Lung colloidal adenocarcinoma - A case report and review of relevant documentation

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Summary

According to the histopathological classification of lung tumors of the World Health Organization (WHO) 2015, update 2021, the adenocarcinoma group includes the following subtypes: (1) minimally invasive adenocarcinoma (MIA); (2) Invasive non-mucinous carcinoma (INMA); (3) Invasive mucinous carcinoma (IMA); (4) Colloidal adenocarcinoma (CA); (5) Fetal cancer (FA); (6) Enteric-type adenocarcinoma (EA). In which group colloidal cancer (CA) is said to be very rare, with high malignancy, rapid progression, very difficult to treat. The definitive diagnosis of lung cancer (LC) in general and Adenocarcinoma in particular is still the absolute role of pathology; The problem of subtype LC diagnosis is essential for treatment and prognosis. We present a rare case of CA with a giant mucinous mass in the lower lobe of the right lung, destroying the diaphragm descending to the abdomen, making preoperative diagnosis extremely difficult. The patient underwent surgery to remove the lower lobe of the right lung, and the postoperative specimens were diagnosed with CA; The prognosis after surgery was very conservative. Through the report, we hope that colleagues will have a better diagnostic approach when encountering a similar case.

Keywords: Adenocarcinoma, invasive mucinous adenocarcinoma; mucinous, computed tomography, pathology, histopathology.

1. Background

Colloidal adenocarcinoma (CA) of the lung is defined as an adenocarcinoma with multiple pools of mucin (colloid) replacing air-filled spaces. In general, tumors are characterized by monocystic or multicystic structures. Histopathologically, large amounts of mucin dilate the alveolar spaces, destroy their walls, and dissect the lung parenchyma. The neoplastic alveolar columnar epithelial cells form an incomplete barrier and float into the mucin-filled alveolar cavities. These pathologic features mimic those of follicular cell carcinomas of the ovary, breast, and pancreas [1, 2].

CT features of CA include single or multifocal, cystic or segmental, low attenuation; The walls and septum are strongly enhanced with contrast after injection and calcified nodules are fixed in the wall or septum. PET/CT with ^{18}FDG showed mild FDG uptake. Since cancer cells are usually found in the wall or septum, uptake of FDG can be seen at these sites [2-5].

Because CA tumors often have mucinous cyst-like structures, CT-guided bronchoscopy and transthoracic biopsies are often difficult to capture the malignant tissue. Diagnostic surgery - copper therapy is currently still an effective method, and pathology of postoperative specimens (macroscopic and microscopic) is still the gold standard for diagnosing the case [2-7].

2. Case presentation

A 65-year-old male patient, was transferred to the National Lung Hospital with the diagnosis of lung tumor monitoring from Provincial Lung Specialist Hospital.

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History: 1 month before admission, the patient showed a cough, sore throat, increased cough, cloudy sputum, one time coughing up blood (about 50ml), the next few days there was black sputum. The patient had no fever, no shortness of breath, fatigue, and poor sleep. The patient went to the provincial pulmonology hospital for examination, was hospitalized for 3 days without improvement, and was transferred to the National Lung Hospital.

Examining some patients awake, good contact; average fitness; normal skin and mucous membranes, no edema, no subcutaneous hemorrhage; peripheral lymph nodes are not enlarged; The patient also coughed with sputum, did not cough up blood, did not have any symptoms of shortness of breath, frequent chest pain. Vital indicators (pulse, blood pressure, breathing rate, temperature) within normal limits; weight 54kg. Examination of other organ systems (circulatory, respiratory, digestive, urinary-genital, neurological, musculoskeletal-joint, ear-nose-throat, teeth-jaw-face, eye, endocrine, nutritional) found nothing unusual.

Tests of the patient at the time of visit and the time of admission to the hospital

Complete blood count: WBC increased, ranging from 12.08-13.56-21.24G/L; corresponding percentage of Neutrophils polymorphonuclear leukocytes: 79.8-75.6-92.9.

Blood biochemistry: Urea slightly increased, fluctuating from 11 to 12.2mmol/L; CRP increased (84.8mg/L); D-dimer 710ng/mL.

Urine chemistry: Normal.

Blood coagulation test: Normal.

Some markers: Pro GRP increased (80.1pg/mL); CEA increased (7.08ng/mL); CYFRA 21-1 and SCC within normal limits.

TB tests (direct AFB; Gene Xpert MTB; culture; LPA): Negative.

PCR SARS-CoV-2: negative

Some markers: Pro GRP does not increase; CEA within normal limits; CYFRA 21-1 increased (12.99ng/ml).

The patient underwent abdominal ultrasound, cranial magnetic resonance imaging, and the results showed no abnormalities.

The patient had a conventional chest X-ray film, the details of which are shown in Figure 1.

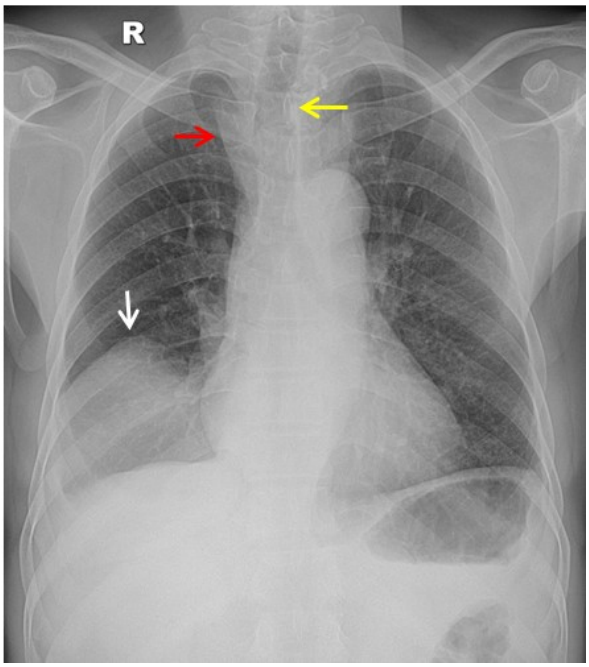

Figure 1. Standard chest X-ray when the patient was admitted to the hospital

Appearance of opacities in the lower of the right lung, clear upper border (white arrow), lateral border bordering the chest wall, erasing the right costophrenic angle. Trachea to the right (yellow arrow), upper mediastinal border to the right (red arrow). Still observing the right mediastinal border (right atrium) => opaque mass not in the middle lobe, posteriorly; The right diaphragm is still observed (not erased) => Pleural effusion is excluded, the opacities are in the lower lobe but not completely adjacent to the right diaphragmatic arch.

Due to the obvious inflammatory Billan (increased WBC; increased CRP), the patient was initially diagnosed with: Pneumonia.

The patient was treated with antibiotics and anti-inflammatory drugs according to the community-acquired pneumonia protocol. After 1 week, the patient's inflammatory condition improved. Interventions were continued.

The patient was underwent chest CT scan with intravenous contrast injection; The results and representative images are shown in detail in Figures 2 and 3.

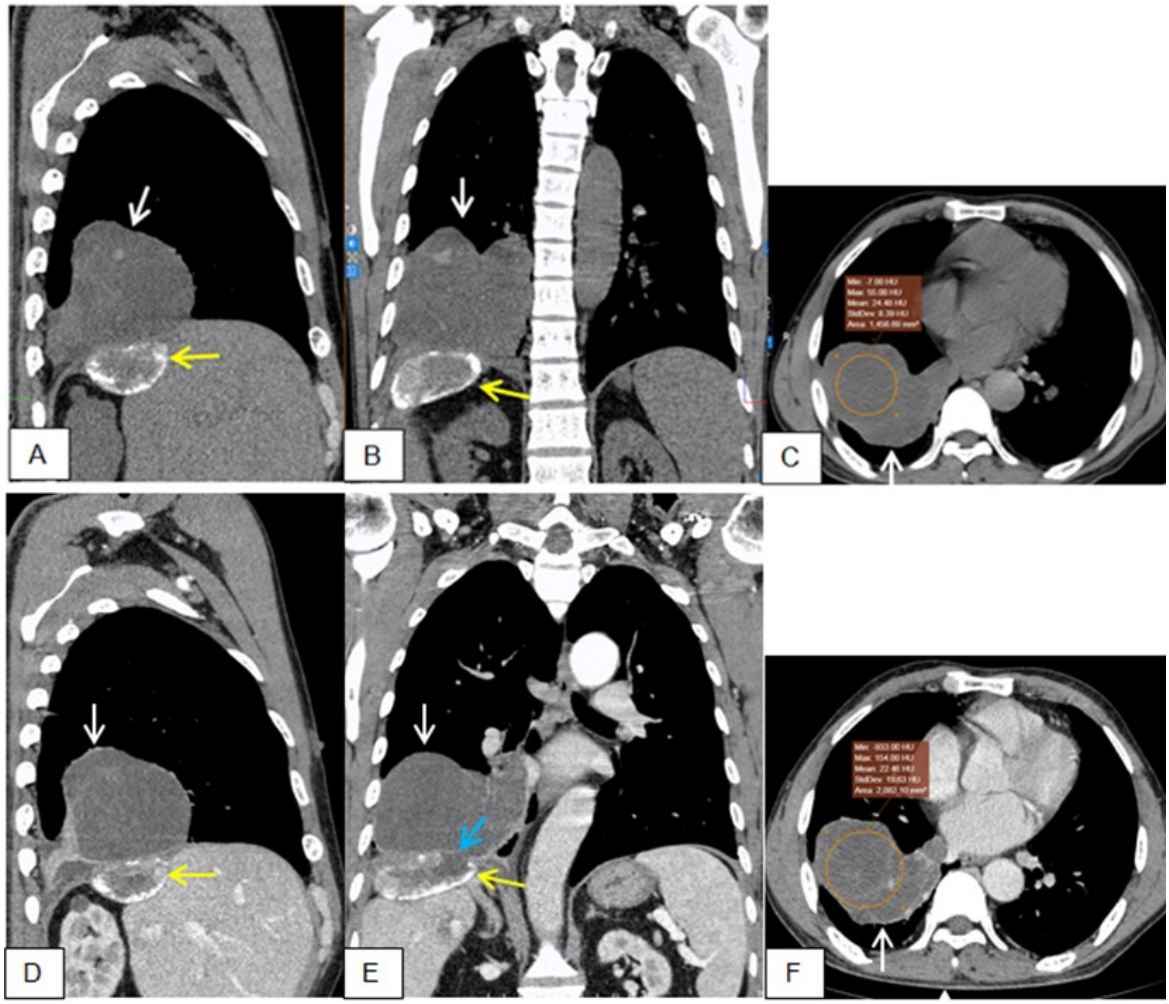

Figure 2. CT image of chest, mediastinal window, anterior (A-C) and posterior (D-F) contrast injection, Sagiatal plane (A, D); Coronal (B, E) and Axial (C, F)

Abnormal mass, clear border (white arrows), clear density ~ fluid (#23HU). Below the right diaphragm appeared another abnormal mass, size # 64 x 46 x 30mm, with a thick, calcified shell that also contained fluid (yellow arrows). In slice E is observed a passageway through the diaphragm connecting the two masses. No large mediastinal lymph nodes were seen. Conclusions of the radiologist: Monitor the possibility of bronchial obstruction of the right lower lobe causing stasis, creating large bronchial fluid pockets; Thick lime is localized to the right pleura close to the diaphragm.

The patient was underwent an interdisciplinary consultation. The decision to do bronchoscopy and CT-guided transthoracic biopsy of the tumor was made later.

Results of of bronchoscopy: Necrotic tissue causes complete occlusion of the right bronchial apertures of segments 8, 9, and 10. Take samples for testing: BACTEC, fungal culture, bacteria culture (tuberculosis, non-tuberculosis), Gene Expert MTB; Biopsy of the right lower lobe mucosa. Subsequent microbiological test results were negative, pathology results of necrotizing ulcerative lesions.

The patient was underwent a transthoracic biopsy under CT guidance, detailed images and pathology results are shown in detail in Figure 3.

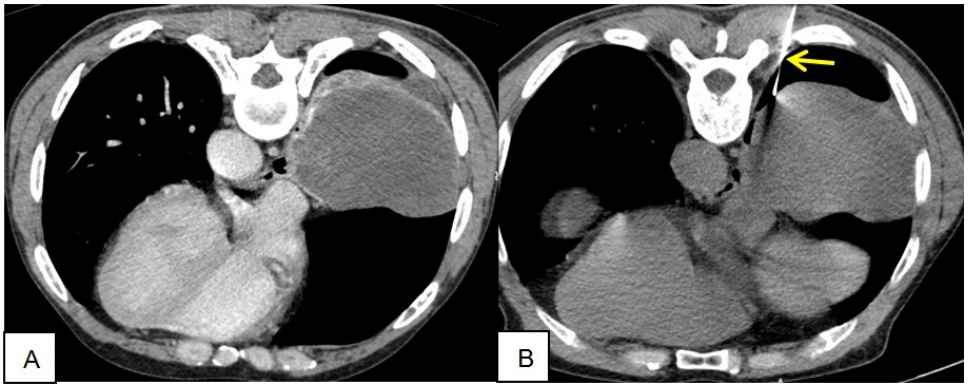

Figure 3. Transthoracic biopsy under computed tomography guidance

A: CT chest, mediastinal window, with slice contrast injection to select the biopsy site. B: The biopsy needle (yellow arrow) enters the right cyst margin. Safe procedure, 4 pieces of specimen to send to pathology, microbiology, reserve for gene mutation and Immunohistochemistry. Biopsy pathology results: The biopsy piece is an area of connective tissue, was infiltrated polymorphonuclear leukocytes, mononuclear inflammatory cells, macrophages, no malignant cells.

3. Discussion

Chronic inflammatory lesions

Thus, post-biopsy through bronchoscopy and X-ray under CT guidance both showed inflammatory results. The patient was consulted, and the decision to undergo diagnostic surgery was agreed upon by the council, the patient and the patient's family. Cranial magnetic resonance imaging was performed, the results were not abnormal (prevent/exclude the possibility of lung metastases to the skull); Preoperative tests were performed. The results allow for surgery.

The patient was operated on by laparoscopic technique, the main features of the operation are shown in the operating report: The parenchyma of the right lung in the upper and middle lobes is pink and beautiful; The lower lobe surface is deformed, sticking to the chest wall, the diaphragm; In the picture shows a solid mass, size # 7 × 7cm, inside the mass contains many white pus-like thick fluid, a part of this mass passes through the diaphragm in the apex region to the sub-abdominal mass. The sub-abdominal mass has a solid shell, and the border is sclerotic. Proceed to remove the entire lower lobe pulp from the chest wall and diaphragm. Dissection of lower lobe pulmonary artery, lower vena cava, lower lobe bronchus with 3 Stapler; Dissect and cut the lung parenchyma adherent to the diaphragm with 3 Stapler. Surgical removal of the entire remaining right lung from the chest wall. After surgery, the parenchyma does not fully expand the cut space. Insert 01 tube to drain the pleural space at the base, close the chest wall anatomically. Safe surgery. The whole specimen mass was properly preserved and submitted to pathology (histopathology test, tissue culture, *EGFR* mutation, *KRAS*).

After surgery, the patient progressed smoothly, had a postoperative drainage tube removed on the 6th day and transferred to the Oncology Department to continue cancer treatment according to the protocol.

Post-operative pathology results

Macroscopic: The lung specimen is solidified, the cut through shows fibrosis, with cocoon-forming area, thick wall, mucus-containing lumen.

Microscopic: The biopsy piece is an area of connective tissue, see many clusters of

adenocarcinoma cells infiltrating, nuclei cells are hyperchromatic and lose polarity. These cells are arranged to form glandular structure and strong mucus secretion. *Conclusion*: Infiltrating colloidal cancer (Lung adenocarcinoma colloid subtype).

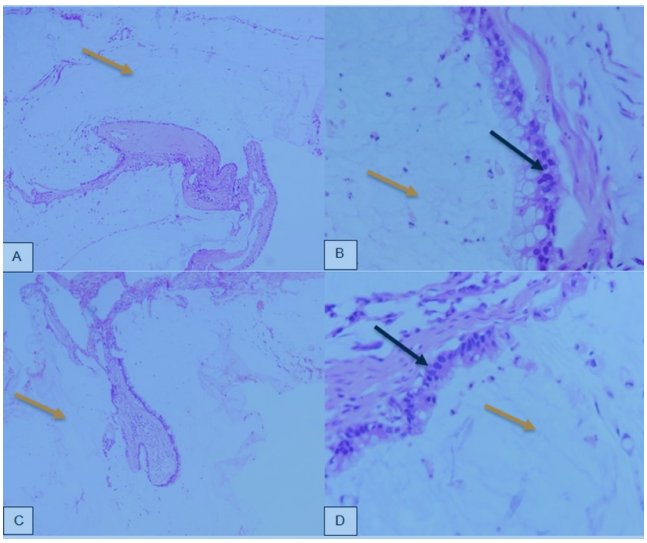

Figure 4. Postoperative specimen HE specimen A-C: HE × 100; B, D: HE x 400. Mucous zone (Orange arrow): glandular epithelial cells (Black arrow)

EGFR gene mutation test result: Negative.

Final definitive diagnosis of the case: Case of patient with colloidal, invasive adenocarcinoma of the lung (Colloid adenocarcinoma - CA).

4. Discussion

Lung cancer (LC) is the most common malignancy in humans and a major cause of cancer death worldwide. Adenocarcinoma currently accounts for nearly half of all LC cases. The 2015 World Health Organization approved classification recommended by the International Association for the Study of LC, the American Thoracic Society and the European Respiratory Society, recommended for use and updated 2021. This classification of tumours combines up-to-date radiology, molecular biology, and oncology knowledge, providing terminology and diagnostic criteria for each type of histopathology. For post-operative specimens, entities were identified as in situ/minimally invasive carcinoma. For invasive adenocarcinoma, the new classification introduced histological subtypes according to 6 variants (under type): MIA; INMA; IMA; CA; EA (as described in the summary) [1, 2].

How can we get an accurate diagnosis of primary lung colloidal carcinoma?. Ogusu S et al in their paper showed that CA is classified as a variant form of invasive adenocarcinoma, which is histologically characterized by the presence of multiple mucins in the tumor. CA is extremely rare, accounting for 0.24% of all cancers. On chest CT, CA is usually seen as a low-density mass (~fluid), with poor contrast enhancement, whereas on magnetic resonance imaging (MRI) is characterized by a mass with low signal intensity on T1WI and intensity high on T2W (possibly from the mucin component of the tumor). However, CT and MRI cannot distinguish between benign and malignant disease. The distinction between CA and IMA is also mentioned by the authors. Immunohistochemically, CA tumor cells were positive for CK7, CK20, MUC2, and CDX2; these features are consistent with colloidal adenocarcinoma [2-4]

In the World Health Organization (WHO) guidelines the diagnosis of CA is based on findings of cancer cells floating in large puddles of mucus and lining the inside of alveolar spaces. Ogusu S et al also reported 13 cases (7 men and 6 women) with pulmonary CA; The mean age was 64.5 years old (50-79 years old) with cough (5 cases), hemoptysis (2 cases), and chest pain (1 case). The five reported cases were asymptomatic and discovered incidentally during routine physical examination. CA tumors have been described as nodules or masses with well-defined borders in the peripheral lung field, measuring 1.8 to 6.5cm. The report described the findings of low density and poor contrast enhancement on CT, low intensity on T1WI and high intensity on T2WI of MRI, and low absorption of 18-FDG on PET; These findings may be due to the abundant mucin that accounts for the majority of tumours.[5] The case we report is also very similar to the imaging features described in this literature.

Kim HK et al also reported on imaging characteristics of 7 cases of CA caught from 2010 to 2017, which were surgically demonstrated CA on

histopathology. CT findings (both contrast and non-contrast) and PET/CT were analyzed; Imaging features were compared with histopathological reports; Clinical and demographic characteristics were also analyzed. The study results showed that 6 tumors had low density on non-contrast CT [(-16.5 to 20.7HU (mean, 9.2HU)]. After contrast injection, the increase in HU was very low (0.4-29.0HU), mean increase 4.1HU (not significant). All tumors have a borderline is segmental line. Tumor calcifications were seen in 1 patient. 18-FDG tumor uptake values on PET/CT ranged from 1.5 to 4.5 SUV (median: 3.5). Six out of seven patients FDG accumulation was seen within the wall of the tumor (curve absorption); 3 patients were seen in both the tumor wall and the tumor septum (cross-absorption). Six patients were alive without recurrence after a median follow-up time of 2.3 years (2 months to 5 years); one patient survived for 4 years (with concurrent adjuvant radiotherapy after lobectomy). Recommendations of the study: On CT, CA of the lung presenting as homogenous hypodense masses, 18-FDG uptake along the mass wall or cross-section is seen in the tumour, where tumor cells line the wall or bulkhead. In addition, the authors note that because CA appears as a low-density tumor or as a cyst on CT, the differential diagnosis should include cystic or cystic lesions such as intrapulmonary bronchial cysts, bronchiectasis, bronchial ataxia, fluid-filled lung cysts, mucinous adenocarcinoma of the lung, metastasis from mucinous adenocarcinoma [6].

Colloidal adenocarcinoma may present with other histological forms of lung cancer. Liu Y et al reported a case of a combination of CA and squamous cell carcinoma (SCC) in a 79-year-old man who was admitted to the hospital with chest pain and dyspnoea (15-year history of dyspnea). The patient underwent surgical resection of both the upper lobe (where the SCC mass appeared) and the right lower lobe of the lung (where the CA mass appeared). After surgery, the patient was treated with 3 rounds of adjuvant chemotherapy with pemetrexed and lobaplatin. The patient was still alive and well at the time of reporting after more than 2 years of surgery [7].

Nakamura D et al reported a case of CA presenting as a giant right upper lobe tumor (diameter # 11cm) that was successfully operated on in a 69-year-old female patient, discovered incidentally without any symptoms. The patient was underwent bronchoscopy, a large amount of mucus was obtained during bronchoscopy but no malignant cells were found on cytology and CT-guided transthoracic biopsy did not give the expected results as malignant cells were floating in the mucus. Chest CT with contrast showed a big cystic mass with calcification and contrast in the cyst wall. The hilar or mediastinal lymph nodes are not enlarged. Magnetic resonance imaging shows a low T1W signal and a high T2W signal in the giant mass. CT and MRI showed a massive tumor compressing the superior vena cava but not infiltrating. A PET/CT scan showed 18-FDG uptake in the cyst wall, with an SUV value of 12.8 (strong positive). Right upper lobe resection with longitudinal sternal dissection and ipsilateral hilar and mediastinal lymph node dissection (10R, 11R, 2R, and 4R) was performed. Pathological examination of the resected specimen confirmed the presence of a large amount of mucin in the tumor. Microscopic examination of the specimen revealed goblet-like tumor cells along the wall of the cyst and disrupted the alveolar cavity by polycystic mucin. A few tumor cells float in mucin reservoirs. Immunohistochemistry showed that tumor cells were positive for CK7, CK20, CDX2, MUC2; and negative for transcription factor TTF-1. Differential diagnosis of CA with metastatic mucinous carcinoma from the gastrointestinal tract is also proposed. The latter possibility was excluded because there was no significant tracer accumulation in the gastrointestinal tract on preoperative PET/CT and no tumor lesions in the gastrointestinal tract on postoperative endoscopy [5]. Field The case we report has similar CA block characteristics as mentioned by the author. The difference and uniqueness is that the tumor has destroyed the right diaphragm, creating a second CA mass under the abdomen with luck due to its thick shell, calcification, so this mass is only localized on the upper surface of the liver, no effect on the

abdominal cavity. To the best of our knowledge, this is the only case reported to date [8].

CA mass in the lung may metastasize to bone. Morita K et al described a primary mucinous adenocarcinoma of the lung in an 80-year-old man. - CT of the thorax showed an abnormal mass with 3.2cm in diameter in the right middle lobe. Transbronchial biopsy via endobronchial ultrasound did not reveal malignancy. A right medial lobectomy was performed and the pathological results subsequently confirmed the case of CA. Twenty-eight months after surgery, the patient developed a solitary nodule on the 5th finger bone of the left hand. CT scan followed by biopsy followed by pathology biopsy revealed an internal mucin-filled tumor, confirming the tumor was secondary to pulmonary CA [9].

Colloidal adenocarcinoma (CA) of the lung represents a rare variant, especially primary CA, which usually presents a favorable prognosis and very rarely presents with hilar, mediastinal enlargement. Murai T et al had a rather special case report. A 70-year-old man was found to had a CA mass in the right upper lobe of his lung with multiple calcified nodules attached to the wall and within the mass. Contrast-enhanced chest CT showed a strong contrast-enhanced mass wall and a few large mediastinal lymph nodes (group 10R; 2R; 4R). The patient underwent surgery to remove the right upper lobe of the lung, with dissection of the ipsilateral hilar and mediastinal large nodes. After surgery, the patient progressed smoothly, but after 4 months, CT and PET scans detected many bone metastases at many locations in the body. Author's recommendation for cases of CA with large regional lymph nodes, postoperative specimens should be noted for differential diagnosis between CA and IMA because mucinous carcinomas often have high malignancy [10].

Returning to the reported case and comparing with the literatures, we found that the difference of CA from other adenocarcinoma subtypes was that the tumor appeared like a mucinous sac on CT images. Due to the rare combination of imaging features very similar to a benign lung tumor, we still initially focused more on the possibility that it was not malignant. The point that is not suitable for the diagnosis of benign lung tumor is that there is damage to the right diaphragm, an abnormal foci located below the abdomen, localized to the upper surface of the liver, with a clear calcified shell. The definitive diagnosis of the case was made only after surgery and the pathology of HE fully demonstrated the histopathological features of typical CA without the need for immunohistochemistry. Unfortunately for us, it was after a confirmed diagnosis that the patient proposed to be transferred to a specialized oncology hospital for treatment. Staging techniques (bone scintigraphy, PET/CT) were also not performed at our hospital and treatment options were not established.

4. Conclusion

Colloidal adenocarcinoma is a rare subtype of lung cancer. Due to limited case data, judgments about the malignancy of CA are unclear. The initial diagnosis is usually based on CT and MRI findings with the use of contrast and contrast agents to demonstrate the cystic structure of the tumor. Malignant cells of the tumor often adhere to the wall and wall of the cyst, so care should be taken when doing PET/CT to determine the extent of 18-FDG arrest of these cells. Diagnosis (cytology, histopathology) before surgery is extremely difficult due to the dispersion characteristics of tumor cells. Tumor resection and postoperative pathology are still considered to be the most effective, providing the gold standard for definitive diagnosis. Postoperative chemotherapy for Colloidal adenocarcinoma tumors is necessary, but the prognosis is uncertain.

Ethical aprroval

All producers performed in studies involving human participants were in accordance with the standards of the NLH Ethics Board and with the 1964 declaration of Helsinki and subsequent amendments, or equivalent ethical standards.

Consent for publication

The patient received informed writen consent form for release of clinical detail. However, in the article the identity of the patient was hidden.

Disclosure

The author report no conflicts of interest for this work.

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