Group A streptococcal infections during the seasonal influenza outbreak 2010/11 in South East England

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We present a series of 19 cases of invasive Group A streptococcal (iGAS) infection reported to the Thames Valley Health Protection Unit from 1 December 2010 to 15 January 2011. Ten patients died and a prodrome of influenza-like illness was reported in 14 cases. Influenza B co-infection was confirmed in four cases, three of which were fatal. Our report provides further evidence that influenza B co-infection with iGAS has the potential to cause significant morbidity and mortality.

On 10 January 2011, the United Kingdom (UK) Chief Medical Officer issued a statement advising primary and secondary care doctors to remain vigilant to the possibility of severe bacterial co-infection in patients with influenza [1], because preliminary data indicated an increase in bacterial diseases known to cause co-infection with influenza.

Streptococcus pyogenes, a Lancefield group A streptococcus, is known to be one of the major pathogens causing severe systemic disease during seasonal and pandemic influenza outbreaks. Invasive group A streptococcal (iGAS) disease is notifiable in the UK, and the infection has become a public health issue since the resurgence of invasive disease in the late 1980s [2].

Because iGAS has an increased incidence in winter months, it has been suggested that this may be related to seasonal influenza [2]. As reported by the World Health Organization (WHO) on 14 January 2011 [3], the current seasonal influenza outbreak has resulted in increased consultation rates across northern and western Europe. The WHO sentinel practices reported that 44% of swabs were positive for influenza. Of these, 74% were influenza A and 26% influenza B.

Since the start of the influenza season, we have noted a marked increase in iGAS disease in the Thames Valley area (Oxfordshire, Buckinghamshire and Berkshire) of South East England, with a catchment population of 2.2 million people (Figure). At the same time, a similar rise in iGAS incidence was noted across the whole of

England as described by Zakikhany *et al.* in this issue of *Eurosurveillance* [4].

Data collection

Data were collected during the routine investigation of iGAS cases reported to Thames Valley Health Protection Unit (TVHPU) from 1 December 2010 until 15 January 2011. The data gathered included demographic information, presence and nature of a prodromal illness, presence and nature of chronic conditions, influenza immunisation status, details on the hospital stay and reports from the Health Protection Agency (HPA) reference laboratory for *emm* typing of invasive isolates as well as viral swabbing. Where these data were incomplete, further information was obtained by telephone interview with the patient's treating hospital physician and general practitioner.

Further data on cases in the South East region (approximately 8 million inhabitants) were obtained through the national reference laboratory and regional epidemiology unit for the same time period. Clinical and demographic information was collected from the data entered routinely in the HPA case management database (HPZone).

Results

Table 1 shows the characteristics of the 19 iGAS cases reported to TVHPU during the reporting period.

Fourteen patients were female, and five were male. The average age was 43 years, ranging from 2 to 83 years. Fourteen patients had no significant past medical history, three had a chronic respiratory condition, two had a history of alcohol dependence, one was pregnant and one was post-partum. All 14 patients reported influenza-like symptoms lasting for a mean of six days prior to hospitalisation with iGAS. Influenza-like illness was defined as at least two of the following three symptoms: fever (included if reported as subjective symptom), cough and upper airway congestion. In 12 patients, influenza-like symptoms in the family were also elicited.

Respiratory infection with iGAS was predominant in 12 cases, followed by blood culture positive disease with no focus of infection in four cases, and septic arthritis in two cases. Only three patients received antivirals. All but one received antibiotics. Of the seven patients who had received seasonal influenza vaccinations, four had received trivalent seasonal influenza vaccine in each of the last two years, two patients had received the vaccination in late 2009 and one only in late 2010. For those vaccinated in 2009, information was not available about the type of vaccine given and if it included vaccination against influenza A(H1N1)2009.

All 10 patients who died had been admitted to hospital and died within two days of admission. These patients were older than the patients who survived (55 versus 29), but had a similar duration of prodromal illness.

Viral swabs were taken from 10 patients, of which six were positive. There were four co-infections with influenza B, one with influenza A(H1N1)2009 and one with human metapneumovirus. None of the cases with proven influenza co-infection had received vaccination against influenza. The predominant iGAS *emm* type was st1.0, which was isolated from eight patients. This was followed by st89.0 with three cases and st1.52 with two cases and corresponded to the dominant types in the UK as mentioned in the most recent Health Protection Report [5].

Three of the four cases with confirmed influenza B died. These patients had a mean age of 26 years (range 10–47 years). They were previously healthy, and none had received influenza vaccination. All four cases had a prodrome of influenza-like illness and iGAS disease

FIGURE

Incidence of invasive group A streptococcal disease in Thames Valley Health Protection Unit area, United Kingdom, 2009–10

^a Number of cases per month in the population of Thames Valley (2.2 million people).

TABLE 2

Comparison of Thames Valley Health Protection Unit with other Health Protection Units in South East England, 2010/11

	Thames Valley Health Protection Unit	South East England Health Protection Units including TVHPU
Population covered	2.2 million	8 million
Number of iGAS cases reported	19	57
Deaths reported	10	12
Influenza co-infection cases reported	4 influenza B, 1 influenza A(H1N1)2009	No further co-infections identified
Sex	26% male, 74% female	49% male, 51% female
ICU admission	52%	44%

ICU: intensive care unit; iGAS: invasive group A streptococcus; TVHPU: Thames Valley Health Protection Unit.

TABLE 1

Cases of invasive group A streptococcal disease, Thames Valley, United Kingdom, 1 December 2010–15 January 2011 (n=19)

No	Age group (years)	Sex	Comorbidities ^a	Seasonal influenza vaccination	Prodrome	Time from onset to admission (days)	ILI in close contacts ^b	iGAS disease	emm type	ICU admission	Intubated	Death	Length of stay in hospital (days)	Antivirals received	Antibiotic received	Viral swab result
1	10-19	F	None	No	ILI	6	Yes	Bilateral empyema	st1.0	Yes	Yes	No	≥32	Yes	Yes	Lost
2	10-19	M	None	No	ILI	14	Yes	Splenic, laryngo-tracheobronchitis	st89.0	No	Yes	Yes	≤1	No	No	Influenza B
3	80-89	F	None	No	None	N/A	No	Pneumonia	st89.0	No	No	Yes	≤1	No	Yes	Not taken
4	30-39	F	None	No	ILI	3	Yes	Pneumonia	st1.0	Yes	Yes	Yes	2	No	Yes	Influenza B
5	0-9	M	None	No	ILI	7	No	Septic arthritis	st12.0	No	No	No	1	No	Yes	Not taken
6	80-89	M	Type 2 diabetes mellitus, gout	2010 and 2009	None	1	No	Pneumonia	st1.0	Yes	Yes	Yes	≤1	No	Yes	Not taken
7	10-19	F	None	No	ILI	7	Yes	Pneumonia	st1.0	Yes	Yes	No	≥20	Yes	Yes	Influenza B
8	30-39	F	None	No	ILI	5	Yes	Pneumonia	st1.52	No	No	No	3	No	Yes	Influenza A(H1N1)2009
9	50-59	F	Alcoholism	2009	ILI	4	Yes	Pneumonia	N/A	Yes	Yes	Yes	2	No	Yes	Negative
10	40-49	F	Post-partum	No	None	N/A	Yes	Endometritis	st28.0	No	No	No	5	No	Yes	Not taken
11	0-9	F	None	N/A	Fever, joint pain	5	No	Septicaemia	st3.1	No	No	No	≥14	No	Yes	Not taken
12	70-79	F	None	2010 and 2009	ILI	3	No	Pneumonia	st1.0	Yes	Yes	Yes	2	No	Yes	Not taken
13	30-39	M	Alcoholism, lung lobectomy	No	ILI	7	Yes	Pneumonia	st1.0	Yes	Yes	Yes	1	No	Yes	Not taken
14	50-59	F	Bedbound due to back pain, asthma	2010 and 2009	ILI	14	Yes	Pneumonia	st1.52	Yes	Yes	Yes	≤1	No	Yes	Negative
15	40-49	F	Asthma, cerebral artery aneurysm	No	Diarrhoea and ILI	10	Yes	Septic arthritis	N/A	No	No	No	≥9	No	Yes	Negative
16	70-79	M	None	2010 and 2009	Diarrhoea and ILI	3	No	Septicaemia	st1.0	Yes	Yes	Yes	1	No	Yes	hMPV
17	30-39	F	Pregnant	2010	ILI	7	Yes	Bacteraemia	st3.4	No	No	No	≥10	No	Yes	Negative
18	40-49	F	None	No	ILI	6	Yes	Pneumonia	st1.0	Yes	Yes	Yes	1	Yes	Yes	Influenza B
19	80-89	F	None	2010	None	N/A	No	Septicaemia	st89.0	No	No	No	1	No	Yes	Not taken

F: female; hMPV: human metapneumovirus; ICU: intensive care unit; iGAS: invasive group A streptococcus; ILI: influenza-like illness; M: male; N/A: not available.

^a Conditions likely to affect outcome.^b Close contacts defined as someone who has had prolonged close contact (includes at least one overnight stay) with the case in a household type setting during the seven days before onset of illness.

affecting the respiratory system. The patient who survived had a prolonged stay in an intensive care unit (ICU) and has been in hospital for more than 20 days.

The increase in iGAS infections in the Thames Valley catchment area was only partially reflected in the reporting for South East England. Other surveillance units in our area also noted an increase in cases of iGAS disease, from a background rate of 12 cases per month between January and November 2010. However, the severity of iGAS infection was not replicated in the iGAS outbreak in South East England. Table 2 shows the data from TVHPU on the background of regional data. This includes all patients with a sample date on or after 1 December 2010 received by the national reference laboratory by 15 January 2011.

Discussion

The association and pathogenic synergism of influenza and bacterial disease is well known and has been best described for *S. pneumoniae* [6]. Co-infection with *S. pyogenes* is thought to be uncommon. Few case series have reported influenza A complicated by group A streptococcal infection, the largest of which was a series of 10 cases during the influenza A(H1N1)2009 pandemic [7] that reported a 70% mortality rate.

Our case series is notable for the high frequency of prodromal influenza-like illness preceding hospitalisation with iGAS and the high rate of respiratory involvement: a large German study reported that pneumonia only accounted for 5.6% of all iGAS disease manifestations [8]. We were able to provide microbiological evidence of concurrent viral infection in almost a third of our cases. We also note that all fatal cases died within two days after hospitalisation.

Influenza B virus is generally considered less pathogenic than influenza A and thought to cause less morbidity and mortality in previously healthy adults. Co-infection of influenza B and streptococci has only been reported once in a series of three previously healthy female cases aged 27, 40 and 61 years, one of whom died [9]. Two of those cases had tested positive for *S. pyogenes*, one for *S. pneumoniae*.

The high proportion of confirmed influenza B in our series is striking, considering the predominance of influenza A(H1N1)2009 in the UK during the report period. Similarly to the only other case series reported to date, our patients co-infected with influenza B and iGAS were young and did not fall into any risk group. In conclusion, our paper provides further evidence for the potential morbidity and mortality associated with influenza B virus in the context of co-infection with iGAS.

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References

1. United Kingdom Department of Health Chief Medical Officer. Influenza, meningococcal infection and other bacterial co-infection including pneumococcal and invasive group A streptococcal infection (iGAS). London:DH; 10 January 2011. Available from: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_123647.pdf
2. Lamagni TL, Darenberg J, Luca-Harari B, Siljander T, Efstratiou A, Henriques-Normark B, et al. Epidemiology of severe *Streptococcus pyogenes* disease in Europe. *J Clin Microbiol*. 2008;46(7):2359-67.
3. World Health Organization (WHO) Regional Office for Europe. Widespread influenza activity in countries of northern and western Europe. *EuroFlu*. 14 January 2011;384. Available from: http://www.euroflu.org/cgi-files/bulletin_v2.cgi?display=1&code=384&bulletin=384
4. Zakikhany K, Degail MA, Lamagni T, Waight P, Guy R, Zhao H, et al. Increase in invasive *Streptococcus pyogenes* and *Streptococcus pneumoniae* infections in England, December 2010 to January 2011. *Euro Surveill*. 2011;16(5):pii=19785. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19785>
5. Health Protection Agency (HPA). Increased incidence of invasive bacterial infection potentially linked to influenza activity. Health Protection Report. 2011;5(2). Available from: <http://www.hpa.org.uk/hpr/archives/2011/hpro211.pdf>
6. McCullers JA. Insights into the interaction between influenza virus and pneumococcus. *Clin Microbiol Rev*. 2006;19(3):571-82.
7. Jean C, Louie JK, Glaser CA, Harriman K, Hacker JK, Aranki F, et al. Invasive group A streptococcal infection concurrent with 2009 H1N1 influenza. *Clin Infect Dis*. 2010;50(10):e59-62.
8. Imohl M, Reinert RR, Ocklenburg C, van der Linden M. Epidemiology of invasive *Streptococcus pyogenes* disease in Germany during 2003-2007. *FEMS Immunol Med Microbiol*. 2010;58(3):389-96.
9. Aebi T, Weisser M, Bucher E, Hirsch HH, Marsch S, Siegemund M. Co-infection of Influenza B and Streptococci causing severe pneumonia and septic shock in healthy women. *BMC Infect Dis*. 2010;10:308.