Catamenial Hemoptyisis From Tracheobronchial Endometriosis*

Reappraisal of Diagnostic Value of Bronchoscopy and Bronchial Brush Cytology

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Objectives: To analyze the clinical data of four patients with a diagnosis of tracheobronchial endometriosis, and to reappraise the diagnostic value of bronchoscopy and bronchial brush cytology in these patients.

Methods: We conducted a retrospective study of four patients with documented tracheobronchial endometriosis treated at National Taiwan University Hospital from 1994 to 1998. The complete histories, diagnostic time interval, results of physical examinations, laboratory data, bronchoscopic findings, cytologic results, chest radiographs, and chest CT of these patients were analyzed.

Results: These patients tend to be younger and nonmultiparous as compared to other patients with thoracic endometriosis. Bronchoscopic examination performed within 1 day or 2 days of menses disclosed multiple purplish-red submucosal patches bilaterally that bled easily when touched. Cytologic evaluation of the brushing specimens demonstrated clusters of small cuboid cells consistent with an endometrial origin. Follow-up bronchoscopic examination in the middle of the menstrual cycle showed disappearance of the previous tracheobronchial lesions. The mean diagnostic interval was 3.25 months. All four patients were successfully treated with danazol therapy.

Conclusions: Tracheobronchial endometriosis consists of a special subgroup of patients with thoracic endometriosis. Proper timing of bronchoscopic examination plays an important diagnostic role in these patients. Cytologic features as well as cyclic changes in bronchoscopic findings are sufficient to warrant the diagnosis. The results of treatment with danazol in these patients seemed favorable.

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Key words: bronchial brush cytology; bronchoscopy; catamenial hemoptyisis; tracheobronchial endometriosis

Periodic hemoptyisis occurring at the time of menstruation (catamenial hemoptyisis) is a rare disorder and generally signifies the presence of thoracic endometriosis. Since the first case published by Schwarz in 1938, <20 cases have been reported. All of the reported cases have been attributed to pulmonary endometriosis, although less than one third have had histologic evidence. Since most reported cases of thoracic endometriosis have involved the distal pulmonary parenchyma rather than the airways, the diagnostic yield from bronchoscopic examination in these patients has been low. Some investigators have even suggested that when appropriate clinical and radiographic findings are present, further tests, including fiberoptic bronchoscopy, are not indicated. We previously reported a case of tracheobronchial endometriosis diagnosed by bronchoscopic examination, and have subsequently made bronchoscopic diagnosis of tracheobronchial endometriosis in three more patients. Owing to the paucity of cases of tracheobronchial endometriosis in the literature, information regarding the natural history and therapy of this disease is also limited. In this study, we analyzed the clinical data of these four patients, who were found to belong to a special subgroup of patients with thoracic endometriosis, and we reappraise the diagnostic value of bronchoscopy in these patients.

Materials and Methods

We conducted a retrospective study of four patients with a diagnosis of catamenial hemoptyisis with tracheobronchial endometriosis, who were treated at National Taiwan University Hospital from 1994 to 1998. The diagnosis was made by bronchoscopy and bronchial brush cytology in all patients. The time interval from the appearance of catamenial hemoptyisis to a definite diagnosis of tracheobronchial endometriosis was recorded. Complete histories, physical examinations, laboratory data, bronchoscopic findings, cytologic results, chest radiographs, and chest CT were obtained. All patients were treated with danazol. The duration of danazol treatment and time of follow-up after cessation of danazol were recorded. The treatment results among these patients were analyzed.

Results

All four patients were women (mean age at diagnosis, 32 years; range, 26 to 41 years), without a history of hemoptyisis at any other time in their menstrual cycles. There was
no prior history of dysmenorrhea or abnormal vaginal bleeding. One patient underwent two previous cesarean sections. No pelvic operation history was found in the other patients. Gynecologic examinations revealed no evidence of pelvic or abdominal endometriosis. Physical examination results were unremarkable. Laboratory investigations revealed normal complete blood counts, coagulation parameters, urea and electrolyte levels, and liver function tests. Sputum smears were negative for acid-fast bacilli and malignant cells. Chest radiographs during hemoptysis were normal. CT scan of the chest during hemoptysis was normal in three patients, and demonstrated mild thickening of the bronchial wall and peribronchial infiltrates over the right middle lobe in one patient. Bronchoscopic examination performed within 1 or 2 days of menstruation disclosed multiple purplish-red submucosal patches in the trachea and bilateral bronchial trees, with easy touch oozing in all four patients (Fig 1). The location of lesions in each patient is shown in Table 1. Cytologic evaluation of the brushing material demonstrated clusters of small cuboid cells consistent with an endometrial origin (Fig 2). Biopsies were performed in two patients: one showed hemorrhage and normal mucosa, and the other showed subepithelial fibrosis. Cultures of bronchial brushings were negative for *Mycobacterium tuberculosis* and fungi. Follow-up bronchoscopic examination in the middle of cycles showed disappearance of the previous tracheobronchial lesions. Two patients received bronchoscopic examination during the next episode of hemoptysis concurrent with menstruation. These examinations disclosed recurrence of the purplish tracheobronchial lesions. The locations and characteristics of the lesions were the same as in the previous bronchoscopic findings. The brush cytology again revealed distinctive features of endometrial cells. The mean diagnostic interval was 3.25 months (range, 1 to 6 months; Table 1). All patients were treated and cured medically with danazol. Among these patients, one received an initial dosage of 400 mg/d and treatment was continued for 8 months; however, her hemoptysis recurred 3 weeks later after discontinuation of danazol. Danazol treatment was reinstituted at a higher dosage, 600 mg/d, for 6 months. No further hemoptysis was reported in the following 3.5 years. Danazol, 600 mg/d, was administered to the other three patients. The treatment was maintained for 6 months in one patient and for 9 months in the other two patients. No recurrent hemoptysis developed. The median follow-up time was 25 months.

**Discussion**

Hemoptysis is a common clinical problem with many potential etiologies. With a history of hemoptysis that is concurrent with menstrual periods, it helps to differentiate catamenial hemoptysis from hemoptysis of other causes. The diagnosis of thoracic endometriosis is usually made on the basis of the clinical history and the exclusion of other causes of recurrent hemoptysis.

According to its localization, thoracic endometriosis has been categorized as either pleural or parenchymal (pulmonary endometriosis). The pleura is the most commonly involved structure in thoracic endometriosis. Reports of catamenial hemoptysis suggesting intrapulmonary or bronchial involvement are less common. Tracheobronchial endometriosis occurs only in a small portion of cases of thoracic endometriosis with parenchymal involvement. However, the results of this study suggest that tracheobronchial endometriosis should be categorized as a subgroup of thoracic endometriosis. It differs from other subgroups of thoracic endometriosis with respect to clinical history, diagnostic role of bronchoscopy, diagnostic...
time interval, and treatment results with danazol. It has been reported that women with cyclic hemoptysis caused by pulmonary endometriosis tend to be older and multiparous, which is different from the patients with tracheobronchial endometriosis in this series (39 years vs 32 years). The diagnostic yield from bronchoscopic examination is low, since most cases of pulmonary endometriosis involve the distal parenchyma rather than the mucosa of large bronchi, and the washings and biopsy specimens often yield inconclusive results. This explains why histologic confirmation has been obtained in less than one third of reported cases and more invasive diagnostic procedures were required. A case of pulmonary arteriovenous malformation mimicking catamenial hemoptysis has been reported. Hence, the need for histologic or cytologic evidence to diagnose pulmonary endometriosis should be emphasized to prevent misdiagnosis or unnecessary drug therapy. In this series, the cytologic features as well as the cyclic changes of the bronchoscopic findings were sufficient to warrant the diagnosis of tracheobronchial endometriosis in all patients. The diagnostic time interval was short because of prompt clinical suspicion and proper timing of bronchoscopic examinations, which avoided unnecessary diagnostic procedures or the need for "doctor shopping," due to lack of a definite diagnosis. The disabling complications perpetuated by a delay in diagnosis and ineffectual therapy can be prevented. The need for serial CT scan of the chest both during and in the interval between menses has been suggested by some investigators. However, the diagnostic role of CT scan of the chest was minor in this series.

Medical treatment has usually been the first line of treatment for pulmonary endometriosis. Current treatment regimens include danazol and gonadotropin-releasing hormone analogs. Although most patients have an excellent response while receiving therapy, remission rates after cessation of therapy vary widely. All four patients in this series were cured by danazol alone, and no recurrence of hemoptysis was noted after complete treatment. Although the case number in this series was small and the follow-up period was short, the results of treatment with danazol in this group of patients seemed favorable.

In conclusion, tracheobronchial endometriosis consists of a special subgroup of thoracic endometriosis. These patients tend to be younger and nonmultiparous, compared to types of patients with thoracic endometriosis with parenchymal involvement. The diagnostic role of CT scan of the chest is minor. Proper timing of bronchoscopic examination plays an important diagnostic role in tracheobronchial endometriosis. Cytologic features as well as cyclic changes of bronchoscopic findings were sufficient to warrant the diagnosis. The results of treatment with danazol in this group of patients seemed favorable.

**REFERENCES**


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**Table 1—Clinical Features of Tracheobronchial Endometriosis in Four Patients**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, yr</th>
<th>Obstetric History</th>
<th>Pelvic Endometriosis</th>
<th>Diagnostic Time Interval, mo</th>
<th>Location of Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>Gravida 0 Parity 0</td>
<td>Nil</td>
<td>6</td>
<td>Lower trachea, left second carina</td>
</tr>
<tr>
<td>2</td>
<td>41</td>
<td>Gravida 2 Parity 2</td>
<td>Nil</td>
<td>3</td>
<td>Mid-trachea</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>Gravida 0 Parity 0</td>
<td>Nil</td>
<td>1</td>
<td>Lower trachea, carina, left main bronchus</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>Gravida 0 Parity 0</td>
<td>Nil</td>
<td>3</td>
<td>Upper trachea, orifice of right bronchus B9</td>
</tr>
</tbody>
</table>

*G-gravid; P-para; B9-lateral basal segment of right lower lobe.*

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**Figure 2.** Photomicrograph of smear from bronchial brush performed during menstruation in patient 3. Clusters of small cuboid cells consistent with endometrial stromal shedding are shown (arrows); some bronchial ciliated epithelial cells are also demonstrated (arrowheads). *Top, A: Papanicolaou stain, original × 143. Bottom, B: Riu’s stain, original × 573.*
Methemoglobinemia After Infusion of Ifosfamide Chemotherapy*

First Report of a Potentially Serious Adverse Reaction Related to Ifosfamide

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Acute formation of methemoglobin is a life-threatening condition caused by multiple medications. In this article we report the first case of methemoglobinemia in a patient with metastatic uterine leiomyosarcoma, after infusion of ifosfamide chemotherapy. The patient recovered after prompt diagnosis and treatment of the condition. A mechanism for the formation of methemoglobin as a result of the ifosfamide infusion is offered.

(CHEST 2000; 118:1208–1210)

Key words: ifosfamide; methemoglobin; methylene blue

Methemoglobinemia is a condition that results from formation of abnormal hemoglobin. Acute methemoglobinemia is life threatening. Multiple medications can cause methemoglobin formation, and the list is constantly growing, as more and more therapeutic agents enter the market. Prompt diagnosis, removal of the offending agent, and treatment can quickly reverse methemoglobin formation. We report the first case in the literature, to our knowledge, of methemoglobinemia induced by the chemotherapeutic agent ifosfamide, and we offer a mechanism for the formation of methemoglobin.