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Case Report

An extensive surgical resection in stage T4 small cell lung cancer with cardiac invasion: A case report and literature review

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ABSTRACT

Introduction and importance: We report a rare case of a patient with a mass involving both the hilum and the heart, but its specific nature could not be determined. SCLC was confirmed by postoperative pathology. It revealed that radical surgical resection for T4 SCLC should be considered an important part of multimodality treatment.

Case presentation: A 49-year-old gentleman complained of mild chest tightness for a week. Two large mass lesions were detected on CECT in the left atrium and left hilum. After an MDT discussion, an extended resection was recommended. Postoperative pathology denoted a complete excision with no residuals and negative lymph nodes.

Clinical discussion: Due to the rarity of lung metastases to the heart, it is vital to determine the homology between the hilar mass and the cardiac mass. Based on this, simultaneous surgical treatment is done and it is very beneficial for patients by eliminating those hazards, such as acute mechanical cardiac obstruction, and cardiac embolism. Our literature review demonstrates that the SCLC tumour progresses rapidly after cardiac metastasis, limiting the chance of a complete resection. Furthermore, complete resection of T4 tumours in NSCLC has been attempted many times, so it should also be tried on SCLC.

Conclusion: It is common for SCLC tumours to progress rapidly once they havemetastasized to the heart. An aggressive operation such as radical resection can reduce tumor burdens, minimize the risk of sudden acute death and improve patient follow-up treatment, all of which may prolong the survival of patients.

1. Introduction

This work has been reported in line with the SCARE 2020 criteria [1].

Cardiac tumours are classified into two broad types, primary and secondary. The former may be benign or malignant whereas the latter are malignant by definition. We describe a clinical case and the diagnostic approach of a hilar and atrial mass of unknown cause. The pathological diagnosis of this patient remained uncertain preoperatively, with suspicion of lung carcinoma could not being ruled out. Despite the patient's family refusing biopsy and PET/CT, extensive resection of the lung tumour was performed after the MDT discussion.

2. Case presentation

A 49-year-old gentleman of Chinese origin with no significant medical diagnosis complained of mild chest tightness and discomfort predominantly in the precordial region for one week. His physical activities of daily living were not affected. He is a non-smoker, and his social history and family history of cancer were unremarkable. He had no known history of drug allergies. An echocardiogram at a local hospital indicated a left atrial myxoma. He was referred to cardiac surgery at our hospital for expert management.

2.1. Timeline

A repeat echocardiogram revealed an isoechoic, non-pedunculated, mobile mass with a smooth edge and a size of 60 mm × 48 mm,

Abbreviations: AFP, alpha fetoprotein; CT, computed tomography; ECG, electrocardiogram; FNA, Fine needle aspiration; PET, Positron emission tomography; PSM, propensity score matching; SEER, Surveillance, epidemiology, and end results; SCLC, small cell lung carcinoma; NSCLC, non-small cell lung carcinoma.

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which was attached to the atrial sidewall and had a base width of 28 mm (Fig. 1). The margins of the left pulmonary vein were indistinct (the left pulmonary vein appeared to be dilated by 20mm), and there was diastolic obstruction of the mitral valve orifices (no prolapse into the left ventricle), systolic function was normal. The myocardium of the left posterior ventricular wall was thinner with decreased motion. The ECG showed a normal sinus rhythm. Routine laboratory blood tests, biochemical tests, and tumour markers CEA, AFP, and CA19-9 were normal. The initial diagnosis was left atrial myxoma. However, the chest X-ray showed a dense homogeneous patchy opacity in the left upper and middle lung zones (81 mm × 58 mm) with unclear boundaries. Contrast-enhanced chest and abdomen computed tomography revealed two large mass lesions in the left atrium and left hilum respectively, with embolization of the pulmonary trunk and obliteration of the left pulmonary artery (Fig. 2). No other metastases were found in the brain or abdomen CT. The thoracic surgeons were asked to consult the patient for further investigations. Considering the risk of mitral valve obstruction by the left atrial mass, which could lead to the sudden death of the patient due to suspension of stroke volume. His family and the patient himself urgently requested immediate surgery and refused PET/CT, bronchoscopy, and FNA. Therefore, surgery was successfully performed on cardiopulmonary bypass by senior thoracic consultant and cardiac consultant sequentially, without any adverse effects on the patient perioperatively. Controlling crystalloid fluid intake, supplementing albumin, maintaining diuresis, and avoiding pulmonary oedema after surgery are crucial.

The postoperative pathological findings were as follows: small cell lung carcinoma (SCLC) in the left upper lobe, size 7 cm × 5.6 cm x 4.2 cm, extending into the inferior pulmonary vein, with lymphovascular invasion, there is no invasion of artery and bronchus. There were 16 hilar lymph nodes, 5 lymph nodes in the large mediastinal soft tissues, and 5 lymph nodes in the fifth zone, all were negative (Fig. 3). No cancer was found in the left atrial appendage and the TNM staging was T4N0M0. He recovered well, adhered to the treatment given in ward and was discharged 15 days after surgery. At the patient's request, he travelled back to his hometown for concomitant chemotherapy.

Advanced lung cancer involving the pulmonary veins is common, but large intra-atrial masses are rare. The standard treatment of choice in such cases is a pathological biopsy followed by adjuvant chemotherapy, radiotherapy, and surgery. However, the left atrial masses can block the mitral valve at any time, which puts patients at risk of sudden death, and a worse long-term prognosis. Therefore, alternative treatment such as direct radical resection, which can mitigate the dual crisis of chronic suffering caused by the disease psychologically and physically, is imperative. Several cases of mandibular osteosarcoma leading to lung and atrial metastases have been reported and the combination of both lung foci and atrial lesions were removed. However, there are few surgical cases of this type of SCLC leading to a huge hilar mass combined with a huge atrial mass, and we expect the patient to have a better prognosis. This is a new idea for the management of advanced lung cancer in the future.

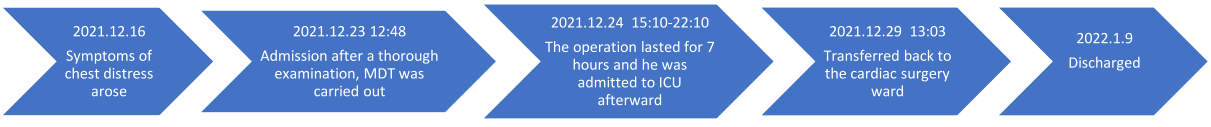
3. Discussion

The incidence of primary cardiac tumours is very low, ranging from 0.001% to 0.03% [2]. Most cardiac tumours are benign, approximately half of which are myxomas. A quarter of cardiac tumours are malignant, which encompasses various types of sarcomas, with distant metastases constituting the remainder of the malignancy. Metastatic cardiac tumours are 100 times more common than primary cardiac tumours [3].

On the CT image of our case, the intra-atrial mass has a smooth surface with no lobulation, associated with a hilar mass, that does not look like a myxoma. Differentiating the mass from primary malignant cardiac tumours such as sarcomas, from the metastatic cardiac tumours such as lung cancer or mediastinal tumours to the heart is the core of diagnosis. Meanwhile, it is also crucial to distinguish whether the cardiac mass is a giant thrombus. It is distinctive that a clear blood flow signal was seen within the mass, which is not consistent with the CT signs of a thrombus. The most common type of primary cardiac tumours are sarcomas originating primarily from the left atrium, and these should be ruled out first [4]. Sarcomas such as osteosarcomas, leiomyosarcomas, and hemangiosarcomas are very uncommon and usually present with a predilection for lobulation [5]. This distinguishes the characteristics of the cardiac mass in our case. Given the presence of significant hilar masses, lung carcinoma or mediastinal tumor is more likely to present, and primary tumours are more preferably metastasize to the heart. In rare cases, the possibility of concurrent metastasis to the hilum and heart is not excluded. In 2002, Woodring, J. H. et al. reported a case of chondrosarcoma with simultaneous metastasis to hilum and heart [6]. Lung biopsy and PET/CT examination are recommended for our patient consequently. Recent studies have reported that left atrial invasion is indeed an independent risk factor for pulmonary embolism [7]. The patient was concerned about the fatal risk of mitral valve obstruction, pulmonary embolism, or pulmonary hemorrhage during the puncture. In addition, there is a lack of PET/CT facilities at our hospital and it is time-consuming for the patient to have it done in other institution. A biopsy and PET/CT were refused by the patients' relatives, who demanded immediate surgery for the patient. Combined resection of the cardiac tumour and hilar tumour with extracorporeal circulation was successfully after a multidisciplinary team discussion. It was confirmed that both tumours were SCLC based on the histopathological findings.

After an extensive search, we discovered that none of the 7 precedents reported cases involving cardiac invasion of SCLC had surgical resection of the lung cancer (Table 1) [8–14]. Most patients were not eligible for surgery because of poor health or the presence of multiple extrapulmonary metastases. A case reported by Kim, A. C., et al. did not include information about the treatment and its outcome [12]. Similarly, in the case reported by Ratican, S et al. the primary lung foci were not seen and were presumably too small to be detected by MRI or PET/CT [13]. Of the remaining cases with cardiac metastases, 3 cases had concurrent brain metastases, 1 case had extensive liver, intestinal, and bone metastases, and 1 case had local rib metastases. Collectively, surgical resection of combined SCLC with cardiac metastases is uniquely rare. The reason may be that SCLC has a high degree of malignancy and rapid metastatic spread. It is easy for metastases to recur in other parts of the patient shortly after the appearance of cardiac metastases, losing the opportunity for surgery and resulting in a poor prognosis. With regards to the NCCN guidelines for SCLC, surgery is recommended as the treatment of choice for stage I, and PCI may be beneficial for patients with stage IIB or III SCLC who have undergone complete resection, as in some cases accurate pre-operative staging is not possible. There is no repudiation on whether stage III cases can be treated surgically.

Although there are some clinical researchers that have attempted to treat T4 stage NSCLC with cardiac invasion by complete surgical resection, this is relatively rare in SCLC compared with NSCLC. One-fifth of all patients with metastatic cancer in which lung cancer was predominant were found to have metastasis to the heart [15]. This



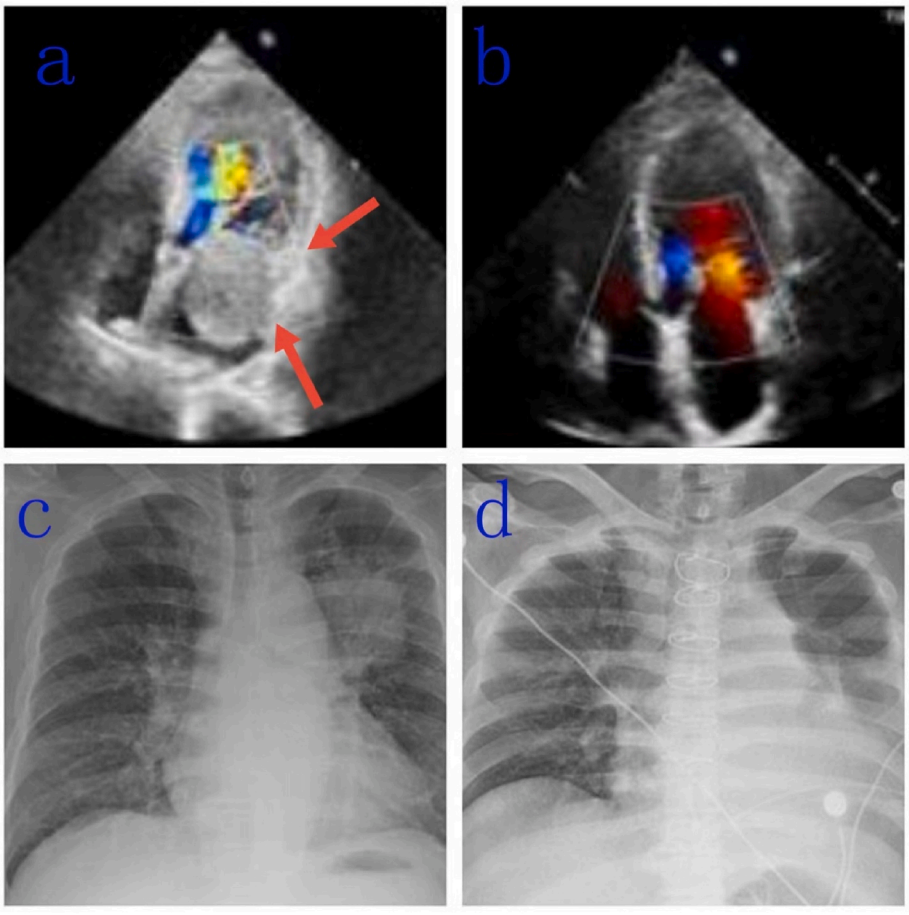


Fig. 1. (A) Transthoracic echocardiography in apical 4-chamber view demonstrated a mass (60 × 48 mm) in the left atrium adherent to the lateral wall (red arrow), obstructing the opening of the mitral valve during the diastolic period, and not exiting into the left ventricle. (B) Upon postoperative transthoracic echocardiography, the mass disappeared and showed normal mitral valve flow (C) The CXR revealed a round mass in the middle of the left upper lung field. (D) The CXR showed absence of a mass in the left upper lung field. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

elucidates that it is an inevitable consequence of the progression of an original neoplasm. On the contrary, direct metastasis to the heart without metastasis to other sites outside the lung is rare which may caused by failingto diagnose and treat in a timely manner.

Notwithstanding much literature has reported the establishment of combined resection of lung cancer and large vascularized heart tumour with or without cardiopulmonary bypass as the treatment of choice in patients with locally advanced T4 NSCLC, it is incredibly rare to perform the same procedure as combined resection of lung cancer and cardiac tumour for SCLC. According to the NCCN guidelines, the backbone of managing stage II or higher stages of SCLC is non-surgical chemotherapy, so there are fewer opportunities to perform an overall surgical resection. In addition, because of the rapid progression of SCLC, it is easy to miss the best treatment time if screening is not done promptly. A handful of recent cases have discussed the feasibility and advantages of surgical treatment for stage II-III SCLC patients, suggesting that surgical resection as part of a multimodality treatment regimen for them is beneficial.

Zhang C et al. demonstrated that OS (overall survival) was significantly better in the surgery group than in the non-surgery group in stage III SCLC patients, and surgery was also an independent prognostic factor along with age and radiotherapy [16]. Yang, Y. et al. analyzed the SEER database for 5 years between 2000 and 2015, and the survival rate of the surgical group of T1, T2, and T4 SCLC patients was significantly better than that of the non-surgical group, while the surgical group was better than the non-operative group in patients at stages IIB and IIIA before and after PSM [17]. The non-operative group had a higher risk of cause-specific death. A single-center study by Weckler, B. C. et al. retrospectively enrolled 47 patients of SCLC with stage IA-IIIB who underwent combined treatment including surgery (including 6 stage T4 patients), resulting in a postoperative 30-day mortality rate of 0% and good long-term survival with a median overall survival of 56 months. His study evaluated that R0 resection was the only factor influencing long-term survival [18].

Therefore, extended lung cancer resection for T4 SCLC with cardiac invasion can effectively reduce tumour burden, interrupt rapid tumour spread, and improve patients' long-term survival. At the same time, surgery can eliminate the risk of fatal embolism and sudden death due to mechanical obstruction, which is conducive to subsequent stable comprehensive treatment.

In our study of 7 cases of SCLC with cardiac metastases, about half of the patients had brain metastases, which were associated with a worse prognosis. Hence, in patients with SCLC, if the overall situation is good and there are no distant metastases to other parts apart from the lung and heart, comprehensive treatment such as complete surgical resection combined with postoperative chemotherapy may be of great benefit to patients. Our patient is well and fit 4 months postoperatively and is scheduled to receive his 4th cycle of EP chemotherapy soon. To the best of our knowledge and review of the literature, along with advances in surgical techniques and anaesthesia, R0 resection is increasingly feasible for many stage II-III SCLC. However, it is common that non-surgical patients to develop refractory drug resistance in the later phase of chemotherapy, due to excessive tumour load and prolonged treatment process, which can lead to tumour cell mutation and subsequently increase treatment challenges. This case serves to conclude that a multimodality treatment plan including surgical intervention should be attempted in eligible patients to achieve a satisfactory outcome in debulking the tumour burden for patients, increasing their tolerance for chemotherapy and/or radiotherapy, and improve their long-term prognosis when there is a cardiac invasion concurrent with stage II-III

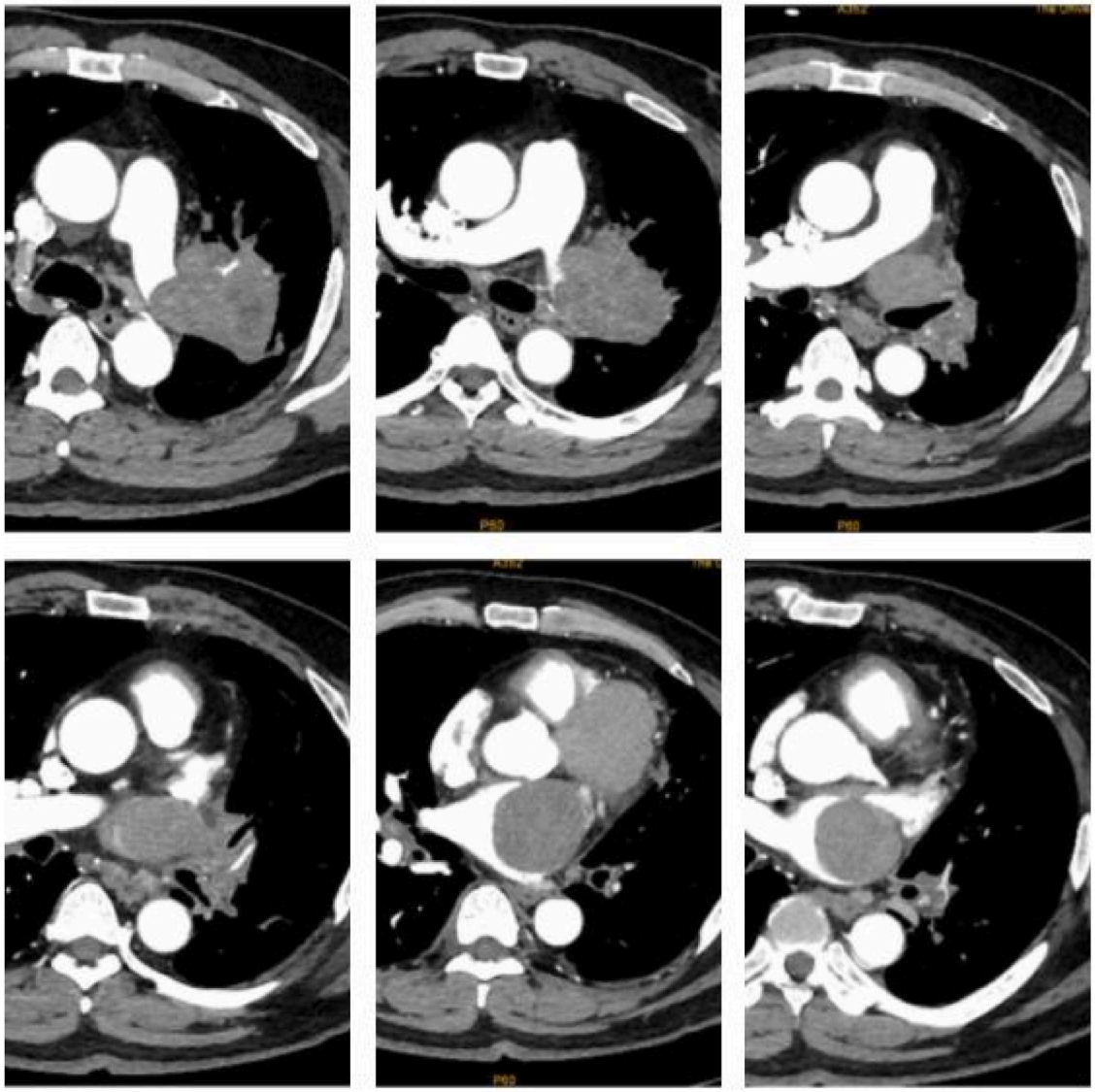


Fig. 2. Upper row of the CT scan showed a large left hilar mass with infiltration around the hilar vessels and trachea, coexisted with subcarinal lymph node enlargement. Lower row of the CT scan showed a round mass at the left atrium.

SCLC. It is of pivotal role to strengthen the early detection of lung cancer and prevent the further development of metastatic SCLC.

4. Conclusion

In spite of the high degree of malignancy of SCLC and the rarity of prompt detection, most patients present with multiple metastases at diagnosis and direct invasion of the heart can be fatal. Timely treatment is crucial to restoring the patient's health and improving prognosis.

According to NCCN guidelines, surgical treatment is not recommended for stage III-IV NSCLC and surgical treatment is recommended commonly for stage I SCLC. The benefit of surgical treatment in stage II-III NSCLC has been gradually documented in the literature. The prognosis of 7 reported cases of SCLC with cardiac invasion was poor and there was some evidence proving the merits of surgical intervention in stage II-III NSCLC patients, thus surgery is probably the better choice for our patient to avoid sudden death.

We share our experience regarding the management of stage II-III SCLC, surgery may be recommended in the future for SCLC patients with acceptable physical conditions, who has only limited metastasis such as direct metastases extended to the heart from the lung. Comprehensive treatment in the form of extended lung cancer resection combined with concomitant chemotherapy could be performed in patients at stage III SCLC with cardiac invasion if the conditions for complete resection are met. Complete resection may prevent cause-specific death and improve patients' long-term survival prognosis. Last but not least, the surgical intervention embraces an amelioration in patient's overall psychophysical health, significantly reduces the psychological distress of patients, and is conducive for them to cooperate better in subsequent treatment. Prospective clinical trials are needed to determine appropriate management for stage II-III SCLC.

Declarations

Ethical approval and consent to participate

The ethics committee of the University of Hong Kong-Shenzhen Hospital approved this study.

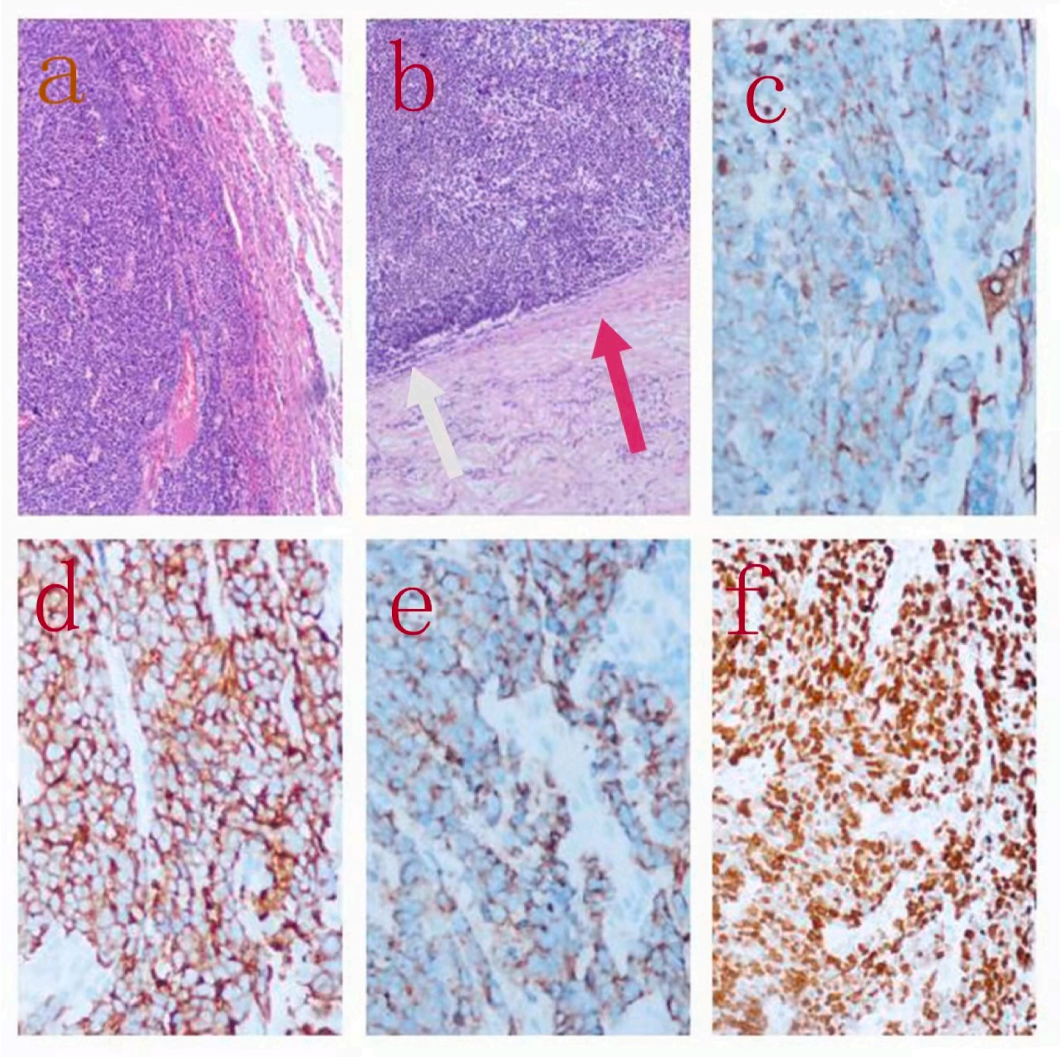


Fig. 3. **(A)** Normal lung tissue composed of alveolar cavities is shown on the right while the tumour is shown on the left, tumour is composed of diffusely growing small cells arranged in solid sheets, trabeculae, or rosettes. (Hematoxylin and eosin staining, x200). **(B)** The red arrow indicated the smooth muscle tissue of the vascular wall while the white arrow showed the disappearance of smooth muscle, which indicated invasion of vascular wall. The tumor cells demonstrated positivity for **(C)** AE1/AE3, **(D)** synaptophysin **(E)** chromogranin-A, **(F)** Ki-67 index 90%. (x400). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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Author's contributions

Shengchun Xiong: Conceptualization, Validation, Writing: Writing – original draft preparation, Supervision; Keiyui Tang: Writing: Review & Editing; Feifei Luo: Visualization; All authors read and approved the final version of the manuscript

Consent for publication

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.

Availability of data and materials

Not applicable.

Guarantor

Shengchun Xiong.

Patient perspective

The patient had no interest in sharing his cancer experience any further.

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The following information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories then this should be stated.

Please state any conflicts of interest.

All authors must disclose any financial and personal relationships

Table 1
Baseline information of 7 precedents reported cases involving cardiac invasion of SCLC.

Patient number	1	2	3	4	5	6	7
Author of the literature	Orcurto, M. V [8]	Shah, R [9]	Duncan, M. D [10]	Pham, N [11]	Kim, A. C [12]	Ratican, S [13]	Pallangyo, P [14]
Published year	2009	2016	2017	2018	2020	2021	2022
Sex, Age, Smoking history	M/68/Y	M/68/Y	F/63/Y	F/66/Y	M/67/Y	M/31/Y	M/67/Y
Lung tumour size (cm x cm)	10 × 6.5	9 × 6.3	NP	7.8 × 8.5	[a]	[a]	[a]
Cardiac tumour size (cm x cm)	[a]	6.6 × 6.2	5.5 × 4.4	[a]	[a]	[a]	NP
Lung tumour location	RUL	RUL	L hilar	RLL	L hilar	[b]	R lung
Cardiac mass location	RV	RV	LA	LA,LV	LA	LA,RA,IS	LA
Other metastasis	2-5 ribs	Brain	Cerebellum	Brain	N	N	Liver
Surgery	N	N	N	N	N	N	N
Symptom	pain	CNS	CNS	CNS	NP	SOB	SOB
Chemotherapy	Y	N	Y	N	NP	Y	N
Radiotherapy	Y	N	Y	N	NP	Y	N
Biopsy	Y	Y	Y	Y	N/CES	Y	Y
ECG changes	RBBB	ST	NP	normal	NP	AF	CHB
PET/CT	Y	N	N	N	N	Y	Y
Prognosis (month)	20	1	[c]	[d]	NP	6	18

NP: not provided.
Y: Yes.
N: No.
CES: Cytological Examination of Sputum.
CHB: Complete heart block.
IS: Interatrial septum.
AF: Atrial flutter.
SOB: Shortness of breath.
[a] No specific data were given, the size of the mass was similar to the aortic diameter or larger or equal to it within the same CT layer.
[b] No obvious primary lung lesion was seen.
[c] The patient was discharged from the hospital after receiving chemotherapy and 10 fractions of whole brain radiation.
[d] The patient died before radiotherapy after craniotomy, probably less than 1 month after surgery.

with other people or organisations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

The authors declare that they have no competing interests.

Please state any sources of funding for your research.

All sources of funding should be declared as an acknowledgement at the end of the text. Authors should declare the role of study sponsors, if any, in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. If the study sponsors had no such involvement, the authors should so state.

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Ethical approval

Research studies involving patients require ethical approval. Please state whether approval has been given, name the relevant ethics committee and the state the reference number for their judgement.

The ethics committee of the University of Hong Kong-Shenzhen Hospital approved this study.

Consent

Studies on patients or volunteers require ethics committee approval and fully informed written consent which should be documented in the paper.

Authors must obtain written and signed consent to publish a case report from the patient (or, where applicable, the patient's guardian or next of kin) prior to submission. We ask Authors to confirm as part of the submission process that such consent has been obtained, and the manuscript must include a statement to this effect in a consent section at the end of the manuscript, as follows: "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".

Patients have a right to privacy. Patients' and volunteers' names, initials, or hospital numbers should not be used. Images of patients or volunteers should not be used unless the information is essential for scientific purposes and explicit permission has been given as part of the consent. If such consent is made subject to any conditions, **the Editor in Chief** must be made aware of all such conditions.

Even where consent has been given, identifying details should be omitted if they are not essential. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note.

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

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgments

Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104448.

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