Immunogenicity of pneumococcal vaccination in a patient with sickle hemoglobinopathy: a case report

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Introduction

*Streptococcus pneumoniae* is a common infectious agent, which carries an increased morbidity and mortality risk due to invasive pneumococcal disease (IPD) in the sickle cell population compared to pediatric and adult populations with normal immunity [1]. The pneumococcus and other encapsulated organisms increase mortality risk secondary to functional asplenia, occurring as early as 2 months of age in patients with sickle hemoglobinopathies, with the most severe defect being in those with SS [22].

Public health initiatives have greatly impacted the sickle cell population in the fight against pneumococcal disease over the past three decades: the 1984 initiative for 23-valent pneumococcal polysaccharide vaccination to be given to children with sickle cell anemia ages 2 years and older [2]; the 1986 publication of prophylactic penicillin trial demonstrating reduction in IPD with penicillin prophylaxis [3–5]; recommendations for newborn screening for sickle cell disease; and more recently the development of the 7-valent pneumococcal conjugate vaccine (PCV-7) and 13-valent pneumococcal conjugate vaccines (PCV-13) recommended for children aged 2 months and older [6–8]. Adults with sickle cell disease constitute a small subset of adults with increased risk of IPD. It is not clear if the guidelines concerning pneumococcal vaccines for adults are the most appropriate for this subset. In the midst of promising advances in the control of IPD, there may exist a cohort in whom there is weak efficacy of vaccination.

Presentation of Case

We present the case of a 22-year-old African-American male with hemoglobin SD disease with gram-positive meningitis, sepsis, pneumonia and vaso-occlusive pain crisis after experiencing a headache and fever for 1 week. Lumbar puncture gram stain demonstrated gram-positive...
coccii in pairs and was treated with meningitic doses of ceftriaxone, vancomycin, and dexamethasone. Four days after admission, his respiratory status progressively worsened with persistent fever and a leukocytosis of >30,000, which led to additional antimicrobial coverage change to piperacillin/tazobactam and meropenem. His CSF cultures from the local hospital grew *S. pneumoniae* sensitive to vancomycin, ceftriaxone, and penicillin. Four of four blood cultures also from the admitting hospital grew *S. pneumoniae* sensitive to ceftriaxone, moxifloxacin, penicillin, and vancomycin. Follow-up blood cultures on days 14, 16, and 18 of his illness were negative. The patient was started on prophylactic penicillin at the time of discharge.

His medical history was significant for the diagnosis of sickle cell disease (double heterozygosity for hemoglobins S and D) and asplenia was incidentally noted at eleven years of age. At age 13, he had an episode of multiorgan system failure including severe acute chest syndrome. Additionally, his history included osteomyelitis, avascular necrosis of bilateral femoral heads, and leg ulcers. He had two additional episodes of acute chest syndrome following multiorgan system failure. He was noted to be noncompliant with hydroxyurea. His childhood immunizations were complete. He was last immunized with PPSV23 6 months prior to admission. Prior to this he had received the PPSV23 at ages 7 and 13.

His immunologic evaluation showed elevated IgG (1730 mg/dL) and IgG subclasses, normal IgM and IgA levels. C3 was just below the lower limit of normal (81 and 85 ng/dL with LLN being 88). C4 was normal. IgG responses to diphtheria and tetanus were normal. HIV-1 antigen and antibody and HIV-2 antibody were not found in his serum. His immunoglobulin levels for the pneumococcal strains in PPSV23 are shown in Table 1; the initial levels were drawn on hospital day 7. These levels were found to be lower than expected, with eight of the serotypes having levels well below 1.3 μg/mL, which is considered to be the minimum protective level [21].

### Discussion

Despite having received his most recent PPSV23 vaccination within the year, the patient had inadequate specific IgG levels against eight of the strains in the vaccine despite the lack of evidence from history and laboratory data that he had an immunodeficiency not accounted for by functional asplenia. A limitation to our case presentation was our inability to type the patient’s pneumococcal isolate, and therefore do not know if his infection was due to serotype in the vaccine. The efficacy of the vaccine cannot be determined, as the serotype of the causative organism remains unknown. Yet, 2 months after his hospitalization for IPD he received his fourth PPSV23 booster produced normal protective levels at 2 and 8 months subsequently.

As this case illustrates uncertainty about the effectiveness of PPSV23 in adults in general and those with sickle cell disease in particular. Antibody concentrations, after administration of PPSV-23, appear to decline within 3–7 years back to prevaccination levels in elderly patients [14]. Postvaccination pneumococcal sepsis occurred in a significant fraction of splenectomized adults who had received PPSV23 [22]. Our patient received only PPSC2 vaccines as part of his immunization regimen. Under the newest guidelines, all adults should receive PCV-13 in addition to PPSV23 [12–13]. Administration of the conjugate vaccine in our patient may have provided enhanced immunity and a longer duration of protection.

There is reason to be optimistic about the rate of invasive pneumococcal infections in the sickle cell population with the data from recent studies showing significant reductions in total IPD in the pediatric population of sickle cell patients [9–10]. These studies reflect the effect of the first pneumococcal conjugate vaccine.

| Table 1. Patient’s pneumococcal antibody levels during and posthospitalizations. |
|----------------------------------|---------------|---------------|---------------|
| Pneumococcal serotype | Hospital day 7 | 4 months posthospitalization | 10 months posthospitalization |
| SEROTYPE 1 | 4.1 | 6.2 | 12.1 |
| SEROTYPE 2 | 0.6 | 2.1 | 6.0 |
| SEROTYPE 3 | 0.2 | 1.4 | 3.6 |
| SEROTYPE 4 | 2.2 | 4.6 | 4.8 |
| SEROTYPE 5 | 4 | 6.5 | 14.1 |
| SEROTYPE 8 | 2.4 | 6.6 | 13.1 |
| SEROTYPE 9N | 1.1 | 3.9 | 17.0 |
| SEROTYPE 12F | 1 | 1.8 | 1.7 |
| SEROTYPE 14 | 3.6 | 6.6 | 9.0 |
| SEROTYPE 17F | 6.7 | 19.0 | 31.6 |
| SEROTYPE 19F | 4.2 | 8.0 | 8.7 |
| SEROTYPE 20 | 0.6 | 3.6 | 5.1 |
| SEROTYPE 22F | 6 | 31.0 | 62.4 |
| SEROTYPE 23F | 5.8 | 34.6 | 83.6 |
| SEROTYPE 6B | 2 | 7.9 | 29.4 |
| SEROTYPE 10A | 2 | 12.2 | 24.7 |
| SEROTYPE 11A | 1.2 | 4.0 | 4.2 |
| SEROTYPE 7F | 3.6 | 17.2 | 30.9 |
| SEROTYPE 15B | 2.6 | 3.7 | 3.2 |
| SEROTYPE 18C | 0.2 | 0.6 | 1.6 |
| SEROTYPE 19A | 3.4 | 7.7 | 22.8 |
| SEROTYPE 9V | 2.7 | 14.5 | 27.1 |
| SEROTYPE 33F | 0.7 | 1.8 | 2.2 |

The patient was immunized with PPSV23 15 years, 9 years and again 7 months prior to the hospitalization, and 2 months posthospitalization. In bold are the levels that are considered to be below the protective level.
(PCV7), showing the epidemiologic results of its use [17–18]. These studies do not report on the antibody responses of the vaccinated cohort. There are no similar population-based studies on the effectiveness of PPSV23 on the adult population with sickle cell disease, nor are there large studies on the presence of antipneumococcal antibodies and response to the vaccine in this group making the evaluation of our patient’s serology difficult [15–16, 19–20].

Currently there are no population-based studies with invasive pneumococcal disease as a primary outcome of vaccinated adults in the sickle cell population. Such a trial would be very difficult to do in the United States, and might have to be done in a country where the sickle cell population is larger. The interval for booster doses of PPSV 23 in the sickle cell adult population remains an estimate.

Conclusion

This case reminds us that a high level of vigilance for the possibility of IPD is needed in the case of patients with sickle cell anemia with functional asplenia, even if they have been previously immunized with pneumococcal vaccines. Documentation of their immune response to the vaccine should be obtained and reimmunization completed if they have fallen below protective levels, specifically in patients who have had an episode of IPD. Prophylactic penicillin should also be considered. For adults with sickle cell disease who have not experienced IPD, the guidelines from Advisory Committee on Immunization Practices should be followed but with the awareness that the schedule may be inadequate for some individuals with sickle cell disease. This is especially true now that the recommendations only require two vaccinations of PPSV23 as an adult as opposed to the former recommendation of revaccination every 5 years.

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Conflict of Interest

The authors have no competing interests.

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