patients. The disease is the most common non-epidemic encephalitis and the most common sporadic encephalitis in the United States (2).

Mycoplasma encephalitis. Mycoplasma pneumoniae is a common cause of respiratory infections but also leads to extra pulmonary manifestations. A ten-year-old boy with a history of malaise and a fever for a week. The day before the reception he was in severe lethargy with photophobia, neck rigidity and seizures. His speech was incoherent and confused. EEG with signs of encephalopathy. Brain CT and MRI were normal. Serum with high titer of mycoplasmal antibodies. Cerebrospinal fluid with mild pleocytosis (3).

Tick-borne encephalitis in Europe. Since 2012, tick-borne encephalitis has been declared in the European Union and by 2016 there were 12,500 cases. It is caused by a Flavavirus and is transmitted by Ixodes ticks. It can very rarely be caused by drinking milk. The disease proceeds in two phases. The incubation period is eight days, and then the first few days there is a toxic infectious syndrome, followed by a symptom-free week and mild meningoencephalitis. There is a vaccine with good efficacy, as can be seen from the mass vaccination in Austria. The highest number of registered cases was in the period from June to September, peaking in 2006 (4).

West Nile encephalitis. West Nile encephalitis was first described in 1937, named after an area in Uganda. It is caused by an RNA virus from the group of flaviviruses and is transmitted by Culex mosquitoes. Birds are the primary reservoir. There are two manifestations of the virus - West Nile fever and West Nile encephalitis. From 1999-2016 there were 40086 cases. Most patients are in August. The largest epidemics were in 2002, 2003 and 2012 (5).

Encephalitis caused by Toxopalsma Gondii. Seventy-six-year-old man with complaints of worsening headaches for a month. MRI showed a 2.2 cm tumor mass in the left parietal lobe. A craniotomy with tumor resection was performed. After the operation, he started having seizures. Patroanatomical examination of the material suggested infection with Toxopalsma Gondii. Treatment with Trimethoprim / Sulfamethoxazole 5 mg / kg was initiated and proved immune histochemical. Leukocyte and lymphocyte levels were normal (6).

Rabies encephalitis. Eleven-years-old boy with complaints of vomiting, fever, strabismus, dysarthria, weakened reflexes and normal brain CT with leukocytosis in the laboratory. Two weeks ago, he was bitten on the face by a dog when he was vaccinated against rabies. Four hours later he had hyper salivation. His condition quickly deteriorated and this led to his death. The autopsy revealed positive antigens from the virus in the cerebral cortex, hippocampus and medulla oblongata (7).

Paraneoplastic encephalitis associated with lung cancer: This is a rare autoimmune neurological syndrome in patients with lung cancer. It affects the limbic system, hippocampus, hypothalamus and amygdala. The disease presents with cognitive impairment, personality changes, short-term memory loss and seizures. It is immune mediated by the neuronal antibodies GABABR and ANNA-1. Patients with GABABR encephalitis are thought to respond better to immunotherapy (8).

Autoimmune anti-NMDA receptor encephalitis. A nineteen-years-old woman with hallucinations and status epilepticus without pathological MRI data and nonspecific EEG changes was tested positive in serum and cerebrospinal fluid for anti-NMDA receptor antibodies. Four months later, after a re-EEG, extreme delta waves and significant behavioral and cognitive abnormalities were found (9).

Japanese encephalitis in Malaysia. This is a tick-borne zoonosis caused by the Japanese encephalitis virus through the Culex mosquito in East Asia. Of particular importance is the disease in children. The first reported case was of a nurse who fell ill with symptoms of general malaise, pain in the left half of the face and a headache. She died and during the autopsy the virus was detected in the cerebrospinal fluid, where the samples were positive on the seventh day and in the blood on the thirteenth (10).

St. Louis encephalitis in America. Since 1999, the epidemics has been significantly reduced by an epidemic in Arizona in 2015 and single incidents in California in 2016. The disease is caused by the St. Louis virus transmitted by the Culex mosquito. Eco-epidemiological studies suggest a recurrence of morbidity due to a new, more pathogenic strain and an increased population of the eared pigeon, which is a natural reservoir (11).

Australian Murray Valley encephalitis is endemic to Australia and New Guinea flavavirus. It is transmitted by Culex mosquitoes. There is a peak between February and June. Especially with the infection is the rapid progression to death and symptoms include paralysis, brainstem involvement with CHM paresis and tremor. A case of an 8-year-old boy with fever, seizures and changes in consciousness has been described. Laboratory changes are leukocytosis with predominant polymorpho nuclear leukocytes and proteinuria. MRI - diffuse leptomingial enhancement and limited inflammation in the left basal ganglia. The diagnosis was confirmed serologically and molecularly (12).

CONCLUSIONS

The presented clinical case is atypical and etiologically unproven. An example of a challenge in diagnosis and treatment that bears no resemblance to the relatively rare neuro infections in our region. We need a revision of the current course of neuroinfections and a new classification based on the clinical picture.

Scientific Responsibility Statement. The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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