P1203

PNEUMOCOCCAL EMPYEMA IN TORONTO, CANADA (1995-2006)

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Abstract (revised)

Background: Several recent studies have documented increases in the rate of pneumococcal empyema (PEMP). We examined trends in the occurrence of PEMP in Toronto, Canada from 1995 to 2006.
Methods: Population based surveillance for invasive pneumococcal disease (IPD) in residents of Toronto and Peel region, Ontario, Canada (pop=3.9M) has been on-going since 1995. In this study, PEMP includes cases with a positive pleural fluid culture, and bacteremic cases with a clinical diagnosis of empyema. Data are collected from patients and their physicians. Antibiotic histories are available for patients from 2000 to 2006.
Results: From 1995 to 2006, 4698 episodes of IPD have been identified: 123 (2.6%) are PEMP. The incidence of empyema increased from an average of 0.22/100,000/y in 1996-2000 to 0.31/100,000/y in 2001-4, while the incidence of all IPD decreased from 12.1 to 9.1/100,000/y averaged over the same period. Patients with PEMP were not significantly different from others with IPD in age (median 56y vs. 50y, P=.14), or proportion that were healthcare acquired, but were somewhat more likely to be male (63% vs 55%, P-/08) and to have underlying lung disease or alcohol abuse (32% vs. 24%, P=.04, 17% vs.. 11%, P=0.04). Population adjusted rates of empyema were significantly greater in those aged >=65 compared to 15-64 and <15, P<0.001).
Isolates from PEMP were more likely to be of serotype (ST) 1 (6/104 PEMP vs. 27/4300 other, P<.001) and were less likely to be stains included in the pneumococcal conjugate vaccine (45/104 vs. 2459/4300, P=.005). They were also more likely to be resistant to TMP/SMX (19/105 vs. 424/4322, p=0.005), macrolides (19/105 vs. 491/4322, p=.03), ciprofloxacin (7/105 vs. 51/4322, p=<0.001), and levofloxacin (5/105 vs. 28/4322, P<.001) but not penicillin (6/105 vs.. 167/4322, P=.33) or moxifloxacin (1/105 vs. 9/4322, p=0.21). Patients with PEMP were more likely to failing out-patient antibiotic therapy when admitted with IPD (15EMP of 127 cases failing antibiotics, vs. 52EMP of 1343 other cases, P=.01). Patients who were failing fluoroquinolone (FQ) outpatient therapy were more likely to have a diagnosis of empyema than other patients (4/26, 15% vs. 65/2275, 3%, P=.008). All 4 EMP patients with FQ resistant isolates were failing FQ: none of these patients died. Similarly, 3/4 EMP patients with erythromycin resistant isolates were failing macrolides (ML); neither of these two patients died,
Conclusion: The incidence of PEMP is increasing. In our population adjusted rates were highest for those over 65. Some serotypes are more likely to cause PEMP than others. The isolates found in empyema were more likely to be resistant to TMP/SMX, macrolides, ciprofloxacin and levofloxacin but not penicillin or moxifloxacin as compared to other invasive pneumococcal disease.

Introduction

Increased use of conjugate and polysaccharide pneumococcal vaccines has been assocaited with substantial reductions in the incidence of invasive pneumococcal disease.

Recently, however, numerous jurisdictins worldwide have reported a paradoxical increase in the incidence of pneumococcal empyema, associated at least in part with the emergence to serotype 1.

The majority of studies have focussed on paediatric empyema. Our objective was to describe the epidemiology of both adult and pediatric pneumococcal empyema in Toronto. Canada.

Methods

Population based surveillance for invasive pneumococcal disease has been ongoing in metropolitan Toronto and Peel region (an urban and suburban population of 3.9M in Ontario, Canada) since January 1, 1995. An adult polysaccharide vaccination program was introduced in this population in October, 1996, and a pediatric conjugate vaccination program in January, 2005.

Demographic and medical data on each case are collected by patient and physician interview and chart review. Isolates are shipped to the central study laboratory where they are confirmed as *S. pneumoniae*. Broth microdilution susceptibility testing is performed to CLSI standards. All isolates are serotyped. Annual audits are performed to ensure complete reporting. Ethical approval is obtained from all hospitals and laboratories.

For this analysis, pneumococcal empyema was defined as a case in which *S. pneumoniae* was isolated from a pleural fluid culture, or gram positive cocci were seen on gram stain in a sample of pleural fluid, and pneumococci were concomitantly isolated from blood cultures. (NOTE: Culture negative pneumococcal empyema is not captured by our surveillance.)

Data for cases from January 1, 1995 to December 31, 2006 are included in the analysis. Statistical comparisons were made using chi-square and Fisher's exact tests with a P value of 0.05 indicating statistical significance.

Results

Table 1 – Demographics

	Non -Empyema N=4698	Empyema N=123	P value
Sex (no. % male)	2574 (55%)	78 (63%)	.08
Age gp			
<15 yrs	1028	10	.001
15 -64	1823	59	
>=65	1944	52	
Institutionally acquired			
Hospital -acquired	205 (4.3%)	8 (6.7%)	.31
Nursing home acquired	307 (6.4%)	5 (4.3%)	.30
Underlying illnesses	(N=4608)	(N=117)	
Lung	1085 (24%)	37 (32%)	.04
Cardiac	916 (20%)	30 (26%)	.13
Cancer	703 (15%)	25 (22%)	.07
Diabetes mellitus	647 (15%)	16 (14%)	.91
Alcohol abuse	491 (11%)	20 (17%)	.04
Kidney disease	234 (5.1%)	2 (1.7%)	.13
HIV infection	208 (4.5%)	5 (4.3%)	.97
No underlying chronic illness	1857/4634 (40%)	37/117 (32%)	.08
Antibiotic exposure			
Received any, last 3 mos	1102/3490 (32%)	22/86 (32%)	.29
Failing AB at presentation	205/223 5 (9.2%)	15/75 (20%)	.004

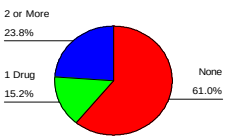
Table 2 – Isolate Details

	Non - Empyema	Empyema	P value
Serotype			
1	27/4300 (0.63)	6/104 (5.8%)	<.001
12F	97/4300 (2.3%)	5/104 (4.8%)	.08
Vaccine type causing infection			
Conjugate vaccine	2459/4300 (57%)	45/104 (43%)	.005
Polysaccharide vaccine	3714/4300 (86%)	83/104 (80%)	.06
Antibiotic resistance	N=4322	N=105	
Penicillin	167 (3.9%)	6 (5.7%)	.30
TMP -SMX	424 (9.8%)	19 (18%)	.005
Erythromycin	491 (11%)	19 (18%)	.03
Ciprofloxacin	51 (1.2%)	7 (6.8%)	<.001
Levofloxacin	28 (0.6 8%)	5 (4.9%)	<.001
Moxifloxacin	9 (0.24%)	1 (1.0%)	.21

Table 3 – Isolate Resistance

		Penicillin		Erythromycin		TMP/SMX		Ciprofloxacin		Levofloxacin	
		Sensitive	Resistant	Sensitive	Resistant	Sensitive	Resistant	Sensitive	Resistant	Sensitive	Resistant
Penicillin	Sensitive			78	11	75	14	79	7	80	6
	Resistant			8	8	2	14	16	.00	16	.00
Erythromycin	Sensitive	78	8			70	16	77	6	78	5
	Resistant	11	8			7	12	18	1	18	1
TMP/SMX	Sensitive	75	2	70	7			69	5	69	5
	Resistant	14	14	16	12			26	2	27	1
Ciprofloxacin	Sensitive	79	16	77	18	69	26			95	.00
	Resistant	7	.00	6	1	5	2			1	6
Levofloxacin	Sensitive	80	16	78	18	69	27	95	1		
	Resistant	6	.00	5	1	5	1	.00	6		

Figure 1 - Isolate Resistance



•Macrolide resistant organisms were more likely to be Penicillin and TMP/SMX Resistant (P <.001)

•All patients failing therapy with a macrolide (2 clari, 1 azi) or a fluoroquinolone (1 cipro, 2 levo, 1 gati) had MICs close to the breakpoint for susceptibility. None of these 7 patients died, compared to 14/68 patients not failing therapy, or failing therapy with susceptible isolates

Results (cont'd)

Figure 2 – Annual incidence (see Legend) of Invasive Pneumococcal Disease and Empyema by Year

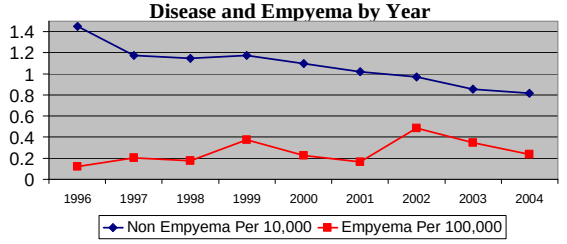


Figure 3 – Annual Incidence of Empyema by Age Group

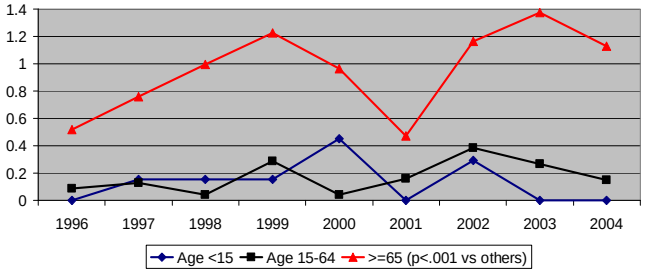
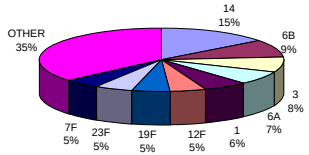


Figure 4 - Isolate Serotypes



Compared with other recent studies of pneumococcal empyema, our isolates were less antibiotic resistant (particularly to penicillin) and while serotype 1 was much more common in empyema than non-empyema IPD, our rates of serotype 1 do not approach the 50% seen in some studies.
PCV7: 4,6B, 9V, 14, 18C, 19F, 23F

Conclusions

In our population

- •Incidence of empyema was highest in patients older than 65, and has been stable or increasing over time despite decreases in IPD
- •Cases were more likely to consume excessive alcohol and have underlying lung disease, and were more likely to be failing outpatient antibiotic therapy
- •Serotype 1 was more common in empyema than in other IPD, and empyema was more likely to be due to non-vaccine serotypes
- •Isolates found in empyema were more likely to be resistant to TMP/SMX, macrolides, ciprofloxacin and levofloxacin but not penicillin or moxifloxacin