SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2011; 28; 153-155

Successful pregnancy complicated by persistent pneumothorax in a patient with lymphangioleiomyomatosis (LAM) on sirolimus

M. Faehling[1], S. Frohnmayer[1], M. Leschke[1], B. Trinajstic-Schulz[2], J. Weber[3], F. Liewald[4]

[1] Klinik für Kardiologie und Pneumologie, Klinikum Esslingen, Esslingen; [2] Lungenfacharztpraxis, Esslingen; [3] Abteilung Innere Medizin, Ermstalklinik, Bad Urach; [4] Klinik für Gefäß- und Thoraxchirurgie, Klinikum Esslingen, Esslingen

Abstract. We report a successful pregnancy in a patient with longstanding LAM on treatment with sirolimus. During temporary discontinuation fo sirolimus in early pregnancy, lung function declined but recovered after resumption of sirolimus. Pregnancy was complicated by a persistent pneumothorax which was treated surgically postnatally. The child has had a normal development despite exposure to low dose sirolimus intermittently during early embryonal and mid-fetal life. *(Sarcoidosis Vasc Diffuse Lung Dis 2011; 28: 153-155)*

Key words: lymphangioleiomyomatosis, LAM, pregnancy, sirolimus, pneumothorax

Four years after histologically confirmed diagnosis of sporadic lymphangioleiomyomatosis (LAM), a 29-year-old patient presented during her first pregnancy for supervision. Ten months ago, treatment with sirolimus (2 mg/d) had been started with marked improvement in respiratory function. Treatment with sirolimus had been discontinued at confirmation of the pregnancy (6 weeks+0). At presentation (11 weeks), dyspnoea was the same as before pregnancy (WHO FC1). Chest examination revealed soft breath sounds, similar on both sides, breathing frequency 14/min.

From 21 weeks onwards, gradually increasing dyspnoea (WHO FC3) and cough occurred. Whereas lung volume was relatively stable, diffusion capacity declined sharply (Table 1). Despite insufficient experience in human pregnancy, available data on sirolimus suggested a low risk to the foetus with the main expected risk being growth retardation. Sirolimus was restarted on 23 weeks+0 at 2 mg/d (serum level after four days 2.2 μg/ml). Dyspnoea improvedly, and diffusion capacity increased markedly.

On 26 weeks+5, dyspnoea and cough acutely increased with reduced breath sounds over the left lung. Chest radiography confirmed a left-sided pneumothorax (Figure 1). A chest tube was inserted with reinflation of the lung and resolution of symptoms. However, a persistent air leak into the pleural space was evident. Temporary interruption of suction resulted in acute dyspnoea and reduced left sided breath sounds indicating persistent pneumothorax. Because of the pregnancy, surgery was deferred until after delivery. Under prophylactic antibiotics, the chest tube was left under permanent suction using a mobile suction system. Sirolimus was discontinued at 29 weeks+0 because of the planned caesarean section which was performed in peridural

Received: 13 January 2011
Accepted after Revision: 18 January 2011
Correspondence: Martin Faehling,
B.M.B.Ch. (Oxford), M.Sc. (Physiol.), M.D.
Klinik für Kardiologie und Pneumologie
Klinikum Esslingen
Hirschlandstr. 97
73730 Esslingen
Tel. (+49)711-3103 82411
Fax (+49)711-3103 2405
E-mail: m.faehling@klinikum-es.de

Table 1. Lung function

	2 months before pregnancy	7 weeks +6	13 weeks +6	17 weeks +0	21 weeks +4	23 weeks +0	24 weeks +0	24 weeks +3	1 months post natally	4 months post natally	8 months post natally
Treatment	Sirolimus	-	-	-	-	-	Sirolimus	Sirolimus	Sirolimus	Sirolimus	Sirolimus
FEV1 (L)	56%	63%	62%	61%	58%	59%	58%	60%	51%	56%	69%
Diffusion capacity (DCO/VA)	46%	46%	45%	49%	33%	31%	58%	59%	41%	46%	51%

anaesthesia on 32 weeks+0 after betamethasone treatment for lung maturation.

Four days later, a thoracoscopic left sided pleurectomy and atypical resection of segment 5 was performed with resolution of the pneumothorax. Histology confirmed the diagnosis of LAM. Ten days postnatally, sirolimus was resumed. Eight months later, the patient is stable with lung function parameters similar to those prior to pregnancy.

The child was a healthy normally developed premature male and has had a normal development until present (8 months).

Discussion

LAM is a rare disease in women characterized by smooth muscle cell infiltration and cystic destruction of the lung (1, 2). LAM may occur with the tuberous sclerosis complex or sporadically. Clinically, LAM is characterized by progressive dyspnoea, recurrent pneumothoraces, chylous fluid collections, and abdominal angiomyolipomas. Lung function declines at 75-120 ml annually, which is 2-3 fold of the normal rate. The diagnosis can be made on high resolution CT, but may require histological confirmation. The standard treatment has been oestrogen antagonism. A meta-analysis, however, revealed that progesterone treatment does not reduce the decline in lung function (3). Since there is no proven medical therapy, lung transplantation is the only treatment for severe LAM. Improved understanding of the pathophysiology of LAM has identified several targets for therapy including the mammalian target of rapamycin (mTOR). Following a proof of principle trial of the mTOR inhibitor sirolimus that showed a reduction of angiomyolipoma size accompanied by an improvement in lung function (4), several trials of sirolimus in LAM are open for recruitment. Pregnancy has been associated with deterioration of lung function and pneumothorax (5), but the risk of pregnancy has not been rigorously studied. In most documented cases of pregnancy and LAM, LAM was not known prior to pregnancy and was diagnosed after a complication (e. g. pneumothorax) had occurred.

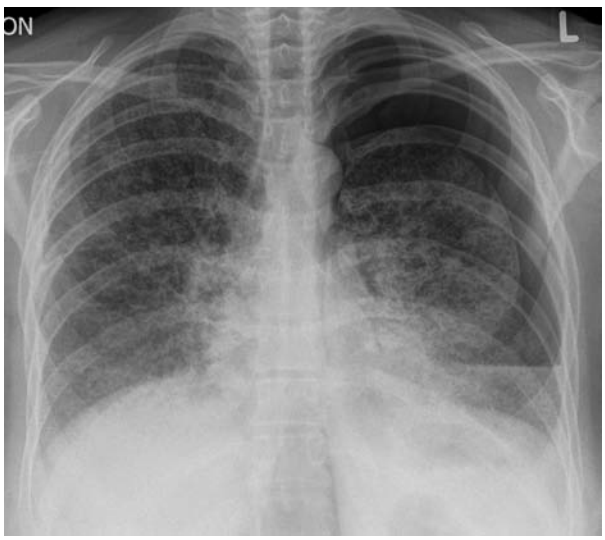

Fig. 1. Chest radiograph (exspiration) at 26 weeks+5: A left sided sero-pneumothorax, bilateral cystic changes and a reticular pattern involving all lung zones are evident

In summary, we describe a successful pregnancy in a patient with longstanding LAM showing stable lung function on treatment with sirolimus. The child has had a normal development despite exposure to low dose sirolimus intermittently during early embryonal and mid-fetal life. LAM patients should be treated within clinical trials since evolving treatment options such as sirolimus are promising but as yet unproven.

References

1. McCormack FX, Lymphangioleiomomatosis. A clinical update. Chest 2008; 133: 507-16.
2. Johnson SR, Cordier JF, Lazor R, et al. European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis. Eur Resp J 2010; 35: 14-26.
3. Taveira-DaSilva AM, Stylianou MP, Hedin CJ, Hathaway O, Moss J. Decline in lung function in patients with lymphangioleiomyomatosis treated with or without progesterone. Chest 2004; 126: 1867-74.
4. Bissler JJ, McCormack FX, Young LR, et al. Sirolimus for angiomyolipoma in tuberous sclerosis complex or lymphangioleiomyomatosis. N Engl J Med 2008; 358: 140-51.
5. Johnson SR, Tattersfield AE. Clinical experience of lymphangioleiomyomatosis in the UK. Thorax 2000; 55: 1052-7.