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CASE REPORT

Recurrent invasive pneumococcal disease in a child living with HIV

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Abstract

Invasive pneumococcal disease remains an important cause of morbidity and mortality in children living with HIV (CLWHIV). Antiretroviral therapy (ART) and pneumococcal vaccination are important strategies to minimize risk. However, uncertainties remain around optimal vaccination policies in CLWHIV. We describe a case of a severely immunocompromised 10-year-old CLWHIV with recurrent invasive pneumococcal disease.

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Introduction

Children living with HIV have increased risk of invasive pneumococcal disease (IPD) such as bacteraemia, meningitis and bacteraemic pneumonia. Treatment with ART and vaccination with a pneumococcal conjugate vaccine (PCV) partially ameliorate this risk and community access to these interventions have significantly altered the epidemiology of IPD in CLWHIV.

Case Presentation

In December 2022 a 10-year-old girl presented to our hospital with a 1-week history of left-sided back, hip and leg pain. Her past medical history was significant for a late diagnosis of HIV, with commencement of ART (Abacavir, Lamivudine and Dolutegravir) in June 2022 (CD4 count of 5 cells/mL at initiation). On clinical examination she was apyrexial with tenderness over the left buttock and thigh.

Bone-scan confirmed left sacroiliitis and an iliopsoas abscess. Ultrasound guided percutaneous drainage yielded 120ml of pus. She was empirically commenced on oral amoxicillin-clavulanate. After 2 days a TB psoas abscess was suspected, empiric anti-TB therapy was commenced and amoxicillin-clavulanate was discontinued. Chest X-ray was normal, tuberculin skin test was negative, and induced sputa were negative for *Mycobacterium tuberculosis* complex on XPert MTB/RIF Ultra and TB culture. Gram-stain of the pus showed neutrophils and gram-positive cocci, *Streptococcus pneumoniae* (sensitive to penicillin and rifampicin) was subsequently cultured. This isolate was resistant to trimethoprim-sulfamethoxazole, erythromycin and clindamycin. The patient's pain improved, and she was discharged home after 5 days on anti-TB therapy, which was inadvertently stopped after 2 weeks. ART was continued, with progressive improvement at follow-up.

In May 2023, the child arrived at a routine follow-up visit acutely unwell. She had a 4-day history of fever, cough, and shortness of breath. On examination she was pyrexial (38.4^0C) tachypnoeic, hypoxic and jaundiced. She had poor air entry, bronchial breathing and dullness to percussion over the left hemithorax. Chest radiograph showed a multilobar pneumonia with white out of the left lung. Ultrasound showed a small effusion, and a pigtail drain was inserted – but did not drain any fluid. Significant blood test results included an elevated C-reactive protein (424 mg/L), a conjugated hyperbilirubinaemia, and a positive blood culture with *S. pneumoniae* susceptible to penicillin, erythromycin, clindamycin, trimethoprim-sulfamethoxazole and rifampicin. Urine lipoarabinomannan (LAM) was negative. Ultrasound of the abdomen excluded re-accumulation of the psoas abscess. Empiric intravenous amoxicillin-clavulanate was commenced, with de-escalatation to intravenous ampicillin once penicillin susceptibility was confirmed. She received 10 days of antibiotics and was discharged home well.

Serotyping of the two *S. pneumoniae* isolates revealed that the initial isolate was serotype 9N (present in the pneumococcal polysaccharide vaccine PPV23), and the second was serotype 13, not present in any pneumococcal vaccine currently available. Vaccine responses to *S. pneumoniae* were also done; IgG: 1.95mg/L (protective levels >35 mg/L), however her vaccination history could not be confirmed.

Discussion

This case demonstrates an atypical manifestation of IPD and recurrence 4 months later at a different site with a different *S. pneumoniae* serotype. It also raises the question of whether specific guidelines for vaccination of CLWHIV should be developed.

Invasive pneumococcal disease causes significant morbidity and mortality in people living with HIV (PLWHIV). In a study from South Africa, the relative risk of IPD amongst those 5 years and older was 43 times greater in PLWHIV compared to HIV-uninfected individuals[1]. Not receiving ART, having an unsuppressed viral load, and a lower CD4 count were all associated with increased risk of IPD in a national cohort of adults living with HIV in England between 1999 – 2017. [2] These findings are consistent with data from South African CLWHIV that showed a marked decline in incidence of IPD temporally associated with increasing ART coverage, prior to the introduction of pneumococcal vaccination[3]. In that study however, despite an estimated 74% of eligible children having been initiated on ART between 2007 – 2008, the incidence of IPD remained 42 fold higher in CLWHIV compared to those uninfected[3]. PLWHIV are also at greater risk of recurrent IPD. In the cohort study from England 6% of the 1453 PLWHIV who developed IPD had multiple episodes during the study period[2]. In an early study from Baltimore on recurrent pneumococcal disease, the recurrence rate was 6.4 times greater in PLWHIV compared to HIV-uninfected individuals, with reinfection (with a different serotype) being more common than relapse (recurrent infection with the same serotype)[4]. The patient described in this case study had both a low CD4 count and was not on ART, identified risk factors for IPD, and her recurrent disease was a reinfection rather than a relapse.

Our patient's presentation with a *S. pneumoniae* psoas abscess is uncommon. Psoas abscesses are classified as primary, resulting from haematogenous or lymphatic seeding of the causative organism, or secondary from direct extension of an adjacent infectious process (e.g. appendicitis, Crohn's disease)[5]. *Staphylococcus aureus* is the organism most commonly isolated from primary psoas abscesses, and in countries with high burden of

Tuberculosis, *M. tuberculosis* psoas abscess is a recognised complication of TB spine[5]. In a literature review of 14 published cases of pneumococcal psoas abscess, trauma was a possible preceding factor in 4/14 cases, and 2/14 had a preceding respiratory tract infection[6]. Our patient had no history of preceding trauma or respiratory tract infection, but did have advanced HIV, an identified risk factor for psoas abscess caused by *M. tuberculosis* and *S. aureus*[5]. Treatment options include open surgical drainage or image guided percutaneous drainage, in conjunction with appropriate antimicrobial agents. Duration of antimicrobial therapy is determined on a case by case basis, but most bacterial cases reported in the literature have had prolonged courses of up to 6 weeks of therapy[6]. Our patient received 2 days of amoxicillin-clavulanate, however the organism was also susceptible to rifampicin and the empiric anti-TB therapy of which rifampicin was a component, and source control measures may have been sufficient to prevent relapse in this severely immunocompromised child.

In addition to ART, vaccination against IPD is critical for reducing the burden in PLWHIV. Two types of pneumococcal vaccines exist, the 23-valent polysaccharide pneumococcal vaccine (PPV23) which is poorly immunogenic in young children, and 10 or 13 valent conjugate pneumococcal vaccines (PCV). Immune dysregulation associated with HIV infection attenuates vaccine responses. CLWHIV have lower vaccine induced antibody geometric mean titres, as well as reduced antibody functionality measured by opsonophagocytosis assays, particularly in the absence of ART and presence of detectable HIV viral loads[7]. Data also suggest a greater and more rapid decline in vaccine-induced antibody levels in CLWHIV in comparison to HIV-uninfected children[8]. One study of a 9-valent pneumococcal conjugate vaccine reported a reduction of vaccine efficacy from 65% at 2 years to 38.8% at 6 years post enrolment in CLWHIV, compared to a decline from 83% to 77.8% in HIV-uninfected children[9]. Furthermore, vaccine-induced immunity prior to ART may not be restored by ART because immune reconstitution in children is thought to be secondary to the generation of naïve T cells and not expansion of memory T cells[10].

Vaccine response and duration of seroprotection are both positively enhanced with early ART initiation prior to vaccination[8]. In a systematic review of immunogenicity of pneumococcal vaccines in adults living with HIV, optimal immunogenicity was attained when vaccination was delayed until immune reconstitution with a CD4 count ≥200 [11]. South African vaccination guidelines make no provision for delay in immunisations in children with newly diagnosed HIV not yet on treatment. The guideline for the vaccination of HIV-infected adolescents and adults in South Africa recommends a prime-boost strategy for pneumococcal vaccination, a dose of PCV followed 8 weeks later by PPV23, ideally when the HIV viral load is <1000 copies/ml[12]. However, the guideline does not clarify if this includes perinatally infected adolescents living with HIV who may have been vaccinated as infants, and if so, at what age this booster dose should be given. It is unknown whether our patient received any pneumococcal vaccines as part of the routine childhood vaccination program, but if she had, it would have been PCV13 given prior to her initiating ART at 6 weeks, 14 weeks and 9 months of age. As a 10-year-old CLWHIV, it is also likely that vaccine induced protection would have waned substantially. Her very low vaccine response to *S. pneumoniae* highlights ongoing vulnerability to recurrent pneumococcal disease, and she would likely gain maximal efficacy from pneumococcal vaccination if administered after immune reconstitution and viral suppression. However, current guidelines do not address when or how such a patient should be vaccinated against future pneumococcal disease.

The role of primary chemoprophylaxis for the prevention of IPD in CLWHIV is limited with vaccination being prioritised. However, secondary prophylaxis may be indicated in CLWHIV who have had >2 serious bacterial infections in a 1-year period despite effective ART, or in those unable to take ART. Criteria for discontinuing chemoprophylaxis includes sustained immune reconstitution.

Conclusion

This case report highlights the ongoing morbidity associated with IPD in CLWHIV as well as a gap in the national vaccination guidelines that should be addressed.

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