

Peer Review File

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Reviewer A

Comment 1: Line 44. The authors could consider changing “multiple nodular and cavitory lesions” to “multiple nodular with subsequent cavitory lesions” so that the audience can appreciate that the nodular lesions are what developed into cavitory lesions. Line 58: The authors can consider changing the statement to “A 72-year-old man presenting with hoarseness was diagnosed with esophageal squamous cell carcinoma....”

Line 62: The authors can remove “:” and put a “.” after the dizziness.

Line 83: The authors can edit the statemen to “...vasoactive administration for septic shock” instead of saying just sepsis.

Reply 1: We appreciate the reviewer’s suggestions. We have revised the sentences as follows (page 6, lines 43-45, page 7, lines 58-59, lines 61-63 and page 8, lines 81-84).

Changes in the text:

Before changes:

Septic pulmonary embolism (SPE) is a rare life-threatening disorder wherein infected thrombi cause an infarction of pulmonary vasculature and the development of multiple nodular and cavitory lesions [1].

After changes:

Septic pulmonary embolism (SPE) is a rare life-threatening disorder wherein infected thrombi cause an infarction of pulmonary vasculature and the development of multiple nodular **with subsequent** cavitory lesions [1].

Before changes:

A 72-year-old man presenting hoarseness was diagnosed as esophageal squamous cell carcinoma with nodal metastases causing left laryngeal nerve palsy.

After changes:

A 72-year-old man presenting **with** hoarseness was diagnosed **with** esophageal squamous cell carcinoma with nodal metastases causing left laryngeal nerve palsy.

Before changes:

However, eight months after esophagectomy, the patient presented with neurological symptoms such as dizziness: multiple brain metastases were detected by non-contrast brain computed tomography (CT).

After changes:

However, eight months after esophagectomy, the patient presented with neurological symptoms such as dizziness. Multiple brain metastases were detected by non-contrast brain computed tomography (CT).

Before changes:

He was treated with appropriate broad spectrum antibiotics and supportive treatment such as adequate volume resuscitation and vasoactive administration for sepsis.

After changes:

He was treated with appropriate broad spectrum antibiotics (piperacillin/tazobactam and vancomycin later switched to cefazolin) and supportive treatment such as adequate volume resuscitation and vasopressor therapy for sepsis shock.

Comment 2: If the authors can indicate when the patient was intubated during the hospital course if it was before the development of pneumothorax or after. It will inform the readers if the positive pressure ventilator contributed to the development of the pneumothoraces.

Reply 2: In the current case, the patient has never been intubated. We have added the sentence as follows (page 8, lines 90-91).

Changes in the text:

Before changes:

The man underwent tracheostomy for better secretion clearance and rehabilitation one week after initiation of right chest tube drainage.

After changes:

The patient underwent tracheostomy for better secretion clearance and rehabilitation one week after initiation of right chest tube drainage.

His respiratory condition did not require mechanical ventilation and thus the patient was

not intubated before and after the development of pneumothorax.

Comment 3: From line 90 and 97, it appeared the pneumothoraces had resolved and there was no air leakage before the intrapleural minocycline pleurodesis was performed. It will be informative if the authors can give justification for the pleurodesis. Example, the incidence of recurrent pneumothorax after septic pulmonary embolism (SPE).

Unfortunately, the patient in this case report died one month after the pleurodesis without recurrent pneumothorax, it will be very informative if the authors can provide information about the timing of recurrent pneumothorax after secondary pneumothorax in patients without pleurodesis.

Reply 3: To the best of our knowledge, the incidence of recurrent pneumothorax with SPE is unknown. One article reported that about 32 % of patients with secondary pneumothorax experienced recurrence in 3 months without pleurodesis [5]. In addition, another article reported that patients with bilateral pneumothorax had a fourfold recurrence rate compared to those with unilateral pneumothorax [6]. Considering these informations, we believed that the patients would be likely to develop the recurrence of pneumothorax in 3 months. Medical pleurodesis was indicated in the present case. We have added the sentence as follows (page 8-9, lines 95-101).

Changes in the text:

Before changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis.

After changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis. Sasaki et al. reported that approximately 32% of patients with secondary pneumothorax experienced recurrence in 3 months without pleurodesis [5]. In addition, another article reported that patients with bilateral pneumothorax had a fourfold recurrence rate compared to those with unilateral pneumothorax [6]. Based on these reports, we assumed that the patient would develop recurrent pneumothorax in a short term. Medical pleurodesis was indicated in the present case, especially for patient's critical condition.

5. Sasaki H, Fukuhara H, Omura I, Mochizuki K. A Study on Recurrent Spontaneous

Pneumothorax. *Iryo*. 1986; 40. 835-841.

6. Ota H, Kawai H, Ogawa J. A clinical study on postoperative recurrence of bilateral spontaneous pneumothorax. *The Journal of The Japanese Association for Chest Surgery*. 2009; 23: 686-691.

Reviewer B

Comment 1: The authors state that blood cultures detected growth of methicillin-susceptible *Staphylococcus aureus* (MSSA) and used appropriate broad spectrum antibiotics. Antimicrobial therapy for sepsis is often challenging; what antibiotics did you actually use?

Reply 1: We appreciate the reviewer's question. We actually used piperacillin/tazobactam and vancomycin. After *Staphylococcus aureus* turned out to be susceptible, we switched to cefazolin. We have revised the sentence as follows (page 8, lines 81-84).

Changes in the text:

Before changes:

He was treated with appropriate broad spectrum antibiotics and supportive treatment such as adequate volume resuscitation and vasoactive administration for sepsis.

After changes:

He was treated with appropriate broad spectrum antibiotics (**piperacillin/tazobactam and vancomycin later switched to cefazolin**) and supportive treatment such as adequate volume resuscitation and **vasopressor therapy** for sepsis **shock**.

Comment 2: The authors speculated CRBSI as one of the causes of sepsis. Did the patient receive peripheral parenteral nutrition or total parenteral nutrition?

Reply 2: The patient received peripheral nutrition. We have added the sentence as follows (page 11, lines 152-154).

Changes in the text:

Before changes:

However, catheter-related bloodstream infection could occur due to peripheral venous line [17].

After changes:

However, catheter-related bloodstream infection could occur due to peripheral venous line [19]. **Indeed, the patient received peripheral parental nutrition.**

Comment 3: The patient required a tracheostomy and continued ventilatory management. What were the ventilator pressure settings; were they managed to cause barotrauma? What was the patient's respiratory management, including airway pressure and oxygenation?

Reply 3: In the current case, the patient has never been intubated. We have added the sentence as follows (page 8, lines 90-91).

Changes in the text:

Before changes:

The man underwent tracheostomy for better section clearance and rehabilitation one week after initiation of right chest tube drainage.

After changes:

The **patient** underwent tracheostomy for better section clearance and rehabilitation one week after initiation of right chest tube drainage.

His respiratory condition did not require mechanical ventilation and thus the patient was not intubated before and after the development of pneumothorax.

Comment 4: What was the negative pressure and how was it managed in this case?

Reply 4: As mentioned above, the patient has never been intubated. We have added the sentence as follows (page 8, lines 90-91).

Changes in the text:

Before changes:

The man underwent tracheostomy for better section clearance and rehabilitation one week after initiation of right chest tube drainage.

After changes:

The **patient** underwent tracheostomy for better section clearance and rehabilitation one

week after initiation of right chest tube drainage.

His respiratory condition did not require mechanical ventilation and thus the patient was not intubated before and after the development of pneumothorax.

Comment 5: Did you mix or use local anesthetics in the administration of minocycline for pain relief?

Reply 5: Yes, we did. We have added the sentence as follows (page 9, lines 101-104).

Changes in the text:

Before changes:

The next day, the patient underwent intrapleural injection of 300 mg of minocycline hydrochloride via chest tube into his left thoracic cavity.

After changes:

The next day, the patient underwent intrapleural injection of 300 mg of minocycline hydrochloride via the chest tube into his left thoracic cavity. Before pleurodesis, 100mg lidocaine was administered via chest tube for pain relief.

Comment 6: Figure 3 shows chest radiographs after pleurodesis. Is it possible to present CT images?

Reply 6: We appreciate the reviewer's question. Unfortunately, we did not take CT images after pleurodesis.

Reviewer C

Comment 1: Refer to patient with gender, male / female instead of Man, woman as it specifies the age. 20 blood cultures and chest computed tomography images, he was diagnosed with 21 secondary pneumothorax due to septic pulmonary embolism triggered by 22 methicillin-susceptible Staphylococcus aureus blood stream infection. Reword it as Pneumothorax secondary to septic pulmonary embolism due to MSSA bacteremia.

Reply 1: We appreciate the reviewer's suggestions. Following the instructions, we have revised the sentences as follows (page 3, lines 18-19 and page 3, lines 19-22).

Changes in the text:

Before changes:

A 72-year-old man previously diagnosed as esophageal carcinoma developed metachronous bilateral pneumothorax while treated for brain metastases.

After changes:

A 72-year-old **male patient** previously diagnosed as esophageal carcinoma developed metachronous bilateral pneumothorax while treated for brain metastases.

Before changes:

Based on blood cultures and chest computed tomography images, he was diagnosed with secondary pneumothorax due to septic pulmonary embolism triggered by methicillin-susceptible *Staphylococcus aureus* blood stream infection.

After changes:

Based on blood cultures and chest computed tomography images, he was diagnosed with pneumothorax **secondary** to septic pulmonary embolism **due to** methicillin-susceptible *Staphylococcus aureus* **bacteremia**.

Comment 2: 81 initiated as well. Continuous and large volume air leakage was observed in both chest 82 tubes. He was treated with appropriate broad spectrum antibiotics and supportive⁸³ treatment such as adequate volume resuscitation and vasoactive administration⁸⁴ for sepsis

Mention vasoactive administration? meaning vasopressors, if yes which ones.

Reply 2: We are sorry for using confusing technical terms. We actually performed vasopressor therapy. We have revised the sentence as follows (page 8, lines 81-84).

Changes in the text:

Before changes:

He was treated with appropriate broad spectrum antibiotics and supportive treatment such as adequate volume resuscitation and vasoactive administration for sepsis.

After changes:

He was treated with appropriate broad spectrum antibiotics (**piperacillin/tazobactam and**

vancomycin later switched to cefazolin) and supportive treatment such as adequate volume resuscitation and vasopressor therapy for sepsis shock.

Comment 3: Mention by what mechanism minocycline affects the pleura and lead to pleurodesis.

Reply 3: We appreciate the reviewer's comment. We should have mentioned the mechanism of minocycline. We have added the sentence as follows (page 10, lines 127-129).

Changes in the text:

Before changes:

Previous reports have already demonstrated the efficacy and safety of minocycline pleurodesis [10-12].

After changes:

Previous reports have already demonstrated the efficacy and safety of minocycline pleurodesis [12-14]. Minocycline inflames the pleural surface and induces dense adhesion, which can prevent recurrence of pneumothorax [12, 28].

Reviewer D

Comment 1: I advise the authors to convince readers that minocycline pleurodesis is indicated for the case described. Septic emboli is a treatable and reversible condition, and the cavities will resolve with proper antibiotic treatment. Why is pneumothorax recurrence required?

Reply 1: We appreciate the reviewer's question. Based on previous reports, we believed that the patient would develop recurrence of pneumothorax without pleurodesis in a short term [5-6]. Minocycline pleurodesis was indicated to prevent the recurrence of pneumothorax. We have added the sentences as follows (page 8-9, lines 95-101).

Changes in the text:

Before changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis.

After changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis. Sasaki et al. reported that approximately 32% of patients with secondary pneumothorax experienced recurrence in 3 months without pleurodesis [5]. In addition, another article reported that patients with bilateral pneumothorax had a fourfold recurrence rate compared to those with unilateral pneumothorax [6]. Based on these reports, we assumed that the patient would develop recurrent pneumothorax in a short term. Medical pleurodesis was indicated in the present case, especially for patient's critical condition.

5. Sasaki H, Fukuhara H, Omura I, Mochizuki K. A Study on Recurrent Spontaneous Pneumothorax. *Iryo*. 1986; 40. 835-841.

6. Ota H, Kawai H, Ogawa J. A clinical study on postoperative recurrence of bilateral spontaneous pneumothorax. *The Journal of The Japanese Association for Chest Surgery*. 2009; 23: 686-691.

Comment 2: was the brain metastases histologically confirmed?

Reply 2: Yes. The brain metastases were histologically confirmed.

Comment 3: for this patient with brain metastases from esophageal cancer, the prognosis was grave and the benefit of pleurodesis was in doubt.

Reply 3: We appreciate the reviewer's comment. We have to admit that pleurodesis was not useful in the current case because the patient actually died of brain metastases from esophageal cancer. However, as mentioned above, we believed that the patient would develop recurrence of pneumothorax without pleurodesis in a short term. We tried to do our best. We have added the sentences as follows (page 8-9, lines 95-101).

Changes in the text:

Before changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis.

After changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis. Sasaki et al. reported that approximately 32% of patients with secondary pneumothorax experienced recurrence in 3 months without pleurodesis [5]. In addition, another article reported that patients with bilateral pneumothorax had a fourfold recurrence rate compared to those with unilateral pneumothorax [6]. Based on these reports, we assumed that the patient would develop recurrent pneumothorax in a short term. Medical pleurodesis was indicated in the present case, especially for patient's critical condition.

5. Sasaki H, Fukuhara H, Omura I, Mochizuki K. A Study on Recurrent Spontaneous Pneumothorax. *Iryo*. 1986; 40: 835-841.

6. Ota H, Kawai H, Ogawa J. A clinical study on postoperative recurrence of bilateral spontaneous pneumothorax. *The Journal of The Japanese Association for Chest Surgery*. 2009; 23: 686-691.

Reviewer E

Comment 1: The authors achieved very good treatments for the patients. But, it was a simple case report, and it is not sure that minocycline was the best choice for his pneumothorax because the leakage of the patient almost stopped before pleurodesis and he died within 1 month after removal of chest tubes. I mean, if he could have survived a bit longer, the pneumothorax might have occurred. According to these backgrounds, it seems that the report does not have enough scientific level.

Reply 1: We appreciate the reviewer's comments. We agree with the idea that minocycline might not be the best choice and the present article did not provide enough scientific evidence. Based on previous reports, we believed that the patient would develop recurrence of pneumothorax without pleurodesis in a short term [5-6]. We selected minocycline because the agent would be safe to use (page 10, lines 127-128). The present case may suggest that minocycline pleurodesis would be optional for critically-ill patients with intractable pneumothorax (page 18, lines 302-303). We have added the sentences as follows (page 8-9, lines 95-101).

Changes in the text:

Before changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural

minocycline pleurodesis.

After changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis. Sasaki et al. reported that approximately 32% of patients with secondary pneumothorax experienced recurrence in 3 months without pleurodesis [5]. In addition, another article reported that patients with bilateral pneumothorax had a fourfold recurrence rate compared to those with unilateral pneumothorax [6]. Based on these reports, we assumed that the patient would develop recurrent pneumothorax in a short term. Medical pleurodesis was indicated in the present case, especially for patient's critical condition.

5. Sasaki H, Fukuhara H, Omura I, Mochizuki K. A Study on Recurrent Spontaneous Pneumothorax. *Iryo*. 1986; 40: 835-841.

6. Ota H, Kawai H, Ogawa J. A clinical study on postoperative recurrence of bilateral spontaneous pneumothorax. *The Journal of The Japanese Association for Chest Surgery*. 2009; 23: 686-691.

Reviewer F

Comment 1: The case is accurately described and pathophysiology of pneumothorax due to septic pulmonary embolism is treated in detail. In literature, there are many different guidelines, even conflicting, on the treatment of pneumothorax. For example, in the presence of a large air leak, a larger caliber drain, or the placement of a second drain, could have reduced the duration of the leaks. Pleurodesis was not mandatory since, once the septic pathology resolved and the cavitated lesions of the lung were reabsorbed, the risk of recurrence would be very low. Pleurodesis produces an irreversible condition in the treated lung. On the other hand, experience teaches that a prolonged presence of the drainage itself acts as a pleurodesic strategy, especially if associated with an inflammatory state of the tissues as happens in septic pulmonary embolism. In this condition the formation of pleural adhesions occurs spontaneously.

The therapeutic strategy described, therefore, may not be shared by everyone; there are no papers that affirm the superiority of one technique over another, given the rarity of the situation.

However, credit must be given to the authors for well-detailing the clinical case and its management, which in the end was effective. Therefore it is suggested that the job be

accepted.

Reply 1: We appreciate the reviewer's favorable comments. We are very pleased if we could share the present case with readers of *Journal of Thoracic Disease*.

Reviewer G

Comment 1: The authors present a case of using intrapleural minocycline for pleurodesis in a patient who experienced a spontaneous pneumothorax. This is in the context of the patient dying of metastatic esophageal cancer. The patient passed away within 1 month of admission. Overall, it's unclear what this article adds to the scientific literature. The authors themselves cite studies showing the efficacy of minocycline for pneumothorax. The case is not unique and there are no specific learning points. It's also unclear if the minocycline would have resulted in reduced recurrence risk at the 1 year mark as the patient passed away within one month. Consequently, there is no unique knowledge being delivered and with inadequate follow up data.

Reply 1: We appreciate the reviewer's comments. Based on previous reports, we believed that the patient would develop recurrence of pneumothorax without pleurodesis in a short term []. We selected minocycline because the agent would be safe to use (page, line). The present case may suggest that minocycline pleurodesis would be optional for critically-ill patients with intractable pneumothorax (page 18, lines 302-303). We have added the sentences as follows (page 8-9, lines 95-101).

Changes in the text:

Before changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis.

After changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis. **Sasaki et al. reported that approximately 32% of patients with secondary pneumothorax experienced recurrence in 3 months without pleurodesis [5]. In addition, another article reported that patients with bilateral pneumothorax had a fourfold recurrence rate compared to those with unilateral pneumothorax [6]. Based on these reports, we assumed that the patient would develop recurrent pneumothorax in a short**

term. Medical pleurodesis was indicated in the present case, especially for patient's critical condition.

5. Sasaki H, Fukuhara H, Omura I, Mochizuki K. A Study on Recurrent Spontaneous Pneumothorax. *Iryo*. 1986; 40. 835-841.

6. Ota H, Kawai H, Ogawa J. A clinical study on postoperative recurrence of bilateral spontaneous pneumothorax. *The Journal of The Japanese Association for Chest Surgery*. 2009; 23: 686-691.

Reviewer H

Comment 1: in figure 2 the patient had bilateral pleural effusions. Was the fluid analysed/sent for microbiology analysis?

Reply 1: Yes, it was. The negative fluid culture was found. We have added the sentences as follows (page 8, lines 84-86).

Changes in the text:

Before changes:

Surgery for pneumothorax was not indicated because of his poor general condition.

After changes:

Surgery for pneumothorax was not indicated because of his poor general condition. **The negative pleural fluid culture was found (Figure 2).**

Comment 2: Some comments below regarding grammar, changes made labelled as " ... "

Line 58: need to add presenting "with" hoarseness and was diagnosed "with" esophageal Squamous cell

Line 65: without any "complications"/ his neurological "symptoms gradually improved"

Line 68: "Because there was a clinical suspicion of sepsis", ...

Line 71: bilateral lung "fields"

Line 78: "A" left sided ...

Line 79: One week after "the left pneumothorax occurred"

Line 87: The "patient" instead of the man

Line 91: Chest X-ray revealed that "the" left pneumothorax

Line 91: recurrence of "the" left pneumothorax

Line 94: 300 mg of minocycline hydrochloride via "the" chest tube
Line 95: Air leakage "remained" (instead of kept) undetected
Line 101: Although pneumothorax "never" recurred after pleurodesis - delete had
Line 102: Instead of due to multiple recurrence, I would write due to recurrence of the brain tumour with multiple lesions
Line 106: His clinical course "is" summarized (instead of was)
Line 112: We reviewed "the literature" (instead of literatures_
Line 118: of recurrence of "the" pneumothorax
Line 132: we did not observe recurrence of pneumothorax (omitted the)
Line 139: of another tissue "are" the sources (instead of were)
Line 155: he finally died "due to his" of worsening condition or rephrase
Line 156: mortality rate of SPE "is" reportedly (instead of was)
Line 158: especially elderly ones (omitted the)

Reply 2: We appreciate the reviewer's suggestions. Following the instructions, we have revised the sentences as follows (page 7, lines 58-59, page 7, lines 64-65, page 7, lines 68-69, page 7, lines 69-71, page 7-8, lines 78-79, page 8, lines 79-80, page 8, lines 88-89, page 8, lines 93-94, page 8, lines 94-95, page 9, lines 101-103, page 9, line 104, page 9, lines 110-112, page 9, line 115, page 9, lines 120-121, page 10, lines 125-127, page 10, lines 141-142, page 11, lines 146-148, page 11, lines 163-165 and page 11-12, lines 165-167).

Changes in the text:

Before changes:

A 72-year-old man presenting hoarseness was diagnosed as esophageal squamous cell carcinoma with nodal metastases causing left laryngeal nerve palsy.

After changes:

A 72-year-old man presenting **with** hoarseness was diagnosed **with** esophageal squamous cell carcinoma with nodal metastases causing left laryngeal nerve palsy.

Changes in the text:

Before changes:

He underwent craniotomy without any complication.

After changes:

He underwent craniotomy without any complications.

Changes in the text:

Before changes:

Because the patient was clinically suspected of sepsis, whole-body CT was taken to detect any sources of infection.

After changes:

Because **there was a clinical suspicion** of sepsis, whole-body CT was taken to detect any sources of infection.

Changes in the text:

Before changes:

It revealed multiple ground-glass opacity and nodular shadows accompanying cavitory lesions observed in bilateral lung field (Figure 1).

After changes:

It revealed multiple ground-glass opacity and nodular shadows accompanying cavitory lesions observed in bilateral lung fields (Figure 1).

Changes in the text:

Before changes:

Left sided percutaneous small caliber (16 Fr) chest tube drainage was placed for left pneumothorax.

After changes:

A left sided percutaneous small caliber (16 Fr) chest tube drainage was placed for left pneumothorax.

Changes in the text:

Before changes:

One week after occurrence of left pneumothorax, he also developed right pneumothorax (Figure 2).

After changes:

One week after **the** left pneumothorax **occurred**, he also developed right pneumothorax

(Figure 2).

Changes in the text:

Before changes:

The man underwent tracheostomy for better secretion clearance and rehabilitation one week after initiation of right chest tube drainage.

After changes:

The **patient** underwent tracheostomy for better secretion clearance and rehabilitation one week after initiation of right chest tube drainage.

Changes in the text:

Before changes:

Chest X-ray revealed that left pneumothorax had disappeared.

After changes:

Chest X-ray revealed that **the** left pneumothorax had disappeared.

Changes in the text:

Before changes:

In order to prevent recurrence of left pneumothorax, we decided to perform intrapleural minocycline pleurodesis.

After changes:

In order to prevent recurrence of **the** left pneumothorax, we decided to perform intrapleural minocycline pleurodesis.

Changes in the text:

Before changes:

The next day, the patient underwent intrapleural injection of 300 mg of minocycline hydrochloride via chest tube into his left thoracic cavity.

After changes:

The next day, the patient underwent intrapleural injection of 300 mg of minocycline hydrochloride via **the** chest tube into his left thoracic cavity.

Changes in the text:

Before changes:

Air leakage kept undetected after left minocycline pleurodesis.

After changes:

Air leakage **remained** undetected after left minocycline pleurodesis.

Changes in the text:

Before changes:

Although pneumothorax had never recurred after pleurodesis (Figure 3B), the man suddenly manifested loss of consciousness due to multiple recurrence of the brain tumor 4 days after removal of the right chest tube.

After changes:

Although pneumothorax never recurred after pleurodesis (Figure 3B), the man suddenly manifested loss of consciousness due to **recurrence of** the brain tumor **with multiple lesions** 4 days after removal of the right chest tube.

Changes in the text:

Before changes:

His clinical course was summarized in Figure 4.

After changes:

His clinical course **is** summarized in Figure 4.

Changes in the text:

Before changes:

We reviewed literatures and summarized the cases of bilateral pneumothorax secondary to SPE in Table 1.

After changes:

We reviewed **the literature** and summarized the cases of bilateral pneumothorax secondary to SPE in Table 1.

Changes in the text:

Before changes:

Intrapleural minocycline pleurodesis could be efficacious against secondary pneumothorax, especially in terms of prevention of recurrence of pneumothorax [10-12].

After changes:

Intrapleural minocycline pleurodesis could be efficacious against secondary pneumothorax, especially in terms of prevention of recurrence of **the** pneumothorax [12-14].

Changes in the text:

Before changes:

Indeed, we did not observe the recurrence of pneumothorax after pleurodesis.

After changes:

Indeed, we did not observe recurrence of pneumothorax after pleurodesis.

Changes in the text:

Before changes:

As shown in Table 1, right-sided endocarditis, central venous catheter-related infection, and abscess of another tissue were the sources of SPE causing bilateral pneumothorax.

After changes:

As shown in Table 1, right-sided endocarditis, central venous catheter-related infection, and abscess of another tissue **are** the sources of SPE causing bilateral pneumothorax.

Changes in the text:

Before changes:

Although the patient had never experienced recurrence of pneumothorax after intrapleural minocycline pleurodesis, he finally died of worsening condition. The mortality rate of SPE was reportedly about 10-20% [1, 21].

After changes:

Although the patient had never experienced recurrence of pneumothorax after intrapleural minocycline pleurodesis, he finally died **due to his** worsening condition. The mortality rate of SPE **is** reportedly about 10-20% [1, 23].

Changes in the text:

Before changes:

Moreover, according to Table 1, patients with bilateral pneumothorax due to SPE would have a poor prognosis, especially for elderly ones.

After changes:

Moreover, according to Table 1, patients with bilateral pneumothorax due to SPE would have a poor prognosis, especially elderly ones.