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TEACHING FILES (GRAND ROUNDS)

PERSISTENT PSEUDOMONAS AERUGINOSA INFECTION IN A CHILD WITH CYSTIC FIBROSIS – HOW TO MANAGE?

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Clinical Problem

A 6 month old girl was diagnosed to have cystic fibrosis (CF) in 2009 in view of recurrent respiratory tract infections and diarrhea with malnutrition. Sweat chloride conductivity test was positive (75 mmol/L equivalent NaCl). She tested positive for both the alleles of F508 mutation. She was started on pancreatin supplements and vitamins A, D, E and K following which her diarrhea subsided. She was hospitalized for the first time in December 2011. Her sputum cultures subsequently grew Bukholderia cepacia, Streptococcus pneumoniae, Klebsiella pneumoniae and Pseudomonas aeruginosa over the next few months. She was put on tobramycin nebulization along with N-acetyl cysteine nebulization. Her sputum cultures continued to grow Pseudomonas aeruginosa on and off. In December 2013, the P. aeruginosa was resistant to tobramycin and she was treated with oral ciprofloxacin and nebulized Colistin for 6 weeks. She was alright till February 2014 when she was hospitalized with pneumonia and was treated with Amikacin and Ceftazidime for 4 weeks. In view of poor weight gain, a percutaneous endoscopic gastrostomy (PEG) tube insertion was done in April 2014. She continued to have recurrent pneumonias due to P. aeruginosa for which she was on nebulized Colistin and finally succumbed to her disease in February 2018.

How to manage persistent pseudomonas aeruginosa infection in cystic fibrosis?

Discussion

Cystic Fibrosis (CF) is an autosomal recessive disorder found commonly in Caucasians reported even from India. (1,2) The gene for CF is located on the long arm of chromosome 7 and there are more than 300 identified mutations in CF. Delta F508 mutation was identified in 44% of CF alleles in a review of genotypes of south Asian patients, considerably lower than the reported frequency of 66% in the worldwide CF population. (3,4) This disease is characterised by abnormally thick secretions in respiratory, gastrointestinal and reproductive tract and sweat glands. The common presentations are meconium ileum in neonates, recurrent lower respiratory tract infections (Pseudomonas spp pneumonia, bronchiectasis), steatorrhoea, azoospermia, and in late stages hepatobiliary and endocrine pancreatic dysfunctions. (2) Respiratory involvement typically causes persistent productive cough, breathlessness, hyperinflation of lung fields on chest X-ray and pulmonary function tests that are consistent with obstructive disease. Transient infections with pathogenic organisms occur early in life. Staphylococcus aureus and Haemophilus Influenzae colonization is common during early childhood but ultimately Pseudomonas aeruginosa is isolated from CF patients due to impaired clearance directly induced by a defective CFTR gene. (5) Pseudomonas aeruginosa colonization is highly prevalent in the lungs of cystic fibrosis patients and leads to progressive pulmonary function decline and its eradication is particularly challenging. (6,7)

Treatment of CF is focused on maintaining lung function near normal by controlling respiratory infection and clearing airways of mucus, administering nutritional therapy and managing complications. Chest physiotherapy along with bronchodilators, antibiotics, mucolytics, anti-inflammatory treatments, and pancreatic enzyme supplements are commonly used. (8,9) Nebulized tobramycin and Colistin are widely used in treatment of Pseudomonal infection which help slow down growth, maintain lung function, and reduce frequency of pulmonary exacerbations.(10,11) When first detected, Pseudomonal infection is treated with only inhaled tobramycin for 28 days. Inhaled Colistin with oral ciprofloxacin is similar in effect. (6) Aerosolized drugs concentrate in the conducting zone of the lung and systemic administrations concentrate in the respiratory zone, since both are colonized, a combination of systemic and nebulized antibiotics is the most helpful. (10) Liposomal amikacin for inhalation is under development that enhances drug delivery and retention in CF airways via drug incorporation into liposomes, it prolongs off-drug periods and helps manage chronic Pseudomonal lung infections. (11)

To cope with malnutrition and improve age-dependent anthropometrics, the CF Foundation recommends enteral tube feeding for adequate nutrition and growth in individuals unable to consume adequate calories and protein. (7,12) As recent as February 2018, a new drug was approved by the FDA called ivacaftor/tezacaftor. It is a CFTR modulator and was approved for use in

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patients above 12 years of age who have two copied of F508 mutation (F508del). In late-stage clinical trials, people with two copies of F508del mutation showed an improvement in lung function by 4% compared to those taking a placebo. Another novel treatment that is under investigation is ataluren which is currently licensed for use in Duchenne muscular dystrophy patients and is being considered for use in CF patients and a nonsense CFTR gene mutation. In addition a new protease inhibitor has been discovered that prevents activation of epithelial sodium channels in the airways of people with cystic fibrosis and hence has the ability to help in airway hydration and mucus clearance. (13) We could not try any of these agents in our patient as they were unavailable.

Compliance with Ethical Standards

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Conflict of Interest: None

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