Pregnancy and alpha-1 antitrypsin deficiency

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Summary: A 29 year old patient with alpha-1 antitrypsin deficiency and bullous emphysema became pregnant against the advice of her physicians. Despite a mid-trimester pneumothorax requiring the insertion of a chest tube, she went on to deliver a healthy child under epidural anaesthesia using a midforceps technique. Vaginal delivery is not necessarily contra-indicated in multiparous patients with bullous emphysema.

Introduction

Alpha-1 antitrypsin deficiency was first described in 1963, and most patients with this deficiency will eventually develop emphysema. In a Swedish study,¹ the onset of dyspnoea in homozygotes occurred at a median age of 40 years in smokers. There are few reports of the outcome of pregnancy in patients with established emphysema. This report documents the successful outcome of pregnancy in a 29 year-old patient with alpha-1 antitrypsin deficiency.

Case report

A 29 year old patient presented with a one year history of progressive shortness of breath on exertion. She had first noticed dyspnoea during the third trimester of a previous pregnancy, but despite a normal delivery and return to prepartum weight, her dyspnoea increased to the extent that she was short of breath on climbing one flight of stairs or walking 200 feet on the level. There was no history of cough, wheeze, sputum production or haemoptysis. She had a 10 year history of smoking two packets of cigarettes per day and was the mother of three healthy children. Her mother and sister, both smokers, were said to have 'bronchitis'.

A chest X-ray 3 years before onset of dyspnoea was normal but a repeat film at the time of presentation

showed bullous emphysema involving the right lung (Figure 1). Alpha-1 antitrypsin level was less than 0.72 ml/min/mm hg (normal 1.4 to 4.2). The actual level was too low to quantitate and phenotyping is unavailable in Atlantic Canada. Ventilation/perfusion lung scanning revealed irregularity in radionucleotide distribution involving both lungs. On the ventilation scan, there were multiple focal filling defects noted in the right upper lobe, right lower lobe laterally, and the left lower lobe. The perfusion scan showed 'matching' defects in these areas and the findings were compatible with multiple bullae involving both lungs. Pulmonary function tests (Table I) indicated severe obstructive impairment with hyperinflation and reduction in diffusing capacity.

The patient was advised against pregnancy and underwent tubal ligation when she later proved to be six weeks pregnant. Prenatal progress was satisfactory until 21 weeks of gestation when she suffered a spontaneous pneumothorax on the right side requiring chest tube insertion. During her pregnancy, repeated obstetrical ultrasound examinations, pulmonary function tests (Table I), and arterial blood gas determinations indicated satisfactory progress. Following induction, she delivered a healthy male child under epidural anaesthesia using a midforceps technique. Post-partum progress was satisfactory.

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Figure 1 X-ray at presentation (PA and lateral).

Table 1 Pulmonary function tests and arterial blood gas determinations

Gestational age	FVC (l)	(% Pred)	FEV ₁ (l)	FEV ₁ /VC(%)	FEF _{25-75%} (l/s)	TLC (l)	(% Pred)	FRC (l)	RV (l)	RV/TLC(%)	DLCO (% Pred)
Before pregnancy	4.13	(121)	2.39	57.8	1.16	5.83	(125)	3.05	1.55	26.6	16.09
30 weeks	4.20	(129)	2.60	62	1.17	5.52	(118)	2.9	1.32	24	11.47
36 weeks	4.07	(123)	2.70	66	1.63	5.97	(129)	2.61	1.76	29	11.36
10 weeks post-partum	4.44	(135)	2.58	58	1.10	6.24	(135)	3.29	1.91	31	12.11

Note: Predicted values for height and weight adjusted for weight gain in pregnancy.
FVC = forced vital capacity
FEV₁ = forced expiratory volume in one second
FEF_{25-75%} = forced expiratory flow 25–75%
TLC = total lung capacity
FRC = functional residual capacity
RV = residual volume
DLCO = OCO diffusion capacity

Discussion

Alpha-1 antitrypsin deficiency is a relatively uncommon condition transmitted as a simple Mendelian trait with low levels of serum alpha-1 antitrypsin being present in homozygotes for the deficiency gene. Homozygotes with phenotype ZZ have less than 10% of normal antitrypsin levels and have a 70–80% likelihood of developing obstructive pulmonary disease, characteristically panacinar emphysema. Homozygotes are rare, and it is thought that smoking hastens the development of emphysema in both homo- and heterozygotes. Pregnancy in patients with established emphysema who have alpha-1 antitrypsin deficiency is very uncommon and review of the literature (National Library of Medicine's Erhill Retrieval System) revealed only one previous reported case.²

Pregnancy is usually associated with a 10–25% reduction in functional residual capacity (FRC) due to diaphragmatic elevation and a 7–22% reduction of residual volume (RV). Inspiratory capacity (IC) often shows a small rise so that vital capacity (VC) and total lung capacity (TLC) remain essentially unchanged.³ Maximum flow rates and FEV₁ are not measurably increased in normal pregnancy⁴ although specific airways conductance increases during normal pregnancy.⁵ Three of four previously reported pregnant patients with emphysema had no clinical evidence of deterioration of their disease during the course of their pregnancy although progression of the obstructive abnormality was demonstrated on maximum expiratory flow volume and forced vital capacity curves.⁴ There was no significant change in FEV₁ during this pregnancy and no change was seen in a previously reported case.² The reduction in diffusion (DLCO) seen in this patient could not be explained on the basis of a fall in haemoglobin. DLCO is said not to alter in the course of normal pregnancies, but previous reviews did not take into account any change in haemoglobin concentration.^{4,6} A rise in DLCO might however be expected to accompany the hypervolaemia of pregnancy in the absence of a fall in haemoglobin.⁷ Arterial blood gases did not appreciably alter between 25 and 37 weeks gestation.

Isolated spontaneous pneumothorax (i.e. without pneumomediastinum or pneumoperitoneum) is rare in pregnancy with only ten reports in the literature.⁸ Bending⁹ described a case of spontaneous pneumothorax occurring at the end of labour in a healthy 17 year old primigravida, and he presented a review of the literature at that time. His patient, however, presumably had pneumomediastinum as she had marked surgical emphysema and pneumomediastinum is much more common, estimates of its incidence range from 1:2000 to 1 in 100,000 with more than 200 cases reported.⁸ The patient presented here had an isolated mid trimester spontaneous pneumothorax requiring chest tube insertion. Pneumothorax and pneumomediastinum most commonly occur in pregnant patients during the second stage of labour with straining against a closed glottis.⁹ Onkar & Didolkar¹⁰ have reported a case of pneumomediastinum in the mother, with pneumomediastinum and pneumothorax in the newborn child. The maternal pneumomediastinum developed one hour and 45 minutes into the second stage of labour and pneumothorax and pneumomediastinum was detected radiologically in the infant within 30 minutes of delivery. In the previously reported case of pregnancy and alpha-1 antitrypsin deficiency in a primigravida, a low forceps technique under epidural anaesthesia was employed.² The risk of pneumothorax and pneumomediastinum was significantly reduced in the patient reported here by use of midforceps extraction under epidural anaesthesia.

Pregnancy and alpha-1 antitrypsin deficiency has illogically been compared with pregnancy and cystic fibrosis.¹¹ These diseases are clearly different clinically and pathologically, and the poor prognosis associated with pregnancy in the latter group (of 129 pregnancies in cystic fibrosis patients, only 86 resulted in viable infants) does not necessarily apply to patients with alpha-1 antitrypsin deficiency.

Vaginal delivery is not contraindicated in patients with alpha-1 antitrypsin deficiency providing careful monitoring in the antenatal period is undertaken and providing the second stage of labour is managed to reduce markedly the expulsive effort required of the patient.

References

1. Larsson, C., Natural history and life expectancy in severe alpha 1 antitrypsin deficiency, *PiZ. Acta Med Scand* 1978, **204**: 345–251.
2. Giesler, C.F., Buehler, J.H. & Depp, R. Alpha-1 antitrypsin deficiency: severe obstructive lung disease and pregnancy. *Obstet Gynecol* 1977, **49**: 31–34.
3. Gaensler, E. Lung displacement: abdominal enlargement pleural space disorders, deformities of the thoracic cage. In *Handbook of Physiology*, Section 3 Respiration Volume II 1965, 1623–1661.
4. Gazioglu, K., Kaltreider, N.L., Rosen, M. & Yu, P.N. Pulmonary function during pregnancy in normal women and in patients with cardiopulmonary disease. *Thorax* 1970, **25**: 445–450.
5. Gee, J.B.L., Packer, B.S., Millen, J.E. & Robin, E.D. Pulmonary mechanics during pregnancy. *J Clin Invest* 1967, **46**: 945–952.
6. Krumholz, R.A., Echt, C.R. & Ross, J.C. Pulmonary

- diffusing capacity, capillary blood volume, lung volumes and mechanics of ventilation in early and late pregnancy. *J Lab Clin Med* 1964, **63**: 648–655.
7. Gibson, G.J. In *Clinical Tests of Respiratory Function*. Raven Press, 1984, p 129.
  8. Karson, E.H., Saltzman, D. & Davis, M.R. Pneumomediastinum in pregnancy. Two case reports and a review of the literature, pathophysiology, and management. *Obstet Gynecol* 1984, **64**: (Suppl): 395–435.
  9. Bending, J.J. Spontaneous pneumothorax in pregnancy and labour. *Postgrad Med J* 1982, **58**: 711–713.
  10. Onkar, N.S. & Didolkar, S. Maternal-fetal pneumomediastinum complicating labour. *J Reprod Med* 1980, **25**: 329–332.
  11. Berkowitz, R.L. Asthma and other severe respiratory diseases during pregnancy. In *Critical Care of the Obstetric Patient*. Churchill-Livingstone, Edinburgh, London, 1983, pp 353–354.