Research Article

Analysis of Anti-Infective Treatment of 9 Neonates with Raoultella ornithinolytica Sepsis

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1.Introduction

In 1989, Sekowska [1] first proposed that Raoule ornithinolytica was an aerobic, amotile, and encapsulated opportunistic pathogen. Raoulella ornithinolytica was first classified as Klebsiella in the 1980s, but was reclassified as Klebsiella in 2001 because 16SrRNA and rpoB gene analysis showed that it was not consistent with Klebsiella [2]. In 2009, Morais et al. [3] reported cases of human infection with Raoulia ornithinolytica. In recent years, the infection of L. ornithine-releasing bacteria is mostly reported in adults, the infection cases in children are less reported, and the infection cases in neonates are even less reported. [4–7]. In order to explore the clinical features and anti-infective treatment plan of neonatal Raul Ornithinolytica sepsis, 9 cases of neonatal Raul Ornithinolytica sepsis in our hospital were retrospectively analyzed.

2. Objects and Methods

2.1. Research Objects. The subjects of this study were children diagnosed with Raoultia ornithine septicemia in the department of neonatology of our hospital from July 2020 to December 2021.

The diagnostic criteria were positive blood bacterial culture, clinical symptoms and signs of bacterial infection, and abnormal laboratory test results (blood routine, C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6) and other infection indicators) [8].

2.2. Research Methods. In this study, a retrospective analysis was performed. Electronic medical records were consulted to record children’s age, gender, maternal and pregnancy status, clinical manifestations, medication history, hospitalization time, hospitalization diagnosis, previous diseases, laboratory tests, auxiliary examinations, treatment, medication status, statistical analysis of the data, and prognosis.

3. Results

3.1. Basic Information. From July 2020 to December 2021, a total of 9 cases of Raoulia ornithinolyticum sepsis were diagnosed in the department of neonatology of our hospital, from 3 neonatal wards, including 2 cases in the NICU ward,
3 cases in the surgical ward, and 4 cases in the general ward. There were 7 boys and 2 girls; only 1 was a full-term neonate (37 weeks of gestation), and the remaining 8 were premature infants, the basic situation of children is shown in Table 1.

Respiratory patterns before infection occurred in 9 patients: case 6 was ventilated by using a noninvasive ventilator, the case 4 was given high-flow oxygen, in case 8 was given oxygen by nasal cannula, and the remaining cases did not need oxygen therapy. She use of antibiotics before infection occurred in 9 children: 3 cases did not use antibiotics; the remaining 6 cases all using broad-spectrum antibiotics, including cefoperazone-sulbactam, meropenem, vancomycin, imipenem, cilastatin sodium, and linezolid from birth to the time of the infection and other antibiotics. She other 9 children all required intravenous nutrition; cases 1 and 6 had PICC intubation.

3.2. Blood Routine and Infection Index Monitoring. All the 9 patients had at least one or more abnormal indicators, and all the children had reduced platelets. In case 7, IL-6 was significantly elevated under normal conditions of other indicators. With effective anti-infective treatment, the levels of CRP and PCT in 7 children returned to normal, and the platelet count also gradually returned to normal. However, in case 4 and case 7, the inflammatory indicators did not decrease significantly or were at a continuous high value, and the platelet count gradually decreased or did not return to normal, as shown in Table 2.

3.3. Clinical Features. Among the 9 children with Raoultia ornithine solution sepsis, 7 had intestinal diseases, including 2 intestinal malformations and 5 neonatal necrotizing enterocolitis (NEC), of which 4 were had a history of intestinal surgery before Raoultia acidic infection. Among the other 9 cases, 2 cases had PICC catheter-related bloodstream infection, 2 cases had abnormal cerebrospinal fluid results and intracranial infection was considered, and 4 cases had different degrees of infection complications. In terms of clinical manifestations, 8 children had fever, of which 7 children showed repeated fever, and the remaining children showed changes in breathing, blood oxygen, and reaction. The length of hospital stay at the time of infection varies from 4 to 50 days, as shown in Table 3. In addition, after the occurrence of sepsis, 4 patients required invasive tracheal intubation for respiratory support, and 4 patients required oxygen therapy.

3.4. Drug Susceptibility Results. 14 strains were cocultured from 9 neonates with Raoultia ornithine solution sepsis, 11 strains were carbapenem-resistant strains, of which 6 strains

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Table 1: Basic information of children with Raoultia ornithine solution sepsis.

| Case | Gender | Gestational week (W) | Cause of premature birth | Cesarean section | Birth weight (kg) | History of suffocation | Whether it is a twin or multiple birth | Is it a test tube baby | Age at admission (d) | Maternal pregnancy history |
|------|--------|----------------------|--------------------------|------------------|------------------|-----------------------|--------------------------------------|------------------------|------------------------|--------------------------|
| 1    | Male   | 30 + 1               | Labor initiation         | Yes              | 1.4              | Yes                   | No                                   | No                     | No                     | 80                       | G2P2, pregnancy-induced hypertension |
| 2    | Female | 27                   | Onset of labor, massive bleeding from placenta previa, and premature rupture of membranes | Yes              | 0.9              | Yes                   | No                                   | No                     | No                     | 68                       | G5P2, hypothyroidism, GDM |
| 3    | Male   | 32 + 6               | Premature rupture of membranes | No              | 2.7              | No                    | No                                   | No                     | No                     | 3                        |                             |
| 4    | Female | 28 + 2               | Premature rupture of membranes | No              | 0.9              | No                    | Twins                               | Yes                    | 84                     | G1P2                     |
| 5    | Male   | 35 + 2               | Placental abruption      | Yes              | 2.4              | No                    | No                                   | Yes                    | <1 (2 h)               | G5P1                     |
| 6    | Male   | 36 + 1               | Labor initiation         | No              | 3.3              | No                    | No                                   | No                     | No                     | 3                        | G2P2                     |
| 7    | Male   | 37                   | Maternal cervical insufficiency and premature rupture of membranes | No              | 2.4              | Unknown               | No                                   | No                     | 15                     | G2P2                     |
| 8    | Male   | 28 + 6               | Onset of labor and premature rupture of membranes | Yes              | 1.45             | No                    | Triplets                            | No                     | 31                     | G5P4                     |
| 9    | Male   | 33 + 3               | Onset of labor and premature rupture of membranes | No              | 2.1              | Yes                   | No                                   | No                     | <1 (6 h)               | G6P2                     |
were resistant to levofloxacin, tigecycline, amikacin, and Compound sulfamethoxazole. 5 strains were only sensitive to tigecycline. The remaining 3 strains were sensitive strains, as shown in Table 4.

3.5. Anti-Infective Treatment and Outcome. Cases 1–6 are children with carbapenem-resistant bacteria infection. Among them, cases 1–3 were selected according to drug susceptibility to two sensitive drugs: the infection was
effectively controlled by levofloxacin combined with amikacin treatment. In cases 5 and 6, the infection was also effectively controlled by removing the PICC catheter, increasing the dose of carbapenem, and prolonging the infusion time. Case 4 died of infection. Cases 7–9 were infected with susceptible strains, and cases 8 and 9 were effectively controlled by selecting sensitive drugs. In case 7, although a sensitive drug was selected for treatment, the effect was not good, and the parents of the child requested to be discharged from the hospital, as shown in Table 5.

Table 3: Clinical characteristics of 9 neonates with Raoulia.

| Cases | Primary disease                                      | Surgery situation                                      | Number of days of surgery at the time of infection | Days in the hospital at the time of infection | Bacterial identification | Clinical manifestations                      | Whether combined with intracranial infection | Infection complications       |
|-------|------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------|---------------------------------------------|---------------------------|-----------------------------------------------|--------------------------------------------|-------------------------------|
| 1     | Ileal scarring strictures after NEC and premature infants | Adhesion bowel release, stricture bowel, and ileocecal resection | 8                                                  | 19                                          | Blood and PICC catheter tip | Fever, shortness of breath, and nasal flaring | No                                        | Liver damage                  |
| 2     | NEC, BPD, premature baby                             | No                                                     | —                                                 | 7                                           | Blood                      | Decreased blood oxygen and heart rate          | No                                        | DIC                           |
| 3     | Congenital jejunal atresia (diaphragmatic type), enteric nerve dysplasia, and premature infants | Enteroplasty                                           | 2                                                  | 6                                           | Blood                      | Fever, poor response, frequent apnea, and decreased blood oxygen | No                                        | Kidney damage                 |
| 4     | Premature infants and chronic lung disease           | No                                                     | —                                                 | 50                                          | Blood                      | Fever, poor mental response, visible markings all over the body, and vomiting of white mucus-like fluid | Yes                                       | Septic shock, multiple organ dysfunction: Liver, kidney, myocardial damage, abnormal coagulation function, and ascites |
| 5     | Necrotizing enterocolitis in premature infants and neonates | No                                                     | —                                                 | 7                                           | Blood                      | Fever                                        | Yes                                       | No                            |
| 6     | Congenital malrotation with midgut volvulus and intestinal necrosis and left testicular torsion with necrosis | Necrotic bowel resection                              | 31                                                | 32                                          | Blood and PICC lateral blood | Fever and slightly poor mental response        | No                                        | No                            |
| 7     | Neonatal necrotizing enterocolitis                   | No                                                     | —                                                 | 4                                           | Blood                      | Repeated fever for 9 days                     | No                                        | No                            |
| 8     | Neonatal necrotizing enterocolitis, premature infants, and BPD | Jejunostomy                                          | 18                                                | 19                                          | Blood                      | Fever and occasional transient oxygen desaturation | No                                        | No                            |
| 9     | Aspiration pneumonia and premature infants           | No                                                     | —                                                 | 27                                          | Blood                      | Fever with shallow and irregular breathing     | No                                        | No                            |

Evidence-Based Complementary and Alternative Medicine
Table 4: Statistics of drug susceptibility results of 9 cases of neonatal Raoulia ornithinolytica sepsis.

| Cases | Specimen     | Positive report time (h) | Amoxicillin-clavulanate potassium | Cefepime | Cefoperazone-sulbactam | Cefoxitin | Ceftazidime | Ceftriaxone | Imipenem | Levofloxacin | Piperacillin-tazobactam sodium | Tigecycline | Amikacin | Cotrimoxazole |
|-------|--------------|--------------------------|-----------------------------------|-----------|-------------------------|-----------|--------------|-------------|-----------|--------------|--------------------------------|-------------|-----------|--------------|
| 1     | Blood        | 9                        | R                                  | R         | R                       | R         | R            | R           | R         | S            | S                               | S           | S         | S            |
| 1     | PICC catheter tip | —                        | R                                  | R         | R                       | R         | R            | R           | R         | S            | S                               | S           | S         | S            |
| 2     | Blood        | 15                       | R                                  | R         | R                       | R         | R            | R           | R         | S            | S                               | S           | S         | S            |
| 3     | Blood        | 16                       | R                                  | R         | R                       | R         | R            | R           | R         | S            | S                               | S           | S         | S            |
| 4     | Blood        | 12                       | R                                  | R         | R                       | R         | R            | R           | R         | S            | S                               | S           | S         | S            |
| 5     | Blood        | 17                       | R                                  | R         | R                       | R         | R            | R           | R         | S            | S                               | S           | S         | S            |
| 6     | Blood        | 12                       | R                                  | R         | R                       | R         | R            | R           | R         | R            | S                               | S           | S         | S            |
| 7     | Blood        | 13                       | S                                  | S         | S                       | S         | S            | S           | S         | S            | S                               | S           | S         | S            |
| 8     | Blood        | 15                       | S                                  | S         | S                       | S         | S            | S           | S         | S            | S                               | S           | S         | S            |
| 9     | Blood        | 13                       | S                                  | S         | S                       | S         | S            | S           | S         | S            | S                               | S           | S         | S            |
Raoultia ornithinolytica is an aerobic, nonmotile, rod-shaped Gram-negative bacterium classified as Enterobacteriaceae of the genus Raoultella. This genus of bacteria also includes cytopathic Raoulia and Raoulia Tulsa. Raoultia is widely present in water, plants, soil and other environments, and mostly colonizes the digestive tract and upper respiratory tract in the human body, and is an opportunistic pathogen [9]. Invasive human infection of Raoulella ornitholyticus is still rare. In recent years, the reports of Raoulella ornitholyticus infection are more common in adults, and the reports of children infection, especially neonatal infection, are relatively rare [10]. Recently, Yaşar et al. [11] reported 14 cases of children infected with Raoulella ornithine, including 5 clinical cases, 3 of which were newborns, including 2 premature infants, and the results showed that all of them were bloodstream infections. Of the 9 infants enrolled in this study, 8 were premature infants. It shows that in the neonatal population, premature infants are at high risk of infection by Raoulia ornithine. However, it is worth noting that, in terms of systemic manifestations, 8 children had fever, suggesting that fever may be one of the clinical features of neonatal Raoultia ornithinolytica infection. In addition to close observation of clinical symptoms in children, early recognition of infection clinically can also be facilitated by assessing risk factors for infection in children and monitoring routine blood tests and infection markers [14,15]. The combination of IL-6, PCT, and CRP is used to continuously and dynamically monitor high-risk groups of sepsis, which is of great significance for early detection and early treatment. Among them, IL-6 is the first elevated serum marker, and it often occurs when elevations occur before overt clinical symptoms [16,17]. For example, the IL-6 of the child in case 7 was significantly elevated before clinical symptoms appeared and other infection markers were normal. Therefore, for children at high risk of infection, dynamic monitoring of CRP and PCT combined with IL-6 can help us identify, thereby winning an earlier treatment opportunity for anti-infective treatment. In addition, after initiating anti-infective treatment, dynamic monitoring of these infection markers will help us evaluate the efficacy and adjust the treatment plan in time. Maseda et al. [18] reported that PCT levels can be rapidly reduced after infection control, and

| Cases | Use anti-infective drugs and time of use (d) | Other drug treatments | Treatment outcome |
|-------|---------------------------------------------|-----------------------|------------------|
| 1     | Meropenem (1d), levofloxacin + amikacin (14 d) | Removal of PICC tube, immunoglobulin, platelets, furosemide, packed red blood cells, frozen plasma, and human albumin | Cure |
| 2     | Meropenem (1d), levofloxacin + amikacin (14 d) | Frozen plasma, furosemide, platelets, immunoglobulin, methylphenidate, packed red blood cells, and human serum albumin | Cure |
| 3     | Meropenem (2d), levofloxacin + amikacin + (14 d) | Furosemide, human albumin, dopamine, platelets, and packed red blood cells | Cure |
| 4     | Meropenem + amikacin (3d) | Immune globulin, platelets, packed red blood cells, frozen plasma, and furosemide | Death |
| 5     | Meropenem (40 mg/kg/time Q8H extended infusion time to 3 h, 21 d) | | Cure |
| 6     | Imipenem cilastatin sodium (25 mg/kg/time Q6H prolonged infusion time 2 h, 14 d) | Remove the PICC tube | Cure |
| 7     | Meropenem (40 mg/kg/time Q8H 8 d) | Human immunoglobulin, furosemide, leukocyte-depleted suspended red blood cells, and platelets | Unknown (request for discharge) |
| 8     | Meropenem (14 d) | No | Cure |
| 9     | Meropenem + amikacin (14 d) | No | Cure |
septic patients can be reduced by 50% within 24 hours after effective treatment.

Due to its special physiological characteristics and the toxic and side effects of drugs, neonates have very few drugs to choose from when facing CRE-resistant infection, which is another major difficulty in neonatal anti-infection treatment. In this study, 14 strains of Raoultia ornithinolytica isolated in this paper were highly resistant to the third and fourth generation cephalosporins, enzyme inhibitor compound preparations, and carbapenems. Eleven of them were carbapenem-resistant Enterobacteriaceae (CRE), which were only sensitive to aminoglycosides, quinolones, and tigecycline. In terms of anti-infective treatment, an anti-infective treatment plan should be formulated based on the basic situation of the child, the severity of infection, and drug susceptibility to achieve individualized treatment. For example, cases 1, 2, and 3 in this article showed that the PCT did not decrease significantly after 24–48 hours of meropenem treatment, suggesting that the curative effect may be poor. By changing the treatment plan in time, the infection of the three children was controlled. At the same time, case 5 had a large gestational age and birth weight, did not need oxygen therapy, and only had fever in clinical manifestations without other infection complications. Drug sensitivity results showed that the MIC value of imipenem and cilastatin sodium was 8μg/ml. According to relevant literature reports [19], in the treatment of CRE infection, when carbapenem MIC is 4–16μg/ml in the treatment of CRE infection, carbapenem antibiotics should be used to increase the frequency or dose and prolong the infusion time. When carbapenems MIC > 16 dou g/ml, carbapenem antibiotics should be avoided. Taking meropenem into consideration, we chose meropenem for anti-infective treatment, increasing the drug dose to 40 mg/kg/time Q8H, optimizing the dosing schedule, and extending the infusion time of meropenem to 3 hours. In the end, the infection of the child was well controlled. In addition, case 6 was a PICC catheter-related infection. Through timely removal of the PICC catheter, increasing the dose of imipenem and cilastatin sodium (100 mg/kg/day, Q6H), and prolonging the drug infusion time to 2 hours, the child also achieved a good anti-infective treatment effect. In case 1, case 2, and case 3, meropenem was selected at the beginning, and then the anti-infective treatment regimen (levofloxacin and amikacin combined therapy) was adjusted promptly in combination with drug sensitivity. After 24–48 hours of treatment, the therapeutic effect was evaluated by strict monitoring of infection indicators. The results showed that all the three children achieved a good therapeutic effect, and no adverse drug reactions were detected. We know that aminoglycosides have ear and kidney toxicity, fluoroquinolones may cause joint and cartilage damage, and tigecycline may cause untoward reactions such as permanent tooth stain, enamel dysplasia, and bone growth inhibition, all of which limit the use of these drugs in the pediatric population [20]. However, when faced with a fatal infection, it should be used with caution after fully weighing the benefits and risks, and the adverse drug reactions should be closely monitored. Regrettably, in case 4, the child eventually developed septic shock and multiple organ dysfunction and died. The child was born very early, with an ultra-low birth weight, and had a variety of underlying diseases such as long-term need for oxygen therapy and extrauterine growth retardation. In addition, the child received multiple antibiotics from birth until infection. For such children, a nosocomial infection is fatal, so hand hygiene, rational use of antibiotics, protective isolation, and other nosocomial infection prevention and control measures are more important.

In conclusion, Raoultella ornithinolytica sepsis in neonates occurred mainly through nosocomial infections and carbapenem-resistant strains were more common. Preterm birth, intestinal disease, and a history of surgery increase the risk of infection; for carbapenem-resistant Raoultella ornithinolytica infection, anti-infection treatment regimens should be formulated based on the basic situation, infection severity, and drug sensitivity of the children, so as to achieve individualized treatment. In addition, dynamic monitoring of infection markers has an important clinical significance for early identification of infection, evaluation of a curative effect, and timely adjustment of anti-infection treatment.

Data Availability

The raw data supporting the conclusion of this article will be available by the authors without undue reservation.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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