CASE REPORT

Endometriosis Associated with Hemothorax

Hung-Tsung Lee[1], Hong-Chung Wang[1]*, Ia-Tang Huang[1], Huang-Chou Chang[2], Jau-Yeong Lu[3]

[1]Division of Chest Medicine, Department of Internal Medicine, [2]Division of Thoracic Surgery, Kaohsiung Veterans General Hospital, Kaohsiung, and [3]Division of Chest Medicine, Department of Internal Medicine, E-DA Hospital, Kaohsiung, Taiwan, R.O.C.

Bloody pleural effusion is rarely associated with endometriosis. To effectively treat this condition, it is important to differentiate the malady from other common diseases such as malignancy or tuberculosis. We describe the case of a 40-year-old multiparous female featuring right-sided hemothorax presenting with right shoulder pain and progressive shortness of breath for the preceding 2 months. Thoracoscopy disclosed grossly negative findings apart from multiple small pores in the right hemi-diaphragm with blood clots within them. Examination of the thoracoscopic biopsy specimens showed chronic pleuritis without evidence of malignancy or tuberculosis. Pelvic endometriosis was considered a possible diagnosis according to the results of abdominal computed tomography (CT) scan, transvaginal sonography, and the results of dilatation and curettage. Periodic episodes of symptoms concurrent with menstruation led to the suspicion of a relationship between these conditions in our patient. Despite the patient undergoing an abdominal total hysterectomy and adhesiolysis without salpingo-oophorectomy, recurrent right-sided bloody pleural effusion developed 1.5 months subsequent to surgery. As a consequence, danazol (400 mg/day) was maintained because of the endometriosis associated with pleural effusion. One year of regular follow-up later, there was no evidence of recurrent pleural effusion. We considered that the bloody pleural fluid arose via seepage from the pelvic endometriosis through the pores of the right hemi-diaphragm during menstruation. [*J Chin Med Assoc* 2006;69(1):42–46]

Key Words: endometriosis, hemothorax, pleural effusion, thoracoscopy

Introduction

Bloody pleural effusion may be a clinical complication of many diseases, such as tuberculosis, malignancies, pneumonia, trauma, pulmonary infarction, some connective-tissue diseases and sarcoidosis, and, on rare occasions, endometriosis.[1–5] To the best of our knowledge, bloody pleural effusion associated with endometriosis was first described by Brews in 1954.[1] Despite the relative rarity of such a condition, the fact that exudative bloody effusion is eminently treatable makes it an important diagnostic condition to consider, when appropriate. Most endometriosis-induced hemothorax involves right-sided pleura with periodic symptoms, like right shoulder pain and shortness of breath.[2–5] In addition, concurrent ascites is often mentioned.[2–5] From a thorough review of the literature, it would appear that mechanisms for the development of the condition are still controversial.[2–5] We herein report a case of endometriosis featuring right-sided pleural effusion, which was evident with trans-diaphragmatic defects rather than ectopic endometriosis of the pleura, which was diagnosed by thoracoscopic findings.

Case Report

A 40-year-old Asian woman (gravida 5, para 3, abortion 2) presented with a 2-month history of progressive shortness of breath and dyspnea on exertion. Abdominal cramping pain, right pleuritic chest pain, fatigue,

*Correspondence to: Dr. Hong-Chung Wang, Division of Chest Medicine, Department of Internal Medicine, Kaohsiung Veterans General Hospital, 386, Ta-Chung 1st Road, Kaohsiung 813, Taiwan, R.O.C.
E-mail: secobarbitalee@yahoo.com.tw • Received: January 3, 2005 • Accepted: August 10, 2005

diarrhea, and right shoulder pain accompanied with deep breathing were noted during menstruation. Right shoulder pain was more severe when the patient was lying down. The patient denied any body weight loss, fever, cough, hemoptysis, and/or drug use. She reported suffering from dysmenorrhea since menarche at age 12, a feature that had become more prominent over the previous 3 years. Her menstruation cycles were reported to be regular, successive episodes being about 22 days apart, each cycle lasting for 3–7 days, with discharge typically being described as heavy. Physical examination of this patient upon admission revealed a temperature of 37°C, a pulse rate of 60 beats/minute, a respiration rate of 21 breaths/minute, and a blood pressure of 111/75 mmHg. The patient featured a clear consciousness level with decreased breathing sounds and dullness of percussion of the right lung. Heart, abdominal, and pelvic examinations revealed no remarkable findings. The chest radiograph (CXR) disclosed right pleural effusion (Figure 1A). Laboratory studies, including complete blood count, serum electrolytes, glucose, creatinine, liver function, a venereal disease research laboratory slide test, human immunodeficiency virus test, and carcinogen embryonic antigen (CEA) test all returned results that were within normal limits, although an elevated serum CA-125 level of 53.8 U/mL (normal < 35 U/mL) was noted. Bloody pleural effusion was drained (approximately 3,000 mL over the 7-day interval subsequent to patient admission). A pleural-effusion analysis revealed lactate dehydrogenase (LDH), 522 U/L; protein, 5.6 g/dL; glucose, 51 mg/dL; white blood cell count (WBC), 660 cells/mm^3; neutrophils, 30%; lymphocytes, 68%; and red blood cell count, 940,000 cells/mm^3. All cultures for bacteria, fungi, and *Mycobacterium tuberculosis*, along with repeated cytologic examinations, revealed negative findings. A rather high CA-125 level of 4,819 U/mL was noted for the pleural effusion, however. Chest and abdominal computed tomography (CT) scans failed to reveal the presence of any mass lesion of lung parenchymal tissue, although such investigation did indicate the presence of moderate amounts of pleural effusion, minimal ascites, and an ovarian cyst of about 5.2 × 3.0 cm in size over the right adnexa. Thoracoscopic findings disclosed smooth surfaces for visceral and parietal pleura without the presence of any nodules, masses, and inflammatory foci or endometriosis bleeding spots. Interestingly, multiple small pores were found in the right hemi-diaphragm with blood clots within them (Figure 2). The emergence of some bloody fluid from these defects was noted during

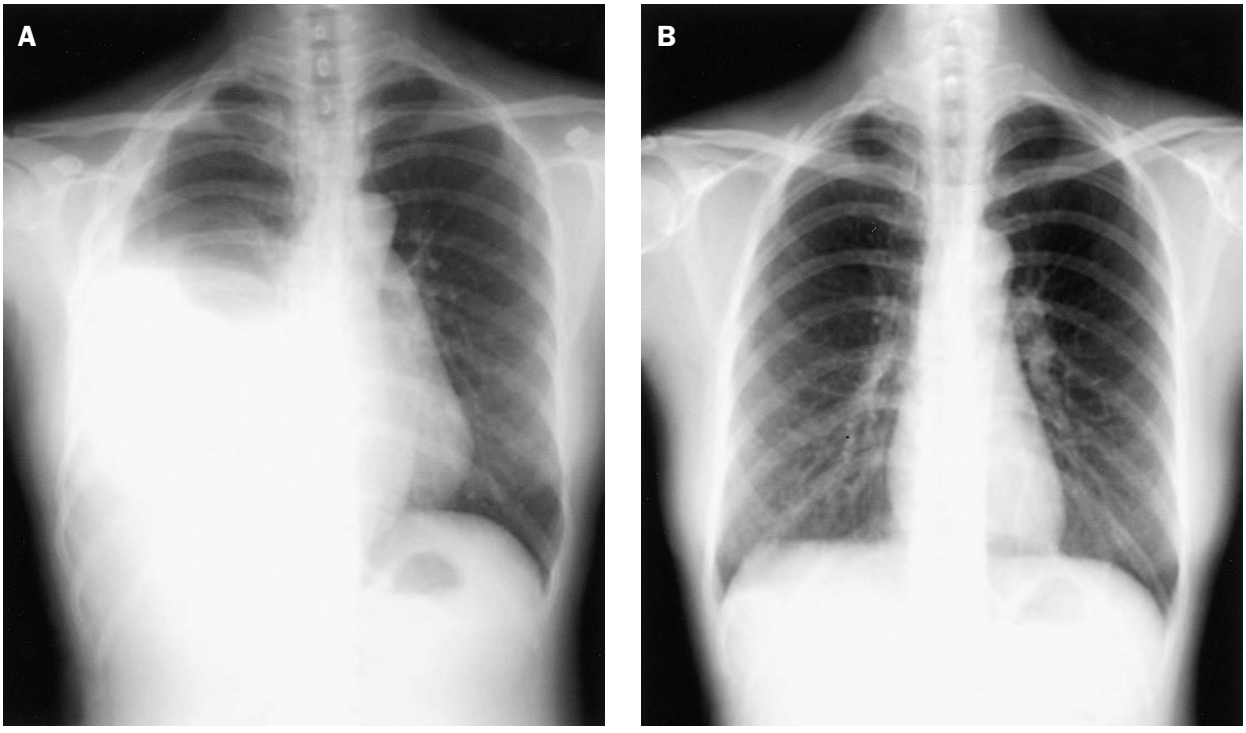

Figure 1. (A) Posteroanterior radiograph at presentation revealing massive right-sided pleural effusion. (B) Posteroanterior radiograph 1 year subsequent to treatment with danazol, the radiograph revealing no recurrent pleural effusion.

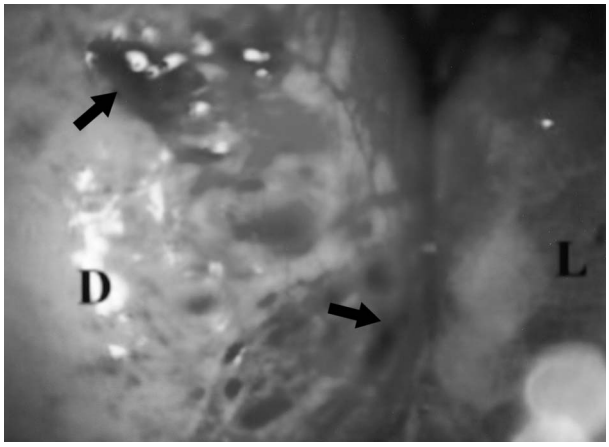

Figure 2. Thoracoscopy revealing bloody pleural effusion in the right pleural cavity, and multiple small pores with some filling with blood clots (arrows) over the right hemi-diaphragm. D = diaphragm; L = lung.

surgery. Examination of thoracoscopic pleural biopsy specimens revealed neither endometriotic tissues nor granulomatous inflammation and/or malignant cells, with only chronic pleuritis being detected. Transvaginal sonography indicated adenomyosis and ascites. The patient also received dilatation and curettage for dysmenorrhea. The histopathology of the endometrium revealed only the secretory phase of the endometrium without the presence of any malignant cells. Subsequent to discharge, dysmenorrhea and right chest discomfort did occur despite the improvement to the patient's earlier shortness of breath. Eventually, the patient returned to our hospital and she underwent abdominal total hysterectomy and adhesiolysis without salpingo-oophorectomy about 1.5 months following her initial discharge. Hemoperitoneum with about 400 mL of old blood and endometriosis-induced severe right adnexa adhesion were noted in her pelvic cavity during hysterectomy surgery. Histopathologic investigation of uterine specimens revealed intramural leiomyoma and a secretory-phase endometrium. Recurrent right-sided bloody pleural effusion did develop about 2 weeks subsequent to her latest surgery, however, for which danazol (400 mg/day) was instituted for endometriosis-related pleural effusion. After treatment for 1.5 months, this patient's residual pleural effusion was drained. Her serum CA-125 level decreased to 20.5 U/mL, and the CA-125 level in the pleural effusion decreased to 4,047 U/mL, and she continued the use of danazol. We noted that there was no recurrent pleural effusion during the follow-up CXR (Figure 1B) approximately 1 year following discharge.

Discussion

Bloody pleural effusion is commonly found in situations of malignancy and tuberculosis, although there is occasionally a rare and benign condition associated with it, such as endometriosis. In this case, we excluded malignancy and tuberculosis by means of negative findings in repeated cytologic studies, mycobacteriologic cultures, and the results of thoracoscopic biopsies, although pleural endometriosis was not visible during the thoracoscopic examination. In addition to the symptoms associated with this patient's aberrant menstruation cycle and the diaphragmatic defects revealed by the thoracoscopic findings, the response to danazol also indicated that the bloody pleural effusion was related to pelvic endometriosis.

The diagnosis of endometriotic pleural effusion and ascites is often based on an examination of a patient's history and/or clinical findings and also on the individual patient's specific response to treatment.[2–6] Biopsy and cytology findings alone would appear to rarely be useful for the diagnosis because the results of such investigations typically reveal evidence of only a nonspecific inflammatory reaction.[2] Just as with the results of thoracoscopic biopsies for our patient, such investigations only reveal chronic pleuritis without the detection of any endometriotic tissue in the biopsied tissue. Additionally, endometriosis often occurs among nulliparous young females.[2–5] This patient's multiparous history may remind us that bloody pleural effusion associated with endometriosis could also arise for older multiparous patients.

In 1996, Flanagan and Barnes[4] presented a case of pleural fluid accumulation due to intra-abdominal endometriosis and suggested that the right pleural effusion was caused by communication between the pleural and peritoneal cavities, even though there were normal thoracoscopic findings for their case. In 1996, Mittal et al[7] demonstrated peritoneopleural communication by scintigraphic studies for 12 patients featuring cirrhotic ascites with pleural effusion; Schuster et al[8] even advocated diagnostic radionuclide ascites scans to facilitate treatment decisions for cases of hepatic hydrothorax. In our case, we directly viewed diaphragmatic pores with blood emerging from them via thoracoscopy, providing further evidence that this mechanism for cases of endometriosis is related to pleural effusion. In 2000, Bhojawala et al[3] reviewed 12 cases of endometriosis with ascites and pleural effusion. From a thorough review of the literature, it would appear that most ascites associated with endometriosis have been described in patients who feature significant accumulations of fluid, this contrasting with the case

for our patient, however, in whom a minimal quantity of ascites was found. Such a scenario was also reported by Ripstein et al,[9] Mentes et al,[10] and Daly et al.[11] All reported hepatic hydrothorax in the absence of ascites, the authors explaining that, once ascitic fluid passes through congenital or acquired fenestrations in the diaphragm and directly into the pleural space, a sort of "one-way valve" mechanism is created. As long as the rate of trans-diaphragmatic flow into the pleural cavity is greater than ascites formation, ascites fluid will not accumulate. Such a hypothesis would appear to be compatible with the presence of small amounts of ascites fluid being present in the peritoneal cavity concurrent with a situation of massive pleural effusion, as was the case for our patient. The large quantity of bloody pleural effusion noted in the drainage bag of our patient might be attributable to repeated episodes (more than 2 times) of menstruation and dyspnea, which might not have been complained about until the accumulated pleural effusion reached a certain critical amount that was able to limit respiratory function.

A tumor marker such as CA-125 commonly reacts with malignant ovarian epithelial cells and has been previously used to monitor ovarian cancer, although, in most such situations there are unusually benign conditions associated with it. In 1995, Myers et al[12] presented a case featuring pelvic endometriosis mimicking advanced ovarian cancer based on an elevated serum CA-125 level of up to 400 U/mL. In our case, a high level of CA-125 in the pleural effusion was initially found, although this level did subsequently decrease following short-term danazol treatment. In 1996, Yucel and coworkers[13] reported a decreased CA-125 level in the pleural effusion following steroid treatment for a case of systemic lupus erythematosus. Thus, we suggest checking the CA-125 level from within the endometriotic pleural effusion when evaluating the relative efficacy of treatment for patients with endometriosis-associated bloody pleural effusion when treatment encompasses only medication.

To the best of our knowledge, it would appear that the definitive therapy for bloody pleural effusion associated with endometriosis is abdominal total hysterectomy with salpingo-oophorectomy.[2–5] For such patients, hormone therapy, including progesterone, danazol, and gonadotropin-releasing hormone agonist, is often initiated prior to surgery, since such patients are often young and nulliparous. Here, as a consequence of the preservation of her ovary and adnexa following total hysterectomy, this patient suffered from recurrent endometriosis and bloody pleural effusion. We used danazol as a rescue therapeutic regimen for which a good response was noted on regular follow-up CXR. In 1996, Mouroux and coworkers[14] used videothoracoscopy for 6 hepatic hydrothorax cases to close diaphragmatic defects that were all localized. Such a surgical technique might be an alternative method for effective treatment of endometriosis-induced bloody pleural effusion that is refractory to medication.

We have presented a case of endometriosis featuring right-sided pleural effusion, which was associated with the presence of trans-diaphragmatic pores, rather than a case of pleural endometriosis diagnosed by the thoracoscopic findings. This supports the mechanism of trans-diaphragmatic communication accounting for bloody pleural effusion associated with pelvic endometriosis. Because this female patient did not undergo salpingo-oophorectomy, she suffered from recurrent bloody pleural effusion. Thus, as long as surgery is considered, the specific surgical procedure intended should be thought out carefully when considering fertility, the menstruation cycle, and any possible recurrence of the disease.

References

1. Brews A. Endometriosis including endometriosis of the diaphragm and Megs' syndrome. *Proc R Soc Med* 1954;47:461.
2. Shek Y, Lia JD, Pattillo RA. Endometriosis with a pleural effusion and ascites: report of a case treated with nafarelin acetate. *J Reprod Med* 1995;40:540–2.
3. Bhojawala J, Heller DS, Cracchiolo B, Sama J. Endometriosis presenting as bloody pleural effusion and ascites: report of a case and review of the literature. *Arch Gynecol Obstet* 2000; 264:39–41.
4. Flanagan KL, Barnes NC. Pleural fluid accumulation due to intra-abdominal endometriosis: a case report and review of the literature. *Thorax* 1996;51:1062–3.
5. Wilkins SB, Thomson JB, Tyras DH. Hemothorax associated with endometriosis. *J Thorac Cardiovasc Surg* 1985;89: 636–8.
6. Olive DB, Schwartz LB. Endometriosis. *N Engl J Med* 1993; 328:1759–69.
7. Mittal BR, Maini A, Das BK. Peritoneopleural communication associated with cirrhotic ascites: scintigraphic demonstration. *Abdom Imaging* 1996;21:69–70.
8. Schuster DM, Mukundan S, Small W, Fajman WA. The use of the diagnostic radionuclide ascites scan to facilitate treatment decisions for hepatic hydrothorax. *Clin Nucl Med* 1998;23: 16–8.
9. Ripstein CB, Rohman M, Wallach JB. Endometriosis involving the pleura. *J Thorac Surg* 1959;37:464–71.
10. Mentes BB, Kayhan B, Gorgul A, Unal S. Hepatic hydrothorax in the absence of ascites: report of two cases and review of the mechanism. *Dig Dis Sci* 1997;42:781–8.
11. Daly JJ, Potts JM, Gordon L, Buse MG. Scintigraphic diagnosis of peritoneo-pleural communication in the absence of ascites. *Clin Nucl Med* 1994;19:892–4.

12. Myers TJ, Arena B, Granai CO. Pelvic endometriosis mimicking advanced ovarian cancer: presentation with pleural effusion, ascites, and elevated serum CA 125 level. *Am J Obstet Gynecol* 1995;173:966–7.
13. Yucel AE, Calguneri M, Ruacan S. False positive pleural biopsy and high CA125 levels in serum and pleural effusion in systemic lupus erythematosus. *Clin Rheum* 1996;15:295–7.
14. Mouroux J, Perrin C, Venissac N, Blaive B, Richelme H. Management of pleural effusion of cirrhotic origin. *Chest* 1996;109:1093–6.