Investigation of a Suspected Nosocomial Infection Outbreak in a Neonatology Department, China

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Background: *To describe the successful management of a multi-strain outbreak of Pseudomonas aeruginosa (Pae) in the neonatal unit, combined with a case control study to identify risk factors.*

Materials and Methods: *The management measures including outbreak investigations and controls were taken to prevent further cases. To analyze the risk factors of infection, neonates were divided into case group and control group. The case group consisted of the 5 infected neonates. The control group consisted of 10 premature infants without infection, but with similar gestational age, body weight, and with >48 hours stay in the hospital. The two groups were matched with the ratio of 1:2. t and chi-square tests were used for comparison between the two groups and P<0.05 was considered significant. Environmental samples were collected from the faucet, sewer, staff hand, body surface of medical instrument, on 15th October, 2020. Cultures were initiated to detect sources of infectious agents.*

Results: *The outbreak comprised of 5 infections over time period. The results were that samples from the environment identified the infection source. It was hypothesized that the organism being transferred from the source to the patients via water. The outbreak was halted by successful control measures. The cases differed from controls only by antibiotic application (type and duration of treatment), length of hospital stays, PICC catheterization time and gastric tube in-dwelling time (P<0.05). When logistic regression was used to analyze relationships between neonatal infection and various variables, all variables were not included in the regression equation (probably due to our small sample size). Pae was identified from the sputum and skin cultures, and from multiple faucet samples. Blood culture analyses indicated inflammation. The Pae outbreaks were associated with exogenous water sources but the infectious agent had different drug resistant patterns.*

Conclusion: *The conclusion is that this was an multi strain outbreak of Pae arising probable from biofilm in faucet water sources, streptococcus, enterococcus, coagulase negative staphylococcus was cultured from the faucet. It was controlled by pre-determined protocols and expert personnel to handle the suspected outbreak efficiently, and successful prevention and intervention processes. The data, therefore, allowed us to exclude the infection as NI outbreak but to conclude exogenous NIs. Furthermore, new hygienic protocols were developed to prevent such occurrences.*

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Financial Disclosures: Financial support for this investigation came from hospital funds of the Xiangtan Central Hospital.

INTRODUCTION

According to reports in 2015 and 2019, neonatal infections were responsible for the third leading cause of neonatal death worldwide, accounting for 750,000 mortality annually[1,2]. Unfortunately, many of these infections occurred in neonatology clinics where intensive cares were provided to critically-ill neonates[3]. Infection prevalence as high as 10.7% in neonatal intensive care unit in developing countries[4].A recent report indicates that nosocomial infections (NIs) were associated with an increased risk of serious neonatal complications, such as brain injury, broncho pulmonary dysplasia (BPD) and death, and were a significant risk factor for adverse motor development at 2 years of corrected age[5]. Therefore, hospitals and clinics have been vigilant in controlling nosocomial infections using rigorous preventive measures.

We describe an outbreak of Pseudomonas (Pae) which manifested from 9th October to 10th November, 2020, 5 cases of suspected NIs occurred in the neonatology department of a hospital in Xiangtan, China. The setting comprised 2,490 beds and 36 for newborns. The infections were particularly worrisome because it occurred during the global COVID pandemic. Immediately, pre-determined protocols for identifying the sources of the infection as well as for initiating prevention and management were initiated. Through various tests and investigations, nosocomial infection outbreak was ruled out and further infections were prevented. The successful effort and process are described in this report.

MATERIALS AND METHODS

General Condition

There are 36 beds, 1200 square meters in neonatal unit, all newborns are treated with superior care.

The case definition was any neonate with Pae infection and refusing to drink milk, bad mental state, effectively by anti-infection treatment who was a patient in neonatology department between 9th October and 10th November, 2020. Patient samples were collected prior to initiation of antibiotics for suspected infection.

The control group consisted of 10 premature infants without infection, but with similar gestational age, similar body weight, and with hospital stay for >48 hours, which were admitted in the same part of the suspected nosocomial infection. The two groups were matched according to the ratio of 1:2.

A total of 43 samples of external environment were collected for routine bacterial culture, including medical staff hands, faucet and water pipe walls, ventilator surface and buttons, warm box, stethoscope and other objects.

Statistical Analysis

The SPSS19.0 software was used for statistical analysis. The quantitative data were expressed as, and t test was used for comparison between the two groups. The qualitative data were represented by the number of cases, and the comparison between the two groups was performed by chi-square test. Logistic regression was used and $P<0.05$ was considered significant.

Protocols In Response to The Suspected Outbreaks

From October 9 to 14, 5 premature infants showed low fever, refused to drink milk and poor spirit, then Pae was cultured in sputum of 3 premature infants. According to the clinical symptoms and manifestations, the infants were diagnosed the hospital infection of the lower respiratory tract, the suspected outbreak of hospital infection were reported to the Department of Infection Control. An alert signal was noted when 3 neonates were diagnosed with suspected NIs. A suspected NIs outbreak generally refers to the occurrence of 3 or more cases of infection with a common infection source and with similar clinical symptoms in a medical institution/ department within a short period of time. Our pre-determined protocol which contained investigation, treatment and verification was initiated immediately. As soon as NIs was suspected, the process involved the head of the hospital administration reporting to the NIs Management Committee regularly on immediate organization of expert consultation and on utilization of effective measures to control the

infections. A joint prevention and control protocol was immediately initiated by the hospital's medical, nursing, infection control, general affairs and the neonatology department. Immediate actions involved: (1) Suspension of new admissions to the neonatology clinic until further notice;
(2) Implementation of isolation management by isolating the infected children;
(3) Intensivemonitoring of diagnosis and therapeutic efficacy of all neonatal children; (4)Strengthening of disinfection, cross infection, personal protection and other hygienic activities; (5)Reporting of any neonates with NIs to the Sensory and Medical departments; and(6)Initiation of expanded surveillance and hygiene activities (on-site air samples of the neonatal intensive care units, internal and external surfaces of warm boxes, humidifying fluid, warm box water, pacifiers, bottles, door handles, outlet of every faucets and water supplies, and treatment of cart tables, hands of medical staff and nurses, and all instruments.)We did this because Pae outbreaks in neonatal outbreaks are associated with 'wet sites' and we did this to identify the reservoirs.

Clinic Activities

Sputum samples were collected through a suction tube from the neonates, skin samples were collected by dipping a cotton swab in saline solution. Sputum and skin samples were immediately collected from affected neonates and were used to set up cultures for detection of infectious agents, conventional microbial culture method was used to calculate the total number of colonies and to observe the growth of pathogenic bacteria. One bottle blood culture was submitted per patient, adequate volumes of blood were collected, and pharyngeal swab samples were also collected for laboratory tests. Environmental monitoring was initiated.
Specific information about gestational age, weight, inpatient days, mother's age, number of antibiotics used, days of antibiotic used, days of invasive ventilator used, days of non-invasive ventilator used, days of umbilical vein, days of PICC, days of gastric tube were collected from 5 infected neonates and the control group consisted of 10 premature infants without infection.

RESULTS

Diagnosis And Test Results

They had a low fever and respiratory distress syndromes. In one month, five neonatal children were suspected to have NIs. They were 4 males and 1 female, with low birth weights of 0.77, 1.35, 1.44, 1.65, 2.25(kg), respectively, and with an average weight of 1.49kg. In addition, they were premature, with gestational ages of 29^{+1}, 30^{+3}, 27^{+6}, 30^{+3}, 32^{+2}, respectively. The blood examination of infection group revealed inflammation but blood cultures and pharyngeal swabs were negative. The case group showed significant differences from the control group in antibiotic application (type and duration of treatment), length of hospital stays, PICC catheterization time and gastric tube in-dwelling time ($P< 0.05$). Tables 1.
When logistic regression was used to analyze relationships between neonatal infection and various variables, all variables were not included in the regression equation. This is possibly due to our small sample size.
Fisher's exact and t tests showed no significant differences in gender, gestational age, birth weight, delivery mode, maternal age, invasive operation (invasive ventilator, non-invasive ventilator, umbilical vein) between the case and control groups ($P>0.05$). Tables 2.

In the external environment monitoring on 15th October, Pae, Enterobacter and coagulase negative staphylococcus were cultured from the surface samples of faucets and water pipes, coagulase negative staphylococcus were cultured from object surface of ventilator button, stethoscope head. In order to track the abnormal cause of environmental monitoring results, the newborn clothes were changed, the surface of the object was disinfected with 500mg/l chlorine-containing disinfectant, and the environment where bacteria were cultured was sampled again on 18th October, only water-related samples were cultured with aeruginosa, Enterobacter, and coagulase-negative staphylococcus. Tables 3,4.

Table 1: Analyses of infection factors among neonates (n=15)

Variant		t	P	95%CI
Gestational age	33+13+4	-1.381	0.191	(-45.387, 9.987)
Weight	1.970.70	-2.115	0.054	(-1.456, 0.016)
Inpatient days	22.0015.28	6.132	<0.005	(17.488, 36.512)
Mother's age	32.274.92	-0.036	0.972	(-6.142, 5.942)
Number of antibiotics used	1.731.16	4.761	<0.005	(1.038, 2.762)
Days of antibiotic used	12.079.37	10.724	<0.005	(14.534, 21.866)
Days of invasive ventilator used	0.200.78	1.472	0.165	(-0.281, 1.481)
Days of non-invasive ventilator used	1.872.26	1.141	0.274	(-1.250, 4.050)
Days of umbilical vein	5.676.61	1.857	0.086	(-1.014, 13.414)
Days of PICC	7.5312.06	5.356	<0.005	(12.231, 28.769)
Days of gastric tube	17.7314.54	7.005	<0.005	(18.328, 34.672)

Table 2: Sex and cesarean section effects on neonatal infection

Variant		Infection status		χ2	P (Fisher 's)	OR	95%CI
		Yes	No				
Sex	Female	2	1	1.875	0.242	0.167	(0.033, 1.429)
	Male	3	9				
Cesarean delivery	Yes	4	3	3.348	0.119	9.33	(0.889, 40.000)
	No	1	7				

Table3: Results of external environment monitoring on 15th October)

NO.	Sample Classification	Source of Samples	Results	Normal range
1	Hands	Doctor Ren	Colony counting< 1 cfu/cm2	Colony counting≤ 10cfu/cm2
2		Nurse Chen	Colony counting< 1 cfu/cm2	Colony counting≤ 10 cfu/cm2
3		Doctor Liu	Colony counting< 1 cfu/cm2	Colony counting≤ 10 cfu/cm2
4	Disinfectant	Hand Disinfectant	Colony counting< 10 cfu/cm2	Colony counting≤ 10 cfu/cm2
5		Complexing iodine	Colony counting< 10 cfu/cm2	Colony counting≤ 10 cfu/cm2
6		Ethanol	Colony counting< 10 cfu/cm2	Colony counting≤ 10 cfu/cm2
7	Water source correlation	Ward faucet	Pae、Enterobacter	——
8		Ward drain	Pae、Enterobacter	——
9		Faucet in isolation room	Enterobacter、Coagulase negative staphylococcus	——
10		Drain in isolation room	Pae、Enterobacter	——
11		Faucet of Doctor's workstation	Pae、Enterobacter	——
12		Drain of Doctor's workstation	Pae、Enterobacter	——
13	Humidification water	NO. 818895	Colony counting< 10 cfu/cm2	Colony counting≤ 10 cfu/cm2
14		NO. 816103	Colony counting< 10 cfu/cm2	Colony counting≤ 10 cfu/cm2
15		NO. 818124	Colony counting< 10 cfu/cm2	Colony counting≤ 10 cfu/cm2

16		NO. 818034	Colony counting< 10 cfu/cm2	Colony counting≤ 10 cfu/cm2
17	Surface of objects	NO.1 Ventilator	Colony counting< 1 cfu/cm2	Colony counting≤ 5 cfu/cm2
18		NO.2 Ventilator	Colony counting< 1 cfu/cm2	Colony counting≤ 5 cfu/cm2
19		NO.3 Ventilator	Colony counting< 1 cfu/cm2	Colony counting≤ 5 cfu/cm2
20		NO.4 Ventilator	Coagulase negative staphylococcus	Colony counting≤ 5 cfu/cm2
21		Doctor Liu's white coat	Coagulase negative staphylococcus	Colony counting≤ 5 cfu/cm2
22		Doctor Liu's keyboard	Coagulase negative staphylococcus	Colony counting≤ 5 cfu/cm2
23		Baby incubator	Colony counting< 1 cfu/cm2	Colony counting≤ 5 cfu/cm2
24		Baby incubator (20007732)	Colony counting< 1 cfu/cm2	Colony counting≤ 5 cfu/cm2
25		Baby incubator (20003091)	Colony counting< 1 cfu/cm2	Colony counting≤ 5 cfu/cm2
26		The door of baby incubator	Coagulase negative staphylococcus	Colony counting≤ 5 cfu/cm2
27		Injection pump	Coagulase negative staphylococcus	Colony counting≤ 5 cfu/cm2
28		Cover cloth for baby incubator	Coagulase negative staphylococcus	Colony counting≤ 5 cfu/cm2
29		Sethoscope	Coagulase negative staphylococcus	Colony counting≤ 5 cfu/cm2
30		ECG monitor	Colony counting< 1 cfu/cm2	Colony counting≤ 5 cfu/cm2

Table 4: Results of external environment monitoring on 18th October）

NO.	Sample category	Specimens	Results	Normal range
1	Water source correlation	Faucet of ward	Pae, Enterobacter	——
2		Water pipe of ward	Pae, Enterobacter	——
3		Faucet of Isolation room	Pae, Enterobacter	——
4		Water pipe of Isolation room	Pae、Enterobacter, coagulase-negative staphylococci	——
5		Faucet of doctor's office	Pae、Enterobacter	——
6		Water pipe of doctor's office	Pae、Enterobacter	——
7	surface of objects	Ventilator button 2 of number five	colony-counting< 1 cfu/cm²	Colony counting≤ 5 cfu/cm2
8		White gown of Doctor C	colony-counting< 1 cfu/cm²	Colony counting≤ 5 cfu/cm2
9		Keyboard of Doctor C	colony-counting< 1 cfu/cm²	Colony counting≤ 5 cfu/cm2
10		The door of incubator	colony-counting< 1 cfu/cm²	Colony counting≤ 5 cfu/cm2
11		Injection pump number two	colony-counting< 1 cfu/cm²	Colony counting≤ 5 cfu/cm2
12		Spread cloth of bed 4	colony-counting< 1 cfu/cm²	Colony counting≤ 5 cfu/cm2
13		Stethoscope head of bed 4	colony-counting< 1 cfu/cm²	Colony counting≤ 5 cfu/cm2

Nosocomial Infections

Pae was identified in sputum and skin swipe cultures from the affected children. From environmental monitoring, the same infectious agent was also found in some faucet and water pipe samples from the department. Therefore, based on the "Hospital Infection Diagnostic Standards" which were issued by the Ministry of Health6, the diagnosis from our investigations was exogenous NI, an infection was caused by a variety of pathogens that are not present in the patient. Because Pae, Enterobacter and coagulase negative staphylococcus were cultured from faucets and water pipes, so we think that biofilms were created on the surface of faucets and water pipes. The exogenous NIs was associated with biofilms.

The duration from the beginning of the investigation to implementation of the test results lasted seven days. So far, no new cases had been detected.

DISCUSSION

This is an outbreak report of Pae in neonatal units，Pae is a virulent pathogen. The infectious agent generally exists in humid environments, even on normal skins, and in intestinal and respiratory tracts. Nevertheless, the bacteria are one of the common opportunistic pathogens in clinical practice and a common pathogen for NIs[7, 8]. In our outbreaks, the time interval between the onset of the 5 children was approximately one month (9 October to 10 November).

Pae was cultured from the sputum of infected children, and through external environmental monitoring, Pae was cultured from taps and pipe walls in various places such as doctors' office, isolation rooms, wards, etc. Active prevention and control measures were taken, including replacing all taps and water pipes in water storage bays and disinfecting the faucet with 500mg/L chlorine-containing every day; In addition, in order to reduce bacterial colonization, faucets and sinks were disinfected at least twice a day. Disposable sterilized milk bottle and pacifiers were used in the department from then on. Special machines were used for more effective cleaning and for disinfection of all clothing in the department. After the targeted systematic treatment of the infected newborn, they gradually recovered.

In the following two years of monitoring, no bacteria were detected in the tap and pipe wall samples, and no outbreak of infection occurred in the neonatal ward. Therefore, it is inferred that this is a nosocomial outbreak of multiple strains of Pa from a presumed water source, and was related to formation of biofilms in faucets and water pipes. These data allowed us to rule out our cases as an outbreak of endogenous hospital infection but as exogenous NIs. But more research is needed to determine the strength of the link between water sources and outbreaks.

Between the case and control groups, our data indicate that the case group showed significantly more infection-related features of inpatient days, number of antibiotics used, days of antibiotic used, days of PICC, days of gastric tube, which is consistent with reported results[9, 10].

Our observations indicate that our pre-determined prevention and control protocols were highly effective in preventing further infections among neonates. In addition, a report recommended an extension of active surveillance protocol to those with very low birth weights (VLBW, <1500 g) in the Neonatal Intensive Care Unit11. Additional hygiene activities may include additional contact precautions, such as discontinuation of “kangaroo care” （Kangaroo care is defined as skin-to-skin contact between mother and baby with frequent and exclusive or nearly exclusive breast-feeding and early discharge from hospital.） and cohorting[12-16].

The outbreak of NIs occurred in our neonatal clinic which could have caused wide-spread infections and serious consequences, especially during the global COVID pandemic. Although 5 cases of the infection were still too many, our predetermined protocols and the dedicated effort from many personnel were essential in successfully containing the outbreak and preventing further infections within a few days. The experience allowed us to implement additional and dedicated effort to prevent future problems, especially in maintaining excellent hygiene on water supplies.

Our successful effort is consistent with recommendations from a recent review which emphasized that “successful prevention efforts have focused on implementing evidence-based practices while eliminating outdated strategies”[17]. Nosocomial infections outbreaks can be reduced through the practice of hand hygiene, breastfeeding, antibiotics management, and less invasive procedures. Another report indicates that the use of single rooms for

neonatal patients did not significantly reduced NIs[18]. Unwavering adherence to hand hygiene practices in single rooms may have further diminished the impact of infection. Although the statement is useful, our experience indicates that patients with suspected NIs should be immediately separated from the non-infected ones until the infection became manageable. And this mainly to interrupt the transmission of pathogenic organisms and prevent NIs is to hospitalize newborn in single rooms, facilitating better isolation from hospital-borne infectious agents and proper execution of standard infection-control measures. Our infected patients had the lowest weighs among our patients. This is consistent with a report which indicates that incidences of NIs in intensive care units showed a decreasing trend from the lowest to the highest birth weight classes[19]. Our report provides additional emphasis that vigorous and dedicated efforts were essential in identifying the source of the infection and in controlling the outbreak[20]. Our effort further identified new protocols which were used to prevent further infections.

CONCLUSION

For the case group, their antibiotic application (type and duration of treatment), length of hospital stay, PICC catheterization time and gastric tube in-dwelling time were significantly higher than those in the control group. Identifying the risk factors for prevention of neonatal infection played an important role in the prognosis of patients.

The infection was most likely caused by colonization of Pae in faucets within the department. In addition, sputum culture results from the affected children were positive for the infectious agent. Therefore, outbreaks of endogenous NIs were excluded and exogenous NIs were concluded.

ABBREVIATIONS

NIs: Nosocomial infections; PICC: Peripherally Inserted Central Catheter; BPD: bronchopulmonary dysplasia; COVID: Corona Virus Disease; NICU: Neonatal Intensive Care Unit; VLBW: very low birth weight.

DECLARATIONS

Acknowledgements

We would like to thank the dedicated support from the hospital leaders, the neonatology colleagues, the microbiology laboratory colleagues, the logistics staff, as well as the relatives of the patients.

Fundings

Financial support for this investigation came from hospital funds of the Xiangtan Central Hospital.

Availability of Data and Materials

Any other datasets used and analyzed during the current study available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The samples involved in the study were all sputum and blood samples that needed to be tested during the treatment, and informed consent to participate was obtained from the patients' legal guardians, the experimental protocols were approved by Xiangtan Central Hospital Ethics Committee.

All experiments and all methods in my research were performed in accordance with relevant guidelines and regulations.

The research had obtained consent from all their legal guardians of the neonates.

Competing Interests

The authors declare that they have no conflict of interest.

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