

CASE REPORT

A three-month-old child with AIDS

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ABSTRACT

Human immunodeficiency virus (HIV) infection in children may lead to severe immunodeficiency and life-threatening conditions during the first years or even months of life. We report a case of three-month-old female child with acquired immune deficiency syndrome (AIDS) presenting severe pneumonia, tracheobronchial candidiasis, and cytomegalovirus (CMV) infection. The child's mother was not tested for HIV in pregnancy. Family history and pulmonary insufficiency in the course of pneumonia in the child resulted in performing an HIV-screening test. Confirmation of diagnosis led to very quick implementation of antiretroviral treatment. Although the girl survived with good neurological outcome, the presented patient shows missed opportunity for prevention of mother-to-child HIV transmission in Poland.

KEY WORDS:

candidiasis, CMV, perinatal HIV infection.

INTRODUCTION

The aim of this paper is to present a case of a three-month-old girl with vertical human immunodeficiency virus (HIV) infection complicated by many comorbidities, including severe pneumonia, tracheobronchial candidiasis, and cytomegalovirus (CMV) infection. The presented patient shows a missed opportunity for prevention of mother-to-child HIV transmission in Poland.

CASE REPORT

The girl was born at term, from uneventful pregnancy and vaginal delivery, weighing 2900 grams, with 10 points on Apgar scale. She was breastfed. She received routine immunisations (BCG – 1×, HBV – 2×, DTP – 2×, IPV – 1×, Hib – 2×).

The girl's mother had been undergoing medical evaluation for fatigue and malaise. Her previous partner died because of tuberculosis. During pregnancy she had vaginal candidiasis and anaemia and had not been screened for HIV. The history of the child's father was unremarkable.

At the age of three months the girl was admitted to a paediatric ward in the regional hospital with a history of diffuse oral thrush, vomiting and increasing dyspnoea. Vomiting and oral candidiasis were observed for two weeks. On admission she was in a poor general condition, yet afebrile, presenting tachycardia 170/min and tachypnoe 90/min. Physical examination revealed generalised lymphadenopathy, oral candidiasis, diminished breath sounds with chest wall retractions, and hepatosplenomegaly. She was cyanotic on exertion and had low (70%) oxygen saturation on ambient air measured by pulse oximetry (90% on oxygen supplementation).

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Her laboratory tests on admission revealed mild anaemia (Hgb 10.2 g/dl.), normal white blood cell count (WBC 13800/mm³), and platelets (PLT 375 G/l). CRP was 4.0 mg/l (normal range < 10 mg/l), liver enzymes were moderately elevated (AST 148 U/l, ALT 64 U/l). Arterial blood gas analysis showed respiratory acidosis. Serological testing for HIV infection was performed and a positive test result was obtained. The blood sample was sent for additional HIV RNA PCR tests. There were confluent consolidations found in both lungs on chest radiograph. Abdominal ultrasound examination was normal. Treatment was started with intravenous cefuroxime, co-trimoxazole (due to suspected *Pneumocystis jirovecii* pneumonia) and oral fluconazole. She required oxygen supplementation and intravenous fluids as well.

She was transferred to the Department of Paediatric Anaesthesiology and Intensive Therapy owing to aggravating signs and symptoms of respiratory failure (oxygen saturation 60%, not responding continuous oxygen supplementation), and she required invasive ventilation.

Chest X-ray showed confluent consolidations in the right lung (in the upper lobe and near the heart) and perihilar consolidations in the left lung. Central vein catheterisation was complicated by right pneumothorax treated with chest drainage. For a few days, dobutamine was used to sustain cardiac output.

Initial treatment was modified – cefuroxime was replaced with ceftriaxone, clarithromycin was added as a prophylaxis of *Mycobacterium avium* complex (MAC) infection, and fluconazole was continued. The therapy with co-trimoxazole was continued with short course of methylprednisolone added for suspected severe *Pneumocystis jirovecii* pneumonia (PJP). However, based on negative blood serologic tests and negative PCR bronchoalveolar lavage for *Pneumocystis jirovecii*, PJP was excluded and, consequently, the therapeutic dose of co-trimoxazole was switched to prophylactic one.

Pharyngeal swab and bronchoalveolar lavage were cultured (among other specimens) and both grew *Candida albicans*. Blood cultures for fungi were negative. Tracheobronchial candidiasis was diagnosed. Considering all the laboratory results along with clinical and radiological findings suggestive of possible *Candida* infection of the lower respiratory tract and critical state of the patient, fluconazole was replaced with liposomal amphotericin B.

Other infections were taken into account. PCR CMV in urine was positive and negative in blood and CSF (central nervous system fluid), it was not possible to distinguish between congenital or postnatally acquired infection. The following infections were excluded: toxoplasmosis, syphilis, hepatitis B and C, TB (tuberculosis), aspergillosis, and cryptococcosis. The initial CD4 lymphocyte count was 488 cells/μl (34%), which meets the criteria of severe immune deficiency in this age group (normal range: above 1500 cells/μl). HIV infection was confirmed by molecular methods: HIV VL (viral load)

amounted to 200,000 copies/ml. Transfontanelar ultrasound and head CT scan revealed mild widening of subdural space. Echocardiography was normal.

A week after admission to the hospital, following genotyping of HIV, exclusion of the drug resistance, and negative results for HLA B5701 antigen, antiretroviral therapy was started with ABC (abacavir), 3TC (lamivudine), and LPV/r (lopinavir/ritonavir). The treatment was followed by Department of Children's Infectious Diseases recommendations.

Further problems in the Department of Paediatric Anaesthesiology and Intensive Therapy included fever and diarrhoea, interstitial infiltrates on chest X-ray: diffuse consolidations in left lung and upper lobe of the right lung, trace amount of air in pleural cavity. The tests for CMV were repeated (two weeks after the first ones), and results of PCR for CMV from blood and urine samples were positive (reactivation/reinfection). CMV disease (gastrointestinal and pulmonary) was diagnosed, without CMV retinitis. Ganciclovir was started. The ganciclovir therapy after a month of treatment resulted in neutropenia (neutrophil count decreased to 360/μl) – treated successfully with filgrastim injections. During the 1.5-month stay in the intensive care unit additional problems included *Staphylococcus haemolyticus* sepsis with positive blood culture, successfully treated with meropenem and vancomycin. The therapy with amphotericin B was discontinued after 24 days; subsequently, fluconazole in a prophylactic dose was re-introduced.

Finally, the girl defervesced and could breathe spontaneously, consolidations on chest radiographs resolved, and she was referred to our clinic for further evaluation and treatment.

After seven months of antiretroviral therapy her CD4 lymphocyte count increased to 1841 cells/μl, which is a normal count for her age. VL HIV became undetectable after 10 months of treatment.

On follow-up lasting for a period of eight years she was successfully treated with ABC, 3TC, and LPV/r. She underwent vaccination according to the national vaccination programme for HIV-infected children. The patient showed no developmental delay and no neurological abnormalities, she went to school in normal conditions. Her weight chart was below the third percentile and height chart on the third percentile. Brain MRI scans were normal. Audiological examination (pure tone audiometry – PTA) was normal. No abnormalities were found on repeated fundoscopy. Spirometry results including vital capacity (VC), forced vital capacity (FVC), and forced expiratory volume in one second (FEV1) were within normal ranges.

DISCUSSION

Despite indications for routine HIV testing during pregnancy in most European countries and in the USA,

there are still high rate of women who are not screened [1–3]. Perinatal transmission can be reduced by antiretroviral treatment in the pregnant woman and prophylaxis in the newborn. The awareness of woman's HIV infection status is crucial to start antiretroviral treatment during pregnancy and prophylaxis in the newborn, both of which along with planned caesarean section and avoiding breastfeeding, reduce the risk of vertical transmission from 15–30% to less than 1%. Despite a decline in perinatal HIV transmission in Poland there are still cases of paediatric HIV infection, which could have been successfully prevented. In the presented case, the mother's medical history (anaemia, vaginal candidiasis) and TB infection in a previous partner underlined the need for HIV testing. The woman should have been tested not only as a screening in pregnancy but also because of her own and her partner's medical conditions.

The progression of HIV infection in children is faster than in adults, with the high risk of development of AIDS - defining conditions during the first two years of life [4]. Severe infectious medical conditions in children indicate the necessity of HIV screening. Opportunistic infections in patients with AIDS are as follows: *Pneumocystis jirovecii* pneumonia, CMV, candidiasis, aspergillosis, tuberculosis (mainly in low-income countries), *Mycobacterium avium* infections, toxoplasmosis, cryptococcosis and, the most commonly diagnosed, serious bacterial infections [5–7]. HIV-related immunodeficiency is a major risk factor for most of them. Our patient developed AIDS with life-threatening clinical presentation of severe pneumonia, candidiasis, CMV disease, and severe immunodeficiency. Detailed medical history and rapid HIV testing on admission allowed the diagnosis of HIV infection at the beginning of hospitalisation and the start of antiretroviral treatment one week later. Initially suspected PJP was excluded.

The most common fungal infections are caused by *Candida* spp. and they are still a major health problem among HIV-infected children [8, 9]. Oesophageal candidiasis often presents with dysphagia and pain. Unlike in adults, many children experience nausea and vomiting (as described in our child), which may lead to dehydration and weight loss. Disseminated candidiasis is infrequent. Risk factors include central venous catheters or intravenous antibiotics. Blood cultures are necessary to confirm candidemia and invasive infection. Systemic antifungals (amphotericin B, echinocandins, fluconazole) are required for effective treatment of invasive candidiasis. The choice of drug depends on the severity of the disease and previous fluconazole exposure. In our patient *Candida albicans* was revealed only in specimens of pharyngeal swab and bronchoalveolar lavage. The course of amphotericin B followed by fluconazole therapy was successful.

HIV-infected children appear to be at high risk of CMV congenital infection and the acquired infection during early childhood [10]. Both HIV and CMV affect

the same cells of the organism, which results in aggravation of the clinical condition of patients. CMV can cause disseminated or localised disease among patients with immunosuppression, with clinical manifestations like retinitis, colitis, esophagitis, and CNS disease. The role of CMV in interstitial pneumonia among HIV-infected children is difficult to assess because it is often isolated with other infectious agents. In children with extraocular disease predominant symptoms are nonspecific (fever, poor weight gain, anaemia, thrombocytopenia).

Late complications of CMV congenital disease include developmental abnormalities, sensorineural hearing loss, chorioretinitis, or neurologic defects. Ganciclovir is the drug of choice in severe cases [9, 11].

In our patient positive CMV PCR in blood together with clinical symptoms confirmed the diagnosis of systemic CMV disease. It was not possible to exclude congenital infection. She was treated with ganciclovir. Neutropenia was noted during IV ganciclovir use, successfully treated with granulocyte colony-stimulating factor.

CONCLUSIONS

Severe infectious medical conditions in children indicate the necessity of HIV screening. Rapid HIV testing on admission to regional hospital allowed us to establish a proper diagnosis and start antiretroviral treatment soon after. The survival of our patient and her overall undisturbed neurodevelopment observed during long follow-up are positive aspects of early diagnosis of HIV infection. Nevertheless, she is a striking example of a case of lifelong and still incurable infection which could have been successfully prevented.

DISCLOSURE

The authors declare no conflict of interest.

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