CASE REPORT

A severe manifestation of primary HIV-1 infection in an adolescent

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SUMMARY

Primary HIV infection (PHI) is symptomatic in 50–90% of patients with symptoms resembling infectious mononucleosis. The diagnosis, however, is seldom made at first presentation. Clinically severe presentations during primary HIV type 1 infection are considered to occur infrequently. We report a case of a severe manifestation of PHI with meningoencephalitis in the setting of HIV seroconversion in an adolescent girl.

BACKGROUND

Primary HIV type 1 (HIV-1) infection represents the initial stage of disease that immediately follows viral entry into the body. It is now known that 50–90% of patients acutely infected with HIV experience at least some symptoms of the primary HIV infection (PHI).¹ The most common findings of the syndrome are fever (80–90%), fatigue (70–90%), rash (40–80%), headache (32–70%) and lymphadenopathy (40–70%). Additional findings include pharyngitis, myalgia, nausea, vomiting, diarrhoea and other symptoms.² Severe unusual presentations have been reported (eg, rhabdomyolysis, meningoencephalitis, multiple organ failure and coma).^{3–7} Neurological features may be associated with more rapid progression of HIV-related disease.⁸ Symptoms usually develop within days-to-weeks after HIV exposure and last from a few days to several months, but usually less than 14 days.⁹ Fewer than 1000 cases have been diagnosed in the first month of infection.¹⁰

CASE PRESENTATION

A 16-year-old Portuguese girl presented in August 2010 with 11 days of high fever (40°C), malaise, cervical lymphadenopathy and sore throat. She had been treated for tonsillopharyngitis with penicillin 1 200 000 UI IM 1 week before without improvement. Serology for Epstein-Barr virus was IgG positive and IgM negative. Four days before admission, the patient developed nausea and vomiting with intolerance to all food. On admission, she was febrile (38.5°C) and tachycardic (125 bpm), with a blood pressure of 79/48 mm Hg. Physical examination was positive for cervical lymphadenopathy, exudative tonsillopharyngitis and oral ulcerations. Whitish enanthems were seen on buccal and gingival mucosa, which suggested oral candidiasis. Physical examination was also positive for anal fissures. No focal neurological signs were evident.

OUTCOME AND FOLLOW-UP

Her initial blood cell count revealed: haemoglobin 13.0 g/dL; neutropenia (white cell count $2.3 \times 10^9/L$,

neutrophils $1300/\mu L$ (57.9%), lymphocytes $800/\mu L$ (36.4%)) and thrombocytopenia (platelets $86 \times 10^9/L$). Serum chemistry showed impaired renal function (creatinine 2.1 mg/dL; blood urea nitrogen 71 mg/dL), normal creatine kinase (68 U/L), elevated lactate dehydrogenase (3622 U/L) and transaminases (aspartate aminotransferase 343 U/L; alanine aminotransferase 133 U/L), alkaline phosphatase 197 U/L, γ -glutamyl transpeptidase 254 U/L and normal bilirubin. C reactive protein was 6.5 mg/dL. Microscopic urinalysis revealed haematuria and pyuria. Chest X-ray was normal.

The patient was empirically treated with intensive fluid and electrolyte replacement, nystatin and fluconazole.

On day 1 after admission, she developed diarrhoea and congested eyes before developing a macular rash affecting face, trunk and extremities. On day 3, she developed oliguria, lethargy, confusion and seizures. Funduscopy examination was normal. Viral encephalitis was provisionally diagnosed and intravenous acyclovir started along with diazepam and phenytoin. At this point the ELISA for HIV-1 and HIV-2 was positive and western blot was positive for HIV-1. Subsequent HIV viral load was $7.3 \log_{10}$ copies/mL. Serologies for herpes simplex 1 and 2, cytomegalovirus, parvovirus B19, hepatitis C virus, *Mycoplasma pneumoniae* and toxoplasmosis were negative. Bacterial cultures of throat, blood, urine and stool were negative. When informed of the diagnosis of HIV-1 infection, the patient revealed history of unprotected intercourse with a new partner 1 month earlier. A history of tobacco, alcohol or illicit drug use was denied. Her medical history was unremarkable. The only prescription medication that she was taking was oral contraceptives.

On day 4, she was transferred to a tertiary hospital and ciprofloxacin, ceftriaxone and afterwards liposomal amphotericin B were added to her previous medication (acyclovir and phenytoin). A CT scan and MRI of the brain were normal. Lumbar puncture revealed: 0.8 cells/ μL , glucose 54 mg/dL (glycaemia 125 mg/dL); proteins 257.2 mg/dL, positive cryptococcal antigen latex agglutination test and negative cerebrospinal fluid (CSF) cultures. EEG showed diffuse slow and irregular posterior wave activity. CSF-PCR for *M. pneumoniae*, *Mycobacterium tuberculosis*, *Treponema pallidum*, Epstein-Barr virus, cytomegalovirus, enterovirus, herpes simplex 1 and 2 and Human herpes virus 6 and 7 were negative. Acyclovir, ciprofloxacin, ceftriaxone and afterwards amphotericin B were discontinued. The patient improved over the next 2 weeks.

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DISCUSSION

The non-specific nature of the acute symptoms of PHI often makes the diagnosis challenging.¹¹ In a cohort of 46 patients with PHI, although 85% sought medical attention, only 25% received a correct diagnosis. This syndrome typically occurs 2–6 weeks after exposure to HIV.¹² Our patient presented, 4 weeks after unprotected intercourse, with many of the common findings of PHI: fever, malaise, tonsillopharyngitis, lymphadenopathy, rash, oral ulcerations, vomiting and diarrhoea which in the beginning resembled infectious mononucleosis. She also presented with an opportunistic infection: oral candidiasis. Typical seroconversion laboratory findings include leucopenia, thrombocytopenia and elevated transaminases,⁹ which were seen in our patient. We believe that the acute renal failure was mostly prerenal in the setting of volume depletion due to vomiting and severe food intolerance. She subsequently developed signs and symptoms of meningoencephalitis: seizures, behavioural changes and a slow and irregular posterior wave activity on EEG. The signs and symptoms of aseptic meningoencephalitis occur in about a quarter of patients with PHI presenting for medical consultation.¹² CSF cryptococcus antigen was positive and thus she was started on amphotericin B. This finding was afterwards considered a false-positive since subsequent CSF cultures were invariably negative and the patient improved after discontinuation of amphotericin B. We believe that this was a severe presentation of PHI with meningoencephalitis probably due to the direct action of HIV as HIV displays a well-known tropism for neural tissues.⁷

The suspicion of PHI should prompt virological and serological analysis. ELISA detects the presence of HIV antibodies as early as 3 weeks up to 8 weeks (median 25 days) after transmission¹³ and thus initial serology in PHI is usually negative; in our case ELISA was positive for HIV 1 and 2. False-positive and false-negative results for this test have been reported.^{14–16} Western blot test confirmed HIV-1 infection.

Learning points

- ▶ Symptomatic primary HIV infection may be difficult to diagnose because it often resembles infectious mononucleosis.
- ▶ Paediatricians should consider primary HIV infection as a possible diagnosis in sexually active adolescents who present with a viral syndrome.
- ▶ Primary HIV infection should be considered in the appropriate setting even if risk factors for acquiring the virus are not disclosed.
- ▶ Recognition of primary HIV infection is especially important for improving prognosis and limiting transmission.

The patient's only risk factor for HIV infection was a history of unprotected intercourse 1 month earlier that she revealed after informed of the diagnosis of HIV-1 infection. This case emphasises the importance of considering PHI even if patients do not initially disclose any risk factors for acquiring the virus. It is imperative that paediatricians maintain a high index of suspicion for sexually active adolescents who present with a viral syndrome. Recognition of PHI is especially important for improving prognosis and limiting transmission.¹⁷

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