

Morbidity of Parainfluenza 3 Outbreak in Preterm Infants in a Neonatal Unit

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Abstract

Introduction: Parainfluenza type 3 virus (PIV-3) is an important nosocomial pathogen which causes pneumonia and bronchiolitis in infants. We report an outbreak of PIV-3 respiratory infection which occurred in the neonatal unit of KK Hospital in June 2005. This is the second PIV-3 outbreak in our unit after the first in December 1994. **Materials and Methods:** The clinical characteristics and outcome of 7 infants tested positive for PIV-3 on nasopharyngeal aspirate in June 2005 were reviewed retrospectively. **Results:** Seven cases were infected with PIV-3 during this outbreak. The median birthweight of affected infants was 970 g (range, 740 to 2585 g), gestational age was 27 weeks and 4 days (range, 24 to 35 weeks), and postnatal age was 84 days (range, 28 to 250 days). Apnoeas and bradycardias were significant symptoms in 3 infants, 5 infants had progressive respiratory distress while the remaining 2 infants had flu-like illness. Five infants required ventilatory support and there were no deaths. The index case was an infant with chronic lung disease who was on oxygen supplementation and subsequently required ventilatory support with nasal CPAP. Despite implementation of control measures to prevent the spread of infection through early identification with strict cohorting of infected cases, contact tracing/screening, and reinforcement of hand hygiene precautions, the outbreak lasted for 24 days. **Conclusion:** PIV-3 respiratory infection in preterm infants can present with non-specific symptoms, leading to significant morbidity especially in those with underlying pulmonary pathology. Early recognition of symptoms and diagnosis by physicians, and prompt institution of control measures are necessary to prevent the spread of infection.

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Key words: Assisted ventilation, Chronic Lung Disease, Nosocomial respiratory infection, Viral

Introduction

Parainfluenza type 3 virus (PIV-3) is an important nosocomial pathogen. It closely mimics respiratory syncytial virus (RSV) in its clinical presentations, and in infants. It is the second commonest cause of pneumonia and bronchiolitis after RSV.¹⁻³ However, PIV-3 has only been infrequently reported in newborns due to passive immunity to parainfluenza in the neonatal period from maternal neutralising antibodies.³ Nosocomial PIV-3 outbreaks in nurseries have been suggested to affect the older infants more commonly, as the protection from maternal neutralising antibodies may no longer be present in the older convalescing premature infant. Moisiuk et al⁴ has shown that the infected infants' mean age to be 42 days compared with 11 days for non-infected infants in a nosocomial PIV-3 outbreak in a nursery.

We report an outbreak of nosocomial respiratory infection with PIV-3 in our neonatal unit in June 2005. This was the second PIV-3 outbreak in our unit after the first in December 1994.⁵ The aim of this series was to study the clinical presentations and morbid consequences of PIV-3 infection, as well as to highlight the importance of early detection of an outbreak necessitating prompt institution of control measures to control the spread of infection.

Materials and Methods

A review of retrospective data of 7 infants tested positive for PIV-3 on nasopharyngeal aspirate (D³ Double Duet™ Respiratory Virus Screening and ID Kit (Immunofluorescence detection), “Diagnostic Hybrids, Athens”) in June 2005 was conducted. Clinical presentations, progress, morbidity and methods employed to control and

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limit the extent of outbreak were studied.

Description of Outbreak

The outbreak occurred in a tertiary neonatal unit in KK Women's & Children's Hospital (KKH) in Singapore on 2 June 2005. The areas involved were the (*Methicillin-resistant Staphylococcus aureus*) MRSA Isolation Intermediate Care Neonatal Nursery which accommodated infants under special care and intensive care, and the Special Care Nursery (SCN). Infants in the MRSA unit were isolated due to MRSA positive nose swabs on routine screening. The MRSA unit is located next to the SCN, both of which are located a distance away from the Neonatal Intensive Care Unit (NICU) on the same level (Fig. 1). The paediatric wards in our hospital are located in a separate tower. There were altogether 6 infants in the MRSA unit prior to the onset of the PIV-3 outbreak, of which 3 infants were the first to be infected (attack rate 50%) and 4 other infected infants were from SCN which managed 107 babies (attack rate 3.7%). The physical layout of the nursery and proximity between cots are specified in Figure 1.

continuous positive airway pressure support (nasal CPAP). The nursing staff had noted that this infant's mother had an upper respiratory tract infection and had been visiting the infant. A nasopharyngeal aspirate (NPA) sent on day 2 of illness was positive for PIV-3. She developed post-viral bronchial hyperreactivity and required continuation of nasal CPAP with increasing oxygen requirements, in addition to prednisolone, theophylline, atrovent and salbutamol nebulisation and monoleukast (Table 2).

Spread of PIV-3 Infection

Cases 2 and 3 were both from the MRSA unit and had underlying CLD (Table 1). Case 2 first became symptomatic on 25 May 2005, but NPA on 27 May 2005 was tested negative. His symptoms of coughing and desaturations worsened on 6 June 2005 (day 12 of illness) and NPA was tested positive for PIV-3 (Table 1, Fig. 2). Both cases required oxygen supplementation during the duration of illness.

Cases 4 to 7 were all from the SCN (Fig. 2). Case 4 developed symptoms of recurrent apnoeas and bradycardias, increased cough and secretions, and was initially managed on



Fig. 1. Physical layout of neonatal unit. MRSA unit was located next to SCN, both MRSA unit and SCN were located a distance away from NICU on the same level. Distance between each side of the baby cot or incubator is 2.5 to 3 feet in SCN and 3 feet in NICU. Distance between the foot-ends of opposite cots or incubators in both SCN and NICU is 9 feet. Hand sinks are marked with the letter "S". Location of index case is marked with a checkered box.

Index Case

The index case was from the MRSA unit, a 250-day-old female infant born at 25 weeks of gestation, with a birthweight of 740 g (Table 1). She had underlying chronic lung disease (CLD) and was on nasal oxygen supplementation. On 2 June 2005, she developed cough and desaturations which required hood oxygen supplementation and subsequently

nasal CPAP but eventually required mechanical ventilation. He was rapidly transferred to the MRSA unit for isolation and intensive care support. Case 5 developed apnoeas and bradycardias which required CPAP support. Cases 6 and 7 had mild coryzal symptoms and did not require any form of assisted ventilation. All these cases were transferred and cohorted in the MRSA unit.

Table 1. Patient Demography

Case	Gestational Age	Birth Weight	Age of Onset/ Date which Symptoms Start	Type of Respiratory Support/ Lung Disease Prior Symptoms
1	25 wks + 5d	740 g	250 days/ 2/6/2005	Hood O ₂ for BPD
2	24 wks + 4d	790 g	102 days/ 6/6/2005	Nasal O ₂ for CLD
3	34 wks + 1d	960 g	84 days/ 7/6/2005	Nasal O ₂ for CLD
4	27 wks + 4d	970 g	59 days/ 13/6/2005	RA/O ₂ (underlying AOP)
5	31 wks	1610 g	28 days/ 18/6/2005	RA (underlying AOP)
6	35 wks + 3d	2585 g	35 days/ 20/6/2005	RA (no underlying lung pathology)
7	26 wks + 2d	1940g	99 days/ 26/6/2005	RA (underlying AOP)

RA: Room air; CLD: Chronic lung disease; O₂: oxygen; BPD: Bronchopulmonary dysplasia; AOP: Apnoea of prematurity

Table 2: Clinical Presentation and Progress of Babies involved in the Outbreak

Case	Clinical Features	Investigations	Respiratory Support during Illness	Other Treatment	Duration of Symptoms
1	Increased retractions, tachypnoea, cough, desaturations	PIV-3 antigen +ve On 2/6/05 (day 2 of illness)	-Nasal CPAP for 10 days -Hood /nasal O ₂ for 13 days	Bronchodilators (Theophylline, Ipratropium bromide & Salbutamol), monoleukast & prednisolone	30 days
2	Cough, desaturations	PIV-3 antigen +ve On 6/6/05 (day 12 of illness)	-Hood O ₂ for 4 days -Nasal O ₂ for 22 days	Nil	26 days
3	Coryza, cough, apnoea, tachypnoea, retractions, feed intolerance	PIV-3 antigen +ve On 10/6/05 (day 4 of illness)	-Nasal CPAP for 3 days -Hood/nasal O ₂ for 5 days -RA	Nil	10 days
4	Apnoeas and Bradycardia, cough, increased secretions	PIV-3 antigen +ve On 14/6/05 (day 2 of illness) CXR: Peribronchial thickening	-Nasal CPAP for 1 day -Mechanical ventilation for 4 days -Post-extubation atelectasis needed nasal CPAP for 5 days	Caffeine, PCT	19 days
5	Apnoeas and bradycardia, Coryza/nasal congestion, Cough	PIV-3 antigen +ve On 21/6/05 (day 4 of illness)	Nasal CPAP for 3 days	PCT	17 days
6	Coryza/nasal congestion, Cough	PIV-3 antigen +ve On 20/6/05 (day 1 of illness)	Stable in room air	Nil	3 days
7	Sneezing, cough	PIV-3 antigen +ve On 27/6/05 (day 1 of illness) PIV-3 antigen -ve On 1/7/05	Stable in room air	Nil	30 days

RA: Room air; O₂: oxygen; CPAP: Continuous positive airway pressure support; PCT: Packed cell transfusion, -ve: Negative

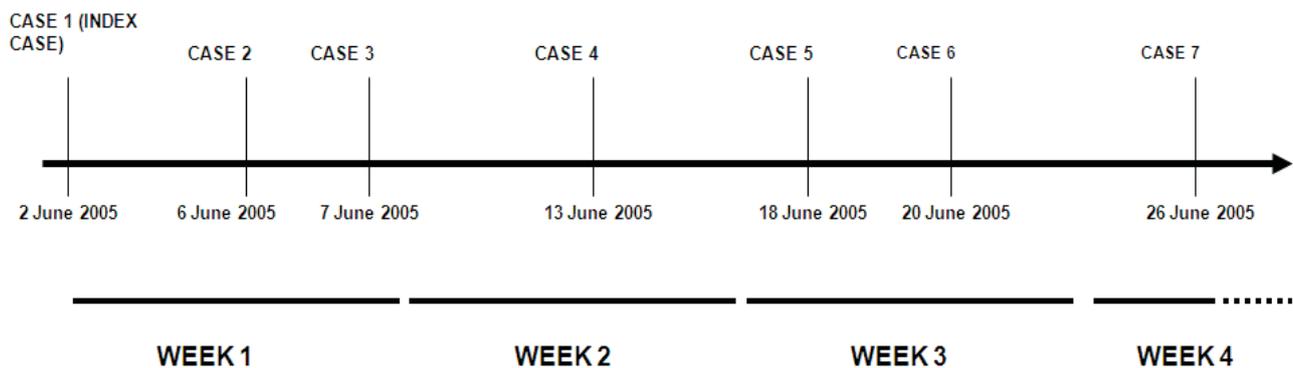


Fig. 2. Timeline of Outbreak Showing Temporal Relationship of Symptoms of Patients.

Infection Control Measures

The nurse to patient ratio in NICU is 1:2 and in SCN 1:5. In addition to the standard infection control policies in the unit, new doctors and nurses undergo formal training for proper hand hygiene and infection control measures. The compliance with hand hygiene precautions varies between 85% and 100%. During the outbreak, hand hygiene precautions were reinforced; every nursing and medical personnel had to adhere to strict handwashing regime or the use of alcohol handrubs before and after handling each patient. Non porous surfaces contaminated with PIV-3 were cleansed with water and detergent. Cot linen was outsourced to an external contractor specialising in hospital linen washing. All the patients in the MRSA unit were screened for PIV-3 on NPA. The MRSA unit was reorganised to cohort the PIV-3 positive cases in the same cubicle. The nursing staff looking after PIV-3 positive cases were kept away from the non PIV-3 infected infants. After the identification of the first PIV-3 positive infant from SCN, contact tracing of all contact cases in SCN was performed. In SCN, only infants with symptoms suggestive of a viral illness were screened for PIV-3 on NPA; asymptomatic infants nursed in different cubicles were not screened for PIV-3. All PIV-3 positive cases were cohorted and isolated in separate cubicles in the MRSA unit.

Results

Seven cases were infected with PIV-3 during this outbreak; 3 cases were from the MRSA isolation unit and 4 cases from the SCN. The index case was from the MRSA unit. The source of PIV-3 was believed to be from the mother of this infant who was having an upper respiratory tract infection and had visited the infant. The spread of PIV-3 infection initially occurred within the MRSA unit on 2 June 2005, and began infecting the other infants in SCN on 13 June 2005.

The median birth weight of infected infants was 970 g

(range, 740 to 2585 g) and median gestational age was 27 weeks and 4 days (range, 24 to 35 weeks). The day of life that the infants were infected ranged from 28 to 250 days, with a median of 84 days.

Apnoeas and bradycardias were the significant symptoms in 3 infants. Other symptoms included cough (7), coryza (4), chest retractions (2), tachypnoea (2), increased secretions (1), and feed intolerance (1). Five infants had progressive respiratory distress while 2 infants had flu-like illness. Five infants required ventilatory support (nasal prong CPAP in 4 infants, mechanical ventilation in 1 infant) and 3 cases were managed on hood oxygen. Four infants required intensive care support while the other 4 only required special care. The duration of symptoms ranged from 3 days (Case 6) to 30 days (index case). The index case also had post-viral bronchial hyperreactivity. There were no deaths.

NPA was positive for PIV-3 for all 7 affected infants. It was positive between day 1 to day 12 of illness. Chest radiography was performed for 5 infants, 2 infants received packed cell transfusion and 1 infant had blood cultures performed and received antibiotics.

Discussion

Clinical presentations of PIV-3 infection in premature infants can often be atypical; they can present with recurrent apnoeas or bradycardias, worsening of bronchopulmonary disease (BPD) with increasing oxygen supplementation requirements, wheezing and even sepsis-like episodes. The diagnosis of PIV-3 infection in preterm infants can be challenging. A high index of suspicion is needed, especially with a background of positive contact history from visitors, medical or nursing personnel. Viral respiratory tract infection should be included in the list of differential diagnoses in premature infants with recurrent apnoeic episodes or sudden unexpected worsening of underlying CLD requiring increasing oxygen supplementation or

assisted ventilation.

In an outbreak of nosocomial respiratory infection in a nursery, more than one virus may circulate concurrently. RSV and PIV-3⁶ infections, RSV and rhinovirus infections⁷ have been previously described in the literature.

There is a high PIV-3 detection rate in our study, 100% of the affected infants were PIV-3 positive. In the PIV-3 outbreak in KKH nursery in December 1994,⁵ all the 5 infected infants also tested positive for PIV-3. Other studies have reported PIV positivity rate of 30% to 50%.^{8,9}

PIV-3 nosocomial infection can result in significant morbidity in premature infants with underlying CLD. In this outbreak, 4 out of 7 infants developed progressive respiratory distress and required assisted ventilatory support while in the outbreak in December 1994,⁵ none of the infants required intubation but all the 5 cases required nasal CPAP support. There were no deaths in our nursery during both of the outbreaks.

PIV-3 nosocomial infection also prolongs the duration of hospitalisation of the affected infants. The average length of symptoms in infected infants in our study was 19.3 days. The duration of symptoms in the index case was 30 days excluding the period after which she developed severe bronchial hyperactivity, and this has resulted in prolonged hospitalisation and the need for home CPAP. During the outbreak in December 1994, the duration of illness ranged from 2 to 17 days with a mean of 7 days. In terms of the severity of symptoms, the degree of assisted ventilation needed, as well as the duration of symptoms, the outbreak in June 2005 had more severe morbid consequences as compared to the outbreak in December 1994. The duration of symptoms of PIV-3 illness was likely to be confounded by the infants' underlying CLD.

The duration of the outbreak in 2005 was 24 days compared to 2 days in the December 1994 outbreak. This outbreak could have been worse but prompt identification of symptoms with a high index of suspicion and implementation of infection control measures controlled the spread of infection in the SCN, despite the fact that many infants in SCN were exposed. In these aspects, the 2005 outbreak was significantly more widespread and had greater morbidity. Cohorting may not be possible in units with space limitation,⁴ and overcrowding contributes to the maintenance of transmission of an outbreak. Experience from the two PIV-3 outbreaks has enabled us to streamline our workflow protocol in the event of any viral outbreak.

Transmission of parainfluenza infection occurs by direct person to person contact as well as inhalation of infected droplets.^{6,10} Parainfluenza viruses have been found to survive for at least a few hours in air and on environmental surfaces.^{11,12} Infectious viruses can be transferred from

environmental surfaces to the hands of hospital personnel who appear to be responsible for the spread.¹³ Good handwashing technique was probably sufficient to control this outbreak. Gloving introduces another barrier of protection and has been suggested to act as a deterrent to touching the eyes and nose, but because PIV-3 can be easily removed from stainless steel with a number of cleaning agents and water alone,¹¹ and considering the rapid decline of virus recovery from the fingers with time, careful adherence to handwashing protocols should be sufficient without the added requirement for gloving.

In the study for potential risk factors for nosocomial respiratory illness in neonates,⁶ the only significant factor found was the use of nasogastric tubes. In our recent PIV-3 outbreak, 2 infected infants had nasogastric tubes while in another study,⁶ none of the infected infants had nasogastric tubes in the situ. Considering how long PIV-3 can survive on non-absorptive surfaces, it is possible that nasogastric tube could be one of the fomites that introduced the virus to mucosal surfaces.

Conclusion

In conclusion, PIV-3 respiratory infection in infants can present with non-specific symptoms in preterm infants and is an important differential to consider. Early detection is necessary to limit the extent of infection and avoid unnecessary investigations and treatment. Though infrequent, nosocomial respiratory infection is a significant cause of morbidity in infants, especially in those with underlying pulmonary pathology. This outbreak has heightened the level of awareness of the importance of infection control among the nursing and medical personnel in our unit. Education on the measures of infection control has been a core curriculum in nursing and medical personnel training in our unit. This outbreak has further emphasised the need for a good team effort in recognising and preventing sick visitors from entering the unit to protect our patients.

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