Catamenial Hemoptysis: A Nationwide Analysis in Korea

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Key Words

Catamenial hemoptysis • Endometriosis • GnRH analogues • Hemoptysis, massive • Tracheobronchial endometriosis

Abstract

Background: Hemoptysis is a potentially serious clinical problem. However, there is no consensus on the clinical characteristics, treatment and patient outcome of catamenial hemoptysis. **Objective:** Clinical characteristics, treatments and outcome in patients of catamenial hemoptysis were evaluated. **Methods:** We conducted a retrospective nationwide observational analysis of Korean patients with catamenial hemoptysis. **Results:** Nineteen patients with catamenial hemoptysis were evaluated from 13 tertiary-care hospitals in Korea. The median age of the patients was 25 years; 8 (42%) were ever-smokers. Eight patients were pathologically diagnosed; 11 were diagnosed by clinical criteria. Sixteen (84%) patients had a history of obstetric or gynecological procedures before developing hemoptysis. The mean amount of hemoptysis (mean $\pm$ SD) was 58.3 ± 71.3 for surgery, 46.4 ± 33.2 for hormonal and 29.1 ± 26.3 for conservative treatment groups. Hemoptysis did not recur in 8 (89%) of 9 patients after surgery. None of the patients in

the hormonal or conservative treatment groups had persistent hemoptysis. There was an excellent outcome (complete remission and partial responses) in all patients with conservative treatment, suggesting that endometrial cells implanted into the lung may have a benign course. **Conclusion:** Patients without massive hemoptysis can be treated conservatively or with hormonal agents.

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Introduction

Catamenial hemoptysis is a rare disorder that is characterized by hemoptysis occurring concomitant with menstruation in female patients. It is presumed to be due to intrabronchial or parenchymal endometrial tissue deposits, and is considered a subset of extrapelvic endometriosis [1]. Currently, there are about 40 cases reported in the English literature. There are no large-scale systematic studies on catamenial hemoptysis due to its scarcity. Most of the information available on this disorder is

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based on anecdotal evidence. The etiological mechanisms remain to be elucidated, and optimal management is debated. Various treatment modalities such as surgery, hormonal therapy or conservative management have been attempted [1–16]. However, the current knowledge on treatment outcomes of catamenial hemoptysis is largely based on case reports of patients with pelvic endometriosis. There is no consensus on the clinical characteristics, treatment and patient outcome of catamenial hemoptysis.

Therefore, we conducted a retrospective nationwide observational study and identified 19 patients with catamenial hemoptysis. Here, we report their clinical characteristics, treatments and outcome.

Patients and Methods

We conducted a retrospective nationwide survey in 2006. Forty tertiary-care hospitals were initially contacted; pulmonary physicians were asked whether they had experience with catamenial hemoptysis. The study protocol was explained and if they had experience with such patients they were invited to participate. For inclusion in the study, subjects were required to have at least one of the two following diagnostic criteria: pathological findings consistent with the diagnosis or a clinical history of at least six synchronous occurrences of hemoptysis with menstruation, characteristic findings on a chest CT performed both during menstruation and between menstruation, and exclusion of other causes of hemoptysis. Of 24 patients diagnosed between March, 1995, and July, 2006, 5 were excluded from this study because of lack of accordance with the inclusion criteria.

The following information (referring to the time of the diagnosis) was requested and obtained by reviewing the medical record, and radiologic and bronchoscopic examinations by a chest physician and radiologist in each institution: smoking habits, maximal amount of hemoptysis per day, number of occasions with synchronous hemoptysis, history of obstetric or gynecological procedures before hemoptysis, results of a chest CT scan and bronchoscopic examination, treatment, response to treatment, follow-up and survival. Response to treatment was evaluated arbitrarily with the following criteria: complete remission was defined as absence of hemoptysis during follow-up; a partial response was defined as a decrease in the amount or frequency of hemoptysis; stable disease was defined as persistence of hemoptysis without any changes in the amount and frequency. The duration of follow-up was calculated from the end of treatment in patients that received either hormonal treatment or surgery, and from the diagnosis in patients who received conservative treatment. The clinical characteristics, treatment and responses were analyzed. To make up for the retrospectively collected data, we tried to contact patients with incomplete data on obstetric and gynecologic history or follow-up by telephone or mail. Of 11 patients, 4 patients (patient 7, 9, 15 and 16) were not contactable. The Institutional Review Board of the Inha University Hospital (Incheon, South Korea) approved this study.

Results

Clinical Characteristics of the Patients with Catamenial Hemoptysis

A total of 19 patients were finally recruited from 13 tertiary care hospitals in South Korea (table 1). The median age of the patients was 25 (range 16–52 years). The mean follow-up lasted 33 months (range 3–82). Eleven (58%) patients were single women and 8 (42%) were ever-smokers. Eight (patients 1–7 and 14) were diagnosed by pathological findings, and 11 (patients 8–13 and 15–19) by clinical findings. Hemoptysis occurred monthly in 16 patients; bimonthly in 2 (patients 3 and 15) and irregularly in 1 (patient 5). The maximal amount of hemoptysis at presentation varied from 5 to 200 ml/day. The mean duration of hemoptysis was 21 months (range 6–120). Sixteen patients (84%) had a history of obstetric or gynecological procedures before developing hemoptysis. The median number of procedures before diagnosis was two (range 0–4).

Chest CT Scan and Bronchoscopic Examination at Diagnosis

On the chest CT scan, ground glass opacities were the findings most often identified ($n = 16$; 84%), consolidation was observed in 6 patients (32%) and a nodule in 4 (21%). No cavitary lesions were found. The size of the lesions was smaller or disappeared between menses. The lesions were more commonly located in the right lung field rather than the left, and favored the distribution in the lower lobe compared to the upper or middle lobes (fig. 1). No lesions were noted in the trachea or bronchi that were suspicious for endometriosis by bronchoscopic examination during episodes of hemoptysis in 16 patients (84%). Sputum examination among 11 patients failed to demonstrate endometrial cells (data not shown).

Treatment Outcome

The mean follow-up duration was 33 months (range 3–81) for the total study group, and for subgroups according to first-line treatment: 41.5 months for surgery, 26.7 months for hormonal treatment and 31.7 months for conservative treatment. The mean amount of hemoptysis ($\pm$ SD) was 58.3 ($\pm$ 71.3) for the surgery group, 46.4 ($\pm$ 33.2) for the hormonal and 29.1 ($\pm$ 26.3) for the conservative treatment groups. No patient died during the follow-up. Surgery was performed in 6 (31.5%) patients as first-line treatment (5 wedge resections and 1 lobectomy). Three patients who had a partial response to other treatment methods received surgery as second-line treatment

Table 1. Clinical characteristics of patients with catamenial hemoptysis at diagnosis

No.	Date of diagnosis	Age years	Smoking habit	Amount of hemoptysis, ml	Synchrony n	Regularity of the synchronicity	OB procedure, n	Dysmenorrhea	Gravida	Para
1	December, 2004	24	current	200	6	yes	3	no	3	0
2	May, 2004	26	never	20	12	yes	1	yes	0	0
3	July, 1996	52	never	50	120	no	2	yes	3	1
4	March, 2005	33	never	50	2	yes	1	no	0	0
5	July, 2004	31	never	20	10	no	2	no	2	2
6	December, 2003	25	current	10	24	yes	3	no	3	0
7	March, 1999	25	former	100	8	yes	2	no	2	0
8	August, 1999	35	current	70	10	yes	2	no	4	2
9	October, 2001	31	NA	20	24	yes	2	no	NA	NA
10	June, 2005	26	never	70	8	yes	1	no	1	0
11	August, 2005	36	never	30	10	yes	2	no	2	2
12	July, 2006	16	never	20	12	yes	0	yes	0	0
13	July, 2001	24	current	15	60	yes	3	yes	7	2
14	May, 2000	26	current	70	10	yes	4	no	6	2
15	April, 2001	21	never	15	6	no	0	no	0	0
16	June, 1999	24	never	30	36	yes	0	no	0	0
17	November, 2001	23	current	5	12	yes	1	yes	1	0
18	November, 2001	24	never	5	15	yes	1	yes	1	0
19	August, 2005	20	current	50	14	yes	1	yes	1	0

Patients 1–7 and 14 were pathologically diagnosed, and patients 8–13 and 15–19 clinically. Hemoptysis was expressed as the maximum amount of hemoptysis per day (in ml), and synchrony as the number of hemoptysis episodes that occurred synchronously with menstruation. NA = Not available; OB = obstetric or gynecological.

Fig. 1. Topographic location of lesions seen on chest CT scans at diagnosis. Numbers in the left and right lobes refer to the lesion site of the corresponding patient.

(table 2). A complete response was observed in most patients receiving surgical resection, except 1 patient (No. 19), in whom endometrial tissue was not found on pathology. Hormonal treatment was initially provided in 7 (37%) patients; a complete response occurred in 3 (43%) patients and a partial response in 4 (57%). Six (31.5%) patients were treated conservatively; 3 of them (50%) had a complete response and 3 (50%) a partial response. Two with a partial response subsequently underwent surgical treatment; despite this, 1 patient (No. 19) still only experienced a partial response.

Discussion

Hemoptysis is a very common clinical problem. Treatment of hemoptysis is usually decided based on its etiology and severity. However, unlike most other causes of hemoptysis, the treatment of catamenial hemoptysis has no specific guidelines because little is known about the characteristic clinical findings, most appropriate treatment and patient outcome. It has been reported that tho-

Table 2. Response to treatment in patients with catamenial hemoptysis

Patients	1st-line treatment	Response	2nd-line treatment	Response	Follow-up, months
1	wedge resection	CR	–		42
2	lobectomy	CR	–		31
3	wedge resection	CR	–		72
4	wedge resection	CR	–		21
5	wedge resection	CR	–		29
6	wedge resection	CR	–		54
7	GnRH analogue	PR	segmentectomy	CR	7
8	GnRH analogue	PR	–		20
9	GnRH analogue	CR	–		6
10	GnRH analogue	CR	–		36
11	progesterone	PR	pregnancy	CR	14
12	oral contraceptive	CR	–		22
13	progesterone	PR	GnRH analogue	CR	82
14	conservative	PR	wedge resection	CR	31
15	conservative	PR	–		4
16	conservative	CR	–		3
17	conservative	CR	–		60
18	conservative	CR	–		59
19	conservative	PR	wedge resection	PR	33

CR = Complete remission was defined as absence of hemoptysis during follow-up; PR = partial response defined as hemoptysis that decreased in amount or frequency and was clinically insignificant.

racic endometriosis is either pleural (83%) or parenchymal (17%) [2]. The pleura is the most commonly involved thoracic location of endometriosis, whereas reports of catamenial hemoptysis suggesting intrapulmonary or bronchial involvement are uncommon [1].

The pathogenesis of thoracic endometriosis is not clear. However, several hypotheses have been proposed, including differentiation of mesothelial cells into endometrial cells (coelomic metaplasia), retrograde flow of the endometrial tissue through diaphragmatic defects (transplantation) and microembolization via pelvic veins [17]. The theory of coelomic metaplasia or transplantation does not explain the presence of endometrial tissue within the lung parenchyma.

The history of an obstetric or gynecological procedure (especially induced abortion) was common in patients with catamenial hemoptysis. This finding suggests that such procedures may be an important risk factor for the development of catamenial hemoptysis. Yeh [18] suggested that pleural endometriosis is caused by retrograde flow of the endometrial tissue through diaphragmatic defects, and that intrapulmonary endometriosis is caused by microembolization of endometrial cells. The findings that the right and lower lung fields were preferred sites,

which was confirmed by chest CT in this study, is in support of the microembolization theory because these findings can be explained by the largest quantity of blood perfusion found in the right and lower lung fields [19].

Interestingly, the frequency of ever-smokers among the patients was found to be much higher than in the general population – the average smoking rate among Korean women aged ≥ 20 years being estimated to be 3.9% in 2006 [20]. This finding does not appear to be related to the disorder.

There has been no report of a patient with catamenial hemoptysis with massive or fatal hemoptysis [17]. In this study, however, 2 patients presented with massive hemoptysis. The severity of hemoptysis may be influenced by the amount of endometrial tissue and the biological activity of this tissue, e.g. hormonal effects, since hemoptysis is observed only during menstruation, and the size of the lesions changes during the menstrual cycle [21]. The fact that hemoptysis was present bimonthly or irregularly in some patients suggests that endometrial tissue in the lungs was not regularly influenced by hormonal effects. Currently, we do not know how long endometrial tissue can survive in the lungs or what factors affect its biological activity. Future studies are warranted to answer these questions.

Ground glass opacities were most commonly encountered on chest CT scans in this study. These lesions might represent parenchymal endometrial tissue or blood only. Tracheobronchial endometriosis is a subtype of catamenial hemoptysis, and the timing of the bronchoscopic examination is important for diagnosis in these cases [3, 4]. Bronchoscopic examination at the time of hemoptysis, however, failed to demonstrate the presence of any central airway lesions in this study. This suggests that tracheobronchial endometriosis accounts for a small subset of patients with catamenial hemoptysis.

Eight of 9 patients that had surgery showed a complete response; the only failure might have been due to difficulty in localizing the lesion (patient 19). This finding suggests that localization is important for the success of surgery. Therefore, every effort should be made to accurately locate the source of bleeding [22]. Among the 9 patients undergoing surgery, 7 patients presenting with non-massive hemoptysis seemed to be over-treated for the following reasons. First, excellent control (complete remission plus partial response) was achieved in all patients with hormonal or conservative treatment. The results of the conservative treatment suggest that endometrial tissue in the lungs might have a benign course. Second, most patients are of reproductive age and sexually active. Third, there was no mortality although 2 patients presenting with massive hemoptysis were subjected to surgery. However, surgery, even including limited resection, can be associated with morbidity and mortality [23] and should be carefully considered before choosing it as the first-line treatment in patients with non-massive hemoptysis.

Even though hormonal treatment with gonadotropin-releasing hormone analogues, oral contraceptives, progestational drugs or danazol is commonly used for catamenial hemoptysis [5, 6], it is expensive, and the symptoms often recur after the treatment is discontinued [7]. Furthermore, since these drugs inhibit ovulation, patients who want to become pregnant refuse to undergo

hormonal treatment [7, 24]. Therefore, hormonal treatment would not be indicated for young women of reproductive age considering pregnancy. The results of conservative treatment were similar to those of hormonal treatment in this study. Therefore, conservative treatment might be considered as first-line treatment in these women, especially those with mild symptoms.

This study may be potentially limited by its retrospective nature and thus the results must be interpreted with some caution. First, follow-up was not regularly conducted and the data on the effects of treatment and relapse were insufficient to draw definite conclusions in some patients. Second, the central form of endometriosis was not observed in this study. Although the diagnostic yield from the bronchoscopic examinations was low, intrapulmonary endometriosis involves more commonly the distal parenchyma; lavages and biopsy specimens often yield inconclusive results [3, 25]. Possibly, clinicians who are not familiar with this disorder might ignore suspicious mucosal lesions from bronchoscopic examinations. Third, none of the patients had a laparoscopic examination or ultrasound at diagnosis; these are standard methods used to detect the concurrent presence of endometriosis [26, 27].

In spite of these limitations, this study reports the clinical characteristics and treatment outcome of the largest number of patients with catamenial hemoptysis published to date. The findings suggest that aggressive treatment should be performed in carefully selected patients with more severe hemoptysis and well-localized lesions, whereas hormonal or conservative treatment appears to be adequate first-line treatment for patients with less severe hemoptysis.

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