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Cluster of Invasive Group A Streptococcal Infection

Since January 2005, six people in the Health Service Executive, Western Area, (the former Western Health Board region) have become ill with invasive group A streptococcal (GAS) infection. This includes two people who have died of necrotising fasciitis, a rare complication of this infection. Preliminary laboratory results on these two patients indicate that the patients were infected with different types of group A streptococci.

Group A streptococcus is a common bacterium which causes infections such as sore throat and impetigo. Up to 15 per cent of people may carry group A streptococci in their throats and have no symptoms. Rarely this bacterial infection can infect normally sterile sites such as blood or muscle, causing severe illness such as necrotising fasciitis and bacteraemia. Invasive GAS infection occurs when the bacteria get past the body defences of the individual who is infected. This may occur when the individual has sores or breaks in the skin that allow the bacteria to get into the tissues, or when the body's ability to fight the infection is diminished because of chronic illness or illness that affects the immune system. Also, some strains of GAS are known to cause more severe disease than others.

Epidemiology

Invasive GAS infection has been a notifiable disease in Ireland since the beginning of 2004 (see case definition at www.ndsc.ie/Publications/ CaseDefinitions/d863.PDF). There were no routinely collected data before that. In 2004, 35 cases were notified to HPSC nationally. Almost equal numbers of males and females were affected. Cases occurred in all age groups but elderly people were more commonly affected. The majority of cases (25) were reported in the Eastern Region, with cases also occurring in the North East, South East and Southern Regions. The number of notifications represents an incidence of 0.9 per 100,000 population per year. The rate of bacteraemia due to GAS in England and Wales, and Northern Ireland was 3.5/100,000 population in 2003.[1]

Clinical Picture

Early signs and symptoms of invasive disease may include fever, severe muscle pain and swelling, redness at the site of a wound, dizziness, confusion or red rash over large areas of the body.

The incubation period is 1-3 days, and the period of communicability is usually 2-3 weeks.

Source and Transmission

The reservoir of infection is humans. Transmission occurs through sneezing, coughing, kissing and skin contact.

Treatment

Invasive GAS infections require treatment with high dose intravenous antibiotics which will usually include benzyl penicillin and clindamycin. Early treatment improves the outcome for invasive GAS disease. For persons with necrotising fasciitis, surgery may be needed to remove damaged tissue.

Household Contacts

Most individuals who come in contact with GAS remain well and symptom free. A small number will develop a sore throat or skin infections. More serious disease, such as invasive GAS infection very rarely occurs in relatives or household contacts of cases.

Antibiotics should only be administered to the following contacts:

- to mother and baby if either develops invasive group A streptococcal disease in the neonatal period (first 28 days of life).
- to close contacts if they have symptoms suggestive of localised group A streptococcal infection i.e. sore throat, fever, skin infection.

If contacts have symptoms suggestive of invasive disease e.g. high fever, severe muscle aches, localised tenderness then they should be immediately referred to A&E for urgent assessment.

Other close contacts should:

- receive an information leaflet outlining the signs and symptoms of invasive group A streptococcal disease (available from Public Health Departments).
- be advised to seek medical attention if they develop such symptoms.

Recommended chemoprophylaxis regimes include
Penicillin V 250-500mgs QID for 10 days is the drug of first choice for chemoprophylaxis.
Azithromycin 12mgs/kg/day p.o. in a single dose (max. daily dose, 500mgs) for 5 days can be used for those who are allergic to penicillin.

The above dosage would have to be adjusted for children. In the unlikely event of an allergy to penicillin and azithromycin the local consultant microbiologist should be contacted to discuss a suitable alternative.

Prevention

The spread of all types of group A streptococcal infection can be reduced by good hand washing, especially after coughing and sneezing and before preparing foods or eating. Persons with severe or persistent sore throats should be seen by a doctor. All wounds should be kept clean and watched for possible signs of infection such as redness, swelling, drainage, and pain at the wound site. A person with signs of an infected wound, especially if fever occurs, should seek medical care.

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R Cloughley, HSE Western Area

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1. HPA. First year of the enhanced surveillance of invasive group A streptococcal infections. *CDR Wkly* 2004; **14**(16). Available at www.hpa.org.uk/cdr/PDFfiles/2004/cdr1604.pdf

Further information on GAS infection
Health Protection Surveillance Centre, Ireland
www.ndsc.ie/DiseaseTopicsA-Z/StreptococcalDiseaseGroupA/

Health Protection Agency, UK
www.hpa.org.uk/infections/topics_az/strepto/pyogenic/groupa_factsheet.htm

Centers for Disease Control, USA
www.cdc.gov/ncidod/dbmd/diseaseinfo/groupastreptococcal_g.htm

Influenza Surveillance in Ireland, 2003/2004 Season

Introduction

Influenza is one of the commonest and oldest diseases known to man. The impact on public health varies depending on the circulating strain of virus and the level of pre-existing immunity in the community each season.[1 2]

There are three types of influenza virus: A, B and C. Influenza C rarely causes human illness. The clinical course of influenza B changes little from year to year and is usually milder than influenza A. Influenza A varies considerably and is responsible for epidemics and pandemics.[3] Influenza A viruses are divided into three subtypes, on the basis of two surface glycoproteins, haemagglutinin (H) and neuraminidase (N). Minor changes in the surface glycoproteins are known as antigenic drift. Antigenic drift occurs between each influenza season, necessitating the annual reformulation of the influenza vaccine, which is based on the current circulating strains. Major changes in the surface glycoproteins occur infrequently and are known as antigenic shift. These result in the emergence of a novel virus that is capable of causing an influenza pandemic. The Spanish influenza pandemic of 1918 is acknowledged as the most devastating, resulting in an estimated 20-40 million deaths worldwide.[3 4]

The 2003/2004-influenza season was the fourth year of influenza surveillance using computerised sentinel general practices in Ireland. The Health Protection Surveillance Centre (HPSC) is working in collaboration with the National Virus Reference Laboratory (NVRL) and the Irish College of General Practitioners (ICGP) on this surveillance project. Very early influenza activity was seen in 2003/2004, with two school outbreaks in September and peak influenza-like illness (ILI) rates occurring in November. Antigenic drift was detected in the circulating influenza A (H3N2) strains with influenza A/Fujian/411/2002(H3N2)-like strain predominating. Widespread highly pathogenic avian influenza (H5NI) outbreaks in Asia also posed a significant threat to human health.

Materials and Methods

Clinical data

Thirty-five general practices were recruited to report electronically, on a weekly basis, the number of patients with influenza-like illness (ILI). ILI is defined as the sudden onset of symptoms with a temperature of 38°C or more, with two or more of the following: headache, sore throat, dry cough and myalgia. Cases were those attending for the first time with these symptoms. In total, the 35 sentinel general practices, comprising 66 general practitioners, represent 2.8% of the national population. Practices were located in all health boards with the number of sentinel practices in each health board based on the population of the health board.

Virological data

Sentinel GPs were requested to send a combined nasal and throat swab on at least one patient per week where a clinical diagnosis of ILI was made. Swabs were sent to the NVRL for testing using immunoflouresence and PCR techniques and results were reported to HPSC. The NVRL also reported the results of respiratory specimens, referred mainly from hospitals, on a weekly basis.

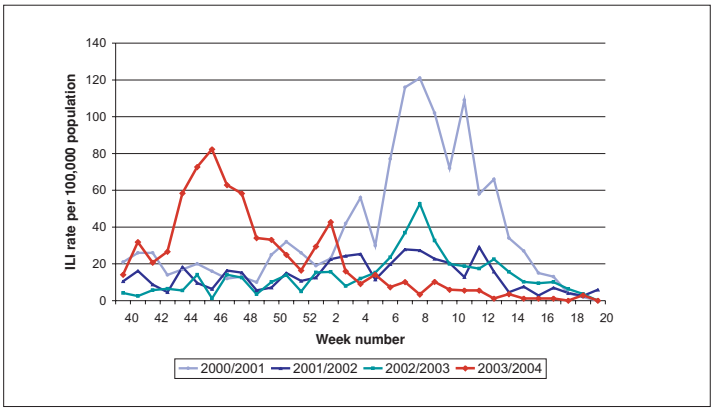

Figure 1. GP consultation rate for ILI per 100,000 population by week, during the 2000/2001, 2001/2002, 2002/2003 & 2003/2004-influenza seasons

Regional influenza activity

The Departments of Public Health sent an influenza activity index (no report, no activity, sporadic-, localised-, regional- or widespread activity) every week, to HPSC. The activity index is analogous to that used by the WHO global influenza surveillance system and the European Influenza Surveillance Scheme (EISS).[5 6] The index is based on sentinel GP ILI consultation rates, laboratory-confirmed cases of influenza, sentinel hospital admissions data and/or sentinel school absenteeism levels. One sentinel hospital was located in each health board. Sentinel primary and secondary schools in each health board were located in close proximity to the sentinel GPs.

Weekly influenza surveillance report

HPSC produced a weekly influenza report, which was posted on the HPSC website each Thursday. Results of clinical and virological data were reported, along with a map of influenza activity and a summary of influenza activity worldwide.

Results

Early school outbreaks

The 2003/2004-influenza season started early, with two school outbreaks of ILI in the ERHA during September. Influenza A (H3N2) was identified in both outbreaks and was later antigenically characterised as the A/Fujian/411/2002(H3N2)-like strain.[7 8] These were among the first cases of confirmed influenza in Europe and 246 students and staff members were affected in total.

Clinical data

Influenza activity also increased earlier than usually observed by sentinel GPs, with GP consultation rates for ILI peaking during week 46 at 82.3 per 100,000 population (figure 1). This was the highest peak rate since the 2000/2001 season when rates peaked at 121.0 per 100,000 during week 8. During the peak in ILI consultation rates, the majority of cases reported were aged between 0-4 and 5-14 years of age (figure 2). A total of 625 ILI cases were reported by sentinel GPs during the 2003/2004 season compared to 348 during the 2002/2003 season.

Virological data

The NVRL tested 350 sentinel specimens for influenza virus during the 2003/2004 season. One hundred and forty-nine (42.6%) sentinel specimens were positive: 142 influenza A (140 A H3N2, and 2 A unsubtyped) and seven influenza B. The predominant influenza virus subtype identified was influenza A (H3N2), accounting for 94.0% of positive specimens (figure 3). The majority of positive sentinel cases were

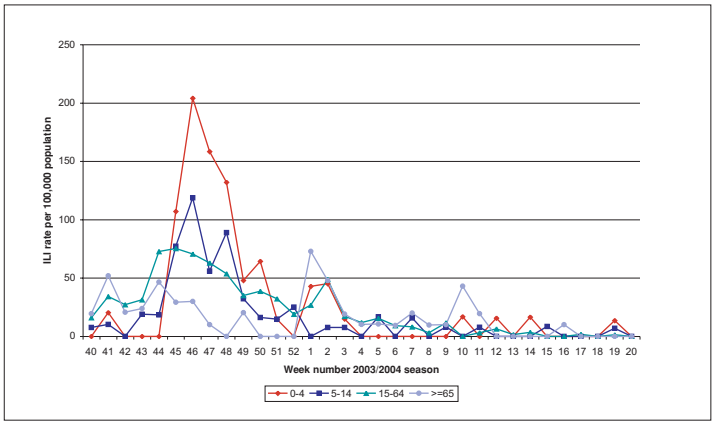

Figure 2. Age-specific GP consultation rate for ILI per 100,000 population by week for the 2003/2004-influenza season

** Please note the denominator used in the age-specific consultation rate is from the 2002 census data; this assumes that the age distribution of the sentinel general practices is similar to the national age distribution.*

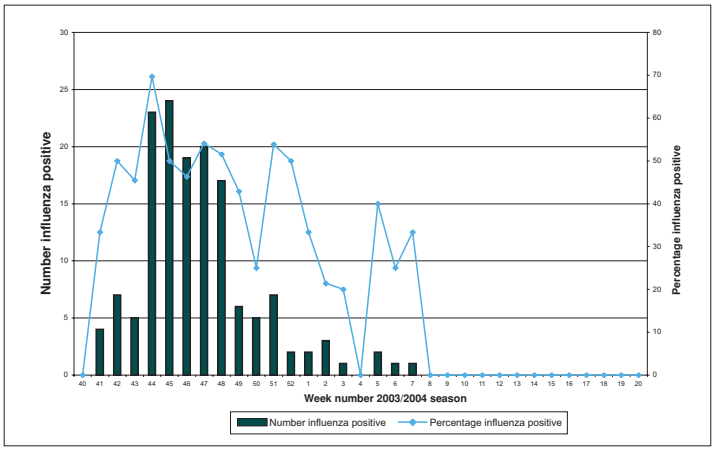

Figure 3. Number and percentage of sentinel specimens positive for influenza virus during the 2003/2004-influenza season

in the 15-64 year age group (75.8%).

Vaccination status and antigenic characterisation

Of the 149 positive influenza virus detections from sentinel specimens, 105 (70.5%) were unvaccinated, eight (5.4%) were vaccinated and vaccination status was unknown in 36 (24.2%) cases. Of the eight cases who were vaccinated, influenza A (H3N2) was detected in seven and influenza A (unsubtyped) was detected in one.

Eight influenza A (H3N2) samples were sequenced at the NVRL and phylogenetic analysis was undertaken at WHO laboratory (Mill Hill) in London. All eight samples were characterised as A/Fujian/411/2002 (H3N2)-like strains. An influenza B virus isolate was antigenically characterised as being closely related to the B/Hong Kong/330/2001-like strain.

Regional influenza activity

Regional influenza activity peaked during weeks 47 and 48 2003, with localised activity reported in the ERHA and NEHB and sporadic activity reported in the remaining health boards.

Mortality data

Two influenza A-associated deaths were reported to HPSC during the 2003/2004 season. These occurred in 0-4 year olds in the SEHB during November 2003.

Influenza activity worldwide

During the 2003/2004 season, influenza activity began early in Western Europe and spread eastwards as the season progressed. Incidence rates were initially highest amongst 0-4 year olds. Early peaks in activity were also seen in the US and Canada.[9 10] Influenza A (H3N2) predominated in most countries worldwide and the vast majority of characterised influenza strains in Europe and North America were influenza A/Fujian/411/2002(H3N2)-like. Influenza A (H1) circulated at low levels globally with outbreaks occurring in Iceland and Ukraine. Influenza B also circulated at low levels.[11] A small percentage of influenza B viruses were characterised, the majority of which were B/Shanghai/361/002-like.[5]

The most significant global influenza event during the 2003/2004 season was the highly pathogenic avian influenza (HPAI) epidemic in Asia. Avian influenza (H5N1) outbreaks spread rapidly and widely across Asia and resulted in mass poultry culls, 44 human infections and 32 human deaths in Thailand and Vietnam. Avian influenza outbreaks were reported to a lesser extent in the US and Canada.[12]

The WHO published its recommendations on the composition of the influenza vaccine for use in the 2004/2005 Northern Hemisphere influenza season on the 27th February 2004. The vaccine included the following strains: A/New Caledonia/20/99(H1N1)-like virus, A/Fujian/411/2002 (H3N2)-like virus and B/Shanghai/361/2002-like virus.[11]

Discussion

Influenza activity peaked early in Ireland during the 2003/2004-influenza season with higher levels of activity reported than in the previous two seasons when low influenza activity levels were observed. During 2003/2004, some antigenic drift was detected in the circulating influenza A (H3N2). The A/Fujian-like strains observed are related to the A/Panama-like strain included in the 2003/2004 vaccine and antibodies induced against this vaccine strain cross-react with A/Fujian-like strains, but generally at a reduced level.

Avian outbreaks of influenza A (H5N1) posed a significant threat to human health in 2004, but there was no evidence of sustained human-to-human transmission of the virus. The greatest concern to human health is that the avian H5N1 virus will remain endemic in Asia and that continued transmission of the virus to humans and other animals will provide opportunities for human and avian viruses to exchange genes (reassortment) to produce a virus that can replicate in humans, is highly pathogenic and is easily transmissible between humans. In a human population with no pre-existing immunity, such a virus could trigger a global influenza pandemic.

The early influenza activity in the 2003/2004 season, coupled with the detection of avian influenza in Asia, Canada and the US emphasises the importance of a timely and effective national influenza surveillance system and pandemic preparedness planning.

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Influenza Vaccine Composition for the 2005/2006 Season

WHO has recommended the following vaccine composition for the 2005/2006 influenza season in the Northern Hemisphere[1]:

- an A/New Caledonia/20/99(H1N1)-like virus
- an A/California/7/2004(H3N2)-like virus[a]
- a B/Shanghai/361/2002-like virus[b]

Reference

1. WHO. Recommendations for influenza vaccine composition Northern Hemisphere: 2005-2006. Available at www.who.int/csr /disease/influenza/vaccinerecommendations1/en/

[a] Candidate vaccine viruses are being developed (for further information please see WHO update at http://www.who.int/ influenza).

[b] The currently used vaccine viruses are B/Shanghai/361/2002, B/Jiangsu/10/2003 and B,Jilin/20/2003.

Community-acquired MRSA and Panton-Valentine Leucocidin in Ireland: a preliminary report

In this brief preliminary communication, we report the first cases of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) in Ireland.

MRSA is a major cause of hospital-acquired (HA) infection but in recent years MRSA is being reported with increasing frequency in the community.[1 2 3] A recent literature review reported that among 10 studies of CA-MRSA between 1998 and 2002, prevalence of MRSA colonisation in community members varied between 0.2% and 7.4%, with highest rates being seen in children.[2] In the past, investigation of apparently CA-MRSA usually revealed some underlying healthcare-associated (HCA) risk factor such as recent hospitalisation, close contact with a patient who had been in hospital recently or previous antibiotic therapy. Whilst HA-MRSA may contribute to the burden of MRSA in the community, MRSA in patients without HCA risk factors in the community is an emerging problem.

Between 1997 and 1999, four children in the USA without HCA risk factors acquired MRSA which caused fatal necrotising pneumonia.[2 3] There have been reports of necrotising pneumonia from other countries but CA-MRSA is more frequently associated with skin and soft tissue infection (SSTI).[3 4] CA-MRSA has caused outbreaks of infection, especially among members of 'semi-closed' communities such as Australian aborigines, North American Indians and Pacific Islanders.[3 5 6] Underlying risk factors in these communities were overcrowding, high rates of skin infection and frequent use of broad-spectrum antibiotics. In the USA, outbreaks have occurred among inmates of jails and among athletes (college football teams, high-school wrestlers and members of a fencing club). Risk factors among these groups were minor skin trauma and poor hygiene practices including sharing of personal items such as towels.[3] CA-MRSA has also been reported in schools, day-care centres, homeless shelters and military bases.[2]

CA-MRSA from different geographical areas share a number of characteristics. Unlike HA-MRSA which are frequently multi-antibiotic resistant, CA-MRSA tend not to be multi-antibiotic resistant, tend to exhibit lower oxacillin minimum inhibitory concentrations and have shorter doubling times.[1 7] In CA-MRSA, methicillin resistance tends to be carried by either of the two smallest staphylococcal cassette chromosome (SCC)*mec* elements recognised to date, SCC*mec* IV (21-24 kb) or SCC*mec* V (28 kb).[7 8] In a study comparing 117 CA-MRSA from three continents, Vandenesch *et al*. showed that all CA-MRSA exhibited SCC*mec* IV and carried the *pvl* genes (*lukS-PV* and *lukF-PV*) which encode the Panton-Valentine leucocidin (PVL).[1] PVL is a toxin which damages host defense cell membranes through the synergistic activity of two proteins LukS and LukF.[3] Another study showed that 70% of MRSA isolates from jail inmates in San Francisco and 69% of isolates from patients attending an outpatient department for treatment of SSTI carried *pvl*. In the latter study, 85% of isolates from SSTI belonged to one of only two clonal groups.[4]

Other studies of CA-MRSA isolates causing outbreaks have also shown clonality suggesting spread occurred by transmission rather than *de novo* development of methicillin resistance.[5 6] However, studies of isolates from geographically distant locations have shown that CA-MRSA may represent several different lineages.[1 7] In the study by Vandenesch *et al*., six different multilocus sequence types were found but the same sequence type (ST) tended to be associated with each continent (ST80 in Europe; ST93 in Australia; ST30 in Oceania, ST1, ST59 and ST8 in the USA). Furthermore, pulsed field gel electrophoresis DNA fingerprint analysis showed that CA-MRSA were unlike the local HA-MRSA in each geographic area.[1] Clinically CA-MRSA appear to be more virulent than MSSA (*pvl* is found in only 2% to 3% of MSSA strains).[3 9] In addition to *pvl*, one strain of CA-MRSA has been shown to carry many additional virulence genes.[1 3 10]

To date, there are no available data on the prevalence of CA-MRSA in Ireland. In a preliminary study of blood culture MRSA isolates submitted to the National MRSA Reference Laboratory (NMRSARL) from Irish hospitals that participated in the European Antimicrobial Resistance Surveillance System during Quarter 2, 2003, two (of 112) isolates carried *pvl*. Six additional isolates from six persons submitted to NMRSARL as possible CA-MRSA over a two-week period in 2004 were also *pvl*-positive. Seven of these eight patients lacked risk factors for hospital acquisition of MRSA. Specifically, there had been no hospital admission for at least two years, no antimicrobial use within the last year and no close contact with a healthcare worker or relative who had recently been in hospital. The isolate from the eighth patient was probably acquired in the community abroad. Four isolates were obtained from one family (a child with a soft tissue infection and three asymptomatic family members). Three of the remaining four patients presented with SSTI and all three were Irish non-nationals.

All eight isolates were non-multi-antibiotic resistant, being resistant only to β-lactam antibiotics. The four isolates from the family mentioned above were resistant to fusidic acid also. All eight isolates were susceptible to ciprofloxacin. Studies to further characterise these isolates and to determine the prevalence of *pvl* among other patient populations are on-going but the results of this preliminary investigation suggest that CA-MRSA may already be a problem in Ireland. NMRSARL would be pleased to receive suspect isolates from microbiology laboratories throughout the country.

Angela Rossney, Pamela Morgan and Brian O'Connell, National MRSA Reference Laboratory.

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