CASE FOR DIAGNOSIS

A common presentation with a rare cause

J.-C. Cutz*, J.S. Woods[#], J.H. Mitchell[#], T.V. Colby[†] and K.O. Leslie[†]

CASE PRESENTATION

A 25-yr-old female presented to a pulmonary clinic carrying a plastic sandwich bag containing 50 mL of bloody sputum. She had experienced approximately eight episodes of haemoptysis similar to this throughout the previous year. Her primary care physician had treated her with antibiotics empirically; however, haemoptysis had recurred.

During a typical episode of haemoptysis, the patient described having a sensation of fullness in her chest. This was followed by an urge to cough, which was productive of ≤ 50 mL of bloody sputum. These episodes would last for up to 3–4 days and would resolve spontaneously. The patient did not have any chest pain associated with the haemoptysis.

The patient could not name any exacerbating factors and denied weight loss, fevers, dyspnoea, palpitations, gastrointestinal complaints or a history of easy bruising or bleeding. She had recently developed a rash on the anterior aspect of her chest after having taken a combination of herbal supplements, including oregano oil and extracts from grape seeds, black walnut, wormwood and cloves. Her rash had resolved after discontinuation of the herbal supplements.

The patient's medical history was unremarkable and she specifically denied a history of cardiopulmonary and rheumatological disease. She also denied a history of thromboembolism. Her surgical history was significant for dilation and curettage 2 yrs previously. No allergies were reported. Current medications included an herbal cough suppressant.

The patient was married without children. She denied smoking, use of alcohol and illicit drugs. She worked at a

natural foods store and enjoyed yoga in her free time. The patient had spent 6 months in India and had also travelled to China. She denied having been ill during her travels and reported a negative tuberculin skin test. Her mother and one of her cousins had rheumatoid arthritis.

Her physical examination was within normal limits, as was pulmonary function testing. Chest computed tomography (CT) scans were performed 2 days after the onset of menstruation and these demonstrated multiple lesions (fig. 1). However, CT angiography was negative and revealed no evidence of pulmonary embolism or other abnormality (not shown). Bronchoscopy revealed mild pitting of the airways along the trachea and in the right upper lobe. Scant amounts of bloody secretions were seen in the lingual. No masses were seen. Lavage fluid cytology was negative. No abnormalities were noted on transbronchial biopsies taken from the right upper lobe. Routine laboratory tests, as well as tests for antinuclear antibody, rheumatoid factor, antineutrophil cytoplasmic antibody, glomerular basement membrane, protein C, S and antiphospholipid antibodies were within normal limits.

The patient was referred for video-assisted thoracic surgery (VATS) lung biopsy. During VATS, subpleural haemorrhagic discoloration was seen within the bounds of lobules or groups of lobules (fig. 2). The parietal pleura appeared free of haemorrhage or other lesions, as did the pleural aspect of the diaphragm. Gross examination of the resected lung tissue, taken from the superior segment of the right lower lobe, did not reveal any abnormalities. The entire tissue sample was submitted for microscopic examination using haematoxylin and eosin stain, and a small panel of immunohistochemical tests were also carried out (fig. 3).

FIGURE 1. a, b) Axial and c) coronal chest computed tomography scans showing multiple scattered and bilateral opacities.

*Dept of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada. [#]Utah Valley Regional Medical Center, Provo, UT, and [†]Dept of Pathology, Mayo Clinic Scottsdale, Scottsdale, AZ, USA.

STATEMENT OF INTEREST: None declared.

CORRESPONDENCE: K.O. Leslie, Dept of Pathology, Mayo Clinic Scottsdale, 13400 East Shea Boulevard, Scottsdale, AZ 85259, USA. Fax: 1 4803018327. E-mail: leslie.kevin@mayo.edu

FIGURE 2. Thoracic videoscscopy showed multiple areas of subpleural haemorrhagic discoloration involving a) the left and b) the right lungs. No effusion, haemothorax, parietal pleural or diaphragmatic lesions were identified.

FIGURE 3. a) A haematoxylin and eosin-stained tissue section showing a characteristic lesion (abnormal glands (arrows), surrounding stroma (black arrowhead) and haemorrhage (white arrowhead)) within a bronchiole. b) An immunostained tissue section showing abnormal CD10-positive stromal cells. c) A dual-colour immunostained tissue section showing ectopic cells positive for oestrogen receptor (pink) with adjacent native lung bronchial epithelium positive for thyroid transcription factor, a marker used to identify cells of lung and thyroid origin (brown). Scale bars=0.5 (a), 0.1 (b) and 0.2 (c) mm.

BEFORE TURNING THE PAGE INTERPRET THE HISTORY, COMPUTED TOMOGRAPHY SCANS AND THORASCOPIC VIDEO IMAGES, AND SUGGEST A DIAGNOSIS.

INTERPRETATION

Chest radiography

The chest radiography showed multiple, irregular peripheral parenchymal opacities scattered throughout both lungs, interpreted as “possible bronchiolitis without evidence of pneumonia” (fig. 1). No pneumothorax or pleural effusion was identified.

Histopathology

Microscopic examination of the wedge biopsy revealed abnormal formations of ectopic glandular columnar epithelium surrounded by spindle stromal cells within lung parenchyma in a bronchovascular distribution. Some lesions were situated within bronchiolar submucosa, with ectopic glandular epithelium in continuity with native bronchial epithelium. Haemorrhage into the bronchiolar lumen was also noted (fig. 3a). There was associated lymphoid hyperplasia and evidence of recent parenchymal haemorrhage in the form of hemosiderosis with encrustation of venular elastic fibres. The pleural tissue submitted did not contain these lesions. To confirm the identity of the abnormal tissue, immunohistochemistry for oestrogen (OR) and progesterone receptors (PR) and CD10 was performed. This showed that both glandular and stromal elements were OR/PR positive and the stroma was CD10 positive, consistent with endometrial tissue (fig. 3b). In addition, thyroid transcription factor (TTF)1 immunostaining was used to confirm the origin of the glandular component. Absence of TTF1 immunoreactivity indicated that the glands did not represent entrapped native lung epithelium (fig. 3c). This finding also helped to rule out the possibility of a metastatic low-grade endometrial stromal sarcoma, which would only contain OR/PR and CD10-positive endometrial stroma.

Diagnosis: catamenial haemoptysis.

CLINICAL COURSE

The patient had no complications from the VATS procedure and refused hormone suppression therapy, alternatively electing to attempt pregnancy.

DISCUSSION

Thoracic endometriosis, depending on the extent and tissue affected, can produce pleuritic chest pain, pleural effusion, pneumothorax, haemothorax and/or haemoptysis (thoracic endometriosis syndrome) [1, 2]. Isolated catamenial haemoptysis, characterised by bloody sputum occurring exclusively at the time of menses, appears to be the rarest presentation of thoracic endometriosis syndromes, with <50 cases reported [2]. Haemoptysis presenting without pleuritic chest pain or pneumothorax suggests that the endometriotic focus is within lung parenchyma or airway mucosa. It is estimated that ~2% of cases of extrapelvic endometriosis involve the thorax and, of these, only approximately one in five cases exclusively involve lung parenchyma, producing catamenial haemoptysis [3–5]. In many instances, a presumptive diagnosis of parenchymal endometriosis is made and the patient is treated by hormone therapy or surgery. A summary of recent literature on bronchopulmonary endometriosis is presented in table 1. In the case of localised, surgically resected lesions, histopathological confirmation of the disease can be made [6]. The current study presents a case of pulmonary peribronchovascular endometriosis where complete radiological, thorascopic,

TABLE 1 Summary of recent case reports of catamenial haemoptysis due to parenchymal and/or endobronchial endometriosis

Reference	Patients n	Age range yrs	Pertinent medical history	Imaging	Pathology confirmation	Treatment	Follow-up* months
[7]	1	26	None	CT, MRI, FOB	Yes	VATS	10
[8]	1	29	G1P1	CT, FOB	No	None	36
[9]	4	26–41	C/S × 2 (1 patient)	CT, FOB	Yes by cytology brushings	Danazol	42
[10]	1	28	G1P1, induced abortion	CT, FOB	Yes	VATS	14
[5]	1	28	None	CT, FOB	No lesions found in specimen	Lobectomy	
[11]	1	28	G3P3, D&C × 2, diagnostic laparoscopy × 2; clomiphene for infertility	CT, FOB, angiography	Negative bronchial biopsy	GnRH therapy	6
[4]	5	19–35	Induced abortion (4 patients)	CT, FOB	Yes	VATS	18
[12]	1	23	Induced abortion	CT × 3	Yes	VATS	6
[13]	1	22	None given	FOB	Yes	Argon laser	3
[14]	1	29	G2P2 by C/S	CXR, CT, FOB	Yes	VATS	6
[3]	4	22–25	1 or 2 D&C each; pelvic endometriosis in 1 patient	CT	No	None	60
[15]	1	22	None	CT	Yes	VATS	5

CT: computed tomography; MRI: magnetic resonance imaging; FOB: fibreoptic bronchoscopy; VATS: video-assisted thoracic surgery; G: gravida; P: para; C/S: caesarean section; D&C: dilation and curettage; GnRH: gonadotropin-releasing hormone; CXR: chest radiogram. #: no patients showed recurrence of haemoptysis at follow-up.

histopathological and immunohistochemical characterisation was carried out.

A few studies have described successful *in vivo* visualisation of parenchymal lesions by CT, magnetic resonance imaging or angiography, but no modality is consistently reliable [16, 17]. Using CT, parenchymal endometriotic lesions are typically described as single or multiple opacities, nodules or cysts, which are most clearly seen during menstruation [4, 8]. Surgical treatment is considered when the disease is limited to a single or several resectable foci and when hormonal suppression is contraindicated, most notably in patients still wishing to become pregnant. In most cases with multiple lesions, some form of hormonal suppression is used. Several studies also indicate that the disease can spontaneously regress without any treatment (table 1).

It is hypothesised that intraparenchymal transplantation of endometrium occurs through lymphatic or vascular embolisation [1]. Surgical manipulation or trauma within or in the vicinity of the endometrial cavity could result in production of endometriotic microemboli [18]. This mechanism is plausible in the present case given the history of uterine curettage.

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