A Case Report of Post Rabipur (Purified Chick Embryo Rabies Vaccine) Acute Disseminated Encephalomyelitis

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Abstract

Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disease that typically occurs following a viral infection or vaccination. The incidence of ADEM following vaccination has become very low since introduction of non-neural rabies vaccine and only few cases had been reported due to pure chick embryo derived rabies vaccine (PCERV). Here we are reporting a rare case of delayed post vaccinal ADEM.

Introduction

ADEM is a rare complication associated with vaccinations,¹ the incidence of which is < 0.1-0.2/100,000 and less than 5% of all ADEM are postvaccinal.² ADEM has been reported at a rate of 1/50000 following non-neural rabies vaccines.³ Onset of symptoms is mostly 1-3 weeks following the last dose.³ The clinical presentations are highly variable and non-specific. It includes focal deficits, optic neuritis, seizures, spinal involvement and variable alteration of consciousness/behaviour.⁴ MRI T2W and FLAIR images show multiple, asymmetrical, supratentorial and infratentorial hyperintense lesions affecting mainly the white matter. The differentiation of ADEM from first attack of multiple sclerosis is often difficult, characteristic location of MRI lesions, involution of the lesions and/ or the absence of new lesions within 6 months, ultimately supports the diagnosis of ADEM.¹

Case Report

A 21 year old girl was admitted with complaints of ‘feeling of stucking of nuts in her throat’ after dinner, altered behaviour and asymmetrical progressive increase of weakness in all four limbs for 3-4 days with nasal twang of voice for 5 days. The disease started twelve days back with blurring of vision followed by bilateral drooping of eyelids. Later on she developed nasal twang in voice and truncal weakness followed by weakness in limbs (UL > LL) without diurnal variation. She consulted a neurosurgeon outside, tab. Pyridostigmine 180 mg/day was given suspecting myasthenia gravis. She was referred to us as her symptoms progressed. She had taken five doses of rabipur vaccine following dog bite (dog alive till 1 year) two months back. She didn’t have fever, seizures or any other illness in last 2 months. There was no h/o major illness in the past.

On neurological examination, cranial nerves 3rd, 4th, 5th, 6th and 9th were involved with bilateral internuclear ophthalmoplegia without evidence of papilloedema /optic neuritis. Motor system examination revealed normal bulk and tone in all four limbs, power 3+ in shoulder, elbow, wrist; 4+ in hips, knee and ankle. All modalities of sensation and cerebellar functions were normal, plantar reflex was extensor bilaterally. There was no other system involvement.

Patient’s haemogram, liver enzymes and renal function tests were normal. Other related biochemical investigations revealed normal serum levels of serum CPK (102 U/L), LDH (33 U/L), cholinesterase (7.6 U/L), TSH (2.03 uIU/ml), Vit-B₁₂ (800 pgm/l) and Folic acid (19.9 ngm/l). Antinuclear antibodies, cantechnophilic cytoplasmic antibodies (ANCA), lupus anticoagulants and serum anticholine receptor assay were
absent. CSF study showed no cells with normal protein and sugar levels; Elisa was negative for CMV, EBV and Mycoplasma. Malarial infection was ruled out. HIV, HBsAg and anti HCV were non reactive. EEG revealed excessive assymetrical slow wave activity. No abnormality recorded in nerve conduction studies (NCV), visual evoked potential (VEP) and SSEP (Median and Tibial) study. Electromyography (EMG) showed no evidence of neuromuscular defect. MRI brain at admission showed multiple confluent scattered and confluent long TR hyper intense lesions in centrum ovale, corona radiata and deep white matter. The lesions were of same age with no gadolinium enhancement (Figures 1a, b). MRI spine showed hyperintensity in C5- D2 suggestive of cord oedema.

During her hospital stay she was managed with I.V. antibiotics and pulse methylprednisolone 1 gm per day for 3 days followed by tapering of oral steroid in one month.

Case Discussion

ADEM is polysymptomatic disease, often produces a widespread CNS disturbance with involvement of the cerebral hemispheres, cerebellum, brainstem, spinal cord and optic nerves. Multiple sclerosis (MS) is an important differential of ADEM initially. MS usually presents as a monosymptomatic disease such as optic neuritis or a sub acute myelopathy. The optic neuritis in ADEM is usually simultaneously bilateral whereas in MS, it is more often unilateral. Fever, meningism and/or psychiatric manifestations which are characteristic of ADEM, are virtually never present in MS. Our patient had no h/o fever, had no signs of meningism but presented with altered sensorium with EEG changes suggestive of encephalopathy.

She had presented with sub acute onset of progressive neurological syndrome affecting multiple cranial nerves, bulbar and pyramidal with asymmetrical motor involvement. Neuromuscular-junction disorders was ruled out by normal EMG, NCV, VEP and SSEP. Thus differentials kept were ADEM (post vaccinal and parainfection), vasculitis and multiple sclerosis. The most widely applied diagnostic tool in ADEM is brain MRI with follow up for at least six months. The diagnosis of ADEM is considered only if the MRI brain is consistent with disseminated demyelination particularly the detection of widespread, multifocal or extensive white matter lesions whereas characteristic findings of MS are well defined lesions located in periventricular, cerebellum and juxtacortical regions with heterogeneity and gadolinium enhancement. Moreover absent of oligoclonal bands and IgG index in CSF defied diagnosis of MS. The presentation of our patient was in favour of ADEM rather than multiple sclerosis as
per revised McDonald criteria. Infectious aetiology and vasculitis syndrome was ruled out by clinically and extensive investigation as mentioned above.

Accepted treatment method include intravenous methylprednisolone, immunoglobulins or a combination of both (Tselis 2001). Few reports highlight the importance of plasmapheresis in ADEM (Lin et al 2004). There was significant neurological improvement in this patient after giving pulse methylprednisolone therapy and subsequent oral therapy for one month.

During her follow up for twelve months, she neither developed any new neurological manifestations nor new findings on repeated MRI (5th and 8th month), it rather revealed partial resolution of previous lesions (Figures 2a, b and 3 a, b). After close follow up of this period she could not fulfill any diagnosing criteria of multiple sclerosis i.e. revised McDonald criteria nor criteria of consensus of international panel on MS. So after ruling out all other possible causes, patient’s presentation was very consistent with post PCERV ADEM.

Literature pertaining to case reports of ADEM following non neural derived rabies vaccination is rare. Bruns et al7 reported a case presented with high fever with vomiting suspected to be encephalitis with no neurological deficits after simultaneous vaccination. Chakrabarty A. reported a case of Guillain – Barre syndrome following Rabipur. Our case had late presentation with multiple neurological deficits following vaccination with characteristic radiological criteria.

References
3. G Guliani, Parry (Minneapolis, US) ,Multiple Sclerosis triggered by purified chicken embryo cell rabies vaccine; 5th Joint triennial congress of the European and American Committees for Treatment and Research in Multiple Sclerosis Amsterdam, The Netherlands 2011;15.30-17.00.