Pulmonary Haemorrhage from Arteriovenous Malformations: Implications and Management in Pregnancy

Calvin SH NG BSc(Hons), MBBS(Hons), MD, FRCS(CTh), FCSHK, FHKAM (Surgery)
Anthony V MANLULU MD
TW LEE MBChB, FRCS (Edin), FCSHK, FHKAM (Surgery)
Randolph HL WONG MBChB, FRCS (CTh), FCSHK, FHKAM (Surgery)
Juan C GARZON MD
Malcolm J UNDERWOOD MD, FRCS (CTh)
Anthony PC YIM MD, FRCS (Eng, Edin, Glasg)
Division of Cardiothoracic Surgery, Department of Surgery, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong

Pulmonary arteriovenous malformations are rare vascular disorders known to produce life-threatening complications. An increased risk of potentially fatal complications has been reported in patients with hereditary haemorrhagic telangiectasia during pregnancy. Due to concerns regarding fetal radiation exposure, the diagnostic and therapeutic management of these patients can be particularly difficult. The problem is even more challenging in patients presenting with complications from pulmonary haemorrhage. We reviewed the literature regarding pulmonary arteriovenous malformations, with an emphasis on pregnancy and focused on the current diagnostic and treatment options available.
Hong Kong J Gynaecol Obstet Midwifery 2011; 11:67-72

Keywords: Arteriovenous malformations; Embolization, therapeutic; Hemothorax; Pregnancy complications; Pulmonary artery; Telangiectasia, hereditary hemorrhagic

Introduction

Pulmonary arteriovenous malformations (PAVMs) are rare vascular disorders known to produce life-threatening complications, including haemoptysis, intrapleural haemorrhage, stroke, brain abscess, and hypoxaemia. Since its first description by Churton in 1897[1], more than 500 cases have been reported in the literature[2]. Pregnancy and PAVM are strongly linked with adverse outcomes, due to an increased risk of complications[3-8]. Management dilemmas arise from concerns about fetal radiation exposure from both diagnostic and therapeutic procedures involving ionising radiation. Furthermore, the ideal treatment modality for this condition during pregnancy is unclear. Surgery has traditionally been regarded as the treatment of choice and is potentially life saving in cases complicated by pulmonary haemorrhage. More recently, in selected cases, transcatheter embolotherapy (TCE) has demonstrated impressive initial results. In this review, we address the diagnostic and management options available for pregnant patients presenting with this rare condition.

The key word "pulmonary arteriovenous malformation" was used in a MEDLINE search of relevant literature for the review that follows, with around 100 articles being identified. The addition of "pregnancy" in the search returned five articles. The relevant articles were individually selected, based on their scientific merit and relevance.

Pathophysiology

PAVMs are characterised by the presence of abnormal communications between arteries and veins through thin-walled aneurysms. These abnormal

Correspondence to: Dr Calvin SH Ng
Email: calvinng@surgery.cuhk.edu.hk

vascular channels function as direct right-to-left shunts; associated clinical features are dyspnoea, fatigue, cyanosis and polycythemia, in the presence of severe shunting. The afferent blood supply is usually from the pulmonary artery, however, an aberrant systemic blood supply may arise from the aorta, intercostals and bronchial arteries. Venous drainage is commonly into one or more branches of the pulmonary veins, although abnormal drainage may occur in the left atrium or inferior vena cava. The majority of lesions are congenital (80%); acquired cases are rare and do not possess malignant potential. The prevalence of PAVM has been reported to be between 2 and 3 cases per 100,000 inhabitants, with a female predominance[9]. PAVM can occur primarily or in association with hereditary haemorrhagic telangiectasia (HHT), an autosomal dominant genetic disorder characterised by the presence of multiple visceral arteriovenous malformations. Identifying patients with both PAVM and HHT is important, because they tend to have multiple arteriovenous malformations associated with more sinister features and higher complication rates. For this reason, screening and regular follow-up for these cases is recommended[10]. In terms of angioarchitecture, PAVMs are simple if supplied by one segmental artery or complex if it receives blood supply from two or more segmental arteries[11]. The lesions may be solitary (40%), multiple (40%), or bilateral (20%), and are most commonly located in the lower lobes. Left untreated, the lesions tend to enlarge and are known to result in life-threatening complications and mortality (Table 1).

Potential Complications

Neurological complications including cerebral infarction or abscess may occur as a result of pathogens bypassing the capillary bed causing the lung to lose its filter function, thereby permitting emboli and bacteria access into the systemic circulation. The frequency of neurological complications varies; it was reported in one study to be 37% for transient ischaemic attack, 18% for stroke, 9% for abscess, and 8% for seizures[12]. Another rare and potentially fatal complication is pulmonary haemorrhage, presenting either as haemoptysis due to intrabronchial rupture of the PAVM or endobronchial telangiectasia, or haemothorax when the lesion ruptures into the pleural space (Figure 1). Pregnancy-induced changes in haemodynamics and hormone levels become more pronounced after the first trimesters, and are believed to provoke adverse effects in PAVMs. More specifically, the progression of this condition during pregnancy may be related to the increased blood volume and cardiac output of the mother, which results in increased pulmonary blood flow and a higher potential for rupture. In addition, elevated oestrogen levels act directly on the vessels and increase venous distensability and together with high progesterone levels can cause further augmentation in blood flow and progression in PAVM size. To illustrate this point, in a review of pregnant patients with PAVM, an annual mortality rate of 12% was reported as well as a high incidence of morbidity. The morbidity included haemothoraces (50%), haemoptysis (26%), worse shunting (15%), and

Table 1. Complications of pulmonary arteriovenous malformations

Complications	Range (%)
Dyspnoea	27-71
Haemoptysis	4-18
Haemothorax	0-2
Cerebral abscess	0-25
CVA or TIA*	11-55

* CVA denotes cerebrovascular accident, and TIA transient ischaemic attack

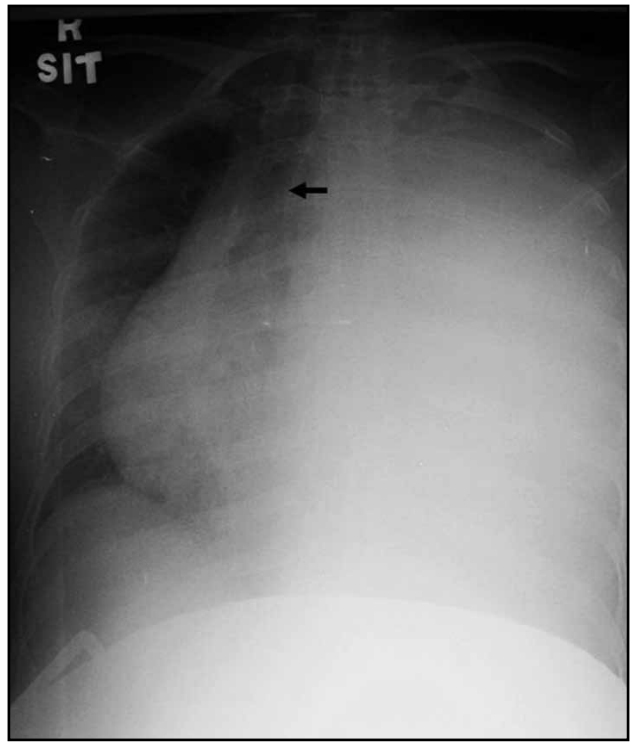

Figure 1. A chest X-ray of a patient at 32-week gestation (note the pelvic shield) presenting with dyspnoea and hypotension. The entire left hemithorax is opacified. There is mediastinal shift and tracheal deviation (arrow)

stroke (8%). Due to the potential for life-threatening complications, screening of women with PAVMs and HHT is highly recommended for those contemplating pregnancy. Moreover, such women should be offered early treatment in order to prevent progression of the PAVM and potentially fatal complications. Shovlin et al[13] reported 11 complications in 23 pregnant patients with PAVM who were managed conservatively; six entailed intrapulmonary shunt deterioration, two had fatal haemorrhages, and three endured cerebrovascular accidents. Caution is therefore advised in selecting conservative management, as such a strategy can result in fetal and maternal death.

Diagnostic Options

The appearance of PAVM on chest X-ray is non-specific; more definitive imaging procedures are required to facilitate the diagnosis (Table 2). Computed tomography (CT) or magnetic resonance imaging (MRI) of the chest (Figure 2) is helpful in delineating the exact size, location, and number of lesions. Such information is crucial to planning treatment. As MRI avoids fetal exposure to ionising radiation, it offers an advantage. However, its limited availability, relatively high cost, and requirement of specially trained radiologists to interpret the images pose a challenge. Contrast echocardiography or radionuclide scanning can suggest the presence of right-to-left shunting and are primarily used for screening or post-treatment following up of patients. The role of contrast echocardiography and radionuclide scanning in planning treatment is limited due to poor anatomical definition of the identified lesions. Pulmonary angiography remains the gold standard for diagnosing PAVM and allows the delineation of feeding vessels, which serves as a suitable guide for subsequent embolotherapy. Its disadvantages are that it is invasive, requires special facilities and personnel, is costly, and the exposure to radiation is intense (compared to other imaging procedures). Concerns about fetal exposure to ionising radiation have limited the application of CT, nuclear scanning, and pulmonary angiography in pregnant patients. If facility for MRI is not available, necessary precautions to limit fetal exposure to radiation during CT or angiography (use of abdominal/pelvic shields) should be deployed.

Therapeutic Dilemmas

Although data regarding the natural history of PAVM are limited, the available literature suggests treatment be offered to all symptomatic patients and those with HHT contemplating pregnancy. Treatment is aimed at improving symptoms associated with shunting and prevention of future complications, but the most appropriate modality to use in pregnancy remains debatable. Use of TCE with detachable balloons or coils to selectively occlude the feeding arteries has been shown to be safe and effective in reducing the risk of

Table 2. Diagnostic modalities for pulmonary arteriovenous malformations

Non-invasive (ionising)
Chest X-ray
Chest computed tomography
Radionuclide scanning
Non-invasive (non-ionising)
Transthoracic ultrasound with colour Doppler
Contrast echocardiography
Chest magnetic resonance imaging
Invasive
Pulmonary angiography

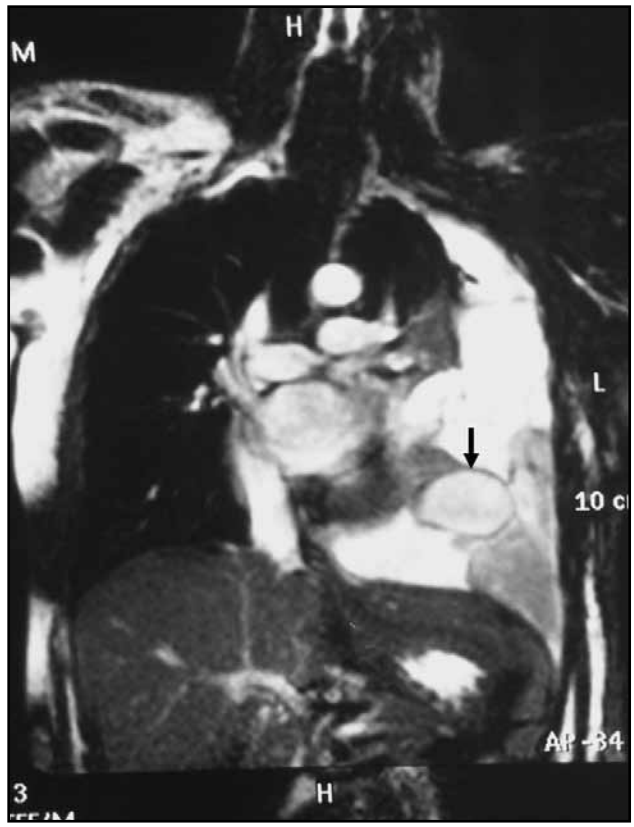

Figure 2. A thoracic magnetic resonance image (coronal view) demonstrating the collapsed left lung as a result of haemothorax in a pregnant woman. Note the well-circumscribed high-signal lesion corresponding to the pulmonary arteriovenous malformation located in the left lower lobe (arrow)

complications[12]. It is widely regarded as the treatment of choice for multiple lesions wherein surgical excision would result in sacrifice of a substantial amount of lung tissue, which could be particularly hazardous in patients at high risk from surgery. Notably, successful outcome from TCE depends upon the ability to adequately embolise all feeding vessels, and often requiring several sessions. Concerns have also been raised about the consequences of fetal radiation exposure (spontaneous abortion, teratogenesis, growth retardation, development of malignancies) and the long-term efficacy of the procedure. The time required to accomplish the procedure successfully should also be taken into account, as it is performed under general anaesthesia. According to Gershon et al's report[14] on a prospective series of pregnant patients, for the most part TCE should be an elective procedure, there being only one previous case of emergency embolotherapy in a pregnant PAVM patient with hypoxaemia. Although initial results of embolisation in centres with experience of the procedure yield high success rates in selected cases[15], long-term follow-up has identified failures, namely: persistence of PAVMs (15%), recanalisation of the occluded artery (10%), growth of an accessory vessels (5%) and interim ischaemic strokes (4.4%)[16,17]. Other complications associated with TCE include: pleurisy (31%), air embolus precipitating angina, bradycardia and device migration with paradoxical embolisation (4%) [Table 3]. Surgery has traditionally been the treatment of choice due to excellent long-term results both in terms of freedom from recurrence and complications[18]. Resection is indicated when embolotherapy is not available or fails and in cases of pulmonary haemorrhage resulting in haemodynamic instability. The extent of pulmonary resection depends on the size, location, and multiplicity of lesions and can range from non-anatomic resections to pneumonectomy (Table 4)[19]. In patients presenting with haemorrhagic complications, surgery is potentially life-saving and the decision to intervene should be made promptly. We advocate the video-assisted thoracic surgery approach, as this permits a less invasive operation than open thoracotomy[20] (Figure 3). In select cases of complex or multiple PAVMs, a hybrid combined transcatheter and surgical approach may allow maximal preservation of

Table 3. Results of embolotherapy for pulmonary arteriovenous malformations

Study	Method*	No. of patients	Mean (range) age (years)	Pregnant patients	Gestation (weeks)	Estimated fetal radiation dose (mrad)
Gershon et al[14], 2001	B/C	7	28 (17-37)	7	16-36	<50 to 220
Saluja et al[15], 1999	C	82	40	0	NA	NA†
Andersen et al[16], 1998	B/C	12	NA	0	NA	NA
Lee et al[17], 1997	B/C	45	41.6	0	NA	NA

* B denotes balloon, and C coil

† NA denotes not applicable

Table 4. Results of surgery for pulmonary arteriovenous malformations

Study	No. of patients	Mean (range) age (years)	Pregnant patients	Operation (No.)
Pick et al[19], 1999	30	37 (18-67)	3	Pneumonectomy (1) Lobectomy (7) Lobectomy+segmentectomy (2) Segmentectomy (7) Wedge (13)
Puskas et al[18], 1993	9	37.5 (15-72)	0	Lobectomy (4) Segmentectomy (5)

* NA denotes not applicable

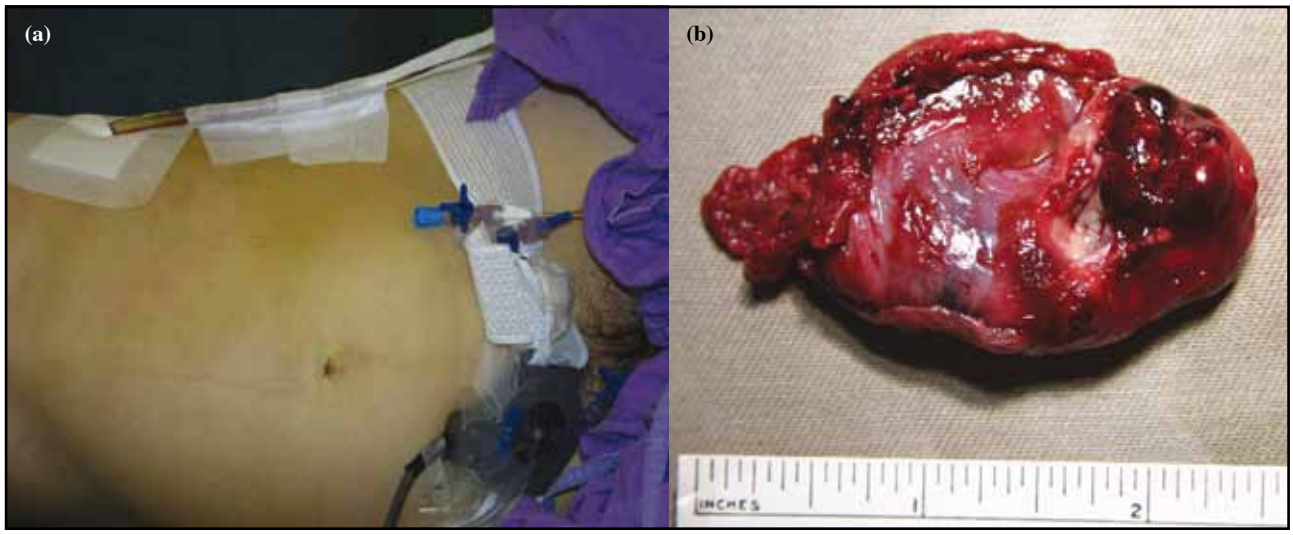

Figure 3. (a) Video-assisted thoracic surgery for bleeding pulmonary arteriovenous malformation (PAVM) with intra-operative cardiotocography monitoring, and (b) the resected PAVM specimen

lung parenchyma[21].

Conclusion

The potential for fatal complications in pregnant patients with PAVMs has been well described. Various modalities are available to aid diagnosis and treatment planning. Prompt treatment should be instituted in order to prevent catastrophic complications. In centres with the available expertise, TCE is currently the treatment of choice as it is safe and effective. Surgery can be life-saving and is reserved for patients presenting with life-threatening pulmonary haemorrhage or failed TCE. After therapy, regular follow-up should be prescribed to monitor the progress of treatment and to rule out recurrences.

Complications	Success rate (%)	Maternal outcome	Fetal outcome	Follow-up (years)
2 Pleurisy	100	All healthy and deliver vaginally at term	All babies well at 1 year old	NA
7 Pleurisy 8 Air embolus 0 Paradoxical embolisation	97.6	NA	NA	Up to 3
1 Pleurisy 1 Fever	100	NA	NA	NA
14 Pleurisy 1 Air embolus 2 Paradoxical embolisation	84	NA	NA	Up to 5.9

Success rate (%)	Surgical complications	Perioperative mortality	Maternal / fetal outcomes	Follow-up (months)
93	1 Mechanical ventilation 1 Haemorrhage and transfusion 1 Prolonged air leak	3%	NA	30
100	NA *	NA	NA	NA

References

1. Churton T. Multiple aneurysms of pulmonary artery. *BMJ* 1897; 1:1223.
2. Khurshid I, Downie GH. Pulmonary arteriovenous malformation. *Postgrad Med J* 2002; 78:191-7.
3. Esplin MS, Varner MW. Progression of pulmonary arteriovenous malformation during pregnancy: case report and review of the literature. *Obstet Gynecol Surv* 1997; 52:248-53.
4. Freixinet J, Sanchez-Palacios M, Guerrero D, et al. Pulmonary arteriovenous fistula ruptured to pleural cavity in pregnancy. *Scand J Thorac Cardiovasc Surg* 1995; 29:39-41.
5. Bradshaw DA, Murray KM, Mull NH 4th. Massive hemoptysis in pregnancy due to a solitary pulmonary arteriovenous malformation. *West J Med* 1994; 161:600-2.
6. Laroche CM, Wells F, Shneerson J. Massive hemothorax due to enlarging arteriovenous fistula in pregnancy. *Chest* 1992; 101:1452-4.
7. Gammon RB, Miksa AK, Keller FS. Osler-Weber-Rendu disease and pulmonary arteriovenous fistulas. Deterioration and embolotherapy during pregnancy. *Chest* 1990; 98:1522-4.
8. Swinburne AJ, Fedullo AJ, Gangemi R, et al. Hereditary telangiectasia and multiple pulmonary arteriovenous fistulas. Clinical deterioration during pregnancy. *Chest* 1986; 89:459-60.
9. Hodgson CH, Kaye RL. Pulmonary arteriovenous fistula and hereditary hemorrhagic telangiectasia: a review and report of 35 cases of fistula. *Dis Chest* 1963; 43:449-55.
10. Begbie ME, Wallace GM, Shovlin CL. Hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu syndrome): a view from the 21st century. *Postgrad Med J* 2003; 79:18-24.
11. White RI Jr, Pollak JS, Wirth JA. Pulmonary arteriovenous malformations: diagnosis and transcatheter embolotherapy. *J Vasc Interv Radiol* 1996; 7:787-804.
12. White RI Jr, Lynch-Nyhan A, Terry P, et al. Pulmonary arteriovenous malformations: techniques and long-term outcome of embolotherapy. *Radiology* 1988; 169:663-9.
13. Shovlin CL, Winstock AR, Peters AM, et al. Medical complications of pregnancy in hereditary haemorrhagic telangiectasia. *QJM* 1995; 88:879-87.
14. Gershon AS, Faughnan ME, Chon KS, et al. Transcatheter embolotherapy of maternal pulmonary arteriovenous malformations during pregnancy. *Chest* 2001; 119:470-7.
15. Saluja S, Sitko I, Lee DW, et al. Embolotherapy of pulmonary arteriovenous malformations with detachable balloons: long-term durability and efficacy. *J Vasc Interv Radiol* 1999; 10:883-9.
16. Andersen PE, Kjeldsen AD, Oxhøj H, et al. Embolotherapy for pulmonary arteriovenous malformations in patients with hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). *Acta Radiol* 1998; 39:723-6.
17. Lee DW, White RI Jr, Egglin TK, et al. Embolotherapy of large pulmonary arteriovenous malformations: long-term results. *Ann Thorac Surg* 1997; 64:930-40.
18. Puskas JD, Allen MS, Moncure AC, et al. Pulmonary arteriovenous malformations: therapeutic options. *Ann Thorac Surg* 1993; 56:253-7.
19. Pick A, Deschamps C, Stanson AW. Pulmonary arteriovenous fistula: presentation, diagnosis, and treatment. *World J Surg* 1999; 23:1118-22.
20. Thung KH, Sihoe AD, Wan IY, et al. Hemoptysis from an unusual pulmonary arteriovenous malformation. *Ann Thorac Surg* 2003; 76:1730-3.
21. Litzler PY, Douvrin F, Bouchart F, et al. Combined endovascular and video-assisted thoracoscopic procedure for treatment of a ruptured pulmonary arteriovenous fistula: Case report and review of the literature. *J Thorac Cardiovasc Surg* 2003; 126:1204-7.