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RESEARCH ARTICLE

ACUTE DISSEMINATED ENCEPHALOMYELITIS POST SARS-COV-2 VACCINATION

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Abstract

Many of the central and peripheral nervous system complications related to severe acute respiratory syndrome coronavirus (SARS-CoV-2) infection have been recently described. An efficient mass vaccination program is required in order to effectively reduce the spreading of the infection and, therefore, minimize long-term sequelae, including neurological ones. Nonetheless, as more patients are accessing the 2019 coronavirus (COVID-19) vaccines, it is important to report potential adverse events. For this reason, we report here, the case of a patient with no remarkable medical history, having developed acute disseminated encephalomyelitis (ADEM) 3 weeks after being vaccinated against COVID-19; Diagnostic criteria for possible autoimmune encephalitis were fulfilled. Our patient showed a good response to plasmapheresis therapy after a failure of corticosteroid one. The Complications of post-vaccination encephalitis following SINOPHARM vaccination still seem to be very rare, but should be diagnosed and treated appropriately.

Introduction:-

Acute disseminated encephalomyelitis (ADEM) is a demyelinating disorder of the central nervous system (CNS) usually occurring in close time-association with a preceding infection or, much less frequently, after vaccination [1].

We describe the case of a patient, having no prior medical history, who developed acute disseminated encephalomyelitis (ADEM) three weeks after vaccination against SARS-CoV-2.

Case presentation

A 34-year-old man with no remarkable medical history was hospitalized in our department for an intracranial hypertension syndrome characterized by a headache, projectile vomiting, and photophobia, and complicated by an acute febrile confusion that had been evolving for 20 days after receiving his second dose of the Sinopharm vaccine against covid 19, without any acute allergic reaction.

The physical examination found a confused patient ; a Glasgow score of 13/15th, with a fever of 38.3°. The meningeal signs were negative (no nuchal rigidity, kernig and brudzinski signs were negative). Bone and tendon reflexes were normal, and no cranial nerve palsies were identified. The remaining clinical examination was unremarkable.

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The brain CT scan showed a badly limited left temporal hypodensity (in a glove finger form) without any acquisition of contrast, confirming the diagnosis of an encephalitis. Lumbar puncture (LP) brought back a clear cerebrospinal fluid (CSF) with 37 elements/mm3, predominantly lymphocytes, without germs on direct examination, a sterile culture, hyperproteinorachy and normoglycorachy. The meningeal PCR was negative as well as the covid PCR on two instances, hence, an encephalitis with covid 19 was excluded.

Lab tests showed a hyperleukocytosis of 17820/uL predominantly neutrophilic (13250/uL); HIV serology was negative; a second lumbar puncture was performed one week later and showed a pleocytosis of 18 elements/mm3 predominantly lymphocytic with a sterile culture, a hyperproteinorachy and a normoglycorachy; a second meningeal PCR was negative (a viral infection was excluded).

The Brain MRI showed a signal defect in the supratentorial and subtentorial white matter with a damage of the basal ganglia and the brainstem suggesting a post-vaccination ADEM rather than an infectious encephalitis. The diagnosis of post-vaccination ADEM was adopted.

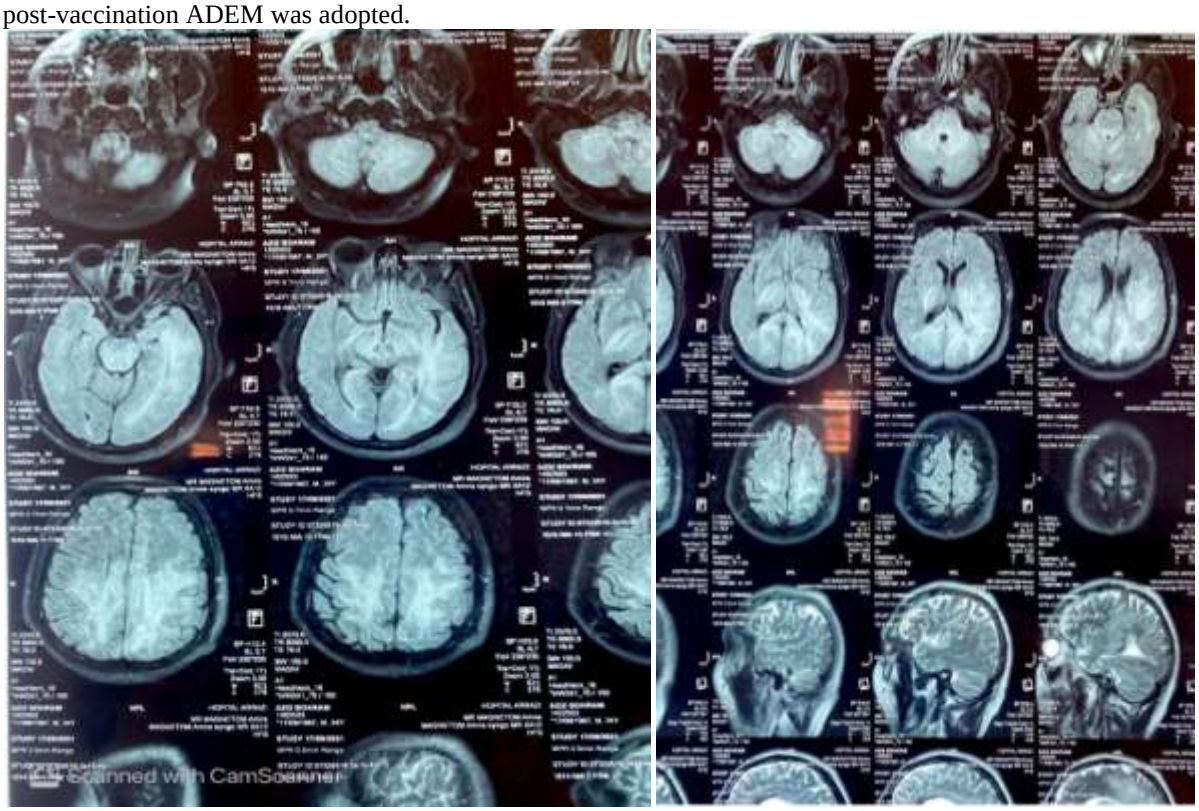

Fig. 1:- Brain MRI angiography images showing a signal defect of the supratentorial and subtentorial white matter along with basal ganglia and brainstem damage suggestive of postvaccination ADEM rather than infectious encephalitis.

At first the patient was treated with high doses of immunosuppressive drugs: solumedrol 1g for 5 days and then oral relay 1mg/kg/d without any significant effect; he then received plasma exchange (05 sessions of plasmapheresis) over 14 days, which led to an immediate clinical improvement. During the period of treatment, a follow-up LP was performed, and showed a decrease in pleiocytosis to 8 elements/mm3.

The outcome was good, marked by clinical and biological improvement; however, cognitive and behavioral disorders remained. A follow-up brain MRI was scheduled.

Discussion:-

ADEM is characteristically developed following an infectious episode or vaccination. There is usually a time gap between the possible triggering factor and the occurrence of clinical signs, which can vary from two to 30 days [2].

The Neurological disorders appear during the days following the settlement of the infection. The onset is sudden or rapidly progressing, and the symptoms develop within hours to days, on average 4.5 days [2].

ADEM has been reported after many vaccinations and, despite its rarity, it is still an issue in developed countries given the vaccination schedules. 3 months is the longest accepted time between a vaccination and the occurrence of neurological symptoms to establish the diagnosis of post-vaccination ADEM [3]. In this report, it is noteworthy that the patient did not have any specific risk factors and that the symptoms of encephalitis appeared within 21 days of the sinopharm vaccination. The criteria for a potential autoimmune encephalitis were fulfilled as follows: (1) subacute onset of neurological disorders, (2) CSF pleocytosis, (3) white matter signal abnormality with basal ganglia and brainstem involvement on MRI, (4) ruling out other causes. Therefore, the diagnosis of a suspected autoimmune encephalitis was established and plasmapheresis treatment was instituted. The patient showed a good response to the treatment, however, he remained with cognitive and behavioral disorders.

Commonly, vaccinations can induce a strong expression of proinflammatory cytokines and a T-cell response. After vaccination, antigens are recognized as potential pathogens both by conserved molecular patterns of pathogen and damaging agents, and by pattern-recognition receptors found on local or peripheral circulating immune cells (e.g., monocytes and macrophages) as well as on residual stromal cells. Induction and transcription of numerous target genes occurs, leading to the synthesis and release of pyrogenic cytokines (i.e., interleukin [IL]-1, IL-6, tumor necrosis factor-alpha [TNF-α], and prostaglandin-E2) thus emulating the response to a natural infection. After stimulation, the immune system triggers a complex series of innate immune events, including phagocytosis, release of inflammatory mediators (chemokines and cytokines), complement activation, and cell recruitment. Mediators and inflammation products in the circulation can affect other body systems leading to systemic side effects and may ultimately cause neuroinflammation for some individuals after microglia activation, depending on the immunogenetic background and innate immune memory [4-5]. We cannot verify this on our patient; however, it could explain a likely correlation between vaccination and a subsequent autoimmune encephalitis. Owing to the lack of antibody detection, the diagnosis of a definitive autoimmune encephalitis cannot be established, whereas a post-vaccination encephalitis could be discussed.

In a 20-year United States survey [6], 396 cases of encephalitis occurred after vaccination. The causing vaccinations were hepatitis B (354 cases), influenza vaccination (208 cases), measles-mumps-rubella vaccination (208 cases) and Haemophilus influenza type B vaccination (120 cases). The onset of encephalitis in the 2-3 weeks after vaccination was reported in 708 patients (50.7%). This is in line with our case.

Public institutions are collecting the occurrence of adverse events for the different COVID-19 vaccines. Recent data from the National Institute of Public Health of Quebec (**INSPQ**) showed that 67 reports of unusual clinical events were submitted in Quebec for every 100,000 administered doses for all vaccines. In the case of AstraZeneca, this proportion rises to 182.5 reports per 100,000 doses. The high proportion of unusual clinical events reported by the INSPQ are described as " non-serious " [7]. A case of ADEM was recently reported following an inactivated SARS-CoV-2 vaccine in China [8].

The therapeutical approach is based on immunomodulatory treatments; The most commonly used treatments are intravenous corticosteroids (CT), polyvalent immunoglobulins (IVIG) and plasma exchange (PE).

The most frequently reported treatment in the literature is high-dose corticosteroids as daily boluses of methylprednisolone; in pediatric series, the doses range from 10 to 30 mg/kg per day, (but no more than 1 g/d) and they should be delivered slowly by intravenous injection for a three- to five-day period [9]. Early relapse appears to be at a higher risk if steroid therapy is less than four weeks [9].

PE has been reported in a small number of cases, mainly if CT fails, as was the case here. the usefulness of this treatment remains undefined, though it seems to be worthwhile when there is no response to CT, especially in ICU patients. PE may be administered as a 14-day schedule of seven plasma exchanges [10].

The recourse to IVIG in ADEM has been reported in 25 cases in children (after IV corticosteroids in 11 of 25 cases) and in eight cases in adults (after IV corticosteroids in six of eight cases). Patients showed a positive response in approximately 70% of cases in children and 50% in adults. IVIG can be provided at 2 g/kg over two to five days [11].

Conclusion:-

We reported a case of post-vaccinal encephalitis matching the criteria of a possible autoimmune encephalitis. The diagnosis was substantiated by : (1) time course association between vaccination and symptom onset, (2) CSF pleocytosis, (3) white matter signal defect involving basal ganglia and brainstem on MRI angiography (4) excluding other etiologies, and (5) response to plasmapheresis therapy.

The complication of autoimmune encephalitis after SARS-COV-2 vaccination appears to be very rare. Obviously, the benefits of vaccination outweigh the risks.

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