Focal seizure associated with human parvovirus B19 infection in a non-encephalopathic child

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Case report

Background: **The incidence of acute symptomatic (at the time of documented brain insult) seizures and single unprovoked seizures are 29-39 and 23-61 per 100 000 per year, respectively. After stabilization of the patient, finding the etiology of the seizure is of paramount importance. A careful history and physical examination may allow a diagnosis without need for further evaluation.**

Methods: **In the literature, severe central nervous system involvement has been reported from human parvovirus B19 infection. We reported a previously healthy 7-year-old girl who presented after an episode of focal seizure. She was afebrile and didn't have any focal neurological abnormalities. She had erythematous malar rash along with reticulating pattern of rash over her both upper extremities.**

Results: **Parvovirus infection was suspected due to the characteristic erythematous malar rash. Serum human parvovirus B19 DNA polymerase chain reaction was positive which was consistent with acute parvovirus infection. Further confirmation of current infection was done with Sandwich enzyme immunoassays showing positive anti-B19 IgM Index (>1.1). IgG index was equivocal (0.9-1.1).**

Conclusions: **We report an extremely rare presentation of non-febrile seizure from acute parvovirus infection in a child without encephalopathy who had an excellent recovery. Timely diagnosis can provide counselling regarding future seizure recurrence risk, curtail expenditure from expensive diagnostic work up and provide additional recommendations about potential risks to a pregnant caregiver.**

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Key words: **erythema infectiosum; human parvovirus B19; nonfebrile seizure**

Introduction

The incidence of acute symptomatic (at the time of documented brain insult) seizures and single unprovoked seizures are 29-39 and 23-61 per 100,000 per year, respectively.[1] In the absence of immediate and obvious provoking etiologies such as head trauma, intracranial infection, brain tumor, hypoglycemia, toxic ingestions, etc., elaborate diagnostic work up is performed utilizing existing practice guidelines. After stabilization of the patient, finding the etiology of the seizure is of paramount importance. A careful history and neurologic examination may allow a diagnosis without need for further evaluation, but the importance of a comprehensive physical examination including other organ system examination cannot be overemphasized. Human parvovirus B19 infection usually produces no or mild symptoms but severe central nervous system involvement with meningoencephalitis and encephalopathy have been reported (Table). We report an extremely rare presentation of non-febrile seizure from acute parvovirus infection in a child without encephalopathy who had an excellent recovery.

Case report

A previously healthy 7-year-old girl presented to an outside emergency department after having first episode of seizure. Her mother noted an erythematous rash on her face earlier that day and also reported an episode of emesis and loose stool. That evening, she developed sudden onset of left sided head and eye deviation followed by generalized stiffening and jerking activity which lasted for approximately 15 minutes. She was taken to an emergency department by emergency medical service where her seizure stopped after 2 milligrams of intravenous lorazepam. She was afebrile

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Table. Clinical manifestations of human parvovirus B19 infection[2]

Well established syndrome	Fifth disease, arthropathy, non-immune hydrops fetalis, intrauterine fetal death, or miscarriage, transient aplastic crisis in chronic hemolytic disorder patients, chronic pure red blood cell aplasia in immunocompromised patients
Cardiac involvement	Myocarditis, dilated cardiomyopathy, left ventricular diastolic dysfunction
Nervous system	Encephalopathy, meningitis, encephalitis and seizure, stroke, cerebellar ataxia, Guillain-Barre syndrome, brachial plexus neuropathy, mononeuritis multiplex, cranial neuropathy, carpal tunnel syndrome
Skin	Generalized erythematous or purpuric exanthem (usually spares the face and can have a reticular or annular shape), asymmetric periflexural exanthema, papular-purpuric gloves and socks syndrome, Gianotti-Crosti syndrome,[3] palpable purpura (vasculitis)[4]
Other organ systems	Acute liver failure, acute renal failure, nephrotic syndrome, vasculitis

and remained post-ictal for 3-4 hours prior to returning to her baseline and for further evaluation she was transferred to our hospital. The parents denied any fever or witnessed ingestions. She had a mild erythematous rash over both cheeks at presentation. She was oriented to time, place and person and normally conversant. Her neck was supple and Kernig's (flexion of patient's hip to 90 degrees and then extending the patient's knee causes pain) and Brudzinski's (flexion of patient's neck causes flexion of patient's hips and knees) signs were absent. Cranial nerve examination was normal. She had normal motor and sensory examination. Complete blood count and basic metabolic panel including blood sugar, calcium, and magnesium were normal. Extensive drug testing was done and was negative. Electroencephalography (EEG) during wakefulness and sleep revealed focal slowing over right parieto occipital head region without any epileptiform abnormality. Magnetic resonance imaging brain (3 Tesla) with and without contrast was normal. During the 2nd day of admission her facial rash became more erythematous and her bilateral upper extremities also showed reticulating pattern of erythematous rash. Serum human parvovirus B19 DNA polymerase chain reaction was sent and came back positive which was consistent with acute parvovirus infection. Further confirmation of current infection was done with Sandwich enzyme immunoassays showing positive anti-B19 IgM Index (>1.1). IgG index was equivocal (0.9-1.1). Epstein-Barr virus panel was negative for infection. The mother of the child was 10 weeks pregnant and advice was given to consult her physician. The child remained afebrile and her rash resolved in 7 days. She had not had any recurrence of seizure activity two months after initial presentation. Her repeat EEG was normal.

Discussion

Human parvovirus B19, a small, non-enveloped, ssDNA virus, can cause variable manifestations from asymptomatic infection to other well established syndrome like erythema infectiosum (EI), arthropathy or pure red aplasia. Asymptomatic parvovirus infection and EI are very common and can affect up to 50% of the school age children.[5] EI presents with characteristic erythematous malar rash (slapped cheek rash) after 2-5 days of nonspecific prodromal symptoms. Pathogenesis of the rash is unclear but may be immune mediated. A wide range of other organ system involvement has been described with this infection including both central and peripheral nervous system disease. Severe forms of encephalopathy, encephalitis and meningitis have been described with Parvovirus B19 infection[6] in both immunocompetent and immunocompromised populations. Generalized and focal seizures as well as status epilepticus have also been reported in the literature.[7] Other neurologic manifestations associated with this infection included stroke, carpal tunnel syndrome, brachial plexopathy, acute cerebellar ataxia and Guillain-Barre syndrome. One previous case report of frontal lobe seizures associated with this infection was reported within one month of uveitis and EI.[8] Direct viral toxicity and cytokine mediated injury from abnormal immune response were proposed mechanisms for nervous system injury. But immunocomplex deposition on the endothelial cells and intracellular accumulation of toxic non-structural protein 1 can also be responsible for the central nervous system (CNS) damage.[9] Generally a prolonged course is expected from parvovirus CNS infection and a review article described a mean duration of illness of 55.7 days (4 patients died secondary to encephalitis).[6]

There is no published report of acute afebrile seizure with concurrent EI in a non encephalopathic patient. Our patient did not have any feature of meningoencephalitis or encephalopathy (no neck rigidity, negative Kernig's and Brudzinsky's sign, and normal mental status). We presume that concurrent malar rash and seizure may likely be due to overproduction of cytokine rather than direct virus toxicity. Her prompt recovery averted a spinal puncture and cerebrospinal fluid assay.

The vast majority of the acute seizures in children are managed by pediatricians and emergency room physicians. Several different guidelines exist to help formulate a plan for these patients. Though a broad idea about the utility

of neuroimaging and electroencephalography can be achieved from these guidelines, optimum management still depends on comprehensive history and physical examination.[10] Diagnosis of infection associated symptomatic seizures can provide effective counselling concerning the lower risk of seizure recurrence compared to an unprovoked seizure. Several other neurotropic agents especially viral infection can cause acute symptomatic seizure, and our study is limited due to absence of comprehensive virologic assessment. But presence of characteristic rash and positive diagnostic assay clearly points towards this particular diagnosis. Efficient diagnosis also may preclude an expensive workup and can provide additional counselling such as in our case in which the mother of the child was advised to consult her obstetrician concerning parvovirus complications of pregnancy.

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