Pneumocystis Carinii Pneumonia in Pediatric Acquired Immune-Deficiency Syndrome

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Pneumocystis carinii pneumonia (PCP) is the most frequent opportunistic infection in children with human immunodeficiency virus (HIV) infection in the developed countries(1). Often it is the presenting manifestation of acquired immunodeficiency syndrome (AIDS) in infants(2). On the other hand, PCP is reported much less frequently in patients with HIV/AIDS, both children and adults, from developing countries such as in Africa and the Caribbean, as well as in India(3-6). It is not clear whether there are differences in the geographical prevalence of PCP, or whether such differences represent inadequate diagnostic facilities in the latter regions. The fact that the prevalence of antibody to Pneumocystis carinii in these regions is similar to that in developed countries argues against the former explanation(7). The published reports of AIDS in India, as well as our own experience (unpublished) suggest that PCP does occur in adult patients with AIDS, but is relatively less common compared to tuberculosis, cryptococcal meningitis and diarrheal disease(8). There is virtually no data on the occurrence or frequency of PCP among children with perinatally acquired HIV infection in India. We describe here two infants with perinatally acquired HIV infection and PCP, proven in one case and presumptive in the second, in order to document its occurrence in this region and to alert pediatricians to search for evidence of Pneumocystis carinii infection in pediatric AIDS.

Case Reports

Case 1

A 4 month old female infant, whose parents were known to be HIV-infected, presented with fever, cough and tachypnea of one week duration. She was admitted and treated at another hospital with parenteral antibiotics for pneumonia and oral gentian violet for extensive oral thrush, but without significant improvement.

On examination, she was ill-looking, febrile, with respiratory rate of 88/min and lower chest indrawing. She had extensive oral candidiasis and palpable cervical and axillary lymph nodes measuring about 0.5cm in diameter. Chest auscultation revealed normal breath sounds with no adventitious sounds. The liver was palpable 3 cm below the right costal margin in the mid-clavicular line, the spleen was not palpable.

Investigations revealed hemoglobin concentration of 8.0 g/dl, total leucocyte count of 24,259/cu mm, differential leucocyte count of band forms 5%, neutrophils 58%, lymphocytes 35% and monocytes 2%, and platelet count 376,000/cu mm. Blood culture was sterile. The HIV ELISA test (Detect HIV, Immunosystems, Montreal, Canada) was repeatedly reactive. Arterial
blood gas analysis revealed pH 7.316, pCO₂ 24.1 mm Hg, pO₂ 29.9 mm Hg and oxygen saturation 51%. Serum IgG was 974 mg/dl, IgM 358 mg/dl and IgA 149 mg/dl. Chest roentgenogram showed bilateral diffuse reticulonodular opacities. Two fasting gastric aspirate samples were negative for acid fast bacilli and endotracheal aspirate was negative for *Pneumocystis carinii* by immunofluorescent staining using a fluorescein tagged monoclonal antibody.

Since PCP was strongly suspected, she was empirically treated with trimethoprim-sulfamethoxazole (TMP-SMX) (20 mg/kg/day of trimethoprim) in addition to intravenous penicillin and gentamicin to cover for other bacterial pathogens. In addition, she received prednisolone, intravenous fluids and oxygen. The patient's condition progressively deteriorated and she died 34 hours after admission. A post mortem lung biopsy showed alveolar spaces filled with a foamy, pale eosinophilic exudate containing cysts of *Pneumocystis carinii* (Fig. 1). A mild interstitial infiltrate of lymphocytes and occasional plasma cells was present.

**Case 2**

A boy, aged nine months, was referred to this hospital with a diagnosis of cystic fibrosis. He had recurrent thrush since 3 months of age and also had delayed developmental milestones. He presented with a history of cough, breathlessness and low grade fever of one month duration. He had not responded to treatment with several broad spectrum antibiotics, including third generation cephalosporins plus aminoglycosides. His father had been transfused with 3 units of blood following a head injury in 1986. The parents denied any other risk factor for HIV infection.

On examination, he was afebrile with respiratory rate of 80/min and lower chest indrawing. He had intermittent episodes of cyanosis. He had oral thrush and small discrete lymph nodes, size about 0.5 cm, palpable in the neck. Normal vesicular breath sound with no adventitious sounds were auscultated over the lungs.

Investigations revealed hemoglobin concentration of 10.6 g/dl, total leucocyte

![Fig. 1. Photomicrograph showing alveolar exudates containing cysts of *P. carinii* (Gomori’s methanamine silver stain x 660).](image-url)
count of 9900/cu mm with 47% neutrophils and lymphocytes 53% and ESR of 40 mm/hour. Mantoux test was non-reactive. Fast ing gastric aspirate was negative for acid fast bacilli. Chest roentgenogram showed diffuse reticulonodular opacities bilaterally. At admission, arterial blood gas analysis showed pH 7.439, pO₂ 36.1 mm Hg and pCO₂ 24.8 mm Hg. Serum immunoglobulin assay revealed IgG 488 mg/dl, IgA 88 mg/dl and IgM 81 mg/dl. Lymphocyte subset enumeration, done by flowcytometry (FACScan, Becton Dickinson, USA), revealed total lymphocyte count of 4290/cu mm, pan T (CD3) cells 3050/cu mm, helper T (CD4) cells 90/cu mm, suppressor T (CD8) cells 2270/cu mm and CD4: CD8 ratio 0.03; the remaining T cells were positive for both CD4 and CD8 markers, indicating that they were as yet undifferentiated T cells. The infant and both parents tested positive for HIV antibody by ELISA and Western blot (IgG, HIV-2.2, Diagnostic Biotechnology, Singapore) assay.

As the patient had diffuse, bilateral pneumonia and hypoxia which was unresponsive to broad spectrum antibiotics and as he was HIV-antibody positive with a very low CD4 count, PCP was suspected. Presumptive treatment for PCP was begun with TMP-SMX and prednisolone, along with other supportive measures. The patient showed a dramatic improvement with progressive improvement in arterial pO₂ and oxygen saturation which were in the normal range in room air within one week after starting treatment. The TMP-SMX dose was reduced to the prophylactic doses 3 weeks after starting treatment and the patient was discharged home. Prednisolone was tapered starting 1 week after treatment and stopped after 3 weeks.

**Discussion**

This report describes two infants with AIDS who presented with PCP. In both the diagnosis of PCP was suspected at presentation but could not be proved because bronchoscopy to obtain specimens for definitive diagnosis was not possible as the patients were considered very high risk for general anesthesia. In one of them the diagnosis was confirmed by post-mortem lung biopsy. In the other, a presumptive diagnosis was made on the basis of the clinical presentation, the immunocompromised status of the child with CD4 counts < 100/cu mm, and prompt response to treatment with TMP-SMX when there had been no response to broad spectrum antibiotics including third generation cephalosporins and aminoglycosides at the previous hospital.

While this report documents that PCP occurs among infants with perinatally acquired HIV infection in India, further studies of infants and children with perinatally acquired HIV infection are required to determine prevalence of PCP in India, to delineate risk factors for and to identify clinical and laboratory correlates of PCP. An increased incidence of PCP has been reported among renal transplant patients at our hospital since the onset of the AIDS epidemic in India, possibly from exogenous infection from contact with AIDS patients(9). It is, therefore, possible that the prevalence of PCP may increase with the increase in prevalence AIDS in India.

Laboratory diagnosis of PCP in infants ideally involves bronchoscopy and identification of *Pneumocystis carinii* in the bronchoalveolar lavage fluid with either methanamine-silver stains or immunofluorescent antibody staining; tracheal aspirates and fasting gastric juice may be used but have a low yield. These procedures may not be possible in most centers in our country. Hence, presumptive treatment based on clinical suspicion may be required and will often be life-saving. Criteria which
may be used to diagnose PCP include: (i) presence of diffuse pneumonia which is unresponsive to common antibiotics; (ii) hypoxemia; (iii) presence of other signs of HIV-infection such as oral thrush, diffuse lymphadenopathy, failure to thrive and developmental delay; (iv) risk factors for HIV in the parents; and (v) when testing is available, low CD4 counts.

The other common pulmonary manifestation of HIV disease is lymphoid interstitial pneumonia (LIP). While this condition also causes diffuse lung involvement, it occurs later in the course of HIV infection in children, usually after the first year of life whereas PCP occurs mainly during infancy. LIP is usually associated with generalized lymphadenopathy, parotid enlargement and hypergammaglobulinaemia and has a slowly progressive course. The condition may spontaneously improve with progressive immunodeficiency and lymphoid ablation. It is very unlikely that the second patient, who was severely immunocompromised, had more rapidly progressive pulmonary disease and had very rapid response to TMP-SMX and steroids, had LIP.

PCP in infants with perinatally acquired HIV infection is a serious disease with a fulminant course and high mortality. In contrast to 37 to 50% of adults, only 26% of children were alive 1 year after the diagnosis of PCP. The increased severity and mortality from PCP in infants is thought to be due to the fact that infants have primary infection with P. carinii whereas in adults, the disease is often due to reactivation of latent infection. Hence, prompt treatment is indicated when PCP is suspected, even if diagnosis cannot be firmly established. The antibiotic of choice is TMP-SMX, given in high doses (20 mg/kg/day of trimethoprim in 4 divided doses). Alternatively, intravenous pentamidine in a dose of 4 mg/kg as a single daily dose may be used. The addition of corticosteroids has been shown to reduce mortality in patients with PCP who have hypoxemia and maybe used as an adjunct to TMP-SMX.

Primary prophylaxis can substantially reduce the risk of PCP. Because of its high frequency of occurrence, associated high mortality and lack of good correlation with CD4 counts during infancy, the Centers for Disease Control, Atlanta (CDC) currently recommends prophylaxis for all infants to 6 weeks of age till the age of 1 year or till HIV infection is conclusively ruled out. At the present time it appears prudent to recommendation in India also. Beyond infancy, recommendations for prophylaxis are based on CD4 counts. Facilities for enumeration of CD4 positive cells are not widely available in India. Guidelines, based on clinical criteria generated from locally available data, are required to overcome this problem.

REFERENCES


