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14. Case Reports

388 Detection of a novel CFTR mutation c.122C>G (p.Pro41Arg) in a young cystic fibrosis (CF) patient with recurrent respiratory symptoms

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Background: At present more than 1800 mutations have been described in the CFTR-gene. Several rare mutations are believed to cause mild lung disease and late onset of symptoms. We present a 5 y old Belgian boy heterozygous for an atypical CFTR variant and a novel variant which was never described before.

Case report: A 5 y old boy with recurrent bronchitis and chronic sinusitis was referred to our clinic with repeated abnormal sweat chloride (Cl) (right 70 mEq/L; left 53 mEq/L) and elevated sweat sodium values (right 86 mEq/L; left 62 mEq/L), performed by Gibson and Cooke gauze method. Chest CT scan showed bronchial wall thickening and mucous plugging, without bronchiectasis. He is pancreatic sufficient, without history of pancreatitis. By screening the coding region of CFTR, using sequencing and MLPA (Multiplex Ligation-dependent Probe Amplification), he was shown to be heterozygous for c.224G>A (p.Arg75Gln – legacy name: R75Q) and c.122C>G (p.Pro41Arg), a novel variant which was never described before. Analysis of the parents is ongoing to prove that both variants are on different alleles.

Discussion: R75Q is described as a variant overrepresented in patients with atypical CF, sarcoidosis, COPD and chronic pancreatitis and rather influences bicarbonate conductance than Cl. Our young patient has already respiratory symptoms and abnormal sweat chloride values. To our knowledge CFTR p.Pro41Arg has never been described before and its clinical relevance is not clear. As this boy has signs and symptoms of CF disease in combination with an atypical CFTR mutation, this novel mutation might be involved. However, mutations outside the coding region cannot be excluded.

389 Prolonged *Clostridium difficile* associated diarrhoea in a cystic fibrosis patient precluding suitability for lung transplant: an important issue for patients awaiting transplantation

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A 21 year old man with cystic fibrosis and declining lung function was assessed for suitability for lung transplant. His sputum was culture positive for *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia* and methicillin resistant *Staphylococcus aureus* for which he received multiple courses of broad-spectrum antibiotics including meropenem, ceftazidime, linezolid, tobramycin, teicoplanin and colistin. In the interim he developed *Clostridium difficile* associated diarrhoea (CDAD) which failed to respond to courses of oral metronidazole and oral vancomycin. A course of pulsed oral vancomycin was administered. This resulted in resolution of symptoms but follow up faecal cultures were found to be positive for *Clostridium difficile* and he was deemed not to be a suitable candidate for lung transplantation.

Deaths directly attributable to CDAD have been described in the CF population following transplantation. Outbreaks of CDAD have increased in incidence in healthcare facilities worldwide, in particular linked to the emergence of hyper-virulent strains. The necessity for multiple, prolonged courses of broad-spectrum antimicrobials in CF patients makes them a group which are potentially vulnerable to the development of CDAD.

Further research is urgently required to ascertain the relationship between CDAD and the CF patient. In the interim it is of paramount importance that infection prevention and control standards are implemented and maintained to prevent cross transmission and emergence of new cases of CDAD in the CF population.

390 Efficacy and safety of colistin for inhalation in children 5 years old and younger with cystic fibrosis with *Pseudomonas aeruginosa* infection

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Aim: To estimate the colistin effectiveness and safety for treatment of children 5 years old and younger with cystic fibrosis (CF) and chronic *Pseudomonas aeruginosa* (PA) infection.

Method: There were 10 children 5 m to 4 y 9 m, average 2 y 3 m with CF confirm diagnosis and having PA in sputum. 2 had chronic PA infection and 8 children had first isolate, 4 girls and 6 boys. They were 1 year follow up. The following characteristics were estimated in time of research: the physical development characteristic (weight/height indicator), the rate of exacerbations, examination of sputum (monthly during half year and every 3 months further). The patients with first isolate were taking colistin inhalation during 21 day (1 mln ×2 times/day) + ciprofloxacin therapy (30 mg/kg/24 h), the patients with chronically PA infection colistin inhalation constantly (in the same dose).

Result: We was noted weight/height increasing average 2 kg/7.6 sm during the treatment. There were no exacerbations, the respiratory syndrome of all patients were significantly reduce. During the examination children with first isolate: PA eradication in 6 case of 8; 1 case PA was revealed in repeated sputum test (sputum test was clean after 3 months colistin course); 1 case reducing of PA titre. 2 patients with chronically PA infection had the clean PA sputum test during the colistin treatment, and PA in sputum test after colistin repeat. All patients were taking medicine felt themselves good. Were not observed adverse event.

Conclusion: Equal clinical efficiency and safety of colistin was shown and it can be used by CF patients 5 years old and younger.

391 Temocillin – drug of choice for *Burkholderia cepacia*?

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Two young women with chronic multi-resistant *B. cepacia* colonisation, seen regularly at our centre, have been treated regularly with iv beta-lactam antibacterials + tobramycin due to exacerbations. Both are severely sick with a lung function (FEV1) of around 30% of expected, chronic productive cough and low grade temperature. One is listed for transplant, the other has been transferred for evaluation. On a licence basis, they were treated with the new semi-synthetic beta-lactam antibacterial, temocillin (Negaban) in combination with tobramycin, intravenously. Temocillin has been reported to be very effective against *B. cepacia* exacerbations. Both patients were started at the hospital, but had home iv treatment with pre-filled Homepump devices causing no problems. Both improved clinically with normal temperature and less cough. The lung function did however not improve. Two weeks later the temperature and cough relapsed. With a traditional iv treatment in between, both had a second iv course, again with clinical improvement. Both are now in for their third iv treatment again after a traditional treatment in between. Temocillin intravenously could be the drug of choice for multiresistant *B. cepacia* patients, but more studies and experience are warranted.