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RESEARCH ARTICLE

ACUTE DISSEMINATED ENCEPHALOMYELITIS AFTER RABIES VACCINATION: ONE CASE REPORT

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Abstract

Acute disseminated encephalomyelitis (ADEM) is an inflammatory autoimmune demyelinating disease of the central nervous system (CNS). There is no typical clinical presentation of ADEM. The combination of multiple neurological disorders occurring during infections or vaccination should alarm the clinician. We report a case of ADEM in a 37-year-old patient, occurred 2 months after an anti-rabies vaccine shot. The diagnosis was concluded as we had the anti-rabies vaccination 2 months before the onset of symptoms, clinical symptoms (of encephalomyelitis) and the outcome of nuclear magnetic resonance imaging (bilateral and symmetrical signal abnormalities of both capsules and both Putamens, hyposignal in T1, hypersignal in T2 and FLAIR). IV corticosteroid boluses were administered, followed by oral corticosteroid therapy then gradual dose reduction. Clinical evolution was marked by improving of consciousness, disappearance of the motor deficit and the persistence of irreversible blindness. ADEM is a rare and serious condition of the central nervous system. Early management is the key to avoid complications.

Introduction:-

Acute disseminated encephalomyelitis (ADEM) is a multifocal demyelinating inflammatory disorder mainly affecting the white matter of the central nervous system [1]. It is an autoimmune disease often triggered by an infection or vaccination after a free interval [2].

Clinical presentation is often acute composed of encephalopathy and focal hemispheric or medullary neurological signs. Magnetic resonance imaging (MRI) is essential for the diagnosis, showing diffuse or multifocal lesions of the white matter in the CNS [3]. The diagnosis is based on anamnestic, clinical and radiological arguments as well as on the absence of previous **demyelinating** disease, CNS infection or other systemic diseases

We are reporting the case of ADEM in a 37-year-old man, which occurred after rabies vaccination.

Our patient is a 37-year-old man who was bitten by a stray dog 2 months prior to the admission date and received an anti-rabies vaccination following the Zagreb protocol (2 doses on D0 then 1 dose on D7 and 1 dose on D14). The patient was attacked for a second time by several stray dogs 48 hours before his admission and was admitted for acute encephalitic syndrome composed of behavioral disorder with loss of deep visual acuity without fever.

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Symptoms started 3 days before his admission by the sudden behavioral disorder with blindness, associated with audiovisual hallucinations and urinary and bowel incontinence, all evolving in a context of apyrexia and deterioration of the general condition. On clinical examination, the patient was confused with a Glasgow score of 14/15, hemodynamically and respiratory stable, with no fever. Paraplegia, an abolished photomotor reflex and negative light perception in both eyes were found. No other abnormalities were noted.

An emergency cerebral CT showed bilateral and symmetrical hypodensities of the Putamens. Lumbar puncture found clear fluid with cells less than 3 elements, glycorachia at 0.74 g/L and proteinorachia at 0.52 g/L, C-reactive protein (CRP) was slightly elevated at 30 mg/L, the blood count showed no abnormality.

Magnetic resonance imaging (MRI) was made after stabilization and revealed bilateral and symmetrical signal abnormalities of the two external capsules and the two Putamens hyposignal in T1, hypersignal in T2 and FLAIR. O**cular fundus** showed total and irreversible optic atrophy. Rabies antibody assessment showed a result > 4 EU/ml.

The diagnosis of post-vaccination ADEM was concluded based on; the anti-rabies vaccination 2 months before the onset of symptoms, previous immunization against rabies given the dosage of anti-rabies antibodies >4 EU/ml, encephalomyelitis clinical symptoms, and the cerebral MRI. Intravenous corticosteroid therapy was initiated; boluses of methylprednisolone (1g/d) for 7 days, followed by oral corticosteroid treatment for 4 weeks, then a gradual decreasing.

Patient had a total recovery of consciousness 3 days after the beginning of the treatment, his paraplegia disappeared completely, however he never gained his vision again (irreversible blindness).

Discussion:-

ADEM is defined as a multifocal autoimmune inflammatory demyelinating damage involving mainly the white matter of the CNS [1]. While it is well described in children, ADEM has rarely been reported in adults and is probably under-diagnosed [4,5]. A male preponderance is reported in several pediatric cohorts with a female/male sex ratio between 0.6 and 0.8 [3]. This trend is less clear in adults (the observed sex ratio is 1.3 to 1.7) [4].

In about 75% of cases in children [1] and in 45 to 50% of cases in adults [4,5] ADEM typically follows an infectious episode or vaccination. ADEM has been observed after numerous vaccinations. The main vaccines reported, besides the rabies vaccine, are: Diphtheria-tetanus-pertussis (DTP), poliomyelitis, measles, influenza, hepatitis B and yellow fever [6]. To make the diagnosis of post-vaccination ADEM the maximum accepted time between neurological symptoms and vaccination is three months [6]. In our case, the clinical signs had occurred 2 months after the rabies vaccination. Clinically, symptoms are acute or rapidly progressive, developing over few hours to few days, on average 4.5 days [7]. Encephalitis frequently involves consciousness disorders, seizures, fever and meningeal stiffness. Consciousness disorders are found in 19 to 69% of cases [3,6]. Meningeal stiffness is reported in 5 to 44% of cases depending on the series [8,9]. Fever is more frequently found in children (43—52%) than in adults (15%) [3,6]. Seizures are reported in 4 to 30% of cases in adults [4] and in 13 to 35% of cases in children [10]. Deficient signs are frequent. Hemiplegia is noted in approximately 75% of cases. Spinal cord involvement is reported in a variable manner (2 to 43% of cases). It is manifested by acute para- or tetraplegia with abolition of reflexes, sensory and vesico-sphincteric disorders progressing to spasticity.

Our patient had consciousness disorders, paraplegia and vesico-sphincteric disorders without fever.

Particularly suggestive, visual impairment is characterized by uni- or bilateral optic neuropathy and is found in 7 to 28% of patients [5]. In our patient, there was bilateral blindness with total optic nerve atrophy in **eye fundus**.

Cerebral MRI with gadolinium injection is the best imaging. It shows characteristic lesions of ADEM appearing as hypersignal on T2-weighted and FLAIR sequences. The lesions are typically multiple, large (>1 to 2 cm), disseminated, poorly demarcated and asymmetrical. Mainly in the white matter at the subcortical regions, the semi-oval centers and at the cortical gray matter-white matter junction of the cerebral hemispheres. Isolated involvement of the gray matter is possible, in particular the central gray nuclei and the thalamus.

In our case, the MRI revealed bilateral and symmetrical signal abnormalities of the two external capsules and the two Putamens; hyposignal in T1, hypersignal in T2 and FLAIR.

CSF assessment is fundamental and makes it possible to exclude infectious meningoencephalitis requiring specific treatment. CSF may show non-specific abnormalities such as lymphocytic pleocytosis associated with hyperproteinorachia. In our case, the lumbar puncture was normal.

Routine biological examinations are generally not disturbed. There is no biological inflammatory syndrome, but discrete abnormalities of the blood formula can be found, such as neutrophilic polynucleosis or lymphopenia [6]. There is no specific biological marker for ADEM. In our patient, the C-reactive protein (CRP) was slightly elevated at 30 mg/L, and the blood count showed no abnormality.

The therapeutic approach is based on immunomodulatory drugs. The most commonly used drugs are intravenous corticosteroids, polyvalent immunoglobulins and plasma exchange (EP). High-dose corticosteroids are the most often reported treatment in the literature, in the form of daily bolus of methylprednisolone. The dosage used in pediatric series varies between 10 to 30 mg/kg per day without exceeding 1 g/d, by slow intravenous route.

Boluses are repeated for three to five days [3,8,9,11,12]. Corticosteroid boluses are followed by oral corticosteroid with gradual dose reduction over four to six weeks [13]. The risk of early relapse seems greater if the duration of corticosteroid therapy is less than four weeks [3,14]. In our case, a bolus of intravenous methylprednisolone was initiated at (1g/d) for a period of 7 days, then relayed by oral corticosteroid treatment for 4 weeks, followed by a gradual reduction.

Currently, more than half of patients treated for ADEM had good outcome with recovery without sequelae [6]. Clinical improvement is generally observed within hours or days of treatment [15].

The most frequent neurological sequelae are limb deficits, ataxia and visual impairment. In our case, we noticed an improvement of consciousness and motor deficit 3 days after the beginning of the treatment. However, the patient kept irreversible blindness.

Conclusion:-

ADEM is a rare cause of adult encephalitis, characterized by inflammatory lesions of the white matter of the CNS. The diagnosis of ADEM must be systematically suggested in front of unexplained acute encephalitis, especially if recent vaccination is found. The existence of central and possibly peripheral nervous system involvement are additional diagnostic arguments.

Cerebral and possibly spinal MRI are essential in the diagnostic process. Clinical improvement is sometimes spectacular with corticosteroids. Thus underlines the importance of an early diagnosis.

Declaration of conflicts of interest

None.

Author contributions

All authors of the manuscript contributed to this work. They read and approved the final version.

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