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Case Report

Pneumocystis pneumonia in children in Calabar, Nigeria

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ABSTRACT

Pneumocystis pneumonia (PJP), initially thought to be rare in this part of the world, has over the years, been diagnosed and treated in our center. PJP should be considered in a young child 3 to 6 months of age with very severe pneumonia, known or suspected to be HIV infected. It should be suspected when severity of illness is out of proportion with the chest findings and chest x-ray is normal or shows minimal or bilateral interstitial infiltrates. Treatment is oral or intravenous high dose cotrimoxazole given 6-8 hourly for 3 weeks and the addition of prednisolone. The objective of this report is to describe the presentation, challenges of diagnosing and management of PJP in children in a developing country. Report of 3 cases aged 3, 4 and 41/2 months, exposed to the HIV. All developed severe pneumonia characteristic of PJP and all responded to treatment with high dose cotrimoxazole and Prednisolone. A high index of suspicion is needed to diagnose PJP in a resource poor setting like ours. It is common in HIV positive children but can also occur in HIV negative individuals as shown by these case reports. A presumptive diagnosis can be made in a young child, usually below 6 months of age, very ill with severe pneumonia and minimal chest findings who responds to cotrimoxazole. Addition of prednisolone has been found to improve the outcome. Antibiotics should continue to cover for co-existing bacterial pneumonia.

Keywords: Pneumocystis Pneumonia, Cotrimoxazole, Prednisolone

INTRODUCTION

Pneumocystic jirovecii pneumonia (PJP), formerly called Pneumocystis carinii pneumonia (PCP), was first described by Otto Jirovec in European infants with pneumonia.[1] It became clear that *Pneumocystis carinii*, first described in 1910, does not occur in humans at all, but only in rats.[1,2] The Pneumocystis species that affects humans is referred to as Pneumocystis jiroveci, not *P.carinii* and *carinii* has now been taken out of the name for the pneumonia.[3] The disease was previously thought to be uncommon in developing countries where, bacterial pneumonia and tuberculosis are the common causes of respiratory illnesses in HIV-infected individuals. Today, many clinical and autopsy studies have confirmed that PJP is more common in developing countries than previously thought.[1] The prevalence of infection among HIV-Infected children hospitalized with pneumonia in Africa has ranged from 10-49% with case fatality rate of untreated PCP almost reaching 100%.[4,5] Autopsy series have described rates of 14 to 51.3% mainly in infants less than 6 months of age.[6]

Pneumocystis infection has proven difficult to study partly due to the lack of reliable culture system for the organism.[7] The mode of transmission is not firmly established but airborne human to human transmission is likely. Infections are almost always limited to the lungs and cannot be cultured reliably outside the lungs.[7,8] Clinical signs and symptoms are non-specific and confirmation is hampered by inability to reliably perform in vitro culture.[5] Definitive diagnosis in resource limited

areas are difficult due to poor diagnostic resources and expertise and so management decisions is primarily clinical.[4] Timely initiation of effective therapy depends on the clinical identification of children with PJP.[4] A valid clinical diagnostic technique to be used by clinicians in these areas is therefore important, using a combination of certain clinical criteria, to diagnose PJP.[4] The outstanding clinical features are fever, dyspnea, tachypnea and cough. In children with pneumonia infected with HIV, four clinical variables are independently associated with PJP: Age under 6 months, respiratory rate greater than 59 cycles/min, oxygen saturation less than or equal to 92% and absence of vomiting. HIV positivity strongly predicts PJP.[8] The findings of young age, with hypoxia, tachypnoea, absent vomiting in a background of maternal HIV infection warrants empirical treatment for PJP.[4]

The World Health Organization had since produced guidelines to ease the management of PJP in hospitals with limited resources.[1] It should be considered in a young child 3-6 months with very severe pneumonia, known or suspected to be HIV infected.[3] The child is usually very ill with dyspnoea and tachypnea, out of proportion with the minimal chest findings on auscultation. Chest X-ray (CXR) may be normal, hyperinflated or have bilateral interstitial infiltrates. Pulse oximetry shows severe persistent hypoxia (paO2 <90%) and response to standard antibiotic treatment is very poor.[3] PJP is also described though much less commonly in HIV-exposed but uninfected infants.[9] Treatment is oral or intravenous high dose cotrimoxazole (CTZ) 20 mg/kg of trimethoprim per day OR 80 mg/kg/day of sulphamethoxazole given every 6-8 hours for 21 days.[3] Addition of corticosteroid therapy during acute infection with PJP in young children with AIDS appears to significantly reduce morbidity and mortality.[10] In 1990, an expert panel recommended the use of corticosteroids in the treatment of PJP. The rationale for using steroids was that 2-3 days into treatment, there is increased inflammation in the lungs as a reaction to killed organisms and steroids reduce this. Therefore when started within 72 hours of treatment, steroids can better control the infection.[11] Prednisone is given at 1-2 mg/kg/day for 14 days and tapered during the next 7 days.[3,10,12] Physicians and policy makers in the lower and middle income countries should therefore familiarize themselves with the presentations of PJP in children in these regions.[13] These case reports aim to describe our experiences in the management of pneumocystis pneumonia in children in a prototype developing country.

METHODS

Report of three cases aged 3, 4 and $4^1/_2$ months respectively, seen in the University of Calabar Teaching Hospital (UCTH) with the diagnosis of pneumocystis pneumonia. All the three babies developed congestive heart failure and responded to anti-infective and anti-failure treatment. All the babies were HIV exposed. Case 1 was confirmed HIV negative and is now 9 years old, alive and well. Case 2 was lost to follow-up after treatment of PJP and later died at home. Case 3 was confirmed HIV infected and has been referred to Paediatric ART clinic for commencement of HAART.

RESULTS

Case 1

A 4 ½ months male child who presented with cough and catarrh for 1 month, fever for 2 weeks and fast breathing for 2 days. Cough was gradual in onset, hacking in nature with associated wheezing and no history of contact with anyone who had chronic cough. Fever was high grade and intermittent. He had made several visits to the Paediatric Out-Patient Department (POPD) and had received ceporex, zithromax, erythromycin, coartem, septrin and nystatin drops on different occasions. Two days prior to presentation he developed fast breathing and this prompted his return to UCTH where he was subsequently admitted in the Children's Emergency Unit (CHER).

He was then a known patient enrolled into the PMTCT programme that was not compliant with his cotrimoxazole prophylaxis and the last child in a family of 4 children. Both parents are seropositive and on treatment. His mother booked for antenatal care at 13 weeks of gestation in UCTH, screened positive for HIV and was started on Highly Active Anti-retroviral Therapy (HAART). Pregnancy was however uneventful. She had elective Caesarian Section at term and baby was given post-exposure prophylaxis after delivery. Birth weight was 2.95 kg with good Apgar scores.

Physical examinations showed an acutely ill-looking child in severe respiratory distress, afebrile, not pale, anicteric, acyanosed, with oral thrush, and weighing 5.3 kg (79% of expected body weight and just below the third percentile on CDC chart). The respiratory rate was 80 cycles per minute with bulging anterior chest wall, hyperesonant percussion notes and occasional expiratory rhonchi only. The heart rate was 160 beats per minute with normal heart sounds. The abdomen was full, soft, moved with respiration, with hepatomegaly of 3cm and splenomegaly of 2-3cm firm, smooth surfaced and tender. A diagnosis of Pneumocystic Jirovecii Pneumonia (PJP) in an exposed baby was made. He was admitted into CHER. Chest X-Ray (CXR) showed hyperinflation with bilateral hilar opacities. Intravenous Ceftriaxone, Gentamycin, oral Prednisolone, high dose oral Cotrimoxazole and oral Nystatin were commenced. Three days later, he was still having fever, with a respiratory rate of 76 cycles per minute, dyspnoic with associated tracheal tug and bilateral creptitations. The liver was enlarged by 5cm below the right costal margin, smooth surfaced and tender. The heart rate was 175 beats per minute with first and second heart sounds only. An additional diagnosis of Congestive Cardiac failure was

considered and digoxin and frusemide were added to the treatment. He gradually responded and was discharged home. HIV serology and DNA PCR results were both Negative. When seen in the follow-up clinic, he was well with a clear chest and no respiratory distress. Prednisolone was tapered off, high dose co-trimoxazole stopped after 3 weeks and cotrimoxazole prophylaxis recommenced. He was since discharged from the PMTCT clinic and is today a healthy 9-year-old boy.

Case 2

A 3 month old baby girl admitted into CHER with complaints of cough, fever and fast breathing of one week duration. The cough was sudden in onset, not in paroxysms and not associated with vomiting. Fever was high grade and intermittent and the mother herself had chronic cough. She started antenatal care in UCTH but stopped after she screened HIV positive. The pregnancy was however uneventful. She had spontaneous vertex delivery at home with no problems. The baby received the first doses of OPV and BCG and mother stopped further immunizations when child became ill. She was yet to attain neck control and had just started smiling before the illness. She was breastfed exclusively for one week. Thereafter formula feeds were introduced when mother's health deteriorated and breast milk became irregular.

She is the 2nd child in a family of 2. The mother was a business woman (selling clothes) and was then on admission in the female ward for AIDS with chronic cough before demise. The father is a supervisor with a construction company.

Physical examination showed an ill looking child in respiratory distress, febrile with temperature of 39oC, moderately pale and mildly dehydrated. Weight was 3.7 kg (61% of expected body weight and below the third percentile on CDC chart). The respiratory system had a rate of 92 cycles per minute, with mild anteroposterior buldging of the chest wall, resonant percussion notes, bronchovesicular breath sounds with no added sounds. The Cardiovascular system had a heart rate of 172 beats per minute with 1st and 2nd heart sounds and no murmurs. The abdomen was full and soft with a tender hepatomegaly of 4cm, while the Spleen was 3cm, firm, smooth surface and non-tender. The central nervous system showed a conscious baby with depressed but normotensive anterior fontanelle, no signs of meningeal irritation and normal tone globally.

A diagnosis of severe Pneumonia in Heart failure was initially made and she was admitted into CHER. CXR showed few patchy opacities, Urgent packed cell volume (PCV) was 28%; Erythrocyte Sedimentation Rate (ESR) was 20mm/hr. The total white blood cell count (WBC) was 10.5 X109/L, Neutrophils – 50%, Lymphocytes- 45%, Eosinophil's – 2% and Monocytes- 3%. HIV screening test was Positive. "Nil per Oral" was instituted and oxygen therapy, cautious intravenous fluids, IV ceftriaxone, IV Gentamycin and digoxin were added to treatment. Despite these measures, she was still dyspnoeic, tachypnoeic, with intermittent fever and a clear chest up to seven days later. A diagnosis of Pneumocystis Pneumonia in an exposed baby was then made to R/O PTB, R/O AIDS. Mantoux test was negative and gastric aspirates were negative for AFB. CD4 count was 1079 cells/mm3. High dose oral cotrimoxazole and oral prednisolone were given for 3 weeks. She improved with these and was subsequently discharged home to complete treatment. Subsequent clinic follow-up showed some weight gain and resolution of all chest signs and was thereafter referred to the ART clinic. Thereafter, she was lost to follow-up and later died at home.

Case 3

A 4 months old female infant admitted on account of fast breathing of 3 days, fever for 2 days, cough and poor sucking of one day's duration. She was well until she developed fast breathing following a prodromal period of catarrh of 2 days, initially mild but progressively worsened even at rest, no history of aspiration of feeds, bluish discoloration of the lips, nor history of foreign body ingestion. The fever was low grade and continuous. The cough was insidious in onset, progressively worsening and associated with poor sucking, for which she presented in CHER for expert management. The pregnancy was booked in UCTH at 4 months of gestation. The mother tested positive to HIV antibodies and was subsequently commenced on HAART. She delivered at term by Spontaneous Vertex Delivery (SVD) and baby has been exclusively breastfed since birth. She's the second child in the family and has received all immunizations for age.

Physical examination revealed an acutely ill-looking child, febrile with temperature of 38.1 degrees Celsius, tachypnoic, and dyspnoic with SP02 of 60% in room air and 90% on oxygen. The weight was 4.8kg (74% expected for age and on the third percentile) and the OFC- 41cm (98% expected for age). The respiratory rate was 52c/min, with a clear chest. The heart rate was 160/min with S1 and S2 only. The Liver was 3cm enlarged, soft, smooth and tender. A diagnosis of PJP in heart failure in an exposed baby was made. CXR had few hilar opacities. The PCV was 37.1%, WBC was 12.9 X109/L with neutrophils of 70%, lymphocytes of 27%, eosinophil's of 3%, platelets of 530 X109/L and a normocytic, normochromic film. Intravenous ceftriaxone and gentamycin, high dose oral co-trimoxazole, oral prednisolone as well as digoxin were commenced. She responded remarkably well and was discharged 10 days after admission to be seen a week later in the respiratory clinic. When seen, she remained well with a good weight gain and a clear chest. Treatment was to continue, after which cotrimoxazole prophylaxis was commenced. HIV Deoxyribonucleic acid Polymerase Chain reaction (DNA

PCR) was positive and she was referred to the Paediatric ART clinic for commencement of HAART.

DISCUSSION

The reported cases aim to document PJP in this environment. Studies have shown that PJP is common in the developed world but has always been regarded as rare in low and middle income countries.[13] It has however remained a public health concern in developing countries.[1,4,5] In Africa HIV infected children have high rates of PJP.[1,4-6]

All the cases in this study were young infants aged below 6 months. Various literature have documented high risk groups as 6 weeks to 6 months, 3 to 6 months and less than 6 months which is in keeping with the age range of children in our study.[3,4,6,8,14,15]

All the three reported cases characteristically had severe pneumonia with severe hypoxia. PJP remains a common cause of severe hypoxic pneumonia and is associated with high mortality.[15] Even with timely use of antibiotics, corticosteroids and supportive interventions, PJP is associated with a high fatality rate of about 50% in HIV-infected children.[5]

Clinical features common to the three cases were fever, cough, fast breathing, severe dyspnea, severe hypoxia, buldging anterior chest wall and unremarkable chest auscultation. This is in keeping with findings from other studies describing similar clinical features.[4,8,14] Also interesting to note is the absence of vomiting in these cases even despite the cough, dyspnea and hyperinflation. Some other studies have observed the absence of vomiting in these infants.[4,8]

The reported CXR findings were minimal showing hyperinflation, hilar opacities and few patchy opacities. Studies have shown that CXR may be normal, show mild lung infiltrates or bilateral diffuse parenchymal infiltrates with ground glass or reticulogranular opacities. Rarely does CXR show pneumothorax, pneumomediastinum, lobar, cavitary, nodular, or miliary lesions.[8] These findings are contrary to one study, which reported complications like pneumothorax and pneumomediastinum in children with PJP.[14] The experience in our center and indeed in these reported cases show that congestive cardiac failure is almost always present as a complication of PJP. No other study has reported this as of date. Further studies and larger sample size need to be done to validate this.

Case 1 was confirmed HIV un-infected. Several studies had since reported PJP in HIV uninfected population where HIV uninfected minority also developed PJP and rates of 9.9 to 48.6% were found in children admitted with pneumonia where 4 non HIV infected children also had PJP.[4,5,15]

Also only one child out of 17 had HIV in a separate study.[14]

Addition of steroids to cotrimoxazole is associated with rapid and remarkable improvement. The benefits of steroid therapy in PJP had since been documented.[3,10-12]

CONCLUSION

A high index of suspicion is needed to diagnose pneumocystis jiroveci pneumonia in a resource poor setting like ours. A presumptive diagnosis can be made in a young child, less than 6 months of age, very ill with severe pneumonia and minimal chest findings who responds to cotrimoxazole. Addition of prednisolone has been found to improve the outcome while antibiotics continue for bacterial pneumonia. Worthy of note is the absence of vomiting and the presence of complication of heart failure as documented by these reports. The importance of early diagnosis cannot be overemphasized for early initiation of treatment to reduce mortality. Doctors practicing in these countries should consider this diagnosis in young infants very ill with pneumonia and severe hypoxia, whether they are known to have HIV infection or not. PJP is common in HIV positive children but can also occur in HIV negative children as shown by these case reports.

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