

Endometriosis of the Lung: Case Report and Literature Review

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Case Report

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Abstract

Background: Lung endometriosis is an extremely rare gynecological disease. Literature reports suggest that most patients will show generic symptoms such as hemoptysis, pneumothorax, and hemopneumothorax, which can often result in misdiagnosis. There are case reports of 18 patients with lung endometriosis describing clinical manifestation, imaging changes, treatment and prognosis. To provide further information on this rare disease, we present a case of pulmonary endometriosis and a review of lung endometriosis.

Case presentation: We report on a 19-year-old female who was admitted to hospital due to repeated menstrual hemoptysis for 3 months. Computed tomography during menstruation showed patchy high-density shadows sized approximately 0.5 cm × 0.5 cm × 0.5 cm in the right middle lobe of the lung. Following menstruation, hemoptysis and changes on CT imaging disappeared. Thoracoscopic right middle lobectomy, right lower lung repair, and closed thoracic drainage were performed. Postoperative histopathology confirmed lung endometriosis. There was no recurrence of symptoms after 6 months of follow-up.

Conclusions: We review the literature on factors associated with lung endometriosis, diagnosis, and treatment options. We propose that the diagnosis for lung endometriosis should be made by comprehensively integrating patient reproductive history, clinical and imaging details as well as histopathology. Surgical resection appears to be an effective treatment for lung endometriosis.

Background

Endometriosis refers to a common gynecological disease in which endometrial glands or stroma with normal endometrial function appear outside the endometrium. The incidence of endometriosis has increased significantly in recent years. Endometrial glands typically grow locally and bleed repeatedly, which can cause pain, infertility, as well as a series of other clinical manifestations. Extra-endometrial growth of endometrial glands or stroma most commonly occurs in pelvic cavity (mainly in the ovaries), or in adjacent tissues (e.g., broad ligament of uterus, rectovaginal lacunae, pelvic peritoneum, abdominal surgical scar, umbilical region, vagina, vulva and vermiform appendix). However, endometriosis can also occur in other organs, such as the lung, pleura, kidney, ureter, bladder, cranial cavity, and mammary gland. Notably, lung endometriosis is very rare and usually accompanies a history of miscarriage or uterine cavity surgery.

Case Presentation

The patient was a 19-year-old female who was admitted for hemoptysis during menstrual period for 3 consecutive months. The patient experienced hemoptysis during the first menstrual period after an abortion one year prior, and hemoptysis with the expulsion of approximately 200 ml of blood recurred in the three months prior to admission. The symptoms appeared on the third day of menstruation and

disappeared after menstruation. There were no accompanying symptoms such as chest pain, respiratory distress, coughing, fever, night sweats, or weight loss.

Our auxiliary examination revealed several patchy high-density shadows in the middle lobe of the right lung in computed tomography of the chest. The high-density shadows had a size of 0.5 cm × 0.5 cm × 0.5 cm (Fig. 1a,b). Laboratory tests assessing routine blood values, liver and renal function, as well as tumor markers, came back normal. A sputum smear test for *Mycobacterium tuberculosis* was also negative. A thoracoscopic right middle lobectomy, right lower lung repair, and closed thoracic drainage were carried out surgically. Tissue specimens were fixed in 10% neutral formalin, embedded in paraffin and stained with H&E. The Envision method was used for immunohistochemistry, and the antibodies used were purchased from Fuzhou Maixin Biotechnology Development Co., Ltd.

Cytopathological analysis of the right middle lobe bronchial brushing found many ciliated columnar epithelial cells and a few lymphocytes, and no malignant cells were observed. Specimen observation of the tissue revealed that the size of lung tissue in the right middle lobe was 9.0 cm × 5.0 cm × 1.0 cm. The section was grey red and soft. A hemorrhagic area (1.5 cm × 0.8 cm × 0.5 cm) was seen locally (Fig. 2a,b). Upon microscopic observation of the right middle lobe lung tissue sent for examination, hemorrhage foci were seen in the alveolar cavity, scattered glandular epithelial cells and inflammatory cells were found in the bleeding foci (Fig. 3a,b), and glandular epithelial cells were seen in the vascular cavity of some lung tissues (Fig. 3c), and hemosiderin deposits were seen in some alveolar cavity (Fig. 3d). The immunohistochemical staining was CK positive (Fig. 4a), but ER, PR, and CD10 expression was negative. Prussian blue staining for hemosiderin was also positive (Fig. 4b). The pathological diagnosis was lung endometriosis with old hemorrhage of the right middle lobe.

Discussion

We analyzed this case as well as 18 other reported cases of lung endometriosis (presented in Table 1). The age of onset was between 19 to 54 years. Patients often sought out doctors due to repeated menstrual hemoptysis, and most patients had a history of miscarriage or uterine cavity surgery. The appearance of hemoptysis was consistent with the occurrence of the menstrual period. After menstruation, the hemoptysis subsided; consistent with this, most patients exhibited imaging changes during the menstrual period, but the imaging findings disappeared after the menstrual period. Almost all patients reported on underwent local lobectomy, and histopathology confirmed the presence of endometrial glands, interstitial cells, hemosiderin deposits, fibrous tissue hyperplasia, or similar pathological findings in the lung tissue. Some patients underwent additional immunohistochemical detection of ER, PR, CD10, or CD68, for instance, and the results suggested the presence of endometrial tissue. In all patients, hemoptysis, pneumothorax and imaging changes disappeared postoperatively, and no recurrence was reported.

Endometriosis is characterized by the growth of the endometrium outside the uterine cavity. It is a common gynecological disease that affects the fertility of women of childbearing age, with an incidence

of approximately 15% in women of childbearing age [4]. It is generally considered to be a hormone-dependent disease [3]. Endometriosis mostly occurs in the pelvic cavity, while it can also occur outside the pelvic cavity. A rare form of endometriosis outside the pelvic cavity is lung endometriosis, which accounts for about 20% of pleural endometriosis [1, 2]. As early as 1938, Schwarz described pulmonary endometriosis for the first time [5]. However, it is an extremely rare disease with complex etiology and unclear pathogenesis, and as its clinical and imaging findings are not specific, it can easily be misdiagnosed.

At present, several clinical features of lung endometriosis have been reported, including repeated hemoptysis, coughing, pneumothorax, hemothorax, and pulmonary nodules consistent with menstrual periods, but not all clinical features will appear at the same time. Among the above-mentioned clinical features, approximately 82% of lung endometriosis patients experience menstrual hemoptysis as their main symptom [6], while the remaining patients may present with menstrual pneumothorax, menstrual hemothorax, or other symptoms. X-ray or CT scans can assist in the diagnosis of lung endometriosis, although it can easily be misdiagnosed due to its non-specific symptoms and rare occurrence. Therefore, other diseases must be ruled out before a clear diagnosis can be made [7]. In our case, the young woman lived in an area with a high incidence of tuberculosis and had symptoms of hemoptysis, but did not have symptoms such as low-grade fever and night sweats. CT showed no nodules, and the sputum smear test for *Mycobacterium tuberculosis* was negative, therefore tuberculosis was excluded.

The typical pathological features of endometriosis are endometrial glands, interstitium and hemosiderin deposition under the microscope [8]. However, compared with pelvic endometriosis, these microscopic features might not all be seen concurrently in lung endometriosis. Ghigna et al. [9] reported that these three characteristics appeared at the same time only in 44% cases of lung endometriosis, while in the remaining cases only endometrial stroma was found. When only a small amount of endometrial stroma is found in lung tissue, the diagnosis is rendered more difficult [10]. In addition, it is sometimes difficult to distinguish endometrial stroma and inflammatory cells by H&E staining. Therefore, immunohistochemical detection is needed to assist in the diagnosis of lung endometriosis [11]. In the case we report here, ectopic endometrium in the lung tissue led to alveolar hemorrhage, hemosiderin deposition, chronic inflammation and fibrosis due to long-term incomplete absorption or excretion. Only few glandular epithelial cells were seen in the alveolar cavity and vascular cavity, and CK markers were positive, while ER, PR, and CD10 were negative. Prussian blue staining for hemosiderin was positive. Combining the above histopathological and immunohistochemical findings with the history of miscarriage, clinical symptoms, imaging changes and the exclusion of other lung diseases, the diagnosis of lung endometriosis was made.

The pathogenesis of endometriosis is still unclear, but 8 theories exist:

1. Endometrial implant theory: This is the most common view. Sampson proposed that when the menstrual blood flows backward, the shed endometrium can enter the pelvic cavity through the

fallopian tube and implants outside the endometrium [12, 13]. Local injuries such as the cervix, vagina, and vulva can therefore easily cause endometriosis [14, 15];

2. Body cavity epithelial metaplasia theory: Meyer et al. proposed that body cavity epithelium has the potential to differentiate into endometrial tissue [16]. It may be transformed into endometrial-like tissue by certain stimulations;
3. Iatrogenic endometrium implantation: This theory suggests a type of artificial endometrial transplantation to certain parts, such as to the abdominal wall scar after cesarean section or perineal side incision after childbirth. A history of multiple uterine cavity operations, repeated abortions, tubal drainage or similar, may therefore lead to endometriosis [16, 17];
4. Embryo theory: In the embryo, the accessory mesonephros, ovary germinal epithelium, pelvic peritoneum, rectovaginal septum, umbilical region, and other tissues evolve from body cavity epithelium, and they are able to differentiate into endometrioid tissue when stimulated by inflammation, which is more common on the surface of the ovary;
5. Induction theory: Under the induction of endogenous biochemical substances, undifferentiated peritoneal tissue can be transformed into endometrial tissue;
6. Genetic factors: Endometriosis has a certain genetic predisposition and family aggregation, and people with a family history are more likely to suffer from this disease;
7. Immune factors: There are reports and studies that speculate that diseased stem cells play an important role in the blood spread of epithelium and long-distance implantation [18, 19].

At present, there is no comprehensive treatment guideline for lung endometriosis. It is generally believed that treatment includes conservative drug treatment and surgical treatment. The most appropriate treatment method is selected based on the patient's clinical symptoms, severity and requirements. The first choice for conservative treatment is Gonadotrophin releasing hormone agonist, which is now widely accepted. This treatment inhibits the release of estrogen and progesterone from the ovaries and results in a decrease in the level of estradiol in the plasma, mimicking a state of pseudomenopause in order to control the growth of lesions. However, gonadotrophin releasing hormone antagonist treatment is costly, can elicit many adverse reactions, needs to be carried out long-term, and is symptomatic rather than a cure [1]. In addition, the recurrence rate is high, and long-time treatment may also harm the patients' ovulation and fertility [20]. Hence, most patients choose surgical treatment, especially pulmonary wedge resection. Compared with drug therapy, the recurrence rate is lower and the prognosis is better.

Conclusions

Our report and literature review highlights that for the diagnosis of endometriosis, the history of abortion, clinical symptoms, imaging changes, histopathology, and immunohistochemistry need to be comprehensively analyzed. Surgical resection appears to be the most effective treatment and offers a good prognosis.

Abbreviations

CT

Computed tomography;CK:Cytokeratin; ER:Estrogen receptor; PR:Progesterone receptor

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report.

Availability of data and materials

As a case report, all data generated or analyzed are included in this article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Jin Y supervised the literature search and wrote the paper. Jia H provided the interesting case that we reported. NaT performed the follow-up. HuiNie,XiaoD performed immunohistochemical tests and Figures processing. Cheng L evaluated the histopathological images and prepared the figures. Wen z provided pictures of imaging. Jin Wang,Hong Z revised manuscript as well as guidance and editing throughout the writing process. All authors have read and approved the final manuscript.

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None

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Tables

Due to technical limitations, table 1 is only available as a download in the Supplemental Files section.

Figures

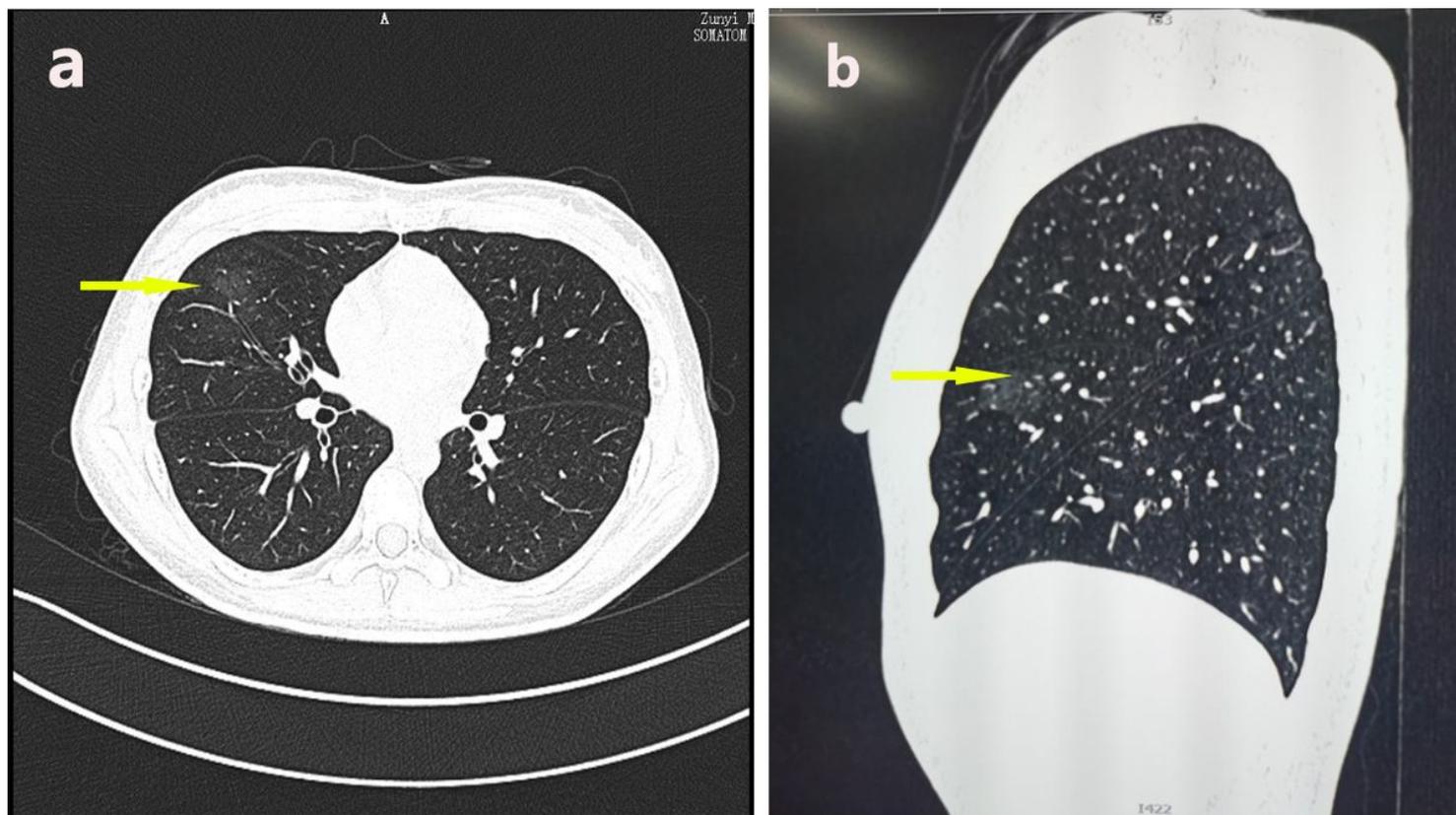


Figure 1

a,b The results of chest CT showed: a little patchy high-density shadow in the middle lobe of the right lung (the yellow arrow).

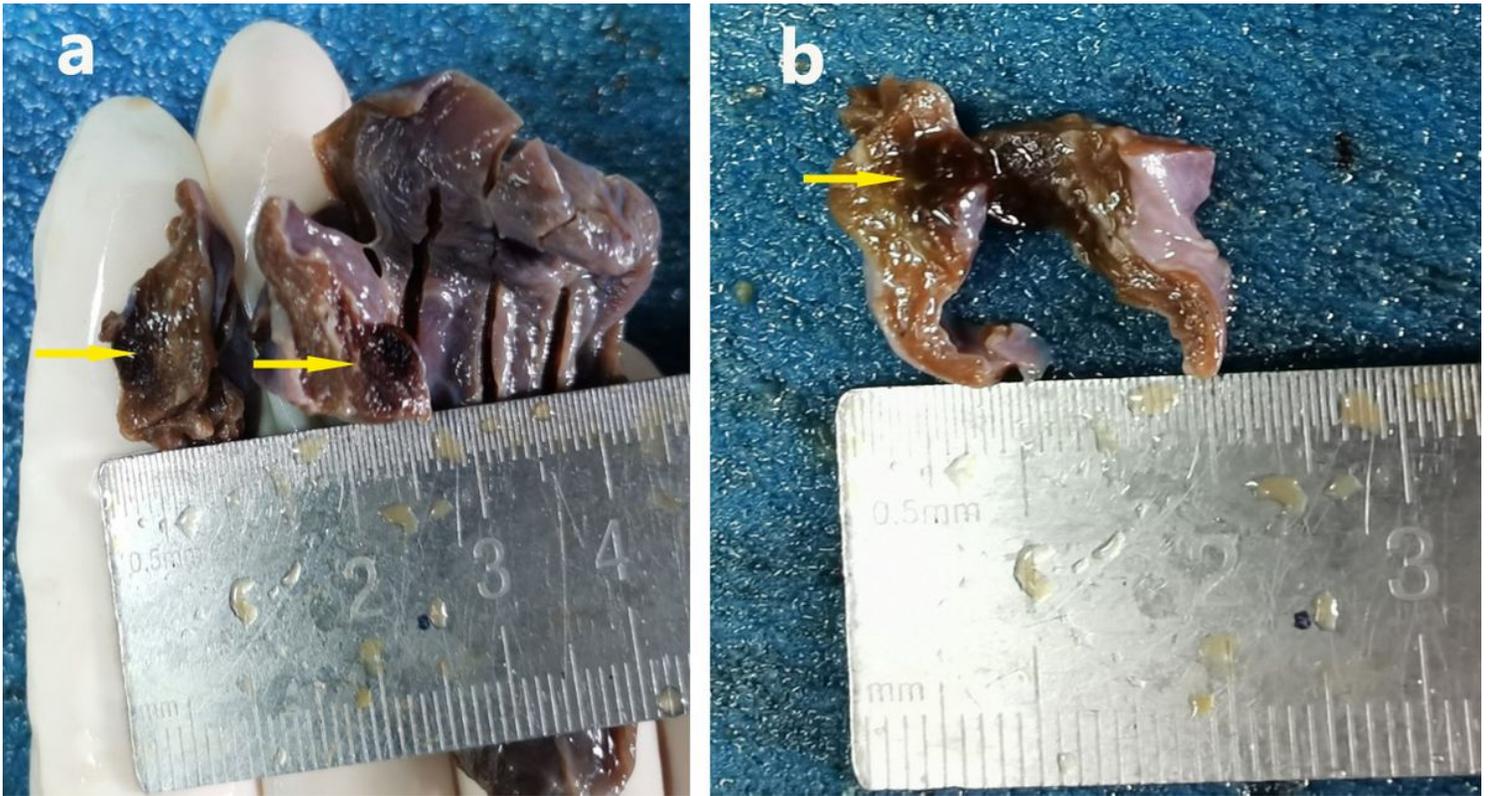


Figure 2

a,b Macroscopic findings: The size of lung tissue in the right middle lobe was 9.0 cm x 5.0 cm x 1.0 cm. The section was grey red and soft. A hemorrhagic area (1.5 cm x 0.8 cm x 0.5 cm) was seen locally (the yellow arrow).

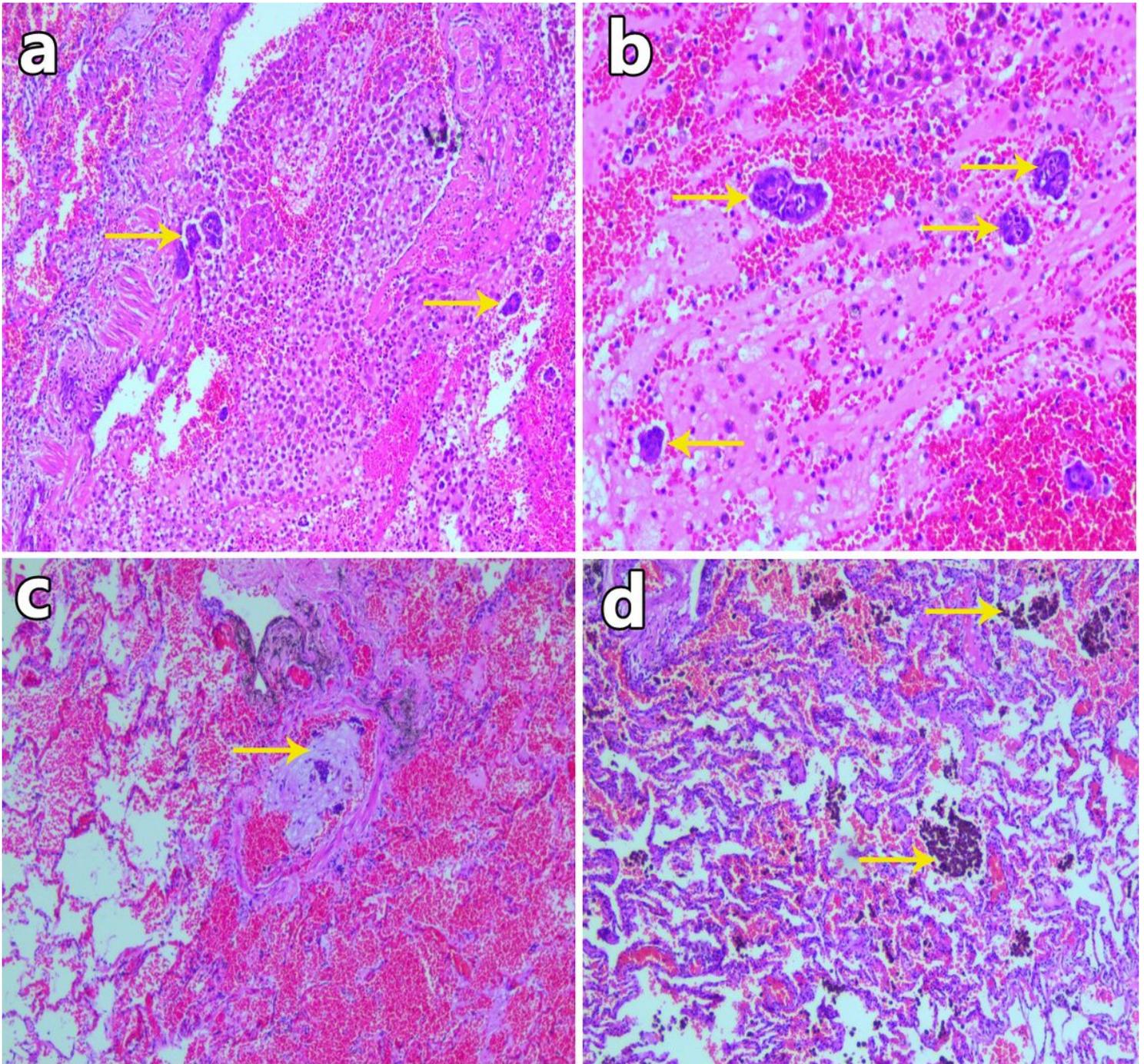


Figure 3

The image of HE. a showed hemorrhage foci were seen in the alveolar cavity, scattered glandular epithelial cells were found in the bleeding foci (100×, the yellow arrow). b Scattered glandular epithelial cells and inflammatory cells are seen in the hemorrhage(200×, the yellow arrow). c Glandular epithelial cells were seen in the vascular cavity of some lung tissues (100×, the yellow arrow).d Hemosiderin deposits were seen in some alveolar cavity (100×, the yellow arrow).

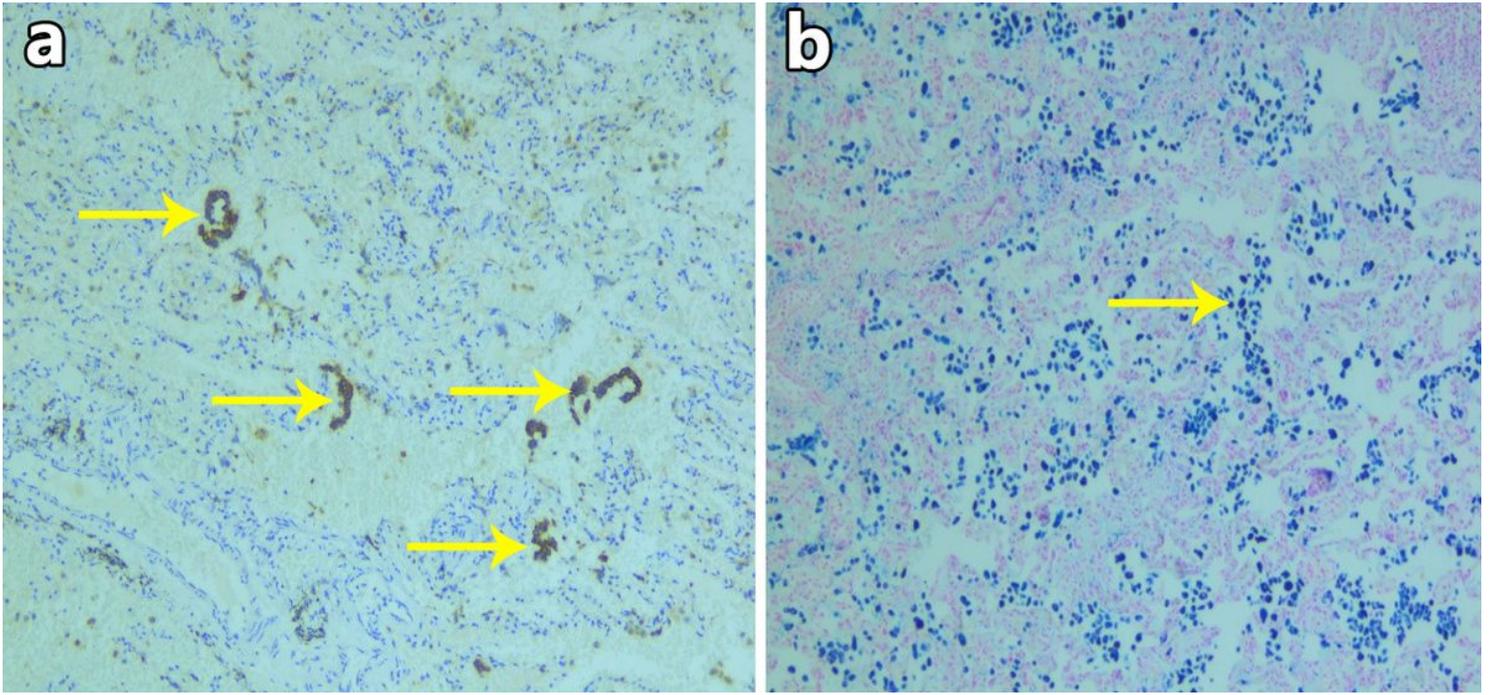


Figure 4

The image of immunohistochemistry. a The immunohistochemical staining was CK positive (100×, the yellow arrow). b Prussian blue staining for hemosiderin was also positive (100×, the yellow arrow).

Supplementary Files

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- [CAREchecklistEnglish2013.pdf](#)