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Asplenic patients and invasive pneumococcal disease—how bad is it these days?

Thomas J. Marrie [a], Gregory J. Tyrrell [b], Sumit R. Majumdar [c], Dean T. Eurich [d,*]

[a] Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada
[b] Division of Diagnostic and Applied Microbiology, Department of Laboratory Medicine and Pathology, University of Alberta, and The Provincial Laboratory for Public Health, Edmonton, Alberta, Canada
[c] Department of Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada
[d] School of Public Health, University of Alberta, 2-040 Li Ka Shing HRIF, Edmonton, Alberta, T6G 2E1, Canada

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SUMMARY

Objectives: Most are aware of pneumococcal infection as a complication of splenectomy and the increased risk of severe invasive pneumococcal disease (IPD) in asplenic patients. However little is known of the current status of this entity in a population with an active pneumococcal conjugate vaccine program for children.
Methods: All IPD cases reported from 2000 to 2014 in Northern Alberta, Canada were collected prospectively. Socio-demographic variables, clinical characteristics, and IPD-related outcomes were compared between patients with and without a spleen using the Student *t*-test, Chi-square test, or Fisher's exact test, as appropriate.
Results: Thirty-seven of 2435 patients with IPD (1.5%) were asplenic. Asplenic patients were significantly more likely to require mechanical ventilation or admission to the intensive care unit and had more complications (e.g., acute kidney injury). However, in-hospital mortality rates were similar in those with and without a spleen (19% vs. 16%, $p = 0.58$). Pneumococcal serotype 22B was 33-fold higher in asplenic patients compared to those with a spleen.
Conclusions: In patients with IPD, those who are asplenic have a more severe infection than those with a spleen; however, the mortality rate is not significantly different. The reason for the predominance of serotype 22B requires further investigation and if replicated may warrant attention to current vaccination strategies.

1. Introduction

Splenic macrophages remove poorly opsonized bacteria (those that are encapsulated, like *Streptococcus pneumoniae*) from the blood stream very efficiently.[1] In addition, the spleen is the major site of synthesis of immunoglobulin M and opsonins such as tuftsin and properidin.[1] It is no surprise then that overwhelming pneumococcal sepsis can occur in splenectomized patients.[2,3] While encapsulated microorganisms other than *S. pneumoniae* can cause bacteremia in splenectomized persons, in a study of 52 asplenic patients with sepsis compared with 52 septic patients with their spleens, *S. pneumoniae* was more frequently detected amongst the asplenic group (42% vs. 12%), whilst the rate of Gram-negative sepsis was similar in the two groups.[4]

There is very little current information on the extent and nature of the problem of pneumococcal sepsis in the asplenic patient, and splenectomy itself is not uncommon. In Alberta, Canada, approximately 150 splenectomies are performed each year (Li Huang, Alberta Health Services, personal communication). Conjugated pneumococcal vaccines have been used in Alberta since the early 2000s. The 7-valent pneumococcal conjugate vaccine (PCV7) was introduced for children in Alberta in 2002 and the 13-valent pneumococcal vaccine (PCV13) in 2010. There is a standardized clinical policy that all patients receive pneumococcal, meningococcal, and *Haemophilus influenzae* vaccines either prior to splenectomy, if possible, or prior to hospital discharge post splenectomy.

* Corresponding author. Tel.: +1-780-492-6333; fax: +1-780-492-7455.
E-mail address: deurich@ualberta.ca (D.T. Eurich).

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Thus, it was sought to determine the effect of asplenia on the manifestations and outcomes of invasive pneumococcal disease (IPD). This study formed part of a prospective 15-year study of IPD in Northern Alberta, Canada.

2. Methods

2.1. Definitions

Cases of IPD were defined as per the Alberta Health Public Health Notifiable Disease Management Guidelines (http://www.health.alberta.ca/documents/ Guidelines-Pneumococcal-Disease-Invasive-IPD-2011).[5] Pneumococcal isolates from cases of invasive disease were collected from normally sterile sites defined as blood, cerebrospinal fluid, pleural fluid, peritoneal fluid, pericardial fluid, bone, joint or specimens taken during surgery. As per the aforementioned guidelines, all IPD isolates were submitted to the Provincial Laboratory for Public Health (PLPH) located in Edmonton, Alberta for capsular serotyping.

2.2. Clinical data collection

Cases of IPD were identified through an isolate database housed at the PLPH. An IPD case list was generated. Research nurses retrospectively collected clinical data for each case using this list. Socio-demographic, clinical, functional, and laboratory data were collected using a standardized case report form (CRF). From 2000 to 2014, data were collected on all patients in Northern Alberta with IPD (approximate population 2 060 039). The research nurses received training on data collection prior to the start of the study. In addition to the CRF, standard operating procedures documents, definitions, drug classification, and underlying illness categorization were part of their working documents. With respect to underlying illnesses, if the attending physician recorded such an illness it was accepted as such for the purpose of the study. Acute kidney failure was specifically defined as an absolute increase in serum creatinine of 100 mmol/l over the baseline creatinine, or any requirement for dialysis. This study received approval from the institutional research review committees of all Northern Alberta health regions, as well as the University of Alberta ethics review board.

2.3. Identification and serotyping of S. pneumoniae isolates

S. pneumoniae isolates were received at the PLPH from acute diagnostic laboratories in Alberta, as per the requirements of the provincial notifiable disease guidelines. *S. pneumoniae* isolates were confirmed as *S. pneumoniae* based on characteristic morphology and optochin susceptibility prior to serotyping.[6] All pneumococcal isolates that exhibited a positive Quellung reaction using commercial type-specific antisera obtained from Statens Serum Institute, Copenhagen, Denmark were assigned a serotype designation.[7]

2.4. Exposures and outcomes

The independent variable of interest was asplenia; it was specifically asked whether the patient had undergone a splenectomy, and patients were categorized into those with or without a spleen based on these data. Patients who had a spleen were classified into the spleen group regardless of spleen function. The primary outcomes of interest were the occurrence of major in-hospital complications defined as the presence of cellulitis, osteomyelitis, septic arthritis, meningitis, admission to the intensive care unit (ICU), need for mechanical ventilation, acute kidney injury, and all-cause in-hospital mortality. In addition, serotyping of all isolates was performed and the results were stratified and described according to the presence or absence of a spleen.

2.5. Statistical analysis

The analyses were largely descriptive in nature. Socio-demographic variables, clinical characteristics, and IPD-related outcomes were compared between patients with and without a spleen using the Student *t*-test, Chi-square test, or Fisher's exact test, as appropriate. All analyses were performed with Stata SE, version 12.1 (Stata, College Station, TX, USA).

3. Results

3.1. General description

Thirty-seven (1.5%) of the 2435 patients identified with IPD in the study were asplenic. Table 1 provides a comparison of IPD patients who were asplenic and those who were not. Patients who were identified as asplenic were more likely to be living at home ($p = 0.026$) and to have had a solid tumor cancer within the past 5 years ($p < 0.001$). They were, however, less likely to be aboriginal ($p = 0.011$), have alcoholism ($p = 0.039$), or use illicit drugs ($p = 0.006$), and were less likely to have chronic obstructive pulmonary disease ($p = 0.13$).

3.2. Outcomes according to the presence or absence of a spleen

Table 2 shows the pre-specified outcomes stratified according to the presence or absence of a spleen. Those without a spleen had a more severe infection as measured by markers of supportive treatment intensity, such as the need for mechanical ventilation ($p = 0.008$) and ICU admission ($p = 0.001$). They were also more likely to have complications of pneumococcal bacteremia such as meningitis ($p < 0.001$), as well as complications of severe sepsis such as acute kidney injury ($p < 0.001$) (Table 2). Although the all-cause in-hospital mortality rate of 19% amongst those with no spleen was higher than that of 16% for those who had a spleen, this 3% absolute difference in mortality was not statistically significant ($p = 0.58$). Even in terms of those with the most severe IPD, 19 (51.4%) of the asplenic patients were admitted to the ICU and six (31.6%) died compared to 664 (27.7%) of the patients with a spleen of whom 192 (28.9%) died.

Table 1
Comparison of IPD patients with no spleen and IPD patients with a spleen

	No spleen	Spleen	*p*-Value
Number	37 (1.5%)	2398 (98.5%)	-
Age, years, mean (SD)	58.6 (13.7)	54.2 (17.9)	0.13
Male	18 (49%)	1362 (57%)	0.32
Aboriginal	0 (0%)	312 (13%)	0.011[a]
Living at home	36 (97%)	1924 (81%)	0.026[a]
Homeless	0 (0%)	184 (8%)	
Fully functional	28 (76%)	1727 (72%)	0.62
Current smoker	8 (22%)	1096 (46%)	0.003
Cancer past 5 years	12 (32%)	295 (12%)	<0.001
Hepatitis C	1 (3%)	306 (13%)	0.078
Chronic renal failure	3 (8%)	124 (5%)	0.44
HIV infection	0	117 (5%)	0.25[a]
Systemic lupus erythematosus	1 (3%)	16 (1%)	0.23
COPD	3 (8%)	438 (18%)	0.13
Alcoholism	4 (11%)	616 (26%)	0.039
Illicit drug use	1 (3%)	481 (20%)	0.006

IPD, invasive pneumococcal disease; SD, standard deviation; COPD, chronic obstructive pulmonary disease.
[a] Corrected for zero cell.