Case Report

Disseminated *Mycobacterium tuberculosis* in an Infant with AIDS

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Abstract

Disseminated *Mycobacterium tuberculosis* with involvement of liver, spleen, and bone marrow is a nonspecific and rare complication in human immunodeficiency virus (HIV) infected infants. Here, we report a six month old girl with fever, recurrent infections, bilateral axilary lymphadenitis, hepatomegaly, huge splenomegaly, and failure to thrive. The infant and her mother had positive enzyme immunoassay (EIA) and Western blot.

HIV DNA PCR test of the infant was positive with subtype A (A1) in genotyping. A positive bone marrow aspirate staining for acid fast bacilli and PCR test on culture revealed *Mycobacterium tuberculosis*.

Keywords: disseminated *Mycobacerium tuberculosis*, HIV/AIDS, infant

Introduction

An estimated 8.8 million new cases of *Mycobacterium tuberculosis* (TB) occur worldwide annually. Currently, TB is one of the leading causes of mortality in children co-infected with human immunodeficiency virus (HIV-1).[1] There are limited studies on the estimates of tuberculosis incidence among HIV infected infants under the age of 12 months.[2] The relative risk of TB among HIV infected infants is more than 24, compared to non-HIV infected infants.[2] Pediatric HIV infection is acquired mainly by transmission from mother to child during pregnancy, labor, or breast feeding. Perinatal transmission accounts for more than 90% of infections in children and is a great challenge in developing countries.[3] Involvement of the spleen, liver, and bone marrow are rare complications due to disseminated TB in the late stage of AIDS.[4] The number of cases of AIDS in children have accounted for less than 1% of all reported cases in the United States.[5] We report a co-infected case of HIV and disseminated TB who presented with anemia, lymphadenopathy, hepatomegaly, huge splenomegaly, and failure to thrive.

Case Report

A six-month-old girl was admitted to the pediatric infectious ward in a university based referral hospital, affiliated with Shiraz University of Medical Sciences in southern Iran, with fever, respiratory distress and lethargy. She developed fever and cough since two months prior to admission, and received antibiotics with no improvement. The patient had a history of BCG immunization at birth and developed suppurative lymphadenitis in the left axilary area, which spontaneously drained after fistulization and healed with a scar at the age of three months. Her deceased father was an injectional drug user (IDU) and her mother an opium addict. Her medical history revealed that she had had frequent illnesses including pneumonia and diarrhea since birth, which resulted in failure to thrive. On admission, her temperature was 39°C, respiratory rate was 60/min and heart rate was 160 beats per minute. The patient was pale, underdeveloped and undernourished. On examination, she had pale conjunctiva, nasal flaring, intercostals retraction, diffuse rales over both lungs, hepatosplenomegaly, and bilateral axilary lymph nodes.

Laboratory data were as follows: Hb, 6 mg/dL; WBC, 9.3 k/μL; ESR, 30 mm/hr; CRP, 96 mg/dL; and blood sugar, 95 mg/dL. Blood urea nitrogen, creatinine, and electrolytes were within normal limits. Arterial blood gas showed mild respiratory alkalosis. Urine analysis, stool examination, and lumbar puncture results were normal. Blood culture, urine culture, Wright, and Widal tests, HBsAg, HBCAb, as well as direct and indirect Coomb's tests were negative. Liver function tests revealed the following results: ALT, 70 U/L; AST, 244 U/L; alkaline phosphatase, 346 U/L; total protein: 5.9 gr/dL; albumin, 2.7 gr/dL; globulin, 3.1 gr/dL; total bilirubin, 2.3 mg/dL; direct bilirubin, 1.3 mg/dL; prothrombin time, 15.5 seconds and partial prothrombin time, 60 seconds. Towards a revolution in COPD health (TORCH) study was negative. Measurement of complements, anti-nuclear antibody, dsDNA, anticardiolipin antibodies, and antibodies to nuclear cytoplasmic antigens (p-ANCA, c-ANCA) were within normal limits. Tuberculin skin test (TST) of both the infant and her mother were negative. Chest X-ray showed mild infiltrations and haziness with no hilar lymph nodes or pleural effusion. Abdominal sonography reported mild hepatomegaly and prominent splenomegaly. Enzyme immunoassay (EIA) and Western blot tests for HIV in the infant's blood and her mother were positive. HIV DNA PCR of the infant was positive. HIV genotyping study revealed genotype A (A1).

Treatment with fluid, oxygen, appropriate antibiotics, and supplements resulted in resolution of respiratory distress. The patient was treated presumptively for *Pneumocystis jirovecii* (PCP) but fever per-

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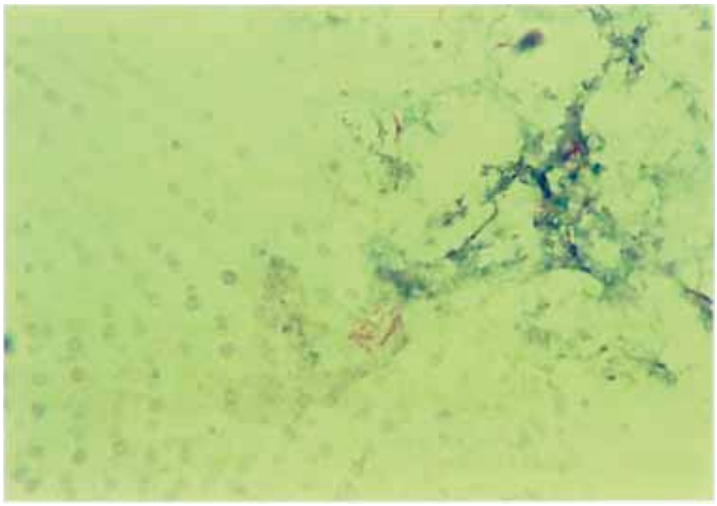

Figure 1. Ziehl-Neelsen stain smear from bone marrow culture (100x)

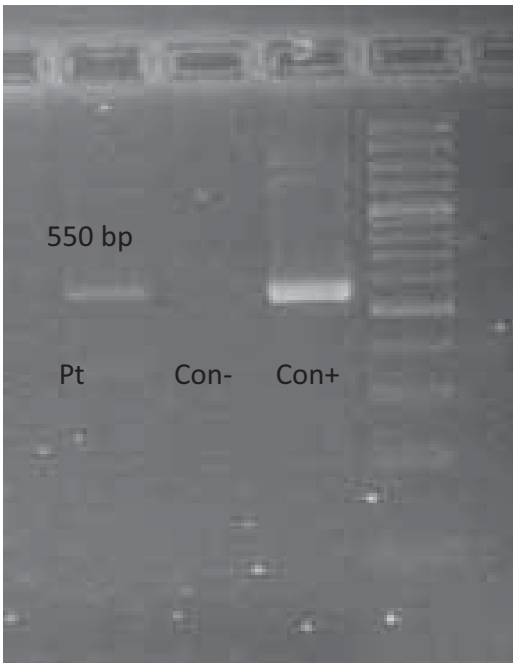

Figure 2. The results of PCR amplification of *M. tuberculosis* in bone marrow culture.

sisted. Bone marrow aspiration cytology was normal. Ziehl-Neelsen staining for acid fast bacilli was three plus positive (Figure 1).

Diagnosed with disseminated BCGitis, the patient received treatment with isoniazid, rifampin, ethambutol, clarythromycin, and ofloxacin; however, because of severe thrombocytopenia rifampin was discontinued. Antiretroviral therapy with ziduvudin, lamivudin, and nevirapin was initiated. One month later, the bone marrow culture was positive. PCR test indicated positive TB genome (Figure 2) and negative BCG genome. Pyrazinamide was added to the drug regimen; in addition, clarythromycin and ofloxacin were discontinued. Prophylactic therapy was started for PCP with trimethoprim-sulfamethoxazole. The patient's body temperature and liver enzymes normalized after one week and body eight slowly increased.

Discussion

It is reported that the incidence rate of TB among HIV infected infants is high.[2] A large study carried out in South Africa over a three-year period revealed a high incidence rate of tuberculosis among HIV infected infants with a relative risk of 24.2 (95% CI: 17 – 34).[2] However, little is known about co-infection of TB and HIV in Iranian infants, therefore our case is one of the rare cases reported thus far.

Extrapulmonary involvement, especially liver, spleen, and bone marrow due to disseminated tuberculosis is a rare complication of HIV/TB co-infection.[4] In countries such as Iran, where BCG vaccine is injected at birth, a predisposing factor for disseminated BCGitis and disseminated TB is HIV infection in infants.[6–8] The patient had extrapulmonary involvement such as bilateral axilary lymphadenopathy, hepatomegaly with hepatitis, and huge splenomegaly. Bone marrow involvement presented with anemia and leukopenia without signs and symptoms of pulmonary TB. Based on clinical findings in the patient that included BCG adenitis and positive acid fast bacilli on bone marrow smear, we initially suggested a disseminated BCGitis, but positive PCR for TB genome in the bone marrow culture revealed disseminated TB. Her mother had documented HIV-infection with positive EIA and Western blot; in addition, the infant was positive for HIV DNA PCR, which is the best confirmatory test for those under 18 months of age. Therefore, we concluded that the transmission route was mother-to-child. It was not possible to determine the time of transmission, if before or after delivery, because she had been breastfed. Her mother was screened for TB by sputum culture, which was negative. Our case was classified as CDC category C (severely symptomatic), based on clinical classification with symptoms and findings such as intermittent fever more than 30 days, failure to thrive and disseminated TB. She also had category B symptoms consisting of fever, anemia, pneumonia, diarrhea, and hepatitis, in addition to symptoms of category A including lymphadenopathy, hepatomegaly, and splenomegaly.[5] As the American Academy of Pediatrics recommended, HIV-infected infants should receive antiretroviral therapy irrespective of clinical symptoms, immune status or viral load,[5] therefore no additional immunological and viral load evaluations were necessary. One of the main complications of anti-tuberculosis therapy in this patient was severe thrombocytopenia that resulted in the discontinuation of Rifampin. Inappropriate anti-tuberculosis therapy and emergence of resistant strains can complicate patients with disseminated tuberculosis.[9]

In conclusion, when evaluating HIV-infected infants with non-specific clinical findings in TB high prevalence areas, physicians should consider mycobacterial infections, in particular the disseminated form. PCR tests on tissue or culture samples can identify the type of mycobacterial infection, which would be necessary for better management of the disease.

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Erratum

In article entitled " Soluble Fas in Pemphigus Vulgaris", published in Archives of Iranian Medicine, Volume 13, Number 3, May 2011, Maryam Yousefi MD[2] should be changed into Maryam Yousefi MD[1].

The author would like to apologize for this mistake.