Section: Case Reports

Myocarditis by human parainfluenza virus in an immunocompetent child initially associated with 2009 influenza A (H1N1) virus

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Abstract:

The association between respiratory viruses and myocarditis has hardly ever been described. We report a case of acute myocarditis in an immunocompetent child associated with the presence of parainfluenza virus type 3 infection, in a context of recent influenza illness, confirmed by molecular and serological studies.

Study:

A 12-year-old girl presented in October 2009 with a 10-day history of fever, cough and coryza. She had no past medical history of note, there was no family history of cardiac illness, and did not received any medications. On 19th of October a nasopharyngeal swab (NPS) sample was taken for microbiological studies. A polymerase chain reaction (PCR) examination was positive for Influenza A/ H1N1 pdm, using the CDC protocol of realtime RT-PCR for influenza A (H1N1). http://www.who.int/csr/resources/publications/swineflu/realtimertPCR/en/index.html. She was admitted in a regional hospital in Ciudad Real, with a diagnosis of viral pneumonia by Influenza A, in the context of pandemic influenza A/H1N1 pdm circulation. She was discharged with antiviral treatment (Oseltamivir [3mg/kg/dose twice daily for 5 days]). Two weeks later she was readmitted to the hospital with dyspnea and signs of heart failure. She needed IV perfusion of inotropic drugs and a diagnosis of severe left ventricular dysfunction was made. After stabilization the patient was treated with Carvedilol® (3.12 mg/12 h), Enalapril® (5 mg/ 12 h), Furosemida® (10 mg/12 h) and Sintromacenocumarol®. On 3rd of November, a new NPS sample was taken and PCR examination was negative for Influenza A/ H1N1 pdm, using the same CDC protocol of realtime RT-PCR protocol.
On 12th of January 2010, after progressive deterioration in cardiac function, she was readmitted in the regional hospital and transferred to one University Hospital in Madrid.

On admission, blood was pressure 91/52 mmHg, pulse 112 bpm, temperature 37.0°C and the O₂ saturation measured 99% while breathing room air. The level of C-reactive protein (CRP) was 4.6 mg/dl. Red cell count and hemoglobin level were normal, white cell count 10700 cells/mm³, with 51.8% polymorphonuclear cells, 41% lymphocytes, 5.7% macrophages. Liver enzymes were ASAT 50 UI/L and ALAT 56 UI/L. The levels of creatine kinase and troponin T were 31 U/L and 0.01 ng/ml.

On 21st of January, she was transferred to our hospital to be listed for heart transplantation, with diagnosis of refractory heart failure. On admission, the patient was hemodynamically unstable (blood pressure 70/55 mmHg, pulse 105 bpm, temperature 37.1°C). Chest X Ray revealed a severe cardiomegaly and 2D doppler echo showed severe left ventricular systolic with ejection fraction of 32% and severe dilatation of left ventricle. Hemoglobin level was normal (12.7 g/dL), as well as platelets 305000/mm³. The girl had no evidence of sepsis or bacterial infection (negative blood, urine, and tracheal aspirate cultures). All serological investigations for herpes simplex (HSV) I, HSV-II, varicella zoster virus (VZV), Cytomegalovirus (CMV), Epstein-Barr virus (EBV) and human herpesvirus 6 (HHV-6) resulted negative, and a PCR examination in a NPS sample was negative for influenza A/H1N1 pdm.

There was progressive heart failure with impending renal failure. She required venoarterial ECMO for stabilization with cannulation of carotid artery and jugular vein. A donor heart was available within 24 hours and she was successfully transplanted.

Pericardial fluid, cardiac biopsy, blood and serum were sent for histological studies, microbiological culture and molecular diagnosis. The multiplex polymerase chain reaction of blood, pericardial fluid and cardiac biopsy samples were negative for HSV-I, HSV-II,
VZV, CMV, EBV, HHV-6 and enterovirus (EV). The multiplex RT-PCR (Clart Pneumovir Version 3.0, Genomica, Madrid, Spain) in pericardial fluid and cardiac biopsy was found positive for Human Parainfluenzavirus type 3 (HPIV-3). A new NPS sample was sent to the National Centre of Microbiology (ISCII) for microbiological studies. In this sample the PCR examination was only positive for rhinoviruses.

The histological studies of cardiac biopsy showed a moderate interstitial infiltration of lymphocytes as well as neutrophils and eosinophils in myocardial and pericardial tissues.

In order to complete the virological findings, both NPS sample taken on 19th October and pericardial fluid, cardiac biopsy and serum samples taken on 22th of January were sent to the National Centre of Microbiology. Nasopharyngeal swab sample taken on 19th October was positive for Influenza A/H1N1pdm, HPIV-3, and coronavirus 229E. HPIV-3 presence was confirmed in pericardial fluid and cardiac biopsy using two different molecular tests: multiplex reverse transcription nested-PCR (RT-PCR) assay (1) and Luminex xTAG respiratory viral panel (RVP) assay. Other virus studied by these methods resulted negative (enterovirus, rhinovirus, coronavirus, influenza A, B, C viruses, respiratory syncytial virus (RSV), adenovirus, bocavirus and metapneumovirus).

The serological tests used for analysis of antibodies against respiratory virus were indirect immunofluorescence assay (IIF), neutralization test (NT), inhibition of hemagglutination (IHA), and complement fixation (FC). The antibody titers of the initial serum sample were significantly elevated for the Influenza A, HPIV-1 and 3. (Table) The NT showed an increase by 1.5-fold of neutralizing antibodies against influenza A/H1N1pdm (A/California/04/2009). The high level of antibody titers against HPIV-1 and 3 can be explained by marked cross-reactivity between HPIV antibodies. Previous studies have documented the cross-reactivity of antibodies against HPIV-1 and 3 of the envelope
glycoproteins, HN and F of these viruses. (6) Influenza A, HPIV-1 and 3 antibody titers remained elevated 2 months after the diagnosis of viral pneumonia.

Postoperative period was uneventful and the patient was discharge from the ICU at day +7 and discharged from the hospital at day +15. She is in functional class I 10 months after transplant without episodes of rejection.

The etiology of myocarditis is multifactorial (infections, immunological, toxins, drugs, and physical agents such as radiation) (5, 13). Molecular studies of cardiac samples obtained through cardiac catheterization of patients presenting with acute viral myocarditis resulted in the identification of viral genomes in a range of 38 to 53% of the cases. Coxsackieviruses, especially group B, appear to be the major agents implicated, but other viruses may also be involved; adenoviruses (12), cytomegalovirus (8), echovirus (11), influenza virus (3), Epstein Barr virus (9), human herpes virus 6 (HHV6) (10), hepatitis C virus (7), parvovirus B19 (2).

The present case illustrates an unusual presentation of myocarditis by HPIV-3 after an upper respiratory tract infection. Others respiratory viruses were detected in the NPS samples (influenza A/H1N1 pdm and coronavirus 229 E), but only HPIV-3 was detected in the cardiac tissues. Recent studies showed high rates of co-detection of two or more respiratory viruses in children admitted with acute respiratory tract infection. (4) Clinical myocarditis and secondary pericarditis to HPIV due to HPIV-3 have been reported previously, although the diagnosis has been established on the basis of serology findings. (13) However, serology for HPIV is difficult to interpret, since the high degree of cross-reactivity amongst them, as previously reported. (6) In our case HPIV 3 was found in the nasopharyngeal swab, cardiac tissues and pericardial fluid diagnosis, thus the diagnosis was confirmed by molecular tests.


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