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Specific Antibody Immunodeficiency Presenting With *Streptococcal pneumonia*-Induced Spontaneous Bacterial Peritonitis

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Abstract

Specific antibody immunodeficiency (SAD) is a primary immunodeficiency disorder characterized by normal levels of serum immunoglobulins (IgG, IgA, and IgM) associated with a dysfunctional immune response. SAD is associated with recurrent infections in the setting of an insufficient response to polysaccharide vaccinations. *Streptococcus pneumoniae* is a well-established cause of respiratory infections in SAD. However, there has been a paucity of evidence of pneumococcal peritonitis in SAD patients, being reported as spontaneous in acquired immunodeficiency such as AIDS. We report the first case of *S. pneumoniae*-induced peritonitis as the presenting sign for SAD.

Keywords

specific antibody immunodeficiency, primary immunodeficiency disorder, *Streptococcus pneumonia*, spontaneous bacterial peritonitis, immunodeficiency

Case Presentation

A 62-year-old woman presented with intermittent generalized abdominal pain without radiation for 10 days. The pain was aggravated by movement and associated with 2 episodes of nonbloody, nonbilious emesis, and 2 episodes of watery nonbloody diarrhea after which she stopped passing both stool and gas. She denied any constitutional symptoms. There was no personal history of recurrent infections or family history of primary immunodeficiency diseases.

The laboratory evaluation revealed a leukocytosis of 17.0×10^9/L. Her chest radiograph was unremarkable. A computed tomography scan of the abdomen and pelvis with contrast showed diffuse small bowel enhancement and bowel thickening sparing the large bowel, and fluid was also noted in Morison's pouch with small loculated fluid collections within the pelvis. A diagnosis of spontaneous bacterial peritonitis (SBP) was concluded, and the patient was started on ciprofloxacin and metronidazole. Her blood cultures grew Gram-positive cocci in pairs and chains and a *Streptococcus pneumoniae* urine antigen was positive. The patient was switched to ceftriaxone, but a repeat CT scan of the abdomen revealed increased multiloculated fluid collections prompting the placement of 3 image-guided peritoneal drains. The cytology of the collected fluid was exudative in nature, but the fluid was negative for abnormal cells or organism growth. *S. pneumoniae* DNA was detected with 16s rRNA primer set within the peritoneal fluid confirming the diagnosis of *S. pneumoniae*-induced peritonitis.

Due to the presence of *S. pneumoniae* SBP, further evaluation for immunodeficiency was explored. HIV antigen/antibody screen was negative. The serum immunoglobulin studies were within normal limits with IgG 1190 mg/dL, IgM 197 mg/dL, and IgA 197 mg/dL. Her B cell phenotype and IgG subclasses are reported in Table 1. There was no decrease in IgG subclasses 1 to 4. Her B cell phenotype showed a relative decrease in

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Table 1. B Cell Phenotype and IgG Subclasses.

B cell phenotype	
CD19%_Marker	8 (6%–19%)
CD 19 Absolute	0.203 (0.070–0/910 × 10^9/L)
CD19+CD27-IgD+% Naïve B cells; percent of CD19	69.3 (58.0%–72.1%)
CD19+CD27+IgD+% Non-switched memory B cells; percent of CD19	4.8 (13.4%–21.4%)
CD19+CD27+IgD+% switched memory B cells; percent of CD19	18.6 (9.2%–18.9%)
CD19+CD24++CD38++% Transitional B cells; percent of CD19	16.4 (1.0%–3.6%)
CD19+CD24-CD38++% Transitional B cells; percent of CD19	1.7 (0.6%–1.6%)
CD45%	100 (%)
IgG subclass	
IgG subclass 1	981 (490–1140 mg/dL)
IgG subclass 2	516 (150–640 mg/dL)
IgG subclass 3	33 (11–85 mg/dL)
IgG subclass 4	300 (3–200 mg/dL)

non-switched memory B cells and relative increase of transitional B cells and plasmablasts. The impaired antibody response to 23-valent pneumococcal polysaccharide vaccine (PPV23) is shown in Table 2, suggesting the diagnosis of a specific antibody immunodeficiency (SAD). In addition, the patient did not respond to subsequent vaccination with streptococcus pneumoniae conjugate vaccine (PCV13).

Table 2. Pneumococcal Antigen Response to PPV23.

Pneumococcal Serotypes	Pretiter (μg/mL) August	Posttiter (μg/mL) September	Posttiter (μg/mL) October
1	0.1	4.3	3
2	0.3	0.2	0.3
3	1.9	1.8	1.4
4	0.1	2.0	1.4
5	0.1	0.6	0.9
8	0.4	1.0	1.0
9N	0.4	0.9	0.8
12F	0.4	0.2	0.2
14	0.2	15.4	13.7
17F	2.5	4.4	4.3
19F	3.1	7.2	5.4
20	1.6	4.2	3.4
22F	0.4	0.8	0.7
23F	0.2	6.8	5.3
6B(26)	0.3	8.4	8.1
10A(34)	0.1	0.2	0.3
11A(43)	0.1	0.2	0.2
7F(51)	0.3	7.9	8.0
15B(54)	0.2	0.4	0.3
18C(56)	1.0	10.9	10.9
19A(57)	1.2	10.6	10.6
9V(68)	0.1	1.9	1.8
33F(70)	2.7	4.1	3.5

Discussion

SAD is a primary immunodeficiency disorder (PIDD) that is classified by impaired IgG responses to polysaccharide vaccines despite having normal serum immunoglobulins (IgG, IgA, and IgM). The prevalence of SAD is unknown.[1] The diagnosis of SAD is usually made with a demonstration of impaired responses to pneumococcal polysaccharide vaccines in the presence of normal serum immunoglobulin levels. However, there are no standardized guidelines when interpreting vaccination responses in SAD. Most agree that an impaired pneumococcal polysaccharide vaccination response is defined as postvaccination titers that fail to reach a threshold of >1.3 μg/mL or postvaccination titers that do not increase 2-fold from baseline in >50% to 70% serotypes.[1–3] Using the aforementioned definition, SAD is classified as mild, moderate, or severe based on vaccination response.[1] A moderate phenotype is designated as having a response to <70% serotypes.[1] Our patient responded to 12 of 23 titers in the presence of normal serum immunoglobulins (including IgG subtypes) and was classified with a moderate form of SAD (Table 2).

Due to a lack of antibody response, patients with SAD can present with recurrent respiratory or severe infections to encapsulated organisms like *S. pneumoniae*.[1] It is important to note the clinical manifestations can vary as in the case highlighted above, however. *Streptococcus pneumoniae* (pneumococcus) is a Gram-positive encapsulated organism that colonizes the nasopharynx after spread through respiratory droplets. Colonization can subsequently lead to infection in susceptible hosts, particularly the young, elderly, and immunocompromised.[4,5] *S. pneumoniae* is the most common agent of community acquired pneumonia, otitis media, and meningitis.[4] Other infections by *S. pneumoniae* can occur by hematogenous spread including SBP in cirrhotic patients.[6]

In addition to cirrhotics, there is evidence of pneumococcal SBP within the immunocompromised patient. A case report showed the presence of a 28-year-old Kenyan

woman who was diagnosed with *S. pneumoniae* peritonitis as the presenting sign of an undiagnosed HIV infection.[7] However, there has not been documented literature of *S. pneumoniae* peritonitis occurring in primary immunodeficiency diseases.

Despite the rare incidence of PIDD, *S. pneumoniae*-induced SBP should always prompt a further investigation for underlying immunocompromised state. In the aforementioned case, a 62-year-old woman presented with complaints of generalized abdominal pain secondary to *S. pneumoniae* SBP in the absence of respiratory symptoms.

A failed response to *S. pneumoniae* vaccination revealed an underlying immunodeficiency disease (Table 2). Mainstay treatment for SAD is prophylactic antibiotics. Although there is some evidence that subsequent vaccination with streptococcus pneumoniae conjugate vaccine (PCV13) may provide therapeutic benefit, the aforementioned patient did not show a response.[1] *S. pneumonia* peritonitis in PIDD may have been encountered previously, we present the first documented case of a patient presenting with *S. pneumoniae*-induced SBP revealing an underlying SAD.

Conclusion

SAD is a PIDD that is characterized by normal serum immunoglobulin levels despite having recurrent infections. SAD is characterized by diminished IgG responses to polysaccharide vaccines, despite a normal level of serum immunoglobulins (IgG, IgA, and IgM). *Streptococcus pneumoniae* is a common agent of respiratory infections; however, there is lack of literature regarding *S. pneumoniae* SBP in primary immunodeficiencies. We report the first case of *S. pneumoniae*-induced peritonitis as the presenting sign for SAD.

Ethical Approval

This study was approved by our institutional review board.

Declaration of Conflicting Interests

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Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

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