SUBMITTED 24 FEB 21
REVISION REQ. 19 APR 21; REVISION RECD. 5 MAY 21
ACCEPTED 3 JUN 21
ONLINE-FIRST: JUNE 2021
DOI: https://doi.org/10.18295/squmj.6.2021.091

The Diagnostic Dilemma of Ruptured Liver Metastasis in a Patient with Lung Cancer

A case report

K S Jayanth,[1] Shivakumar Madan,[1] Balakrishnan Gurushankari,[1] Sathasivam Sureshkumar,[1] Amaranathan Anandhi,[1] Rajesh NG,[1,2] *Vikram Kate[1]

Departments of [1]Surgery and [2]Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India
**Corresponding Author's e-mail: drvikramkate@gmail.com*

Abstract

Spontaneous rupture of a metastatic liver tumour is rarely documented in literature when compared to hepatocellular carcinoma and other liver lesions, especially from a lung primary. Here we report a case of ruptured liver metastasis from an adenocarcinoma of the lung mimicking ruptured liver abscess, challenging the clinical diagnosis. A 42-year-female presented in July 2020 with complaints of abdominal pain, breathlessness, fever. On examination, the patient was tachypneic with a right hypochondriac mass. A contrast-enhanced computed tomography of abdomen and thorax revealed an ill-defined heterogeneously enhancing lesion in the liver with a communicating subcapsular collection and hypo enhancing lesions in the left lobe and heterogeneously enhancing lesion in the left lung. Adenocarcinoma of the lung with hepatic metastasis was confirmed with a core needle biopsy. The patient was managed conservatively with intravenous antibiotics, intercostal drainage tube and Gefitinib. However, despite best efforts, the patient succumbed to the disease.

Keywords: Liver secondaries; Spontaneous rupture; Hepatocellular carcinoma; Thyroid transcription factor; Liver abscess.

Introduction

Carcinoma of the lung is one of the lethal cancers with commonest sites of dissemination being brain, liver, contralateral lung, adrenals, and bone.[1, 2] Although rupture of liver lesions such as liver abscess, hepatic adenomas, hemangiomas, focal nodular hyperplasia has been reported in the literature, rupture of malignant tumors is relatively uncommon.[3] Spontaneous rupture of hepatocellular carcinoma (HCC) is reported in about 10% due to its hypervascularity and decreased coagulation factors due to underlying liver cirrhosis.[4, 5]

However, spontaneous rupture of a metastatic liver tumour is rarely documented in literature when compared to HCC and other liver lesions. [4, 5] Rupture of liver metastasis in a patient with lung cancer is rarer with isolated cases mentioned in the literature. Here we report a case of ruptured liver metastasis from an adenocarcinoma of the lung presenting to our tertiary care hospital in South India in July 2020 with subcapsular collection and massive pleural effusion mimicking a ruptured liver abscess, associated with portal and hepatic venous thrombosis, challenging the clinical diagnosis. To the best of our knowledge, no such case has been reported.

Case Report

A 42-year lady, a homemaker from a village of South India, was brought by ambulance to our emergency department in July 2020 with complaints of dull-aching right upper abdominal pain, breathlessness (modified Medical Research Council, mMRC grade 3), and intermittent high-grade fever for 15 days.[6] The patient had a history of loss of appetite and significant weight loss over 2 months. The patient did not have any history of vomiting or jaundice. The patient had no history of prior hospitalization or surgeries. She had no known medical comorbidities. She gave a history of usage of firewood as fuel for cooking purposes in an ill-ventilated house for past 25 years. She had no history of consumption of tobacco or alcohol. On examination, the patient was afebrile, anemic, anicteric, and breathless with a respiratory rate of 26/min. The patient's blood pressure was 110/70 mm Hg and pulse rate was 110/min. Abdominal examination revealed an 8x6 cm soft, ill-defined, tender mass in the right hypochondrium. On digital rectal examination, no growth or deposits were palpable. On auscultation of bilateral lung fields, reduced breath sounds were heard in both inframammary, infra-axillary and infra-scapular areas, with no added respiratory sounds, possibly suggesting of pleural effusion. Preliminary blood investigations showed hemoglobin of 9.1g/dL and

leukocytosis of 15,510 cells/mm3 with normal renal parameters and electrolytes. Liver function tests showed normal bilirubin and transaminase levels with only mild elevation of alkaline phosphatase- 228 IU/L.

Chest radiograph, ultrasound (USG) abdomen and contrast-enhances computed tomography (CECT) of abdomen and thorax was carried out and the findings are reported in Table 1. The CECT of abdomen and thorax revealed an ill-defined heterogeneously enhancing lesion in the liver with a communicating subcapsular collection and hypo enhancing lesions in the left lobe and heterogeneously enhancing lesion in the left lung. (Figure 1A and 1B) The thrombosis in the portal vein and inferior vena cava (IVC) is depicted in Figure 2A and 2B. The portal vein thrombosis was managed with intravenous heparin as it was an acute thrombosis (<60 days) and thought to be of infective pathology.

Ultrasound-guided aspiration from the subcapsular collection revealed no organism on culture and a fine needle aspiration cytology (FNAC) was carried out from the liver lesion which was non-diagnostic. Pleural fluid aspiration was done twice as a therapeutic procedure and yielded brownish fluid suggestive of sterile necrosis. The aspirate was tested for malignant cytology, but returned negative both times. (Table 1) The effusion was attributed to reactive fluid collection secondary to the large liver lesion, as is well documented in large liver lesions of malignant as well as infective pathologies. With CECT revealing heterogenous ill-defined lesion in the lower lobe of the left lung, an USG guided core needle biopsy from the lung and liver lesion was carried out which revealed features of adenocarcinoma of the lung with hepatic metastasis. (Figure- 3A, 3B & 3C) The findings of core needle biopsies has been documented in detail in Table 1. The patient was managed conservatively with intravenous empirical antibiotics in view of persistent febrile spikes and leukocytosis. She was transferred to intensive care unit (ICU) for intensive monitoring and management in view of respiratory distress and desaturation. An intercostal drainage (ICD) tube was placed in view of the deterioration of tachypnea, as a palliative procedure for the massive pleural effusion which rapidly reaccumulated despite multiple therapeutic aspirations. The biopsy samples of the lung and liver were sent for assessing EGFR status and EGFR mutation was found. The patient was started on oral tyrosine kinase inhibitor Gefitinib. However, the patient's tachypnea continued to worsen and despite best efforts, there was no response to the treatment and the patient succumbed to the disease. The cause of death was reported as severe respiratory failure and acidosis due to intractable pleural

effusion and septicemia secondary to disseminated lung adenocarcinoma with a ruptured liver metastatic lesion.

Appropriate consent has been obtained from the patient and the attenders for inclusion of the case details in the report and publication of the same.

Discussion

We report a case of carcinoma of the lung with ruptured liver metastasis which led to a diagnostic dilemma due to a dubious presentation mimicking a liver abscess. Although carcinoma of the lung is frequently accompanied by liver metastasis, the incidence of rupture is scarce.[7] The mechanism of spontaneous rupture of hepatic metastasis is not clear but there are several factors reported in the literature such as tumour necrosis, vascularity, location (subcapsular) and impaired coagulation.[7, 8] In the present case, the probable cause of rupture may be the subcapsular location and necrotic hepatic metastasis which may be due to the presence of portal vein thrombosis.

The commonly observed symptoms in patients with ruptured liver metastasis are non-specific abdominal pain, discomfort followed by hemodynamic instabilities, fever in case of infected collection or as a part of the systemic inflammatory response (SIRS), acute liver failure and multi-organ dysfunction syndrome (MODS).[8] In the present case, the patient presented with fever, non-specific abdominal pain, SIRS (heart rate >90beats/min and respiratory rate >20/min) and a soft and tender mass in the right hypochondrium.

Abdominal USG is the initial investigation carried out followed by CECT which is ideal in differentiating HCC, liver metastasis and liver abscess. But it has its limitation in hypervascular metastasis. Peripheral location, discontinuity of the hepatic surface with surrounding hemoperitoneum are the characteristics CT findings in a ruptured HCC which can be extrapolated to liver metastasis as well.[4] Similarly, in the present case CT revealed multiple liver lesions with subcapsular collection from primary in the lung. The left lower lobe pulmonary lesion visualised on CT was not characteristic of lung carcinoma but was later proven by pathological examination to be the primary. The patient gave history of firewood usage for cooking purposes. Indoor air pollution with medium particulate matter especially due to usage of biomass fuel has been noted to be an independent risk factor for lung adenocarcinoma in non-smokers.[9, 10]

Portal vein thrombosis is infrequently associated with hepatocellular carcinoma and can be due to tumour extension or due to benign thrombosis in cirrhosis or prothrombotic states. It causes liver hypo vascularity and may induce necrosis in the tumour. Piscaglia et al have reported that portal vein thrombosis in a patient with known hepatic malignancy should be appropriately investigated for benign versus malignant cause for thrombosis.[11] Patients with benign thrombus can be considered for hepatic transplant whereas malignant thrombosis is a contraindication. Hepatic venous thrombosis leading to Budd-Chiari syndrome is most commonly caused by hypercoagulable states and can lead to acute hepatic necrosis and failure. It is very rarely seen due to neoplasms of the liver and can impart poor prognosis for the patient. In our case, a metastatic liver lesion had concomitant portal venous and hepatic venous thrombosis which is an extremely rare occurrence and may have contributed to the significant areas of necrosis and possibly the rupture.[12, 13]

Diagnosis of non-small cell lung carcinoma is based on histopathology with immunohistochemical markers such as TTF1, AE1/AE3, CK7, beta catenin and Napsin A Treatment of spontaneous rupture of hepatic metastasis depends on the tumour as well as the patient factors such as the tumour size, location, severity of bleeding, active bleeding and hemodynamic stability of the patient.[3, 14] There are various treatment modalities available for ruptured liver metastasis ranging from conservative to surgical resection. A staged approach is advocated in recent studies where the active bleeding is managed by less invasive Trans-arterial angioembolization (TAE), hepatic wedge resection, lobectomy, or suture ligation of the bleeder followed by hepatic resection.[14] Conservative management of ruptured liver metastasis focuses on correcting coagulopathy, close-monitoring and stabilization of the patient followed by imaging to confirm haemostasis. There are conflicting studies regarding the conservative management in the literature. A retrospective study from Taiwan reported a higher survival rate at 30 days in patients undergoing immediate hepatectomy or a two-staged procedure (TAE followed by hepatectomy) in comparison to conservative management.[15] On the contrary, a retrospective study on patients with ruptured HCC and a case report on ruptured liver metastasis in a pancreatic adenocarcinoma were managed successfully with conservative management.[14, 16] Similarly, in the present case, the patient was managed conservatively but had a poor outcome.

Although several treatment options are available in the management of ruptured liver metastasis, the prognosis seems to be poorer in these cases. Ruptured liver metastasis is detrimental in a patient with lung cancer, therefore, early diagnosis with a risk assessment for rupture, close monitoring for high-risk candidates with a selective intervention based on tumour biology and patient factors are the key components in the management of these cases. Appropriate consent has been obtained from the patient's attenders for inclusion of the case details in the report and publication of the same.

Conclusion

Spontaneous rupture of the liver metastasis is rare; even rarer is a ruptured liver metastasis in a case of adenocarcinoma of the lung. Close monitoring by risk assessment, especially in subcapsular liver secondaries is warranted for early diagnosis and prompt management in case of rupture. More studies are required to find a suitable treatment in such cases. Physician has to decide between a two-staged approach or conservative management based on the patient's hemodynamic stability, tumour characteristics and availability of resources. This report emphasizes the importance of the knowledge of rare possible complications of the common condition in order to avoid a diagnostic dilemma.

Author Contributions

VK contributed in the concept of the work, supervision and critical review. **SM** contributed in the data collection & processing, literature review and manuscript writing. **BG** contributed in data collection & processing, analysis & interpretation, literature review and manuscript writing. **SS** contributed in the supervision & critical review as well as data analysis and interpretation. **AA** contributed in the supervision & critical review as well as data analysis and interpretation. **RNG** contributed in the supervision & critical review, data collection & processing as well as data analysis and interpretation. **KSJ** contributed in data collection, processing, analysis & interpretation, literature review and manuscript writing.

References

1. Riihimäki M, Hemminki A, Fallah M, Thomsen H, Sundquist K, Sundquist J, et al. Metastatic sites and survival in lung cancer. *Lung Cancer.* 2014;86:78–84. https://doi.org/10.1016/j.lungcan.2014.07.020.

2. Morgensztern D, Ng SH, Gao F, Govindan R. Trends in Stage Distribution for Patients with Non-small Cell Lung Cancer: A National Cancer Database Survey. *J Thorac Oncol.* 2010;5:29–33. https://doi.org/10.1097/JTO.0b013e3181c5920c.

3. Gulati A, Vyas S, Lal A, Harsha S, Gupta V, Nijhawan R, et al. Spontaneous rupture of hepatic metastasis from choriocarcinoma: a review of imaging and management. *Ann Hepatol*. 2009;8:384-7.

4. Choi BG, Park SH, Byun JY, Jung SE, Choi KH, Han J-Y. The findings of ruptured hepatocellular carcinoma on helical CT. *Br J Radiol*. 2001;74:142–6. https://doi.org/10.1259/bjr.74.878.740142.

5. Chen Z-Y. Etiology and management of hemmorrhage in spontaneous liver rupture: a report of 70 cases. *World J Gastroenterol*. 2002;8:1063. https://doi.org/10.3748/wjg.v8.i6.1063.

6. Rajala K, Lehto JT, Sutinen E, Kautiainen H, Myllärniemi M, Saarto T. mMRC dyspnoea scale indicates impaired quality of life and increased pain in patients with idiopathic pulmonary fibrosis. *ERJ Open Res.* 2017;3:00084. https://doi.org/10.1183/23120541.00084-2017

7. Mochimaru T, Minematsu N, Ohsawa K, Tomomatsu K, Miura H, Betsuyaku T, et al. Hemoperitoneum secondary to rupture of a hepatic metastasis from small cell lung cancer during chemotherapy: a case with a literature review. *Intern Med*. 2017;56:695-9. https://doi.org/10.2169/internalmedicine.56.6828

8. Goto Y, Tobino K, Yoshimine K, Sueyasu T, Okahisa M, Sakabe M, et al. An autopsy case of ruptured liver metastases from small cell lung cancer: A case report and literature review. *Respir Med Case Rep*. 2020;30:101039. https://doi.org/10.1016/j.rmcr.2020.101039

9. Mu L, Liu L, Niu R, Zhao B, Shi J, Li Y, et al. Indoor air pollution and risk of lung cancer among Chinese female non-smokers. *Cancer Causes & Control*. 2013;24:439-50. https://doi.org/ 10.1007/s10552-012-0130-8.

10. Behera D, Balamugesh T. Indoor air pollution as a risk factor for lung cancer in women. *J Assoc Physicians India.* 2005;53:190-2.

11. Piscaglia F, Gianstefani A, Ravaioli M, Golfieri R, Cappelli A, Giampalma E, et al. Criteria for diagnosing benign portal vein thrombosis in the assessment of patients with cirrhosis and hepatocellular carcinoma for liver transplantation. *Liver transplantation.* 201;16:658-67. https://doi.org/ 10.1002/lt.22044.

12. Goto Y, Uchino Y, Sasaki S, Shirahama N, Nomura Y, Akiba J, et al. Complete spontaneous necrosis of hepatocellular carcinoma accompanied by portal vein tumor

thrombosis: A case report. *Int J Surg Case Rep*. 2018;1;44:220-5. https://doi.org/ 10.1016/j.ijscr.2018.02.045. Epub 2018 Mar 7.

13. Sabol TP, Molina M, Wu GY. Thrombotic venous diseases of the liver. *J Clin Transl Hepatol*. 2015;28;3:189. https://doi.org/ 10.14218/JCTH.2015.00014

14. Rahul A, Robin F, Adarsh H. Spontaneous rupture of hepatic metastasis from pancreatic adenocarcinoma. *Case Rep Oncol Med*. 2016;2016:6968534. https://doi.org/10.1155/2016/6968534

15. Hsueh KC, Fan HL, Chen TW, Chan DC, Yu JC, Tsou SS, et al. Management of spontaneously ruptured hepatocellular carcinoma and hemoperitoneum manifested as acute abdomen in the emergency room. *World J Surg*. 2012;36:2670-6. https://doi.org/10.1007/s00268-012-1734-6.

16. Leung KL, Lau WY, Lai PB, Yiu RY, Meng WC, Leow CK. Spontaneous rupture of hepatocellular carcinoma: conservative management and selective intervention. *Arch Surg*. 1999;134:1103-7. https://doi.org/10.1001/archsurg.134.10.1103

Table 1: Description of the radiological and histological characteristics

Radiological and histological Investigations	**Findings**
Chest radiograph	Bilateral moderate pleural effusion (right more than left).
Ultrasound abdomen	An ill-defined heterogenous predominantly hypoechoic collection in the right lobe of the liver with no internal vascularity and a large subcapsular collection around segments 7 and 8, possibly suggestive of a ruptured pyogenic abscess or hepatocellular carcinoma. Portal vein showed an echogenic filling defect in the main branch extending into the proximal right and left branches suggestive of portal venous thrombosis.
Contrast enhanced computed tomography abdomen and thorax	An 8.5 x 7.5 x 6.5cm ill-defined heterogeneously enhancing lesion with fluid attenuating areas and hypo enhancing areas in segments 7 and 8 of the liver with hyperdense contents within. This lesion was communicating with a subcapsular collection with a thickness of 2.7 cm, overlying the segments 6 and 7, suggesting a subcapsular rupture. Multiple, clustered, ill-defined and a few discrete heterogeneously hypo-enhancing lesions were noted surrounding the above lesion and two similar hypo enhancing lesions were noted in the left lobe of the liver, around 2 x 2cm. No significant washout of contrast was noted on venous or delayed phases. Portal and hepatic venous thrombosis was noted, but there was no evidence of direct extension of the lesion into the veins, suggesting a benign thrombosis. Right massive pleural effusion with collapse of right middle and lower lobes was noted, but there was no direct extension of tumor into the pleural cavity; left moderate pleural effusion was also noted. A clustered heterogeneously

	hypo- enhancing lesion with lobulated margin measuring 3.6 x 5 x 3cm was noted in the anterior and lateral basal segments of lower lobe of the left lung, which was possibly infective and was suggested for biopsy correlation. A suspicion of infective or malignant pathology was considered.
Core-needle biopsy from the lung lesion	Features of adenocarcinoma of the lung with focal areas of bronchoalveolar pattern of spread and occasional foci of necrosis with tumor cells staining positive for epidermal growth factor receptor (EGFR).
Core-needle biopsy from the liver lesion	A malignant, possibly metastatic tumor focally infiltrating the hepatic parenchyma displaying abundant cytoplasm, pleomorphic nuclei and brisk mitotic activity. Immunohistochemistry showed positive cytokeratin (CK)-7 and thyroid transcription factor (TTF)-1 suggesting the lesion to be metastases from a primary in the lung. CK-20, estrogen receptor and glypican 3 were found to be negative.
Cytology from the pleural fluid	Negative for malignancy.

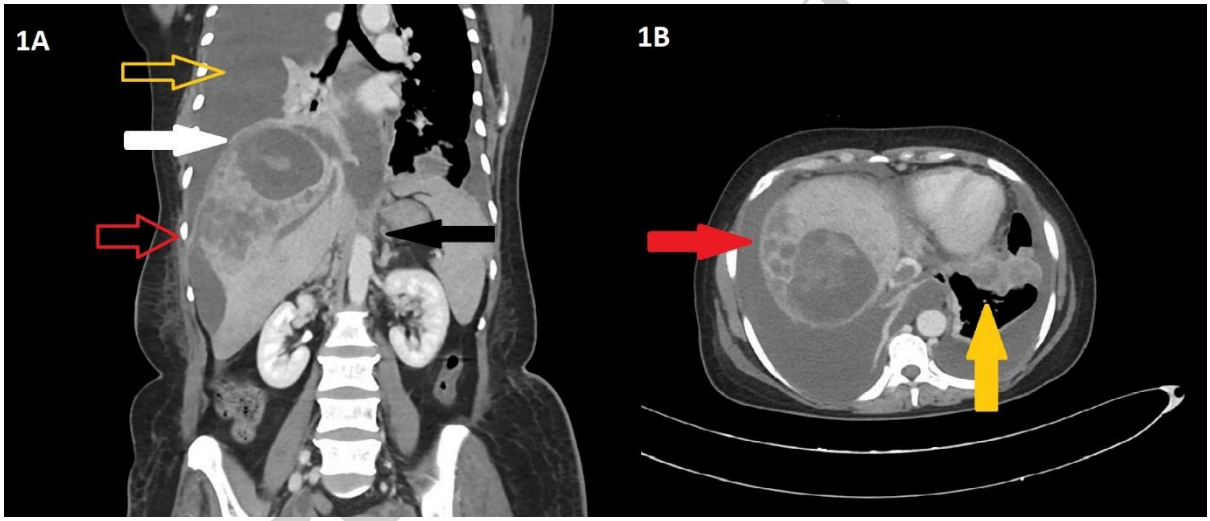

Figure 1: Contrast enhanced computed tomography (CECT) of the abdomen and the thorax **1A-** Coronal section of CECT abdomen and thorax shows heterogenous hypodense lesion in the right lobe of liver (white solid arrows), possible site of subcapsular rupture (red arrow), massive pleural effusion (yellow arrow), inferior vena cava (IVC) compression with hepatic vein thrombosis (black solid arrow). **1B-** Axial section of CECT abdomen and thorax shows left lower lobe lung heterogenous ill-defined lesion (yellow solid arrow) and heterogenous hypodense lesion in right lobe of liver with multiple satellite lesions (red solid arrow).

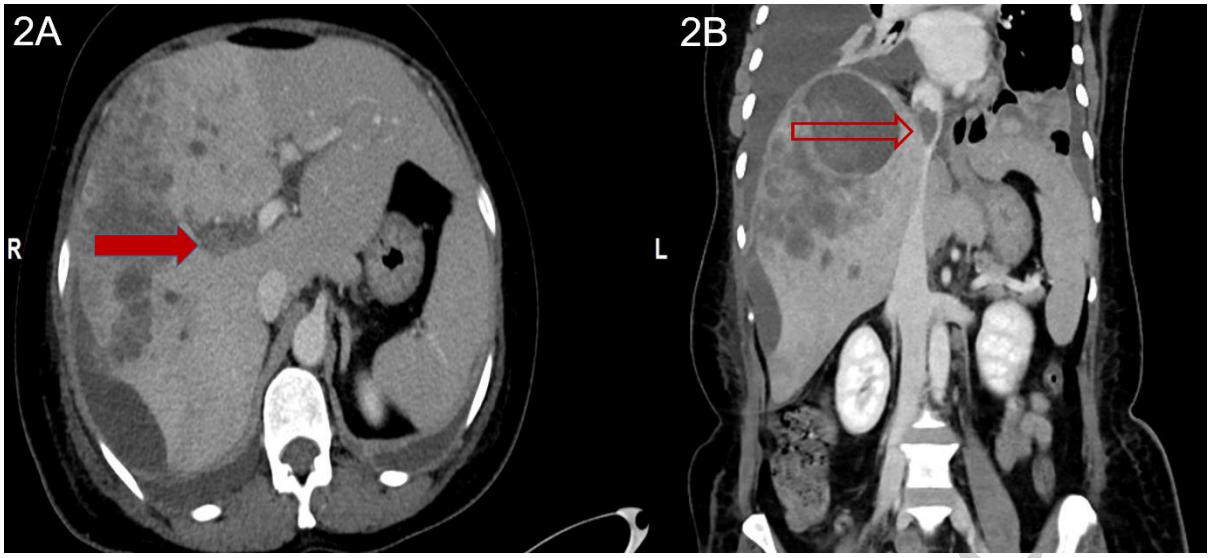

Figure 2: Contrast enhanced computed tomography (CECT) of the abdomen and the thorax. **2A**- Axial section of portal Phase CECT of the abdomen and pelvis shows hypodense filling defect in the right branch of the portal vein (solid arrow). Normally enhancing left branch of the portal vein is seen. **2B**- Coronal reformation of the venous phase of CECT abdomen and pelvis reveals a hypodense filling defect in the supra-hepatic segment of the inferior vena cava (IVC) suggestive of thrombus (arrow).

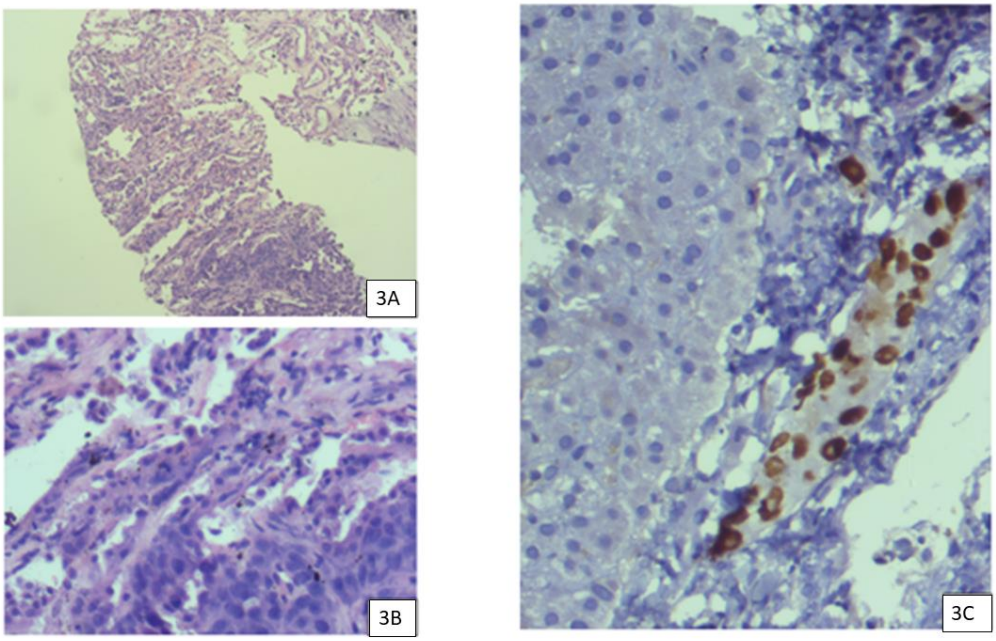

Figure 3: Histopathology of lung and liver lesion. **3A** – Hematoxylin and eosin stain (H&E) at x40 magnification. Section shows a core of lung parenchyma with tumor cells in the lower part of the core arising from the alveolar wall forming a bronchioloalveolar pattern and infiltrating the lung parenchyma. **3B** – H&E stain at x200 magnification showing lung parenchyma infiltrated by tumor cells arising in glandular pattern exhibiting moderate nuclear

atypia and pleomorphism. **3C** – Diaminobenzidine with hematoxylin counterstain at x400 magnification showing liver parenchyma infiltrated by metastatic deposits of adenocarcinoma from lung, highlighted by TTF-1 (thyroid transcription factor – 1), Immunohistochemistry with DAKO monoclonal antibody, USA.