Clinical Case Reports

Open Access

CASE REPORT

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

E. Leila Jerome Clay[1], Tierra Burrell[2], Thomas Belhorn[3] & Rupa Redding-Lallinger[4]

[1]Division of Hematology and Oncology, Departments of Pediatrics and Internal Medicine, Georgia Regents University, Augusta, Georgia, USA
[2]Department of Pediatrics, University of Cincinnati, Cincinnati, Ohio, USA
[3]Division of Infectious Disease, Department of Pediatrics, University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA
[4]Division of Hematology and Oncology, Departments of Pediatrics and Internal Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA

Correspondence
E. Leila Jerome Clay, Division of Hematology and Oncology, Departments of Pediatrics and Internal Medicine, Georgia Regents University, 1120 15th Street, BG 2011, Augusta, GA 30912, USA.
Tel: +(706) 723 0014; Fax: +(706) 721 2643;
E-mail: leila.clay@gru.edu

Funding Information
This manuscript was prepared during the corresponding author's training and was supported by the T32 NIH/NHLBI grant PHS GRANT 5T32 HL 7149–35.

Received: 16 May 2014; Revised: 18 October 2014; Accepted: 4 December 2014

***Clinical Case Reports* 2015; 3(7): 618–621**

doi: 10.1002/ccr3.276

Key Clinical Message

Despite decrease in morbidity and mortality from invasive pneumococcal disease (IPD), individuals with asplenia remain at risk for IPD compared to the general population. This report describes a young adult with hemoglobin SD and documented splenic autoinfarction with pneumococcal sepsis, meningitis, and pneumonia within seven months of immunization with PPSV-23.

Keywords

Invasive pneumococcal disease, PPSV-23, sickle cell disease, *Streptococcal Pneumonia*.

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

cocci 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 immunoglobin 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].

Table 1. Patient's pneumococcoal 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.

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 PPSC23 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

(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.

Acknowledgments

The authors thank the Department of Internal Medicine and Pediatrics of the University of North Carolina Chapel Hill Hospitals for their contribution to this study.

Conflict of Interest

The authors have no competing interests.

References

1. Poehling, K. A., L. S. Light, M. Rhodes, B. M. Snively, N. B. Halassa, E. Mitchel, et al. 2010. Sickle cell trait, hemoglobin C trait, and invasive pneumococcal disease. Epidemiology 21:340–346.
2. CDC. 1984. Pneumococcal polysaccharide vaccine usage United States. Morb. Mortal. Wkly. Rep. 33:273–6281.
3. O'Brien, K. L., A. J. Swift, J. A. Winklestein, M. Santosham, B. Stover, R. Luddy, et al. 2000. Safety and immunogenicity of heptavalent pneumococcal vaccine conjugated to CRM197 among infants with sickle cell disease. Pediatrics 106:965–972.
4. Narang, S., I. D. Fernandez, N. Chin, N. Lemer, and G. A. Weinberg. 2012. Bacteremia in children with sickle hemoglobinopathies. Journal of Pediatric Hematology/oncology 34:13–16.
5. Gaston, M. H., J. I. Verter, G. Woods, C. Pegelow, J. Kelleher, G. Presbury, et al. 1986. Prophylaxis with oral penicillin in children with sickle cell anemia: a randomized trial. New England Journal of Medicine 314:1593–1599.
6. Hord, J., R. Byrd, L. Stowe, B. Windsor, and K. Smith-Whitley. 2002. *Streptococcus pneumoniae* sepsis and meningitis during the penicillin prophylaxis era in children with sickle cell disease. Journal of Pediatric Hematology/oncology 24:470–472.
7. Reinert, P., M. Benkerrou, M. de Montalembert, E. Lesprit, I. Abadie, F. Bernaudin, et al. 2007. Immunogenicity and safety of a pneumococcal conjugate 7-valent vaccine in infants with sickle cell disease. The Pediatric Infectious Disease Journal 26:1105–1109.
8. Centers for Disease Control and Prevention. 2010. Prevention of pneumococcal disease among infants and children—use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morb. Mortal. Wkly. Rep. 59:1–18.
9. Halasa, N. B., S. M. Shankar, T. R. Talbot, P. G. Arbogast, E. F. Mitchel, W. C. Wand, et al. 2007. Incidence of invasive pneumococcal disease amongindividuals with sickle cell disease before and after the introduction of the pneumococcal conjugate vaccine. Clinical Infectious Diseases 44:1428–1433.
10. McCavit, T. L., L. Xuan, S. Zhand, G. Flores, and C. T. Quinn. 2012. Hospitalization for invasive pneumococcal disease in a national sample of children with sickle cell disease before and after PCV7 licensure. Pediatric Blood & Cancer 58:945–949.
11. Adamkiewicz, T. V., B. J. Silk, J. Howgate, W. Bauughman, G. Strayhorn, K. Sullivan, et al. 2008. Effectiveness of the 7-valent pneumococcal conjugate vaccine in children with sickle cell disease in the first decade of life. Pediatrics 121:562.
12. Centers for Disease Control and Prevention. 2011a. Recommended immunization schedule for persons aged 0 through 6 years—United States. http://www.cdc.gov/vaccines/recs/schedules/downloads/child/0-6yrsschedule-pr.pdf

13. Centers for Disease Control and Prevention. 2011b. Recommended immunization schedule for persons aged 7 through 18 years—United States. http://www.cdc.gov/vaccines/recs/schedules/downloads/child/7-18yrsschedule-bw.pdf
14. Sankilampi, U., P. O. Honkanen, A. Bloigu, and M. Leinonen. 1997. Persistence of antibodies to pneumococcal capsular polysaccharide vaccine in the elderly. Journal of Infectious Diseases 176:1100–1104.
15. Castagnola, E., and F. Fioredda. 2003. Prevention of life-threatening infections due to encapsulated bacteria inchildren with hyposplenia or asplenia: a brief review of current recommendations for practical purposes. European Journal of Haematology 71:319–326.
16. Meerveld-Eggink, A., O. de Weerdt, and H. van Velzen-Blad. 2011. Response to conjugated pneumococcal and Haemophilus influenza type b vaccines in asplenic patients. Vaccine 29:675–680.
17. Breukels, M. A., A. Zandvoort, G. P. van Den Dobbelsteen, A. van Den Dobbelsteen, M. E. Lodewijk, M. Beurret, et al. 2001. Pneumococcal conjugate vaccines overcome splenic dependency of antibody response to pneumococcal polysaccharides. Infection and Immunity 69:7583–7587.
18. Givon-Lavi, N., D. Greenberg, and R. Dagan. 2010. Immunogenicity of alternative regimes of the conjugated 7-valent pneumococcal vaccine: a randomized control trial. The Pediatric Infectious Disease Journal 29:756–762.
19. Manci, E. A., D. E. Culberson, Y. M. Yang, T. M. Gardner, R. Powell, J. Jr Haynes, et al. 2003. Causes of death in sickle cell disease: an autopsy study. British Journal of Haematology 123:359–365.
20. Paris, K., and R. U. Sorenson. 2007. Assessment and clinical interpretation of polysaccharide antibody responses. Annals of Allergy, Asthma & Immunology 99:462–464.
21. Sorenson, R. U., L. E. Leiva, F. C. III Javier, D. M. Sacerdote, N. Bradford, B. Butler, et al. 1998. Influence of age on the response to *Streptococcus pneumoniae* vaccine in patients with recurrent infections and normal immunoglobulin concentrations. The Journal of Allergy and Clinical Immunology 102:215–221.
22. Fosrtner, C., S. Plefka, S. Tobudic, H. M. Winkle, K. Burgmann, and H. Burgmann. 2012. Effectiveness and immunogenicity of pneumococcal vaccination in splenectomized and functional asplenic patients. Vaccine 30:5449–5452.

