Pneumomediastinum and hyponatraemic dehydration as presenting features of cystic fibrosis.

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Dear Editor

Newborn screening for cystic fibrosis (CF) promotes early diagnosis and treatment, leading to a reduction in the number of late diagnoses [1]. This is of benefit to patients but contributes to physicians being less aware of the diverse ways in which unscreened patients present. We report a 12 year old boy who presented with pneumomediastinum and hyponatraemic dehydration, subsequent investigations diagnosed CF. Hyponatraemic dehydration is well-documented as a presenting feature of CF but usually occurs during periods of hot weather or after strenuous exercise, neither were present in this case [2]. Although pneumomediastinum is not uncommon in adults with advanced CF [3] it is very rare in children and has not previously been reported in combination with hyponatraemic dehydration.

A 12 year old boy attended the Emergency department with shortness of breath, neck swelling and chest pain. He had been unwell for one week with coryza, pyrexia and a productive cough. He was dehydrated, tachycardic, tachypnoeic and hypoxic. Blood pressure was normal. He had palpable crepitus on the left side of his neck extending onto his anterior chest wall. Chest wall expansion was equal and his trachea central. On auscultation, there were coarse crackles throughout both lung fields. The only other abnormality was grade III finger clubbing.

Blood investigations confirmed dehydration and identified hyponatraemia, hypokalaemia, hypochloraemia and metabolic alkalosis. A chest radiograph (figure 1A) confirmed subcutaneous emphysema. It also identified pneumomediastinum, hyperinflation, increased bronchovascular markings with bronchial wall thickening, dilation of perihilar airways and scattered nodular densities; there was no
pneumothorax. Oxygen was initially given to treat the hypoxia and then continued to promote “nitrogen washout” and aid pneumomediastinum absorption. He received two 20 ml/kg boluses of 0.9% saline and a dose of oral potassium chloride. Maintenance intravenous (IV) fluids and IV co-amoxiclav were commenced. By Day 2 his electrolyte abnormalities had almost completely normalised and his subcutaneous emphysema was no longer clinically apparent. Intravenous fluids and oxygen were therefore discontinued.

Further discussion revealed that the patient had a one year history of cough, this was mainly dry but he occasionally produced sputum in the morning. There was no shortness of breath or wheeze. He had a good appetite and normal bowel habit. Growth was normal (weight 37.8 kg - 25th percentile and height 155.3 cm - 75th percentile). Due to his cough he had been seen by a Paediatric Respiratory Physician 3 weeks prior to his acute admission. A number of investigations had been booked but most had not yet taken place. His U&E’s from that appointment were normal.

Once clinically stable he was fully investigated. A high resolution CT scan of his chest (figure 1B-E) showed widespread mediastinal air tracking into the supraclavicular fossae, the upper arms and posteriorly around the periscapular regions. No intrapleural air was seen. There was striking bronchial wall thickening, with many of the segmental airways showing mild/moderate cylindrical bronchiectatic dilatation. Peripherally, there was a profuse reticular nodularity and widespread "tree-in-bud" opacities reflecting small airways mucus plugging. A sweat test confirmed cystic fibrosis (chloride 111mmol/L) and he was shown to be homozygous
for the Phe508del cystic fibrosis transmembrane conductance regulator (CFTR) mutation. During flexible bronchoscopy, purulent secretions were seen throughout both lungs. Bronchoalveolar lavage (BAL) cultures only isolated Methicillin-sensitive *Staphylococcus aureus* (MSSA). His IV antibiotics were changed to cefuroxime and flucloxacillin and he was taught airway clearance techniques by a specialised CF physiotherapist. Exocrine pancreas insufficiency was confirmed (faecal elastase <15 µg EL/g) and the serum concentrations of fat soluble vitamins were low: vitamin A 0.37 umol/L, 25-OH-cholecalciferol 22.1 nmol/L and vitamin E 6.4 umol/L. The patient was commenced on pancreatic enzyme replacement therapy and vitamin supplementation. The patient was discharged after a two week course of IV antibiotics.

The patient’s 6 year old sister was born 5 months prior to the CF newborn screening programme being implemented across the UK. She had a history of a productive cough and intermittent greasy stools. The day after her brother was diagnosed she attended the hospital for a sweat test which confirmed CF (chloride 102mmol/L). A high resolution CT scan of her chest showed mucus plugging but no bronchiectasis and BAL cultures were positive for a MSSA and *Haemophilus influenza*. She received 2 weeks of IV cefuroxime and flucloxacillin. The same CFTR mutations were identified as was exocrine pancreas insufficiency. Pancreatic enzyme replacement therapy and vitamin supplements were commenced. The simultaneous, late diagnosis of CF in 2 siblings was clearly devastating news for the whole family. Significant care was taken in ensuring that the news was broken to the parents and the children in the most appropriate way. This process was led by the CF consultant with support from the specialist CF nurse and psychologist.
This is the first reported case of CF presenting in a child with pneumomediastinum and hyponatraemic dehydration, it highlights variable ways in which unscreened patients can present. Patients diagnosed late are known to do worse than patients of the same age and CFTR mutation, diagnosed by newborn screening [4]. In addition there are significant psychological consequences. The observation that a child homozygous for the Phe508del CFTR mutation and pancreatic insufficient can reach 12 years of age with relatively normal growth and few respiratory symptoms confirms that other factors can modify disease severity. These factors are likely to include diet, physical activity and polymorphisms in genes other than the CFTR gene.

The association between CF and hyponatraemic dehydration was first recognised during a New York heat wave in 1948 [5] and led to the identification of elevated concentrations of sodium and chloride in the sweat of patients with CF [6]. There has subsequently been multiple reports of patients with CF presenting with hyponatraemic dehydration associated with hypochloraemia and metabolic alkalosis [2, 7]. Virtually all these cases have occurred during periods of hot weather but the average temperature prior to this presentation was 5°C and therefore was not the precipitant of his hyponatraemic dehydration. We hypothesise that the respiratory exacerbation and specifically the associated high pyrexia contributed to excess sweating and therefore electrolyte loss that was seen in our patient. Urinary electrolytes taken at presentation (Na <10 mmol/L, K 0 mmol/L) confirm that the losses were not renal.
Spontaneous pneumomediastinum is defined as air in the mediastinum that appears in the absence of trauma. It is caused by alveolar rupture and dissection of air along the bronchovascular sheath into the mediastinum and hilum. A trigger factor such as the Valsalva manoeuvre or forceful coughing may be identified [8]. Whilst spontaneous pneumomediastinum is not uncommon in adults with advanced CF it is extremely rare in children. There are only 2 previous case reports; one in a 2 year old girl in whom spontaneous pneumomediastinum was the presenting feature of CF [9] and the other in a 10 year old boy with CF in whom it was the presenting feature of ABPA [10]. Neither however, had an associated electrolyte imbalance. We hypothesise that our patient’s pneumomediastinum was caused by excess coughing due to the infective exacerbation.

In summary this is the first reported case of pneumomediastinum and hyponatraemic dehydration as presenting features of CF. In addition this case has highlighted the variable ways in which unscreened patients can present with CF and reminds us that despite the widespread introduction of newborn screening programmes, physicians should continue to consider CF as a possible diagnosis in such patients.
References:


Figure 1.
A: Chest radiograph showing extensive surgical emphysema, pneumomediastinum, bronchial wall thickening and scattered nodular densities. B-E: Computerised Tomography axial images of the chest on lung window settings. Demonstrating extensive surgical emphysema within the soft tissues of the thorax at the thoracic outlet (B), at the superior mediastinal level there is left anterior chest wall subcutaneous emphysema and extensive mediastinal air (C). Within the lungs, there is bronchiectasis, bronchial wall thickening, tree in bud opacities and centilobular nodules, this is most notable below the level of the hila (D&E). Consolidation posteriorly in right lower lobe (E).

Figure 1A
Figure 1B
Figure 1E