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AEROSOLIZED VANCOMYCIN FOR TREATMENT OF AIRWAY COLONIZATION BY MITHICILLIN-RESISTANT STAPHYLOCCUS AUREUS

Recent reports have indicated that aerosolized antibiotics are effective against organisms causing persistent respiratory infections in patients with chronic respiratory diseases while avoiding the toxicity of systemic therapy. Numerous studies in adults have resulted in conflicting information regarding the efficacy of these agents.

We report the use of aerosolized vancomycin hydrochloride for the eradication of tracheal colonization by methicillin-resistant Staphylococcus aureus (MRSA) in a chronically ventilated child with bronchopulmonary dysplasia.

Case. PRF is a 3½-year-old (11-kg) ventilator-dependent white female born at 26 weeks gestation with a birth weight of 610 g. The pregnancy was complicated by preclampsia. She was intubated at birth and remained on mechanical ventilation for the first 6 months of life. Complications of prematurity included severe bronchopulmonary dysplasia, retinopathy of prematurity and hearing loss.

Because of growth failure a decision was made to provide long term ventilatory support in an effort to deliver sufficient calories to achieve growth rather than fuel respiratory work and to avoid respiratory failure as a result of the increased production of CO₂ from the increased carbohydrate intake. A tracheostomy was performed at 20 months of age to provide airway access on a long term basis.

The course of her ventilator dependency was complicated by recurrent pulmonary decompensation requiring increased ventilator support. These episodes were primarily associated with heavy growth of bacteria from the tracheal secretions, a marked increase in the volume and in the number of leukocytes in her tracheal secretions with subsequent bronchospasm or pneumonia.

After tracheostomy she was colonized with MRSA on 4 separate occasions. Successful eradication was accomplished with administration of vancomycin systemically, rifampin orally and gentamicin topically to her tracheostomy stoma.

On May 2, 1989, she became colonized with MRSA that was susceptible only to vancomycin and tetracycline. To avoid systemic side effects of parenteral vancomycin administration, it was decided to attempt eradication of MRSA with aerosolized vancomycin treatment. Each 500-mg vial of the intravenous solution of vancomycin was reconstituted with 5 ml of 0.95% sodium chloride injection (solution pH 3.53) of which 40 mg were delivered three times daily via nebulizer (Dart™ high flow nebulizer; Model 049663) with her scheduled bronchodilator (albuterol) therapy. These medications were aerosolized through the tracheostomy in line with the ventilator circuit. Daily tracheal aspirates were cultured to monitor the results of the therapy. Cultures became negative for MRSA after vancomycin aerosol therapy for 24 hours. Her clinical condition improved with an appreciable decrease in the volume and consistency of her tracheal secretions and in her degree of respiratory distress. After 72 hours of therapy and three consecutive negative cultures the aerosols were discontinued. Tracheal aspirate cultures were followed daily thereafter for 3 days to determine whether the antibiotic merely suppressed culture growth and whether resurgence of the organism occurred. She remained MRSA-free for the ensuing 15 days at which time her tracheal aspirate cultures were again positive for MRSA with the same reported susceptibility pattern.

Treatment was restarted with the addition of vancomycin drops (60 mg/ml of the intravenous solution diluted with 0.97% sodium chloride injection; one drop in each nostril four times a day) delivered intranasally to the same vancomycin aerosol regimen. After therapy for 3 days tracheal and nasopharyngeal cultures were negative for MRSA. After 3 consecutive days of negative cultures, the treatment was discontinued. Nasopharyngeal and tracheal cultures plated weekly for the next 4 weeks were negative for MRSA and she has been free of colonization for the past 4 months.

Discussion. Nosocomial colonization with methicillin-resistant S. aureus is a well-recognized epidemiologic problem in hospitalized patients of all ages. Intravenously administered vancomycin has become the mainstay of therapy to eradicate this organism. In our patient aerosolized vancomycin appeared to be an effective means of therapy to eradicate MRSA colonization of the airway. Antibiotics administered by this method would theoretically be effective only in the treatment of organisms that can be reached on the surface of the respiratory tract. An ideal locally administered antibiotic should be poorly absorbed from the mucus layer, have a potent topical/local effect and not be irritating or allergic. This would avoid the systemic side effects of parenteral therapy and the need for intravenous access. Monitoring of antibiotic concentrations could potentially be avoided based on studies showing insignificant accumulation in the systemic circulation of aerosolized antibiotics delivered via a tracheostomy tube. However, data are needed in a variety of patients, including those with inflamed respiratory mucosa and renal disease which might increase absorption and decrease clearance of vancomycin, respectively.

Bronchospasm is a well-recognized side effect of aerosolized antibiotics. In our patient aerosolized vancomycin therapy was well-tolerated when given via high flow nebulizer in combination with a bronchodilator to a patient with known reactive airways.

Although the cost of vancomycin used for the aerosolized therapy is less on a per day basis (one 500-mg vial/4 days vs. one vial/day if given 40 mg/kg/day by the intravenous route) than for parenteral therapy, the total charge per day is actually greater in our institution as a result of the cost of administering treatment. Until the necessary length of treatment and dosage schedule is established, the cost effectiveness of this form of therapy will not be precisely known.

This case suggests that treatment of MRSA colonization with aerosolized vancomycin may eradicate the organism. However, this finding should be validated by a blinded randomized controlled trial.

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 CITROBACTER DIVERSUS LUNG ABSCESS IN A PRETERM INFANT

Lung abscess is a rare entity in children and only a few cases have been described in the neonatal period. Lung abscesses in the neononate present special problems, especially related to etiology, diagnosis and treatment.1-7 We describe a preterm infant who developed a lung abscess caused by Citrobacter diversus in the 4th week of life. To the best of our knowledge this is the first report of a lung abscess in a preterm infant and the first reported lung abscess caused by C. diversus in infants and children.

Case report. The patient was a preterm boy, an estimated 30 weeks of gestation, with a birth weight of 1820 g. He was the first of dinyotic twins born to young, unrelated parents. Two previous children were healthy. The pregnancy and labor were uneventful.

The patient, born by cesarean section, had an Apgar score of 8 at 1 and 5 minutes. The second twin died during the first day of life from respiratory failure and disseminated intravascular coagulation. Blood, urine, cerebrospinal fluid and peripheral cultures were all sterile.

Immediately after birth our patient developed respiratory distress as a result of hyaline membrane disease and mechanical ventilation was needed. His course was complicated by a left pneumothorax on the second day of life which was drained. He was extubated on Day 5 and the thoracic drain was removed on Day 7.

Sepsis workup was performed on the first day of life and he was empirically treated with ampicillin and gentamicin. The blood, urine, cerebrospinal fluid and peripheral cultures were sterile. Chest roentgenograms were normal at the end of the second week of life.

On the 25th day of life the infant developed respiratory failure with hypotension. On physical examination he appeared pale with cutis marmorata and had decreased peripheral perfusion. The white blood cell count was 38,000/mm³ with many immature forms. The platelet count was 80,000/mm³ and his prothrombin time was prolonged. On chest roentgenogram a right lower lobe density was noted as well as a minimal right pleural effusion. Cefotaxime and tobramycin were administered intravenously.

On the 3rd day of treatment chest roentgenograms revealed a cavity that was partially gns-filled located in the center of the right lower lobe consolidation.

C. diversus grew from two blood cultures taken the day before and one culture on the first day of treatment. Blood cultures became sterile on the second day of treatment. Cerebrospinal fluid, tracheal secretion, urine, stool, ear and throat cultures were negative. The pleural effusion was too small to be tapped. Ultrasonographic examination of the head was normal with no evidence of brain abscess.

The organism was susceptible in vitro to aztreonam and tobramycin; therefore the regimen was changed to those two drugs. Clindamycin was also added to treat possible anerobic infection.

Aztreonam and clindamycin were given intravenously for 28 days and the infant was subsequently treated with ceftriaxone intramuscularly and amoxicillin/clavulanate orally for a total antibiotic treatment of 6 weeks.

Bacteriologic surveillance performed in the nursery did not reveal C. diversus in the environment (water, milk and equipment) or in cultures obtained from other premature infants in the unit (blood, stool, and nasopharynx).

It was possible to perform a computerized tomographic scan of the chest during the 3rd week of his illness. At that time the computerized tomographic scan showed a residual segmental infiltrate-consolidation in the posterior segment of the right lower lobe and residual cavity with thick walls.

When the infant was discharged at the age of 2 months the physical examination was normal. At follow-up at the age of 4 and 6 months the patient showed normal development with no respiratory difficulty. Repeated chest radiograms at those times were normal.

Discussion. Lung abscess is a rare entity in children and especially in neonates.1 To our knowledge it has not been reported in premature infants.

Lung abscess may occur as a primary infection with no underlying abnormality in the lung parenchyma or it may be secondary to an underlying lesion such as a cyst or sequestration. A single abscess can occur as a primary event, where it probably represents a single area of suppuration in a pneumatic process, but it is more likely to be associated with a congenital abnormality.

Lung abscesses in the neonatal period is usually caused by Gram-negative bacteria (Escherichia coli, Klebsiella sp.), or Gram-positive ones such as Group B streptococci. In older children the organisms most frequently cultured are Staphylococcus aureus, Group A streptococci and anoerobes.

It must be emphasized that differentiation between pneumatocele, infected pneumatocele and "true" lung abscess can be difficult even at histologic examination as noted by Wallace and Robinson.4 The location, thick walls and the cavity in the right lower lobe of our patient suggested an infective process.

Our patient had a short prodromal illness, with rapid clinical deterioration and leukocytosis with many immature forms. These findings are consistent with the clinical signs reported previously for neonatal lung abscess and differ from those reported in cases of lung abscess in children, by the lack of prolonged prodromal illness, fever and puritic spumin.4,8

C. diversus, a rod-shaped Gram-negative bacterium, is a virulent organism causing necrosis in various tissues by invasion through intact anatomical barriers.6 C. diversus has been reported as a cause of meningitis,8,9 urinary tract infection, osteomyelitis, gastroenteritis,9 endocarditis,9 upper respiratory infection and sepsis.10

The organism was susceptible to Citrobacter involve the respiratory system and the urinary tract. In children sepsis and meningitis are the most important infections. All infants with Citrobacter brain abscess have meningitis, but only about one-third have bacteremia. Among the infants with Citrobacter meningitis more than 75% develop brain abscesses."