Clinical Case Report

Medicine®

OPEN

Primary pulmonary choriocarcinoma in a male that was successfully diagnosed and treated

A case report and review of the literature

Ran Zhu, MM[a,b], Congwei Jia, MD[a], Jie Yan, MD[a], Yufeng Luo, MB[a], Zhen Huo, MD[a,*]

Abstract

Introduction: Primary pulmonary choriocarcinoma (PPC) is extremely rare, especially in males. It is characterized by a poor response to therapy and shortened survival times. Here, we report a successful diagnosis and modified treatment for PPC in a male and a review of the literature.

Case presentation: This case report describes a 67-year-old male who was discovered to have a left pulmonary mass. The patient underwent a pulmonary lobectomy. Pathological examination showed a poorly biphasic differential tumor. Immunostaining displayed that beta-human chorionic gonadotropin (β-HCG), CD10, and GATA3 were positive, and the increase of postoperative serum β-HCG secretion was also confirmed. Systemic and genital screening was performed, but other abnormal findings were not observed. The diagnosis of PPC was confirmed. Then, the patient received 4 cycles of modified chemotherapy according the condition of his body. The patient has been alive for >13 months without recurrence, and the level of serum β-HCG has already decreased to normal. In addition to reporting this case, we have also summarized the similar previously published cases.

Conclusions: Currently, there is no standard treatment for PPC. A rapid and correct diagnosis is necessary. Surgery and modified chemotherapy, based on the physical condition of the patient, may currently be the best therapy for PPC.

Abbreviations: β-HCG = Beta-human chorionic gonadotropin, CT = computed tomography, ETT = epithelioid trophoblastic tumo–r, HCG-producing GCC= human chorionic gonadotropin-producing giant cell carcinoma, HE = hematoxylin & eosin, MRI = magnetic resonance imaging, PEB = bleomycin etoposide and cisplatin, PPC = primary pulmonary choriocarcinoma, TTF-1 = thyroid transcription factor-1, TPS = tyrosylprotein sulfotransferase.

Keywords: beta-human chorionic gonadotropin, male, primary pulmonary choriocarcinoma

1. Introduction

Nongestational choriocarcinoma consisting of cytotrophoblastic and syncytiotrophoblastic cells is an exceedingly rare neoplasm that secretes beta-human chorionic gonadotropin (β-HCG), arises spontaneously, and is primarily located within midline structures such as the retroperitoneum or mediastinum. However, some cases have been reported to emerge in the lung, gastrointestinal tract, brain, and liver. In the literature, only 29 cases of primary choriocarcinoma in lung have been reported in males, including 25 cases of choriocarcinoma,[1,3–11,13–19,21–22,24–26] 3 cases of choriocarcinoma combined with adenocarcinoma,[12,20,23] and 1 case of mediastino-pulmonary choriocarcinoma,[2] which is even rarer and has a very poor prognosis compared to its counterpart in the midline structures according to the literature. Primary pulmonary choriocarcinoma (PPC) in males is easy to misdiagnose or delay the diagnosis; therefore, a potentially curative chemotherapy or surgery may also be delayed. Herein, we reported a 67-year-old male with a large mass in his lung who underwent a surgical resection of the left upper lobe and a section of the left lower lobe. The diagnosis of PPC was confirmed by its morphology and immunotype combined with the postoperative β-HCG level. The patient received a successful and modified treatment plan and is in good condition now. Next, we have described the clinicopathological features, treatment, and prognosis of PPC with a short review of the literature.

2. Case presentation

A 67-year-old Chinese male was found to have a left pulmonary mass by chest roentgenogram during a routine medical

Editor: Yong Liu.

Consent for publication: Written informed consent for publication of his clinical details and clinical images was obtained from the patient. Copies of the consent forms are available for review by the editor of this journal.

Authors' contributions: ZR was the main author on the article, worked up the cases, and drafted the manuscript. JC and YJ were responsible for the figures. LY carried out the immunohistochemistry. HZ was the main pathologist involved in the cases and the main editor of the body of the text. All authors read and approved the final manuscript.

Ethics approval and Consent to participate: The ethics committee of the Peking Union Medical Collage Hospital specifically approved this study (No. S-K171), and patients provided written informed consent to participate in the study.

The authors have declared that no competing interests exist.

[a] Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, No.1 Shuaifuyuan, Wangfujing Street, Dongcheng District, Beijing 100730, China, [b] Department of Pathology, Changping Hospital of Integrated Chinese and Western Medicine, Beijing 102208, China.

[*] Correspondence: Zhen Huo, Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, No.1 Shuaifuyuan, Wangfujing Street, Dongcheng District, Beijing 100730, China (e-mail: huozhen1976@126.com).

Medicine (2016) 95:52(e5693)

Received: 29 August 2016 / Received in final form: 15 November 2016 / Accepted: 29 November 2016

http://dx.doi.org/10.1097/MD.0000000000005693

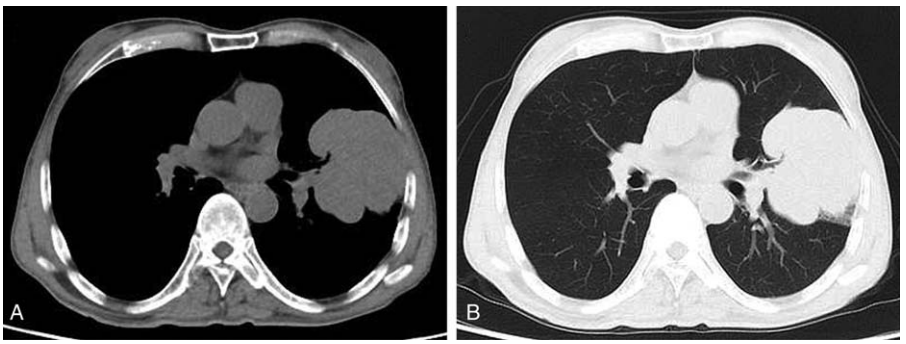

Figure 1. CT scan of the chest. (A) Soft tissue window: A fairly well demarcated left pulmonary mass is adjacent to the pleura and compressed the left oblique crack to camber. (B) Axial 5-mm-thick reconstructed lung window: A well-defined 8 × 6 cm lobulated inhomogenous mass can be seen in the upper lobe of the left lung.

examination. The patient was asymptomatic and was admitted to Peking Union Medical College Hospital (Beijing, China) 15 days later. A high-resolution computer tomography scan of the chest confirmed the presence of a large mass in the left lung adjacent to the pleura that locally compressed the left oblique crack to camber without mediastinal lymphadenopathy (Fig. 1A and B). Pleural thickening and multiple small lymph nodes were detected. The patient was a smoker (1 pack per day) and a drinker (100 g/day) for 40 years and was diagnosed with asthma 15 years ago. Based on the physical examination, he was a typically developed and healthy-appearing man with stable vital signs. The chest was clear of abnormalities during auscultation and percussion. The cardiac and abdominal examination was normal. Physical examination revealed that the testicles were equal in size and without nodules or masses. To determine whether the tumor occurred primarily within the lung, systemic and genital screenings were performed by magnetic resonance imaging (MRI), computed tomography (CT), and ultrasound, and the results displayed no abnormal findings. The results of the routine laboratory examinations were all normal except the tyrosylprotein sulfotransferase (TPS) (>1200 U/L) and Cyfra (21133.86 ng/mL). The preoperative β-HCG levels in the serum and urine were not examined. A cytological diagnosis of non-small cell carcinoma was confirmed by the examination of bronchial brushing cells obtained during bronchoscopy. The cardiopulmonary risk was within acceptable limits for complete resectional therapy. In the absence of distant and regional metastases (stage IIIA, T4 N0 M0), the patient underwent a left whole upper and a partial lower lobectomy.

The macroscopic pathological finding consisted of a large hemorrhagic mass measuring 9 × 7 × 6.5 cm occupying more than one-third of the resected lung with necrosis and a hemorrhage that was adjacent to the lung membrane (Fig. 2A). The specimen was fixed in 10% neutral buffered formalin, routinely processed, and embedded in paraffin. Hematoxylin and eosin-stained sections were examined using optical microscopy and independently reviewed by 2 experienced pathologists. The microscopic examination showed that the majority of the neoplasm was composed of necrotic and hemorrhagic areas. The tumor cells were poorly differentiated and had a characteristic biphasic pattern with polygonal cytotrophoblastic cells growing in a nest-like fashion that were separated or capped by multinucleated giant syncytiotrophoblastic cells (Fig. 2B–D). The tumor was close to the lung membranes and had invaded through the bronchial tubes, but did not exhibit lymph node involvement; the surgical resection margins were clear. Formalin-fixed and deparaffinized sections were examined using immunohistochemistry. A panel of markers in the tumor was detected by an indirect immunoperoxidase method using antibodies against the following markers: ALK-D5F3, CK20, CK7, Napsin A, P40, P63, TTF-1, Ki-67, CD146, HLA-G, β-HCG, HPL, CD10, CAM5.2, and GATA3. The results of the immunohistochemical analysis with the listed antibodies are provided in Table 1. The tumor cells exhibited positivity for HLA-G, CD10 (Fig. 3A), CK7, CAM5.2, and GATA3 (Fig. 3B) and weakly focal positivity for HPL and P63 (Fig. 3C). Staining for β-HCG (Fig. 3D) was strongly positive within the syncytiotrophoblastic cells and weakly positive in the cytotrophoblastic cells. Staining for ALK-D5F3, CD146, CK20, P40, TTF-1 (Fig. 3E), and Napsin A was negative. The Ki-67 labeling index (Fig. 3F) was 75%. Based on these findings, the diagnosis of choriocarcinoma was confirmed.

After the operation, the serum and urine β-HCG levels were measured for the first time. The serum β-HCG level was 38.41 IU/L (normal, 0–5 IU/L), and the β-HCG level of the urine test was suspiciously positive. The patient then received standard combination chemotherapy (PEB scheme) that consisted of cisplatin (25 mg/m^2, intravenous [IV)] drip d1–5), etoposide (120 mg/m^2, IV drip d1–5), and bleomycin (30 mg/m^2, intramuscular injection d1, d8, d15), but the patient developed a pulmonary ventilation disorder with diffusive dysfunction. Then, vincristine (2 mg/m^2, d3) and elemene (600 mg/m^2, d1–7) were administered instead of bleomycin. After the first course of chemotherapy, the levels of TPS decreased to 50.55 U/L, Cyfra decreased to 2112.48 ng/mL, and β-HCG markedly decreased to 2.00 IU/L, which was within the normal range, and the patient was found to have bone marrow suppression (grade 3) as well. Fortunately, the suppression relieved after the patient received recombinant human granulocyte colony-stimulating F (300 μg, qd, 3 d) therapy. The dosage was amended to accommodate patient's status during the second course of chemotherapy, which consisted of cisplatin (25 mg/m^2, IV drip d1–5), etoposide (110 mg/m^2, IV drip d1–5), vincristine (2 mg/m^2, IV drip d1) and elemene (600 mg/m^2, IV drip d1–7). Unfortunately, the patient was found to be in bone marrow suppression again. The dosage was further amended during the third course of chemotherapy, which consisted of cisplatin (25 mg/m^2, IV drip d1–5), etoposide (100 mg/m^2, IV drip d1–5), vincristine (2 mg/m^2, IV drip d1), and elemene (600 mg/m^2, IV drip d1–6). The patient was in good condition during this course of chemotherapy. During the fourth course of chemotherapy, the dosage remained the same as the third course. Dynamic CT evaluation was performed, and no abnormal findings were observed during

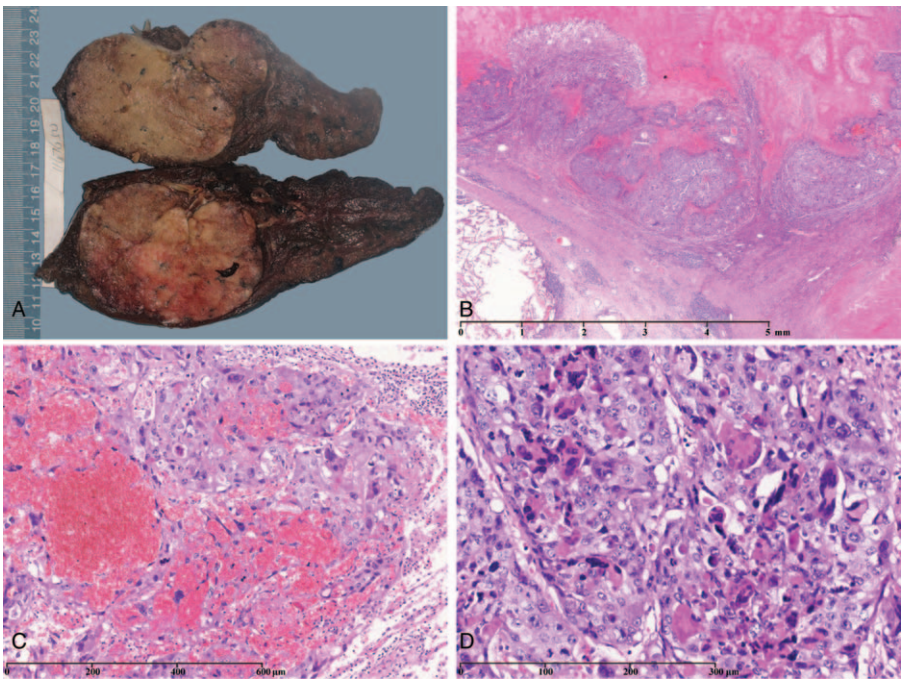

Figure 2. Macroscopic and histologic features of the tumor. (A) Gross specimen compressing the adjacent lung tissue. (B) At low magnification, the tumor cells grow in clusters with a large area of hemorrhage and necrosis (hematoxylin and eosin; original magnification, ×12.5). (C) The cytotrophoblastic cells grow in clusters separated and capped by giant syncytiotrophoblastic cells, thereby forming the characteristic biphasic pattern surrounded by a hemorrhagic area (hematoxylin and eosin; original magnification, ×100). (D) Higher magnification emphasizes the peripheral palisading by bizarre syncytiotrophoblasts (hematoxylin and eosin; original magnification, ×200).

the 4 cycles of chemotherapy. After the fourth course of chemotherapy, the β-HCG decreased to 0.91 IU/L. At present, the patient has survived >13 months of follow-up without any symptoms.

3. Discussion

In our case, the patient presented as an older male without any complaints or disease history. Additionally, the preoperative β-HCG level was absent, and the tumor cells were poorly differentiated. The diagnosis of PPC was based on the histological features combined with immunohistochemical detection. A differential diagnosis is required to exclude other β-HCG-positive tumors, such as human chorionic gonadotropin-producing giant cell carcinoma (HCG-producing GCC), epithelioid trophoblastic tumor (ETT), and metastatic choriocarcinoma. HCG-producing GCC is even rare. According to previous reports, the giant cells of HCG-producing GCC may simulate syncytiotrophoblasts, but they lack the overall greater cytological pleomorphism morphologically. Additionally, the multinucleated giant cells are smaller than those in PPC, and lower levels of β-HCG are detected immunohistochemically. Most importantly,

Table 1

Clones, dilutions, sources and results of antibodies used in the immunohistochemical panel.

Antibodies to	Clone	Source	Dilution	Choriocarcinoma
ALK	D5F3	Roche	Prediluted	–
CK20	EP23	ZSJQ-BIO, Beijing, China	Prediluted	–
CK7	RN7	XYJQ-BIO, Beijing, China	Prediluted	+
Napsin A	IP64	XYJQ-BIO, Beijing, China	Prediluted	–
P40	BC28	ZSJQ-BIO, Beijing, China	Prediluted	–
P63	UMAB4	ZSJQ-BIO, Beijing, China	Prediluted	Weakly focal+
TTF-1	8G7G3/1	Maixin-Bio, Fuzhou, China	Prediluted	–
Ki-67	EP5	ZSJQ-BIO, Beijing, China	Prediluted	Label index 75%
CD146	EP54	ZSJQ-BIO, Beijing, China	Prediluted	–
Beta-HCG	ZSH17	ZSJQ-BIO, Beijing, China	Prediluted	+
HLA-G	MEM-G/1	Abcam, Shanghai, China	1:50	+
HPL	Polyclonal	MX-BIO, Fuzhou, China	Prediluted	Weakly focal+
CD10	EP195	ZSJQ-BIO, Beijing, China	Prediluted	+
CAM5.2	CAM5.2	ZSJQ-BIO, Beijing, China	Prediluted	+
GATA3	L50-823	XYJQ-BIO, Beijing, China	Prediluted	+

– = negative, β-HCG = Beta-human chorionic gonadotropin, + = positive, ALK = anaplastic lymphoma kinase, HLA-G = human leucocyte antigen-G, HPL = human placental lactogen, MX-BIO = Mai Xin Biology, TTF-1 = thyroid transcription factor-1, XYJQ-BIO = Xi Ya Jin Qiao Biology, ZSJQ-BIO = Zhong Shan Jin Qiao Biology.

thyroid transcription factor-1 (TTF-1), which is an immunohistochemical marker of pulmonary epithelial origin,[27] is not expressed in the trophoblast cells of PCC but is strongly positive within the giant cells of HCG-producing GCC.[28] ETT is composed of mononucleated epithelioid cells arranged in cohesive sheets and has a hyaline extracellular matrix background. ETT was immunoreactive for AE1/AE3, p63, HLA-G, and HPL, whereas β-HCG and CD146 were typically negative.[29] The Ki-67 labeling index of ETT is 7% to 20%. In contrast, PPC includes both cytotrophoblastic-like cells and multinucleated syncytiotrophoblasts. The multinucleated syncytiotrophoblasts of PPC reveal strong immunoreactivity to β-HCG, and the cytotrophoblastic-like cells of PPC exhibit weakly focal positivity to p63, whereas both multinucleated syncytiotrophoblasts and cytotrophoblastic-like cells are negative for CD146. The Ki-67 labeling index in PPC is much higher than ETT. The differentiating points are given in Table 2. The patient in our study lacked evidence of a primary genital tumor and had a thorough check-up by MRT, CT, and ultrasound. No tumors were found in other parts of the body. Therefore, the detailed and rigorous clinicopathological analysis made metastatic choriocarcinoma unlikely.

Extragonadal primary choriocarcinoma in males is extremely rare and aggressive with a much poorer prognosis than other histological subtypes most likely related to the hematogenous dissemination. Most cases derive from midline structures such as the mediastinum, retroperitoneum[30,31] and pineal body corresponding with the theory of the mismigration of primordial germ cells along the urogenital ridge during embryogenesis. However, cases involving other organs have also been reported, such as the lung, brain, stomach, intestine, kidney, and adrenal gland.[1–26,32] PPC in males is even more rare, as only 29 cases have been reported.

Our study includes a literature review of PPC in males. The tumorigenesis of PPC remains unclear, although a few theories have been discussed. Some researchers hypothesized that PPC originated from the neoplastic transformation of misplaced primordial germ cells or was generated from an occult primary gonadal neoplasm undergoing spontaneous regression. Other scholars have suggested that the neoplasm could have arisen from metaplasia or the differentiation of somatic tumor cells similar to primary lung cancer. Additionally, Toda et al[16] proposed that epidermal growth factor might play an important role in an autocrine manner in tumor cells of PPC.

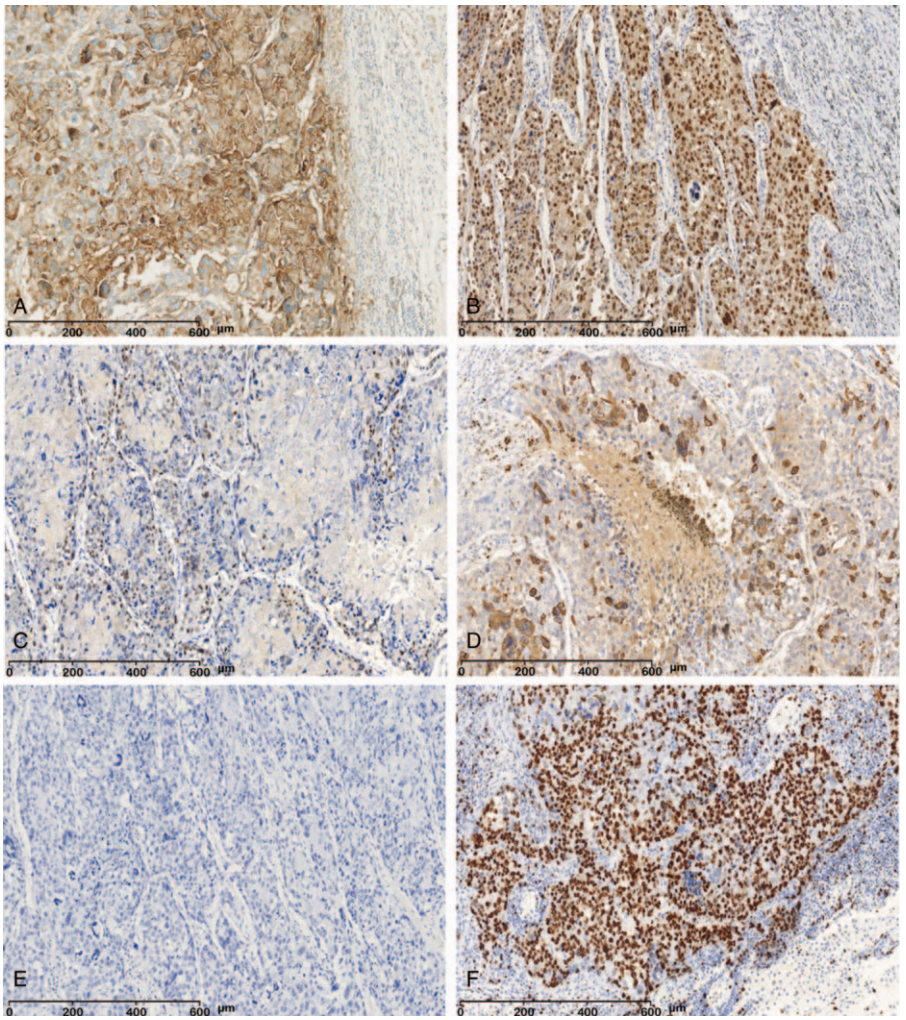

Figure 3. Immunohistochemical findings of PPC. (A) The PPC cells are positive for CD10. (B) The PPC cells are positive for GATA3. (C) The tumor cells are weakly focal positive for P63. (D) Syncytiotrophoblastic giant cells and a few cytotrophoblastic cells are positive for β-HCG. (E) The tumor cells are negative for TTF-1. (F) The Ki-67 labeling index is 75% in the tumor cells (immunohistochemical staining; original magnification, ×100). β-HCG = Beta-human chorionic gonadotropin, PPC = primary pulmonary choriocarcinoma, TTF-1 = thyroid transcription factor-1.

Table 2

Differential diagnosis.

Disease	Morphology	Immunohistochemistry				
		β-hCG	HPL	TTF-1	Ki-67	P63
PPC	Cytotrophoblastic-like cells and multinucleated syncytiotrophoblasts	+	-/ Weakly +	–	70%–80%	Focal +
HCG-producing GCC	Simulate Syncytiotrophoblast	Weakly +	NA	+	NA	–
ETT	Mononucleatedepithelioid cells	-/ Weakly +	+	–	7%–20%	+

ETT = epithelioidtrophoblastic tumor, HCG-producing GCC = human chorionic gonadotropin-producing giant cell carcinoma, NA = not available, PPC = primary pulmonary choriocarcinoma.

Table 3

List of all published cases of primary pulmonary choriocarcinoma in males.

Case Number/Case	Age, y	Symptoms	Diagnostic Method	Therapy	Follow-up
Guichard et al[1]	NA	NA	NA	NA	NA
Starichkov et al[2]	NA	NA	NA	NA	NA
Cacciamani[3]	19	Cough	Autopsy	CT	Died 5 monthsafter diagnosis
Hayakawa et al[4]	45	Gynecomastia	Biopsy postoperatively	IR + RT	Died 4 months after initial symptoms
Hayakawa et al[4]	57	NA	Autopsy	None	Died 2 months after initial symptoms
Kalla et al[5]	27	Pleuritic pain	Biopsy postoperatively	CR + CT	Still alive after 2 years
Zapatero et al[6]	67	Hemoptysis	Biopsy postoperatively	CR	Still alive after 3 years
Uspenskiĭ et al[7]	NA	NA	NA	NA	NA
Kuang[8]	NA	NA	NA	NA	NA
Endou et al[9]	NA	NA	NA	NA	NA
Sullivan[10]	51	Cough, weight loss	Autopsy	None	Died 1 week after admission
Sridhar et al[11]	37	Cough, chest pain	Biopsy postoperatively	Neoadjuvant CT + CR + palliative CT	Died 15 months after diagnosis
Adachi et al[12]	71	Dyspnea,chest pain	Biopsy postoperatively	NA	Died 6 months after initial symptoms
Dura[13]	NA	NA	Two case by autopsy and one case by biopsy postoperatively	NA	NA
Durieu et al[14]	61	Hemoptysis, chest pain	Biopsy postoperatively	CR + RT + palliative CT	died 11 days after; starting chemotherapy
Otsuka et al[15]	4 months	Precocious puberty	Biopsy postoperatively	CR + CT + skull RT	Died 5 months after surgery
Toda et al[16]	69	Hemoptysis	Autopsy	CT	Died 1.5 months after admission
Canver and Voytovich[17]	69	Asymptomatic	Biopsy postoperatively	CR + CT	Still alive 6 months after surgery
Uwatoko and Kajita[18]	NA	NA	NA	NA	NA
Ikura et al[19]	60	Asymptomatic	Autopsy	CT	Died 5 months after the tumor detected
Chen et al[20]	61	Hemoptysis	Biopsy postoperatively	CR + CT + best supportive care	Still alive 6 months after surgery
Tsai et al[21]	23	Hemoptysis and progressive dyspnea	Urine pregnancy test and bronchoscopicbiopsy	Aggressive CT + management in the ICUs	Death 8 days after admission
Vaideeswar et al[22]	60	Cough, dyspnea, hemoptysis	NA	NA	NA
Yamamoto et al[23]	77	Rapid progressive respiratory dysfunction	Autopsy	None	Died 6 days after admission
Hadgu et al[24]	48	Shortness of breath, cough, drenching night sweats	CT-guided biopsy of right lung lesion	CT + CR	Died 5 days after surgery
Jiang et al[25]	45	Fainting	Biopsy postoperatively	IR + CT	Death 10 months after diagnosis
Kamata et al[26]	70	Cough	Biopsy postoperatively	CR	Still alive after 2 years
Our case	67	Asymptomatic	Biopsy postoperatively	CR + CT	Alive >13 months after the tumor detected

CR = complete resection, CT = chemotherapy, IR = incomplete resection, NA = not available, NE = not examined, RT = radiotherapy.

All PPC cases published from 1953 to 2016 involving males were collected, and all results were examined for applicability. Only 29 cases were found within 26 independently published reports. These cases are included in Table 3.[1–26] We only found 19 unequivocal cases with clinical data in 18 published reports. We could not acquire details from the other 10 reports because these reports were either not accessible or not in the English language. The patients with clinical data in the publications were aged from 4 months to 77 years.[1–26] The age of PPC patients showed a higher prevalence rate in the second and third decades of life. The median age of patients was 58.5 years. Most patients saw their doctors with symptoms, such as pleuritic pain, hemoptysis, dyspnea, cough, or precocious puberty, whereas 3 cases (including the present case) were asymptomatic, and the tumor was discovered by chest roentgenogram. Eight cases were diagnosed by autopsy, and only 1 patient was diagnosed by a urine pregnancy test and bronchoscopic biopsy. One patient was diagnosed by a CT-guided biopsy before the operation. The diagnosis is usually delayed until the patient is in the middle-late stage of the disease. Distant metastases are observed in many cases[11–12,14,16,19,23–25] at the time of diagnosis, and the overall prognosis is extremely poor. A total of 18 patients have data about their treatment: 6 patients were treated with surgery and chemotherapy; 4 were treated with chemotherapy alone; 2 were treated with surgery, chemotherapy, and radiotherapy; 1 was treated with surgery and radiotherapy; 2 were treated with surgery alone; and 3 patients did not receive treatment and died quickly. Only 5 patients (including our case) survived for >1 year.

The treatment strategies performed for the patients included complete resection, chemotherapy, radiotherapy, supportive care, or a combination of the above treatments in the published cases.[33] There is no evidence-based treatment recommendation at present, making the planning of further therapy difficult. According to the literature, a complete resection followed by adjuvant chemotherapy with 2 or 3 cycles of PEB protocol and close follow-up examinations tended to yield the best survival chance for the patients. Nevertheless, the patients with PPC had a higher metastatic rate and a poorer survival rate. Some reports found that females with PPC were a lot younger than males and had longer survival periods than their male counterparts,[34] but the reason for this is unknown. In the present case, the tumor was discovered before the onset of symptoms. A complete resection was performed in a timely manner. After a definite diagnosis of PPC was made, 4 cycles of modified chemotherapy were carried out for the patient based on the systemic status of the patient. The present results support a good response to the chemotherapy. So far, the serum β-HCG level of the patient has remained within the normal range, and no metastatic complications have been discovered. We will continue follow-up with the patient.

4. Conclusion

The case highlights a rare disease that was successfully diagnosed before the onset of symptoms, and the patient received modified chemotherapy according to the systemic status of the patient following chemotherapeutics after surgery. The key step for the diagnosis of PPC is based on the histological features combined with immunohistochemical detection, β-HCG levels of the patient, and the differential diagnoses. Although the prognosis is poor, such patients would benefit tremendously from early diagnosis and modified therapy. It is necessary to explore novel treatments for patients with PPC, and more reports of similar cases are warranted to establish optimal management.

Acknowledgements

We thank the medical technologists of Department of Pathology, Peking Union Medical College Hospital for vigorous technical assistance.

References

[1] Guichard A, Cabanne F. Pulmonary chorioepithelioma in man and its so-called primary forms. J Med Lyon 1953;34:235–65.
[2] Starichkov MS, Tager I. Primary mediastino-pulmonary chorioepithelioma in a male. Vestn Rentgenol Radiol 1962;37:50–4.
[3] Cacciamani J. Case of choriocarcinoma of the lung. Clin Notes Respir Dis 1971;10:10–1.
[4] Hayakawa K, Takahashi M, Sasaki K, et al. Primary choriocarcinoma of the lung: case report of two male subjects. Acta Pathol Jpn 1977;27:123–35.
[5] Kalla AH, Voss ECJR, Reed RJ. Primary choriocarcinoma of the lung (a case report). WV Med J 1980;76:261–3.
[6] Zapatero J, Bellon J, Baamonde C, et al. Primary choriocarcinoma of the lung: presentation of a case and review of the literature. Scand J Thorac Cardiovasc Surg 1982;16:279–81.
[7] Uspenskiĭ LV, Denisova OP, Ablitsov IuA. Primary lung chorioepithelioma in a male. Khirurgiia (Mosk, Russian) 1982;5:106–8.
[8] Kuang XW. Primary pulmonary choriocarcinoma in a male: report of a case and review of the literature. Zhonghua Jie He He Hu Xi Xi Ji Bing Za Zhi 1984;383:354–5.
[9] Endou T, Ueno H, Okada H, et al. Primary choriocarcinoma of the lung (a case report of male subject and review of the literature). Nihon Naika Gakkai Zasshi (Japan) 1988;77:1404–9.
[10] Sullivan LG. Primary choriocarcinoma of the lung in a man. Arch Pathol Lab Med 1989;113:82–3.
[11] Sridhar KS, Saldana MJ, Thurer RJ, et al. Primary choriocarcinoma of the lung: report of a case treated with intensive multimodality therapy and review of the literature. J Surg Oncol 1989;41:93–7.
[12] Adachi H, Aki T, Yoshida H, et al. Combined choriocarcinoma and adenocarcinoma of the lung. Acta Pathol Jpn 1989;39:147–52.
[13] Dura J. Primary choriocarcinoma of the lung. Three cases in men Zentralbl Pathol (German) 1991;137:74–7.
[14] Durieu I, Berger N, Loire R, et al. Contralateral haemorrhagic pulmonary metastases ("choriocarcinoma syndrome") after pneumonectomy for primary pulmonary choriocarcinoma. Thorax 1994;49:523–4.
[15] Otsuka T, Ohshoima Y, Sunaga Y, et al. Primary pulmonary choriocarcinoma in a four month old boy complicated with precocious puberty. Acta Paediatr Jpn 1994;36:404–7.
[16] Toda S, Inoue Y, Ishino T, et al. A rare case of primary pulmonary choriocarcinoma in a male: immunohistochemical detection for human chorionic gonadotrophin, epidermal growth factor (EGF) and ECF-receptor. Endocr J 1995;42:655–9.
[17] Canver CC, Voytovich MC. Resection of an unsuspected primary pulmonary choriocarcinoma. Ann Thorac Surg 1996;61:1249–51.
[18] Uwatoko K, Kajita M. Primary choriocarcinoma of the lung: a case report involving a male. J Jpn Assoc Chest Surg 1997;11:662.
[19] Ikura Y, Inouc T, Tsukuda H, et al. Primary choriocarcinoma and human chorionic gonadotrophin producing giant cell carcinoma of the lung: are they independent entities? Histopathol 2000;36:17–25.
[20] Chen F, Tatsumi A, Numoto S. Combined choriocarcinoma and adenocarcinoma of the lung occurring in a man: case report and review of the literature. Cancer 2001;91:123–9.
[21] Tsai JR, Chong IW, Hung JY, et al. Use of urine pregnancy test for rapid diagnosis of primary pulmonary choriocarcinoma in a man. Chest 2002;121:996–8.
[22] Vaideeswar P, Mehta J, Deshpande J. Primary pulmonary choriocarcinoma: a series of 7 cases. Indian J Pathol Microbiol 2004;47:494–6.
[23] Yamamoto S, Tanaka H, Takeo H. Primary pulmonary choriocarcinoma combined with adenocarcinoma. Pathol Int 2006;56:402–7.
[24] Hadgu A, Tindni A, Panda M. Primary pulmonary choriocarcinoma in a male. BMJ Case Rep 2010;02:2712–8.

[25] Jiang F, Xiang Y, Feng F-Z, et al. Clinical analysis of 13 males with primary choriocarcinoma and review of the literature. OncoTargets Ther 2014;7:1135–41.
[26] Kamata S, Sakurada A, Sato N, et al. A case of primary pulmonary choriocarcinoma successfully treated by surgery. Gen Thorac Cardiovasc Surg 2016;5.
[27] Yatabe Y, Mitsudomi T, Takashashi T. TTF-1 expression in pulmonary adenocarcinomas. Am J Surg Pathol 2002;26:767–73.
[28] Attanoos RL, Papagiannis A, Suttinont P, et al. Pulmonary giant cell carcinoma: pathological entity or morphological phenotype? Histopathology 1998;32:225–31.
[29] Chen B-J, Cheng C-J, Chen W-Y. Transformation of a post-cesarean section placental site nodule into a coexisting epithelioid trophoblastic tumor and placental site trophoblastic tumor: a case report. Diagnost Pathol 2013;8:85–9.
[30] Moran CA, Suster S. Primary mediastinal choriocarcinomas: a clinicopathologic and immunohistochemical study of eight cases. Am J Surg Pathol 1997;21:1007–12.
[31] Bokemeyer C, Nichols CR, Droz JP. Extragonadal germ cell tumors of the mediastinum and retroperitoneum: results from an international analysis. J Clin Oncol 2002;20:1864–73.
[32] Fine G, Smith RW, Pachter MR. Primary extragenital choriocarcinoma in the male subject: case report and review of the literature. Am J Med 1962;32:776–94.
[33] Kini U, Babu MK. Primary pulmonary choriocarcinoma: is it still an enigma? Indian J Chest Dis Allied Sci 2007;49:219–26.
[34] Serno J, Zeppernick F, Jäkel J, et al. Primary pulmonary choriocarcinoma: case report and review of the literature. Gynecol Obstet Invest 2012;74:171–6.