

Progressive Multifocal Leukoencephalopathy as a Presenting Manifestation of Acquired Immunodeficiency Syndrome in a Child

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Received: 18 July 2017; Accepted: 13 August 2017

Citation: Mamoun Al-Qaseer, Saroj Bala Grover, Mariam Al-Fadhli. Progressive Multifocal Leukoencephalopathy as a Presenting Manifestation of Acquired Immunodeficiency Syndrome in a Child. *Microbiol Infect Dis*. 2017; 1(1): 1-3.

ABSTRACT

Progressive multifocal leukoencephalopathy is caused by JC virus and mainly affects human immunodeficiency virus infected patients. The disease is exceptionally rare in children. The diagnosis is based on magnetic resonance imaging and on the detection of JC virus DNA in the cerebrospinal fluid. This is a report of a 14 year old girl, not previously known to have human immunodeficiency virus, who was admitted to the hospital in a semicomatose state after complaining of progressive neurologic symptoms for 4 months. Initially she complained of being tired and had an unsteady gait. This was followed by worsening myoclonic and generalized tonic-clonic convulsions. Brain magnetic resonance imaging revealed asymmetrical, diffuse subcortical white matter demyelination. Polymerase chain reaction test of the blood was positive for JC virus. Despite the initiation of antiretroviral therapy, the patient died in the intensive care unit 42 days after her admission.

Keywords

Encephalitis, Viral infections, Human immunodeficiency virus, Progressive Multifocal Leukoencephalopathy.

Introduction

Progressive multifocal leukoencephalopathy is a subacute demyelinating disease of the central nervous system. It is caused by JC virus, a human Polyomavirus which belongs to the Polyomaviridae family [2]. Reactivation of latent JC virus infection in the setting of cellular immunodeficiencies can result in progressive multifocal leukoencephalopathy [1]. This is a case report of a human immunodeficiency virus infected girl who presented with progressive multifocal leukoencephalopathy.

Case description

A 14 year old girl was admitted to the hospital in a comatose state. By reviewing the medical record and interviewing the relatives, it was found that the patient was complaining of progressive neurologic symptoms for 4 months. Initially she felt tired. This was followed by unsteady gait. Later, she complained

of worsening myoclonic and generalized tonic-clonic convulsions which resulted in the loss of consciousness. There was no history of fever, vomiting, headache, head injury, jaundice nor ear discharge. There was no history of any prior medical illness. On examination, the patient was afebrile with tachycardia of 130 beats per minute. The pupils were reactive to the light. She was responding to pain and had exaggerated reflexes. Abdominal examination showed massive hepatomegaly. The rest of the examination was unremarkable. Soon after admission, the patient was transferred to the intensive care unit for mechanical ventilation. Laboratory investigations revealed white blood cell count 13200/mm³ (59% neutrophils, 28% lymphocytes, 9% monocytes, and 4% eosinophiles), normal platelet count, hemoglobin of 11.2 g/dl, and marked elevation of Gamma-glutamyltransferase 476 IU/L, alkaline phosphatase 382 IU/L and aspartate aminotransferase 173 IU/L. Cerebrospinal fluid analysis at presentation showed normal cytology, a protein concentration of 0.99 g/L, glucose of 6.12 mmol/L, no acid-fast bacilli, and no bacterial growth on culture. The cerebrospinal fluid was also negative for toxoplasma, Cryptococcus and Venereal Disease Research Laboratory test

reactivity. Magnetic resonance imaging of the brain revealed asymmetrical, diffuse subcortical white matter demyelination without mass effect and contrast enhancement. The lesions were hypointense on T1-weighted images, hyperintense on T2-weighted images and on fluid attenuated inversion recovery images (Figures 1 and 2). Ultrasound and computed tomography of the abdomen were suggestive of an enlarged fatty liver (Figure 3).

Biopsy of the liver was consistent with a fatty liver, there were no other remarkable findings. Other investigations done included serum copper level, caeruloplasmin level, direct and indirect Coomb's test, brucella serology, Venereal Disease Research Laboratory test, cold agglutinins test, blood electrophoresis and blood culture for Mycobacterium avium complex, echocardiogram and skeletal survey. All of which were unremarkable.

Due to the unusual presentation and manifestations of the case, a serological test for human immunodeficiency virus was done which was positive. This was confirmed by western blot assay. Viral load was 256,000 copies/mL, and CD4 and CD8 count were 0 cells/ μ L. At this stage, 16 days after admission, the diagnosis of progressive multifocal leukoencephalopathy was considered. JC virus was also detected by polymerase chain reaction in the blood and urine by polymerase chain reaction. However, polymerase chain reaction testing of the cerebrospinal fluid was not done due to sampling refusal by the caretakers.

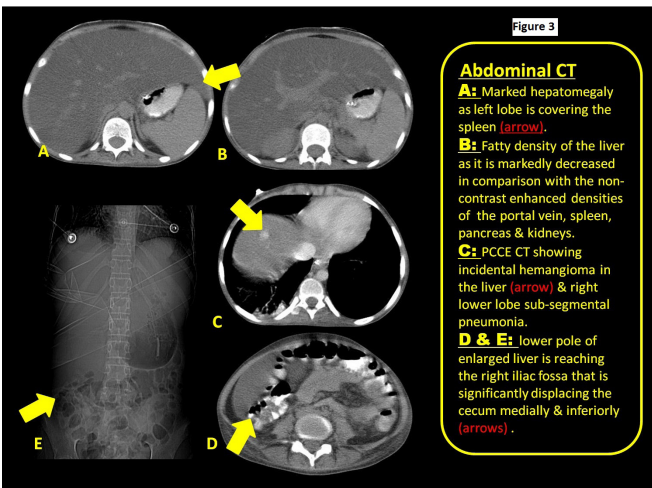
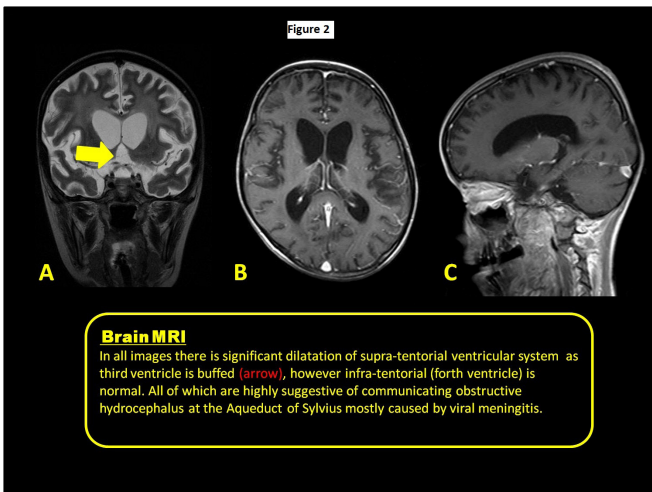
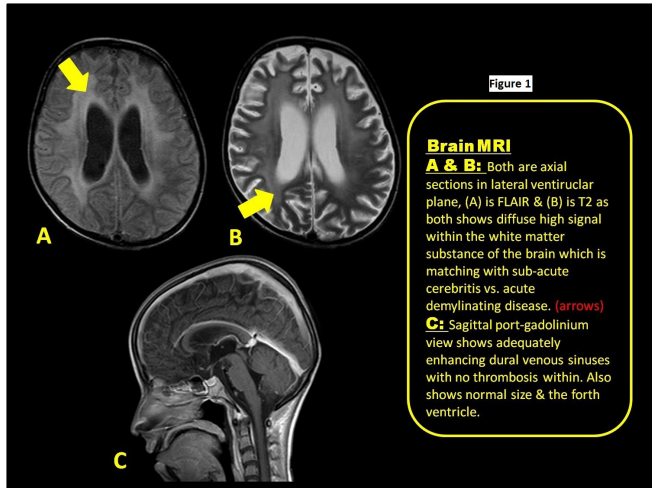
During her stay in the intensive care unit, the patient developed a number of complications. She developed interstitial pneumonia. Tracheal aspirate for bacterial culture was negative, but the polymerase chain reaction showed the presence of cytomegalovirus. Real-time polymerase chain reaction of the blood showed the presence of 300,000 copies/ml of cytomegalovirus. The patient also suffered from continuous normochromic normocytic anemia which required repeated blood transfusion. In addition, she developed urinary tract infections and an infected bed sore. The patient received multiple antibiotics, antiretroviral therapy, and supportive care. However, she died in the intensive care unit 42 days after her admission.

Other similar and contrasting cases in the literature

Extensive search of the MEDLINE database and Google Scholar search engine using the terms "leukoencephalopathy" and "acquired immunodeficiency syndrome" or "human immunodeficiency virus" showed the presence of only 12 reported cases of progressive multifocal leukoencephalopathy in children with human immunodeficiency virus infection [3-13]. Five of these cases were girls [4,5,7,9,10] and seven were boys [3,6-8,11-13]. The age of the patients at presentation with progressive multifocal leukoencephalopathy ranged from 6 to 17 years, with 3 of the girls presenting at an age of 13 years [7,9,10]. The neurologic symptoms and signs at presentation of these cases are variable, most likely depending on the affected area of the brain. One patient represented a case of immune reconstitution inflammatory syndrome [11]. Survival for more than 12 month was reported in 3 cases [6,11,13].

Discussion

Progressive multifocal leukoencephalopathy is a subacute demyelinating disease of the central nervous system caused by reactivation of the latent polyomavirus JC virus in the presence of immunosuppression 1. This case represents the first paediatric progressive multifocal leukoencephalopathy case reported in Kuwait. To our knowledge, no similar case (progressive multifocal



leukoencephalopathy in human immunodeficiency virus infected child) has been reported from any Arabic country.

This case demonstrates how difficult it can be to make a diagnosis of progressive multifocal leukoencephalopathy, especially when the human immunodeficiency virus status of the patient is unknown or when progressive multifocal leukoencephalopathy is the initial manifestation of acquired immunodeficiency syndrome. In spite of suggestive neuroradiology, progressive multifocal leukoencephalopathy was not initially considered in the differential diagnosis which, in turn, led to delayed diagnosis and a large number of unnecessary investigations and clinical consultations. In general, definitive diagnosis requires brain biopsy. However, this can be avoided if, in the presence of a compatible radiologic (brain magnetic resonance imaging) picture, JC virus DNA is detected by polymerase chain reaction in the cerebrospinal fluid [2]. The brain magnetic resonance imaging of the case in question was consistent with progressive multifocal leukoencephalopathy as it showed characteristic asymmetrical subcortical lesions of the white matter with no mass effect or contrast enhancement. Another difficult aspect of this case was the massive hepatomegaly for which no possible cause could be identified.

The patient probably had mother to child transmission of human immunodeficiency virus. The father of this patient died of *Pneumocystis jirovecii* pneumonia in another hospital about ten years ago, his human immunodeficiency virus status was not determined. There were no data available about the mother, who has also passed away seven years ago, however, the patient has a twin brother who was investigated for human immunodeficiency virus after the admission of his sister and was found to be human immunodeficiency virus positive as well.

Progressive multifocal leukoencephalopathy, despite being more frequently seen in adult patients with acquired immunodeficiency syndrome, is quite rare in human immunodeficiency virus infected children [3-13]. The exact reason for this is not known but is believed to be related to the early mortality of human immunodeficiency virus-positive children with perinatally acquired human immunodeficiency virus [3]. These children may not survive long enough to acquire the primary infection or reactivate latent infection [3,14].

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