Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Medical thoracoscopy with cryobiopsy as diagnostic tool for pleural metastatic in cutaneous squamous cell carcinoma: a rare case report

Jimmy Tanamas, MD[a,*], Melissa Angela Chionardes, MD[c], Thomas Handoyo, MD[a], Fathur Nur Kholis, MD[a], Farida, MD[a], Banteng Hanang Wibisono, MD[a], Agus Suryanto, MD[a], Eric Daniel Tenda, MD, PhD[f], Gurmeet Singh, MD, PhD[f], Eko Adhi Pangarsa, MD, PhD[b], Bambang Satoto, MD, PhD[d], Faiza Rizky Septarina, MD[e], Dik Puspasari, MD[e]

Introduction: Distance metastasis of cutaneous squamous cell carcinoma (cSCC) to pleural is rarely reported, and meets difficulties in diagnosing due to quality of pleural biopsy sample. This case presented a novel technique by using cryobiopsy to obtain adequate sample and was first conducted in our hospital.

Case presentation: A 62-years-old man admitted to hospital with dyspnoea due to massive right pleural effusion. Lung multi-sliced computed tomography showed right lung pleural effusion with compression atelectasis as well as collapse of medial lobe and upper lobe, multiple solitary nodules on mediastinal, costal antero-posterior and right diaphragm pleural part. Medical thoracoscopy was performed to obtain pleural samples by using cryobiopsy and forceps biopsy. Pathological analysis with Immunohistochemistry (IHC) revealed metastatic squamous cell carcinoma.

Discussion: Recurrence rate of cSCC remains high even after treatment, with worse prognosis. Distant metastasis to pleural is rarely reported. Clinical approach for malignant pleural effusion by using medical thoracoscopy has 80% sensitivity with minimal complication. Pleural cryobiopsy is a novel technique used for obtaining sample from pleural biopsy with significant larger size of the specimen, less crush artefacts, fragmented and better tissue integrity, although the diagnostic yield and bleeding severity between cryobiopsy and conventional forceps biopsy are not significant

Conclusion: Medical thoracoscopy with cryobiopsy should be considered as a preferrable diagnostic tool for obtaining better sample specimen, especially for pleural metastatic.

Keywords: Cryobiopsy, cutaneous squamous cell carcinoma, interventional pulmonology, malignant pleural effusion, medical thoracoscopy

Introduction

Cutaneous squamous cell carcinoma (cSCC), a non-melanoma skin cancer is the second most common skin cancer, secondary to basal cell carcinoma (BCC)[1]. Although cSCC can be treated by surgery followed by chemotherapy, the incidence of recurrence, distant metastasis and mortality remain high[2]. Distant metastasis can be presented as exudative / malignant pleural effusion (MPE)[3] and also can be a way of establishing the diagnosis from the pleural biopsy. Semi-rigid medical thoracoscopy (sMT) has good sensitivity (91%) and specificity (100%) in the diagnosis of unknown exudative pleural effusion, followed by good modalities of pleural biopsy[4]. Cryobiopsy yields larger and deeper tissue specimens with less crush artifacts[5]. This is the first case of using single use cryoprobe 1.7 mm for cryobiopsy in semi-rigid

HIGHLIGHTS

- Distant metastasis of cutaneous squamous cell carcinoma to pleural is rarely reported and difficult to establish the diagnosis.
- Clinical approach for malignant pleural effusion by using medical thoracoscopy has good sensitivity and minimal complication rate.
- Pleural biopsy specimen obtained from cryobiopsy is significantly larger in size, less crush artefacts, fragmented and has better tissue integrity.
- Medical thoracoscopy with cryobiopsy should be considered as a preferrable tool for obtaining samples from pleural metastatic.

[a]Division of Respirology and Critical Care Medicine, [b]Division of Hematology and Medical Oncology, Department of Internal Medicine, Departments of [c]Internal Medicine, [d]Radiology, [e]Anatomical Pathology, Kariadi Hospital Medical Center, Faculty of Medicine, Diponegoro University, Kota Semarang, Jawa Tengah and [f]Division of Respirology and Critical Care Medicine, Department of Internal Medicine, Cipto Mangunkusumo National Reference Hospital, Faculty of Medicine, University of Indonesia, Kota Depok, Jawa Barat, Indonesia

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Division of Respirology and Critical Care Medicine, Internal Medicine Department, Kariadi Hospital Medical Center, Faculty of Medicine Diponegoro University, Kota Semarang, Jawa Tengah 50244 , Indonesia. Tel.: +628 121 525 1543. E-mail: tanamasjimmy@gmail.com (J. Tanamas).

Annals of Medicine & Surgery (2024) 86:1734–1738

Received 4 December 2023; Accepted 11 January 2024

Published online 9 February 2024

http://dx.doi.org/10.1097/MS9.0000000000001814

medical thoracoscopy procedure for diagnosis of MPE in patient with history of cutaneous squamous cell carcinoma. Cryobiopsy provides better adequate tissue specimens for pathological analysis.

Case report

A 62-years-old man was referred to hospital with dyspnoea since one month before admission. The patient underwent several times of thoracocentesis due to recurrent pleural effusion. The patient also complaint of weight loss, cough, loss of appetite, and lumps in right armpit. There was no history of chronic diseases such as diabetes mellitus, hypertension, chronic liver disease, chronic kidney disease, and smoking. Formerly, the patient was diagnosed with squamous cell carcinoma from hand biopsy in 2015 and underwent 3 times of platinum-based systemic chemotherapy as well as 25 times of external radiation. The patient decided to stop chemotherapy due to the side effects. There was no family history of skin cancer or other cancer.

Upon admission the patient was fully conscious and laid semi fowler, vital signs were blood pressure 134/82 mmHg, heart rate 92 times beats per min, respiratory rate 26 times per min, body temperature 36,6°C, and 96% blood saturation level with nasal cannula of O_2 3 l per min. The chest examination revealed abnormalities: from inspection right side chest was left behind during active breathing, dullness on percussion, decreased on tactile fremitus, and during auscultation normal vesicular sound was disappeared. There were enlargement of axillary and posterior coli lymph nodes with springy consistency, fixed and painless. His chest X-ray showed full opacity on right lung and mediastinum were shifted contralaterally (Fig. 1). His blood test during admission revealed: haemoglobin (Hb) 14.9 gr/dl; white blood cell count (WBC) 10.2×10^9/l, platelet count 312×10^9/l, random blood glucose 102 mg/dl, lactate dehydrogenase (LDH) 509 U/l, albumin 3.2 g/dl, total protein 6.0 g/dl, blood urea 17 mg/dl, creatinine 1.2 mg/dl, sodium 137 mmol/l, potassium 3.9 mmol/l, and chloride 101 mmol/l. Initial treatment was lifesaving from massive right pleural effusion by inserting the chest tube and connected to water sealed chamber for drainage. Pleural fluid analysis revealed: colour was yellowish cloudy, Rivalta positive, protein level 3.4 g/dl, LDH 348 U/l, mononuclear 262 cell, polymorphonuclear 159 cell with erythrocytes 6000 cell. Light's criteria showed exudative pleural effusion with pleural cytologic analysis revealed no metastatic cell / malignancy were found.

After patient were stabilized with chest drainage, patient underwent right axilla lymph nodes biopsy. Histopathology result of the lymph nodes biopsy showed metastatic malignant epithelial tumour. On the fifth day after placement of chest tube, chest and lung multi-sliced computed tomography (MSCT) was performed and showed right lung pleural effusion with compression atelectasis and collapse of medial lobe and upper lobe, multiple solitary nodules on mediastinal, costal antero-posterior and right diaphragm pleural part with the biggest size ~2.5×2.1 cm on mediastinal part. The nodules were also confirmed by lung ultrasound at right forth zone / postero-lateral alveolar pleural syndrome (PLAPS) (Fig. 2).

Multi-disciplinary team (MDT) discussion were conducted, consisted of internist-pulmonologist and critical care medicine, thoracic and cardiovascular surgeon, thoracic radiologist, pathologist, and anesthesiologist. After deep analysis and appropriate clinical consideration, medical thoracoscopy under general anaesthesia was performed. Patient were placed left lateral decubitus (LLD) with the impact side on the top. Skin incision were taken placed on the fifth intercostal space at mid axial line with 2 cm in width. The incision were deepened by blunt dissection until reaching pleural space. Thoracoscope trocar were placed, followed by semi-rigid thoracoscope LTF-16 from Olympus. Drainage of massive pleural fluid and inspection for the pleural space were performed. Multiple nodules on parietal pleural at diaphragm part and mediastinal part were found. Several biopsy by using single used cryoprobe

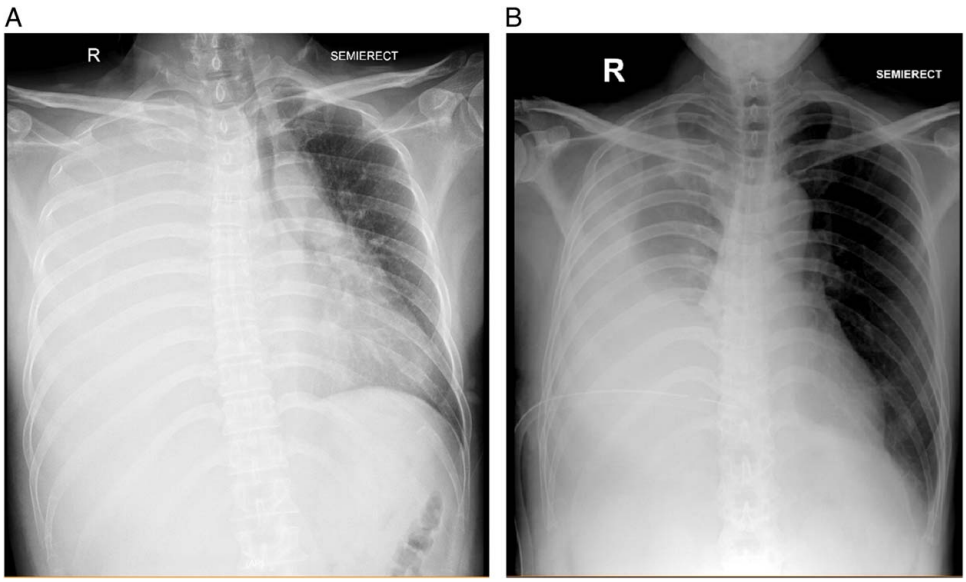

Figure 1. (A) Massive pleural effusion, shifting mediastinum to contralateral. (B) Reduced pleural effusion after inserting chest tube.

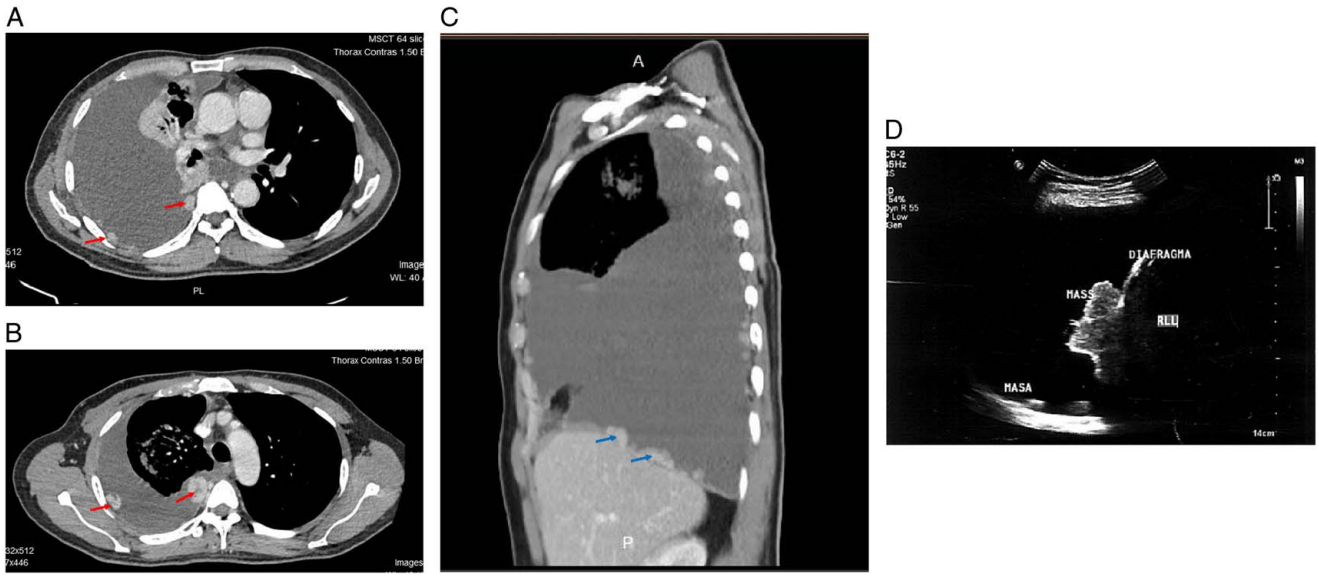

Figure 2. (A, B) Post-contrast thoracic MSCT axial view showed nodules on pleural parietal (red arrow). (C) Post-contrast thoracic MSCT sagittal view showed multiple nodules attached to diaphragm (blue arrow). (D) Right postero-lateral alveolar pleural space (PLAPS) Thoracic ultrasound showed mass attached to diaphragm.

size 1.7 mm followed by conventional forceps biopsy were performed (Fig. 3). After completing medical thoracoscopy procedure, a 24 Fr chest tube were placed and connected to water sealed chamber system with active suctioning of – 10 Kpa. Several days after medical thoracoscopy, production of pleural fluid reached minimal level and chemical pleurodesis by using bleomycin 60 mg was conducted to overcome malignant pleural effusion, and 2 days after, chest tube was removed.

Histopathology of pleural biopsy sample, both from cryobiopsy and forceps biopsy, revealed same results, but the sample from cryobiopsy showed better field of apparition with less crust. The result was nested malignant proliferation epithelial cell infiltrated fibrous connective tissue stromal with collided inflammatory lymphocyte, histiocyte, malignant cells with oval nucleus, pleomorphic, hyperchromatic, rough chromatin with visible nucleolus, wide eosinophilic cytoplasm and no visible lymphovascular invasion. From immunohistochemistry (IHC) examination of malignant cells showed squamous cell carcinoma (Table 1).

Discussion

Medical thoracoscopy plays important role in diagnosis and evaluation for suspected malignant pleural effusion or exudative pleural effusion[5]. Meta-analysis showed medical thoracoscopy was 0.929 times more sensitive than thoracocentesis for malignancy cases with lower rates of complications[6]. The first recommendation for diagnosing suspected malignant pleural effusion is cytologic examination of pleural fluid. Repeated thoracentesis may enhance sensitivity for about 50–70%[7,8]. Another safe and promising procedural for sampling the pleura with 80% sensitivity to diagnose malignant pleural effusion is medical thoracoscopy with minimal complication rates[9,10]. Pleural cryobiopsy is a novel technique used for diagnosing pleural pathology with significant larger size of the specimen, less crush artefacts, fragmented and better tissue integrity compared to forceps biopsy. Besides, the difference of diagnostic yield and bleeding severity between cryobiopsy and forceps biopsy are not significant[5]. This case of using medical thoracoscopy with pleural cryobiopsy was first conducted in our hospital. Cryobiopsy with VIO3 Electrosurgical Unit from Erbe, with single use flexible cryoprobe 1.7 mm, was supervised by Indonesian Key Opinion Leader (KOL) appointed by ERBE. Forceps biopsy was performed after cryobiopsy. The pleural specimens were significantly differed for the size, crust and artefacts, but not for the diagnostic yield.

After obtaining sample from cryobiopsy and forceps biopsy, staining and immunohistochemistry was performed for establishing the diagnosis. Positive P40, negative TTF-1 and Ki67 (+) > 20% showed diagnosis of squamous cell carcinoma with high proliferation tends to be malignant. Based on patient history of squamous cell carcinoma from his hand, and negative result of TTF-1, can lead to squamous cell carcinoma with primary from skin.

Cutaneous squamous cell carcinoma represent 20% of all non-melanoma skin cancer and is a deadly threat owing to its ability to metastasis to any organ in the body[11]. Study from Joseph and colleagues showed that the mortality rate of SCC were 70.6%. In 2013, a large study reviewing 603 patients with metastatic cSCC found that 89% of patients with distant metastatic died from their disease, were much higher than those with regional metastasis[12,13]. In 2005, Veness and colleagues conducted one of the largest studies of metastatic cSCC and reported patterns of recurrence, outcome and predictors for survival rate after treatment. They reported that there was 28% recurrence rate following treatment and worse prognosis[14]. The vast majority of metastases are found in the parotid or cervical lymph nodes (73.6%) followed by axillary nodes, inguinal nodes and distant

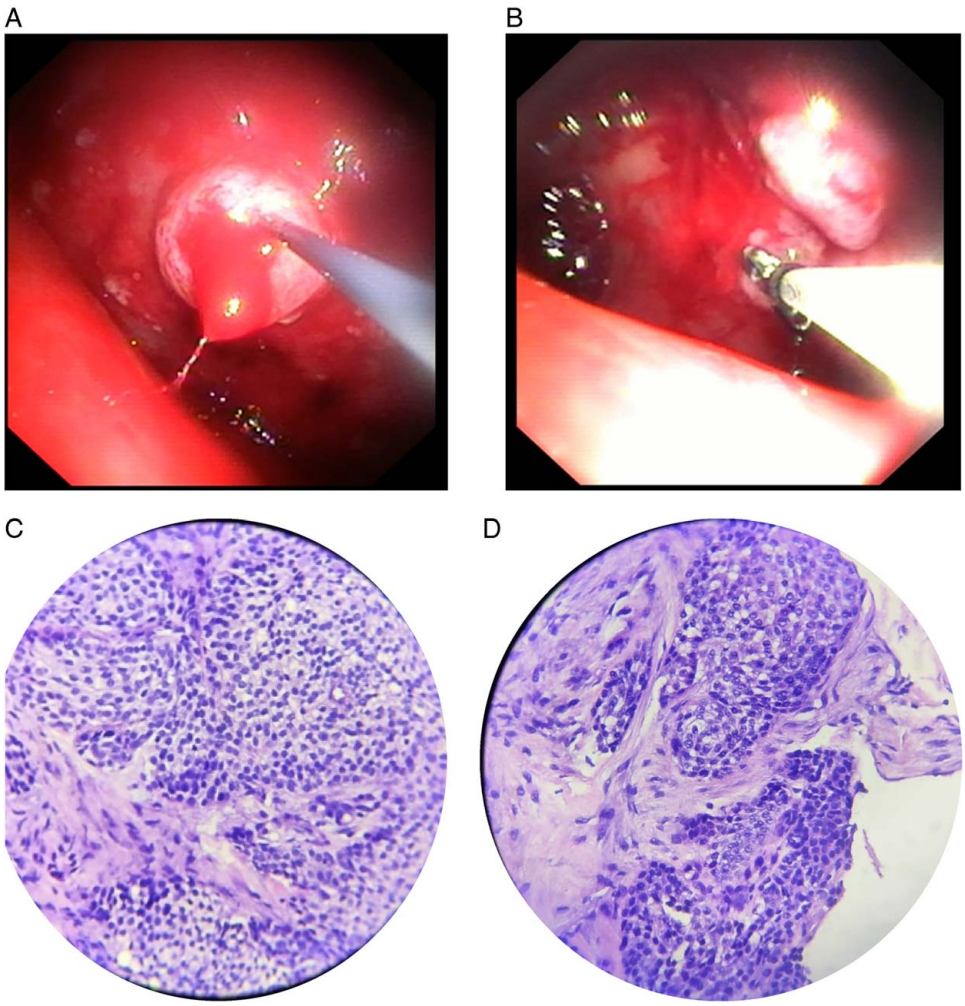

Figure 3. (A) Biopsy of pleural mass using single use cryoprobe 1.7 mm. (B) Biopsy of Pleural Mass using forceps biopsy. (C) Histopathology sample of pleural biopsy obtained by single use cryoprobe 1.7 mm, with 400 times magnifier. (D) Histopathology sample of pleural biopsy obtained by forceps biopsy, with 400 times magnifier.

metastasis such as lungs, liver, brain, and bones[15,16]. Recurrent of cSCC indicates an aggressive tumour as the metastatic rates are 25–30%[11]. Distant metastasis, especially in pleural was rarely being reported. Guidelines used are both the American Joint Committee on Cancer (AJCC) and the National Comprehensive Cancer Network (NCCN) for distinguishing a low versus high risk cSCC. AJCC and NCCN have similar high risk criteria, such as : tumour depth greater than 2 mm, tumour diameter greater than 2 cm, poor differentiation, perineural invasion, or involvement of the ear or lip mucosa[17]. In this case, there was poor information regarding the history of cSCC from his hand and the patient didn't complete the chemotherapy. Hence, the risk of cSCC couldn't be ruled out and differentiated whether the patient's condition developed to remission or relapsed with distant metastasis, or the disease hadn't resolve and developed to metastasis.

Table 1

Immunohistochemistry examination

Immunohistochemistry	Result
P40	Positive
TTF-1	Negative
Chromogranin	Negative
Synaptophysin	Negative
Calretinin	Negative
Ki67	Positive > 20%

Conclusion

Pleural nodules with massive recurrent pleural effusion, as in this case was metastatic from cutaneous squamous cell carcinoma (cSCC), requires appropriate and adequate diagnostic tools. Medical thoracoscopy should be considered as a powerful diagnostic tool for exudative pleural effusion or malignant pleural effusion to obtain pleural biopsy specimen. Cryobiopsy is preferred as one of modalities that can obtain better sample in size, less artefact and crush, compared to forceps biopsy, although the diagnostic yield between two modalities are same.

Ethical approval

This article type (case report) that does not require a formal ethical committee approval. Approval has been given by the Director of Kariadi Hospital Medical Center, Semarang, Indonesia.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Source of funding

The authors declare that they have no funding.

Author contribution

J.T. : conceptualization, data curation, formal analysis, investigation, writing original draft, project administration. M.A.C.: data curation, formal analysis, methodology, project administration, writing—review and editing, visualization. T.H.: investigation, supervision, validation, methodology. F.N.K.: investigation, supervision, validation, software. Farida: investigation, supervision, validation, formal analysis. B.H.W.: supervision, validation, writing—review and editing. A.S.: supervision, validation, writing—review and editing. E.D.T.: project administration, supervision, validation. G.S.: formal analysis, supervision, validation. E.A.P.: writing—review and editing, visualization. B.S.: validation, writing—review and editing. F.R. S.: resources, data curation. D.P.: resources, data curation

Conflicts of interest disclosure

The authors declare that they have no competing interests.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Jimmy Tanamas, Melissa Angela Chionardes.

Data availability statement

Not applicable.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Patient perspective

The patient did not present his point of view.

References

[1] Rogers HW, Weinstock MA, Coldiron BM, *et al*. Incidence estimate of nonmelanoma skin cancer (keratinocyte carcinomas) in the US population 2012. JAMA Dermatol 2015;151:1081–6.
[2] Karia PS, Han J, Schmults CD. Cutaneous squamous cell carcinoma: estimated incidence of disease, nodal metastasis, and deaths from disease in the United States, 2012. J Am Acad Dermatol 2013;68: 957–66.
[3] Fania L, Didona D, Di Pietro FR, *et al*. Cutaneous squamous cell carcinoma: from pathophysiology to novel therapeutic approaches. Biomedicines 2021; 9:1–33.
[4] Ahuja AV, Shah J, Goyal R. Comparative study of cryobiopsy and forceps biopsy on thoracoscopy in undiagnoses pleural effusions at a tertiary care centre in India. Eur Respir J 2018;52:PA902.
[5] Giri M, Dai H, Guo S, *et al*. Efficacy and safety of pleural cryobiopsy vs forceps biopsy for evaluation of undiagnoses pleural effusion: a systematic review and meta-analysis. Front Med 2022;9: 847146.
[6] Martinez-Zayas G, Molina S, Ost DE. Sensitivity and Complications of thoracentesis and thoracoscopy: a meta-analysis. Eur Respir Rev 2022; 31:220053.
[7] Roberts ME, Neville E, Berrisford RG, *et al*. Management of a malignant pleural effusion: British Thoracic Society pleural disease guideline 2010. Thorax 2010;65(suppl 2):ii32–40.
[8] Bennett R, Maskell N. Management of malignant pleural effusions. Curr Opin Pulm Med 2005;11:296–300.
[9] Metintas M, Ak G, Dundar E, *et al*. Medical thoracoscopy vs CT scanguided Abrams pleural needle biopsy for diagnosis of patients with pleural effusions: a randomized, controlled trial. Chest 2010;137:1362–8.
[10] Bing WY, Li XL, Wang XJ, *et al*. Diagnostic value of medical thoracoscopy in malignant pleural effusion. BMC Pulmonary Med 2017;17:109.
[11] Burton KA, Ashack KA, Khanchemoune A. Cutaneous squamous cell carcinoma: a review of high—risk and metastatic disease. Am J Clin Dermatol 2016;17:491–508.
[12] Brunner M, Veness MJ, Ch'ng S, *et al*. Distant metastases from cutaneous squamous cell carcinoma: analysis of AJCC stage IV. Head Neck 2013; 35:72–5.
[13] Joseph MG, Zulueta WP, Kennedy PJ. Squamous cell carcinoma of the skin of the trunk and limbs: the incidence of metastases and their outcome. Aust N Z J Surg 1992;62:697–701.
[14] Veness MJ, Morgan GJ, Palme CE, *et al*. Surgery and adjuvant radiotherapy in patients with cutaneous head and neck squamous cell carcinoma metastatic to lymph nodes: combined treatment should be considered best practice. Laryngoscope 2005;115:870–5.
[15] Venables ZC, Autier P, Nijsten T, *et al*. Nationwide incidence of metastatic cutaneous squamous cell carcinoma in England. JAMA Dermatol 2019;155:298–306.
[16] Fu T, Aasi SZ, Hollmig ST. Management of high-risk squamous cell carcinoma of the skin. Curr Treat Options in Oncol 2016;17:34.
[17] Schmults CD, Karia PS, Carter JB, *et al*. Factors predictive of recurrence and death from cutaneous squamous cell carcinoma: a 10-year, single-institution cohort study. JAMA Dermatol 2013;149:541–7.