Pneumococcal vaccine and HIV infection: report of a vaccine failure and reappraisal of its value in clinical practice

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Abstract

A clinical failure of pneumococcal vaccine is reported. A 22 year old African woman was given 23-valent pneumococcal vaccine at her initial presentation with HIV infection. She was asymptomatic and had a CD4 + lymphocyte count above 500 cells/mm³. Eighteen months later she died of meningitis and septicaemia due to *Streptococcus pneumoniae* type 9 (an antigen included in the 23-valent vaccine). Pneumococcal antibody levels performed on stored blood demonstrated no serological response to the vaccine. This is the first reported case of clinical failure of pneumococcal vaccine in an HIV infected patient who received vaccine whilst at the asymptomatic stage of HIV infection and with relatively intact immune function. The literature pertaining to pneumococcal vaccination in the context of HIV infection was reviewed. Pneumococcal vaccination is recommended for HIV positive patients in the UK by the Departments of Health. It is likely that many physicians are not aware of these recommendations or are concerned about the poor efficacy of the vaccine, and it may consequently be underused in clinical practice. But the potential gain to the HIV positive patient is such that the vaccine should be offered to all HIV positive patients as soon as they present for medical care, irrespective of the stage of HIV disease. Physicians and patients should be aware that the vaccine is not fully protective and that episodes of sepsis, pneumonia and meningitis could still be pneumococcal in origin and should be treated appropriately. Awareness of the substantial risks of pneumococcal disease in HIV infected patients with prompt diagnosis and effective treatment is the most important strategy to decrease morbidity and mortality.

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Introduction

The incidence of pneumococcal disease in HIV infected patients has been calculated at up to 30 times that of the general population and is particularly high in HIV positive drug users, African and AIDS patients.¹⁻⁵ The most common presentation is with pneumococcal community acquired pneumonia which is

more likely to be bacteraemic, recurrent and fatal in HIV infected patients.³⁻⁷

The UK Departments of Health recommend that "pneumococcal vaccine should be considered for all those aged over two years... with immunodeficiency... including HIV infection at all stages".⁸ From US data, immunisation has been under-utilised in clinical practice, perhaps because of the literature emphasis on lack of serological response to vaccine.^{5 9-12} The extent of use of pneumococcal vaccine in the context of HIV infection in the UK is not known.

The prevention of pneumococcal disease is now even more vital with the world wide spread of penicillin resistant pneumococci.^{4 13-15} We report a clinical failure of pneumococcal vaccine in a patient who received pneumococcal vaccination when at an early stage of HIV infection.

Case report

A 22 year old African woman was diagnosed HIV positive at a genitourinary medicine clinic. She had in the past had a left salpingo-oophorectomy and appendicectomy in Africa and gave a history of blood transfusion 10 years previously. On her initial visit she was found to have positive syphilis serology (VDRL -, TPHA +, FTA +) and was given a course of procaine penicillin injections. She was also given 23-valent pneumococcal vaccine 0.5 ml intramuscularly.

At follow-up visits she remained well although was admitted on one occasion with malaria following a visit to Africa. Her CD4 + lymphocyte count was persistently above 500 cells/mm³ and she was not receiving any prophylaxis.

Eighteen months after her initial HIV diagnosis and pneumococcal vaccination she attended for routine repeat syphilis serology. She was asymptomatic and had a normal neurological assessment. That same night she felt unwell and was admitted to hospital 60 hours later, moribund and with a fever of 40°C. She died shortly after admission. *Streptococcus pneumoniae* type 9 (an antigen included in the 23-valent vaccine) was subsequently grown from her CSF and blood. Pneumococcal antibody levels were assayed on stored sera. The pre vaccination antibody level was 15 units/ml and this fell to 9 units/ml 10 months after vaccination. The normal level in unimmunised adults is above 20 units/ml and at least a two fold rise in levels would be expected after vaccination (Helen Griffiths, personal communication).¹⁶

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Discussion

This is at least the sixth reported case of pneumococcal vaccine failure in a patient with HIV infection and without other risk factors, and is the second reported case from the UK. Of the previous five cases, full details are not available on two,^{17,18} two patients had AIDS or ARC^{6,19} and the UK patient was vaccinated when he was already antigenaemic and his CD4+ lymphocyte count was below 200 cells/mm³.²⁰ This is the first reported case of clinical failure in a patient who received vaccine with relatively intact immune function (CD4+ lymphocyte count above 500 cells/mm³) and who was at the "asymptomatic" stage of HIV infection.

The pneumococcal serotypes causing disease in HIV positive patients are the same as in any other group of patients from that geographical area²¹ and 80–100% of bacteraemic isolates from HIV positive patients are included in the 23-valent vaccine.¹⁷ So any clinical failure is most likely to be due to poor response to the vaccine.¹⁷

HIV infected patients often have low baseline antibody titres to many pneumococcal serotypes and impaired antibody responses after immunisation.^{9–12} A poorer antibody response has been correlated with declining T-cell function and more advanced clinical disease.²² But despite lower levels of antibody responses, many HIV positive patients are able to mount adequate titres to one or more type-specific antibodies.²³ There is no clear correlation between antibody levels and clinical response to vaccination but assessment of antibody responses to pneumococcal vaccine may be useful. Although the present data show no convincing evidence of efficacy, and the extent of vaccine use in the UK clinical practice is not known, it is not ethically possible to conduct a study on clinical efficacy since vaccination is already recommended by the UK Departments of Health.⁶

Although the efficacy of pneumococcal vaccine may be lower in HIV infected patients the potential benefit is great because of the high rate of disease.²¹ The cost-effectiveness of pneumococcal vaccine was elegantly demonstrated by Rose using a hypothetical cohort of 30 year old patients at different stages of infection.²⁴ For a cohort of patients with a CD4+ lymphocyte count of 650 cells/mm³, 17 vaccinations must be administered to prevent one admission for pneumococcal infection and 94 to prevent one death. For a cohort with less than 350 CD4+ lymphocyte cells/mm³, between 18 and 368 vaccinations must be administered to prevent one hospitalisation and 104 to 1,842 to prevent one death. The authors concluded that even under the worst case assumptions the vaccination saves money over the lifetime of the cohort because relatively few vaccinations must be given to prevent a hospitalisation or death.

One caveat in the use of pneumococcal vaccine is that physicians and patients should be aware that pneumococcal vaccination is not fully protective and that any episodes of sepsis, pneumonia or meningitis could still be pneumococcal in origin and should be treated appropriately. Awareness of the substantial

risks of pneumococcal disease in HIV infected patients with prompt diagnosis and effective treatment is the most important strategy to decrease mortality.²⁵ Additionally, pneumococcal vaccine should be offered to all HIV positive patients as soon as they present for medical care, irrespective of the stage of HIV disease.

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