CASE BASED DISCUSSIONS

Massive haemoptysis and ventilatory failure in pregnancy

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Ivan Tang, Core Medical Trainee (IT): A 36-year-old pregnant woman presented to her local hospital with massive haemoptysis. At the time of admission, she was at 34 weeks of gestation with her first pregnancy. She reported a 6-week history of breathlessness, productive cough and fatigue. On the day of presentation she had expectorated two cupfuls of fresh red blood.

The patient had been diagnosed with bronchiectasis in her teens in her native Lithuania before moving to the United Kingdom 15 years earlier. At the age of 21 years, she had an episode of pleural infection requiring thoracotomy and rib resection.

The patient's body mass index (BMI) at booking was 16 kg/m^2. Fetal nuchal translucency and a fetal morphology ultrasound scan were normal. Fetal abdominal circumference at 28 weeks was on the fifth centile.

Initial management included supplemental oxygen and intravenous antibiotic therapy with piperacillin–tazobactam to ensure coverage against potential *Pseudomonas aeruginosa* infection. A CT pulmonary angiogram showed severe bronchiectasis with a large cavity and consolidation in the left upper lobe (see figure 1). There was evidence of bronchial artery hypertrophy bilaterally. Transfer to our hospital as the regional tertiary centre for both respiratory and obstetric medicine was arranged.

William G Flight, Consultant Respiratory Physician (WGF): Bronchiectasis is recognised as a frequent cause of massive haemoptysis, accounting for up to two-thirds of episodes in published case series.[1] The source of haemoptysis in bronchiectasis is usually from the bronchial arterial circulation.[1]

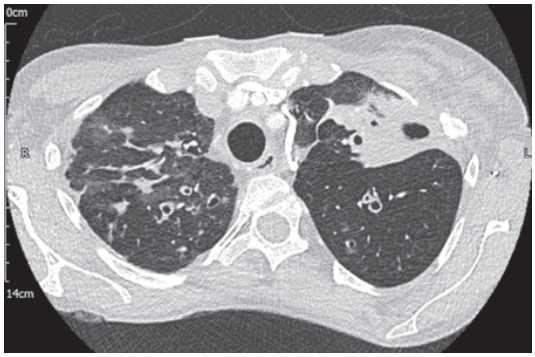

Figure 1 CT pulmonary angiogram showing severe bilateral bronchiectasis with consolidation and a large left upper lobe cavity.

Bronchial artery hypertrophy can be demonstrated through a contrast-enhanced CT scan or conventional angiography, whereas bronchoscopy is only rarely helpful in identifying the site of bleeding.

Gold standard treatment for massive haemoptysis in bronchiectasis is bronchial artery embolisation (BAE). BAE may be performed through a femoral or radial arterial approach to allow selective catheterisation of the bronchial arteries from their origin in the thoracic aorta. Abnormal vessels are identified by angiography and embolised with materials such as polyvinyl alcohol or metal coils. BAE is typically effective in initial control of haemoptysis in between 60% and 90% of cases although recurrent bleeding is common.[2] Serious complications of BAE have been reported including limb ischaemia, paradoxical embolism and hypoxia.[2]

There have been a small number of case reports of massive haemoptysis in pregnancy. BAE has been reported during pregnancy,[3] but its safety has not been established and there are no consensus guidelines covering this scenario. We discussed the case with colleagues in interventional radiology and as the haemoptysis appeared to have settled with conservative treatment, BAE was not pursued. In the event of recurrent haemoptysis or worsening respiratory status, this decision would be reconsidered.

IT: Sputum samples cultured methicillin-sensitive *Staphylococcus aureus*. Spirometry revealed severe airflow obstruction with FEV_1 0.54 L (16% predicted). Respiratory physiotherapy input was provided twice daily and the patient was referred to the Obstetric Medicine team.

Alison Gates, Respiratory Physiotherapist (AG): Effective clearance of sputum is essential in the management of bronchiectasis. Positive pressure techniques to aid airway clearance are relatively contraindicated during active haemoptysis but may be restarted once the bleeding has settled. There is no consensus on how long airway clearance and positive pressure techniques should be withheld after an episode of haemoptysis. In our practice, this is influenced by both the severity of haemoptysis and the impact of stopping these treatments on the patient's respiratory status. Our patient was taught autogenic drainage and intermittent positive pressure breathing was introduced within 48 hours of transfer to our service which was helpful in improving airway clearance.

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IT: Arterial blood gases on air revealed a compensated respiratory acidosis with daytime pCO_2 6.63 kPa and bicarbonate 32.0 mmol/L. Supplemental oxygen was trialled, targeting saturations of >92% to maintain adequate fetal oxygenation, but unfortunately resulted in worsening hypercapnia. The patient was established on overnight non-invasive ventilation (NIV) using spontaneous timed mode with an inspiratory positive airway pressure (IPAP) of 12 cmH_20 and an expiratory positive airway pressure (EPAP) of 5 cmH_20. The backup rate was set at 18 breaths/min with an inspiratory time of 1.1 s.

Lucy Mackillop, Consultant Obstetric Physician (LM): This patient has severe lung disease and potentially life-threatening complications of respiratory failure and massive haemoptysis with significant implications to mother and fetus. Outcomes of pregnancy in bronchiectasis have been little studied to date. Extrapolating from the cystic fibrosis (CF) literature, we would expect increased risk of adverse outcomes with lower FEV_1 and other factors such as low body weight.[4]

It is important to exclude pulmonary hypertension due to the high risk of peripartum morbidity and mortality with this condition, and our patient had a normal echocardiogram. Further detailed fetal ultrasound at 35 weeks estimated the fetal weight to be lower than the fifth centile with a normal umbilical artery Doppler signal. Fetal cardiotocograms were satisfactory. Our aim was to support the patient to 36 weeks' gestation to allow time for optimisation of lung function and the administration of intramuscular betamethasone to aid fetal lung maturation.

WGF: In addition to stabilising the patient and planning for a safe delivery, it is important to consider the potential underlying causes of her bronchiectasis. The 2019 British Thoracic Society bronchiectasis guidelines advise on the investigation of newly diagnosed bronchiectasis with an emphasis on identifying treatable underlying conditions. It is recommended that a full blood count, immunoglobulins and either a specific IgE or skin prick test for *Aspergillus fumigatus* are checked in all cases of bronchiectasis to exclude primary immunodeficiency and allergic bronchopulmonary aspergillosis. Primary ciliary dyskinesia should be considered in people with a history of sinonasal disease since childhood. In our case this was considered unlikely given the absence of a history of neonatal respiratory distress and upper airway symptoms.

CF is another genetic cause of bronchiectasis that should be suspected in patients with upper lobe predominant disease, undernutrition, pancreatic pathology or *Staphylococcus aureus* airways infection. Diagnosis of CF is made on a combination of clinical features, identification of two pathogenic mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (*CFTR*) gene and a raised sweat chloride level. Nasal potential difference or intestinal current measurement may be helpful in equivocal cases.

In our case, the sweat chloride was raised at 79 mmol/L (with values >60 mmol/L consistent with CF). Genetic analysis identified two CFTR mutations: c.3718–2477C>T and c.2052dupA p.(Gln685Thrfs), a combination which typically leads to classical CF. Given the clinical setting, genetic results and sweat test, we made a confident diagnosis of CF. Input was sought from the CF multidisciplinary team to optimise her condition prior to delivery.

Jo Snowball, CF Dietitian (JS): Addressing the patient's poor nutritional status was a priority. A stool sample revealed a faecal elastase of 51 µg/g indicating severe pancreatic insufficiency. Pancreatic enzyme replacement therapy was started alongside oral nutritional supplements, aiming for a calorie intake of 3000 kcal/day.

AG: Nebulised dornase alpha therapy was commenced, helping reduce sputum viscosity and work of breathing associated with airway clearance.

LM: Caesarean section under epidural anaesthesia was performed at 36 weeks' gestation and a healthy baby girl weighing 1895 g (lower than third centile for gestation) was delivered. NIV was continued throughout the delivery. The patient was transferred to the intensive care unit (ICU) and patient-controlled anaesthesia was provided. Physiotherapy input for airway clearance restarted within a few hours of delivery.

It was important to ensure that the baby did not have CF herself. Carrier testing of the baby's father was negative for 53 common CFTR mutations. The baby underwent newborn screening for CF with a normal heel-prick immunoreactive trypsin level.

Stephen J Chapman, Consultant Respiratory Physician (SJC): Having made the diagnosis of CF and navigated successful delivery of the baby, our attention turned toward optimising the mother's maintenance therapies. Huge strides forward have been made in CF care through the adoption of specialist multidisciplinary CF teams and, more recently, the advent of CFTR modulator therapies.

Ivacaftor is an oral medication that has shown dramatic effectiveness for CFTR gating mutations such as G551D which affects approximately 5% of people with CF. In this population, ivacaftor showed an improvement of around 10% predicted in FEV_1 as well as improved BMI and a significant reduction in exacerbations.[5] Ivacaftor has since been shown to exhibit activity in a range of other CFTR mutations, including the splice mutation c.3718–2477C>T. NHS England does not currently fund ivacaftor for this mutation, so access to the therapy was secured through the manufacturer's managed access programme. Ivacaftor was started at the standard dose of 150 mg two times per day and was tolerated well.

IT: The patient was stepped down from the ICU to the postnatal ward 24 hours following delivery. She received a further 10 days of inpatient multidisciplinary CF care before discharge.

WGF: The patient was followed up regularly after discharge and at 6 months postpartum, she reported feeling well with a reduction in sputum volumes. Her blood gases had improved with normalisation of her pCO2 and bicarbonate despite discontinuing NIV. She had experienced one minor pulmonary exacerbation requiring oral antibiotics but had not needed further hospital admissions. Spirometry had modestly improved with FEV_1 0.79 L (23% predicted), but her BMI remained low at 16.4 kg/m^2. The focus of her care has turned toward improving her physical fitness and BMI with a view to referral for lung transplantation assessment.

SJC: This case demonstrates a number of important learning points. First, cross-specialty, multidisciplinary input was key with contributions from respiratory medicine, the CF team, obstetrics and critical care. This combined effort allowed the successful management of pregnancy in the face of multiple life-threatening complications including massive haemoptysis, ventilatory failure and severe malnutrition.

Our case also illustrates the importance of a thorough work-up for underlying causes of bronchiectasis. As highly effective CFTR modulator therapies increasingly reach clinical practice, it is vital that a diagnosis of CF is made as early as possible in life to prevent progression toward end-stage lung disease. The diagnosis of CF in adulthood often represents a significant psychological challenge, all the more potent when combined with

becoming a parent. Support from clinical psychology and the CF multidisciplinary team has been invaluable for our patient and her family. It is likely that this need will continue as our patient contends with motherhood, a substantial treatment burden and the prospect of lung transplantation.

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REFERENCES

1 Radchenko C, Alraiyes AH, Shojaee S. A systematic approach to the management of massive hemoptysis. *J Thorac Dis* 2017;9(Suppl 10):S1069–S1086.
2 Flight WG, Barry PJ, Bright-Thomas RJ, *et al*. Outcomes following bronchial artery embolisation for haemoptysis in cystic fibrosis. *Cardiovasc Intervent Radiol* 2017;40:1164–8.
3 Downs TW, Chao CR. Massive hemoptysis in pregnancy treated with bronchial artery embolization. *Am J Perinatol* 1997;14:51–3.
4 Edenborough FP, Borgo G, Knoop C, *et al*. Guidelines for the management of pregnancy in women with cystic fibrosis. *J Cyst Fibros* 2008;7 Suppl 1(Suppl 1):S2–S32.
5 Ramsey BW, Davies J, McElvaney NG, *et al*. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. *N Engl J Med* 2011;365:1663–72.