

## CASE REPORT

## A Case of Miliary Adenocarcinoma of Lung Masquerading as Miliary Tuberculosis

NIK AZLAN NM

*Department of Emergency Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia*

### ABSTRAK

*Adenokarsinoma paru-paru miliari adalah sangat jarang dan agresif. Adenokarsinoma paru-paru biasanya menunjukkan sifat ketulan pada peparu yang berkaitan dengan kerosakan paru-paru dan efusi pleura. Adenokarsinoma ini jarang jarang berpunca daripada tapak selain daripada tapak primer, tidak seperti kanser-kanser lain contohnya kanser tiroid, koriokarsinoma dan sarcoma. Kami membentangkan di sini kes seorang suri rumah berusia 50 tahun yang mengadu batuk-batuk, hilang selera makan dan sukar untuk bernafas selama 1 bulan. Perawat perubatan primer telah merawat beliau sebagai jangkitan kuman pada paru-paru. Disebabkan keadaan yang tidak pulih dan semakin melarat, beliau dibawa ke Jabatan Kecemasan. Oksigen beliau dikesan sebanyak 93% atas udara bilik. Berdasarkan sejarah pesakit dan penemuan X-ray paru-paru, rawatan untuk tuberculosis miliari telah di beri walaupun ujian Mantoux dan kahak negatif. Berikutan peningkatan tanda-tanda dan intubasi, bronkoskopi kemudian mendedahkan diagnosis adenokarsinoma paru-paru. Sebagai pelajaran, penampilan miliari radiografi tidak dikelirukan kepada tuberculosis sahaja, kerana sebab-sebab berbahaya yang lain perlu disiasat. Bronkoskop dengan analisis histopatologi diperlukan, terutamanya jika Mantoux dan sputum adalah negatif.*

*Katakunci: adenokarsinoma, bronkoskopi, tuberculosis miliari*

### ABSTRACT

Miliary lung adenocarcinoma is a highly deceptive and insidious form of cancer. It commonly presents as a mass lesion accompanied with a collapsed lung and significant pleural effusion. Adenocarcinoma presenting in this manner rarely originates from other primary sites such as thyroid, choriocarcinoma, and sarcomas.

**Address for correspondence and reprint requests:** Nik Azlan Nik Muhamad. Department of Emergency Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +603-9145 5555 Email: nizat78@yahoo.com

This was a case of a 50-year-old housewife, who presented with increasing severity of shortness of breath, cough and loss of appetite for the past one month. Primary care physician treated her as community-acquired pneumonia, which did not improve. She then arrived at the Emergency Department with pulse oximetry to be 93% on room air. She was slightly tachycardic. Bilateral widespread miliary patches were seen on chest radiograph. Based on the history and chest X-ray, she was initially treated for miliary tuberculosis, despite negative Mantoux and negative sputum. Following worsening of symptoms, she was intubated and admitted to the intensive care unit. Bronchoscopy revealed the diagnosis of primary miliary lung adenocarcinoma. As a lesson, the radiographic miliary appearance is not confounded to tuberculosis alone, as other insidious causes should be investigated. A bronchoscope with histopathology analysis is warranted for miliary picture, especially if the Mantoux and sputum turn out to be negative.

Keywords: adenocarcinoma, bronchoscopy, miliary tuberculosis

---

## INTRODUCTION

Pulmonary carcinoma is the most common cancer among cancer-related death worldwide (Chen et al. 2016). Misdiagnosis leads to delay in proper treatment. Radiology is the main tool used for diagnosis, nevertheless pulmonary infections such as miliary tuberculosis can present as a miliary metastasis of the lung. Several lung infections such as bacteria, mycobacteria, fungi and viruses can be a cause (Zhao et al. 2017).

Miliary lung metastasis is rare and often misdiagnosed as miliary tuberculosis due to similar presenting complaint and radiological features. Diagnosis is difficult, especially in regions where tuberculosis is common. Prevalence of tuberculosis in Malaysia was 29,000 (25,000-33,000) in the year 2018, with the rate of 92 (79-106) per 100,000 of the population (WHO 2019) and this can be a factor leading

to misdiagnosis.

This was a case report of a patient who presented with signs and symptoms of pulmonary tuberculosis. Chest X-ray was similar to miliary tuberculosis. Only after a delayed bronchoscope, histopathology revealed primary miliary adenocarcinoma. Pre-treatment baseline of epidermal growth factor receptor (EGFR) mutation was established and targeted chemotherapy was initiated. It was reported previously that this radiological presentation of adenocarcinoma (miliary pattern) was detected early and a pretreatment (baseline) activating EGFR mutation via bronchoalveolar lavage had a better outcome with early chemotherapy and improved oxygen saturation (Schaller et al. 2014). A lesson that can be learnt is that miliary nodules can be the manifestation of multiple diseases other than pulmonary tuberculosis. Treating physicians should have a broad differential diagnosis once

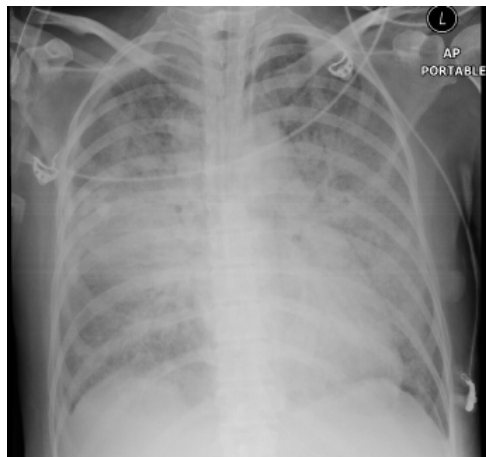


Figure 1: Bilateral reticulonodular opacities at plain chest x-ray. Middle zones are prominently opacified. A typical findings of miliary picture.

these lesions are encountered in conventional radiographs (Bueno et al. 2017).

### CASE REPORT

A 50-year non-smoker housewife complained of shortness of breath which increased in severity over the past one month. This was associated with cough, whitish sputum and loss of appetite. There was also a loss of weight of 7 kg for the past 1 month. Prior to Emergency Department (ED) referral, she was attended by a private general practitioner and was prescribed two courses of antibiotics which was ciprofloxacin. The clinic then referred her to a periphery hospital, where she was then prescribed another course of antibiotics which was amoxicillin/clavunalic acid and azithromycin. The arrays of antibiotics did not improve her condition. She was also investigated for pulmonary tuberculosis, where sputum culture was taken. A relative

recommended a tertiary hospital where she then attended.

Upon arrival at the tertiary hospital, her initial pulse oximetry was 93% on room air. She was slightly tachycardic (pulse rate 103/minute), afebrile and respiratory rate was at the upper limit of normal (20/minute). There were minimal right lower zone crepitations and the liver was palpable. She had no significant past medical or social history. She was known to be taking vitamin and mineral supplements. She had no contact with any foreign worker and did not travel recently.

Sputum culture from the periphery hospital yielded *Klebsiella pneumoniae*. However, an acid-fast bacillus (AFB) for tuberculosis (TB) was negative. Chest X-ray revealed bilateral homogenous reticulonodular opacity (Figure 1). White cell count (WCC) was  $13.2 \times 10^9/L$  and C-reactive protein (CRP) was not elevated (0.32). Other tests such as Human Immunodeficiency Virus (HIV), Venereal Disease Research Labarotary (VDRL) screening and hepatitis were unremarkable. Following the initial presentation, she was admitted in an isolation ward and treated as partially treated pneumonia and miliary tuberculosis. Mantoux test was done in the ward and it was non-reactive. She was discharged with anti-tubercular drugs (ethambutol hydrochloride, isoniazid, pyrazinamide and rifampicin). She was re-admitted two weeks later with worsening dyspnoea. After failed trial of non-invasive ventilation she was intubated and was admitted to the intensive care unit (ICU). Tracheal aspirate for AFB, Polymerase Chain

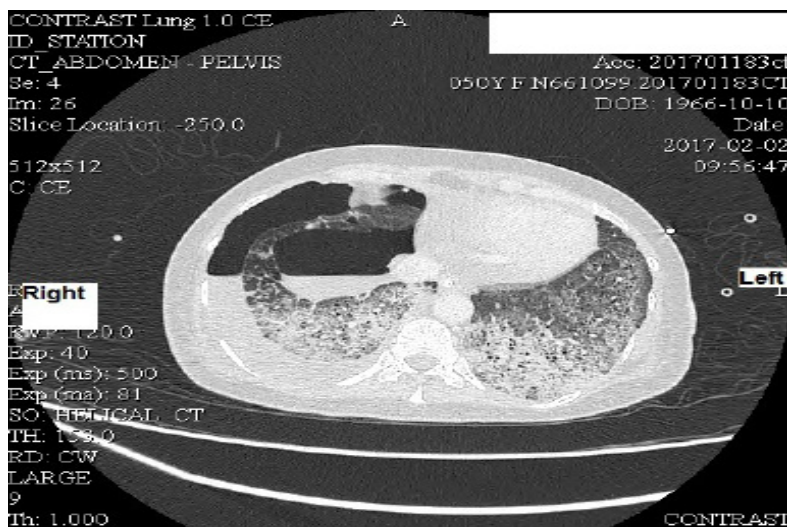


Figure 2: A slice of CT thorax reveals bilateral reticulonodular opacities with right lung collapse and pleural effusion

Reaction (PCR) TB was negative. She was treated with antibiotics and anti-tuberculosis medication throughout her stay in the ICU. Computed tomography (CT) thorax revealed right lung collapse with pleural effusion and scattered multinodular hyperdensity at bilateral lungs (Figure 2). Due to no improvement in oxygenation and radiographic features, bronchoscopy was done and lung tissue showed adenocarcinoma. Pretreatment baseline of EGFR mutation was detected from the bronchoscopy. The staging was subsequently done with contrasted CT to reveal liver metastasis. She was started on oral chemotherapy which was tyrosine kinase inhibitor targeting specifically EGFR mutation of the tyrosine kinase at the cancer cells. This was the first case in Malaysia that on oral EGFR was administered via nasogastric (ryles) tube on an intubated patient. Elective tracheostomy was performed for prolonged intubation

after two months of ICU admission. She passed away shortly after the procedure.

## DISCUSSION

Treatment for pneumonia and miliary TB was started based on mixed evidence. The points supporting miliary TB were bilateral homogenous opacity on chest X-ray, prolonged cough and loss of weight. However, infective markers were not initially elevated, sputum culture for AFB and Mantoux test were negative. White cell was only  $13 \times 10^9/L$  at that time and could suggest infection. A similar case was reported in India, where bilateral miliary patches were seen on the radiograph of a 62-year-old housewife. It was similar to this case where she was initially misdiagnosed and treated for miliary tuberculosis, where later it turned out to be miliary adenocarcinoma (Prajapat et al. 2015).

A case reported by Liu et al. 2019 highlighted a 34-year-old lady with miliary metastasis, diagnosed with an incidental finding from pain at the region of left thigh. She refused treatment and passed away one year later. A case reported by Schaller et al. had the same presentation, in which a 47-year-old male had a history of weight loss from 97 to 92 kg within one month, cough and fatigue. His chest X-ray showed similar bilateral multiple micronodules described as miliary. The patient had no fever, and his oxygen saturation was 90% (rest time without oxygen), improving to 94% under oxygen therapy. CT and bronchoscopy for histopathology and immunology for EGFR mutation was done early, followed by treatment with Erlotinib, cisplatin-pemetrexed and bevacizumab. The patient improved subsequently.

Adenocarcinoma was also suspected to result in immunodeficiency which led to the subsequent arrays of infection. In this patient, immunodeficiency was evident with a low WCC and a non-reactive Mantoux test, with regard to a widespread mottling of the chest X-ray. According to a cohort study in Taiwan, the incidence rate of lung cancer (269 of 100,000 person-years) was significantly higher in patients with pulmonary TB (Wu et al. 2011). In population that is latently infected with TB, occult lung cancer can occur due to TB induced immunodeficiency. (Feld et al. 1976).

In terms of management, there is no effective treatment for this carcinoma once metastasis has occurred. In Louyang, China, a 48-year-old

man with miliary adenocarcinoma which metastasised to the bones and brain, underwent two cycles of chemotherapy. The chemotherapy was paclitaxel and followed by two cycles of pemetrexed, cisplatin and Endostar (human recombinant endostatin). However, this was ineffective. The patient was then treated with icotinib (Guangsheng et al. 2016).

## CONCLUSION

Lung carcinoma should be suspected in all tuberculosis patients with no infective evidence, negative sputum and negative Mantoux. Early bronchoscope should be done in cases of radiological evident miliary tuberculosis without sputum, haematological or Mantoux positive results. CT of the possible primary or secondary source should be done early which could reinforce the diagnoses of carcinoma. This could avoid future delays in initiating chemotherapy.

## REFERENCES

- Bueno, J., Chung, J., Hobbs, S. 2017 Thoracic Radiology Section Editors: Miliary Nodules: Not Always Tuberculosis. *Annals ATS* 14(12): 1858
- Chen, W., Zheng R., Baade P.D., Zhang, S., Zeng, H., Bray, F., Jemal, A., Yu X.Q., He, J. 2016. Cancer statistics in China, 2015. *CA Cancer J Clin* 66(2): 115-32.
- Feld, R., Bodey, G.P., Groschel, D. 1976. Mycobacteriosis in patients with malignant disease. *Arch Intern Med* 136(1): 67-70.
- Guangsheng, P., Weijiao, Y., Gang, L., Xiaoli, W., Lingxia, L., Yimin, M. 2016. Miliary lung adenocarcinoma: a case report. *Int J Clin Exp Pathol* 9(2): 2563-6.
- Liu, S.Z., Zhou, X., Song, A., Wang, Y.P., Liu, Y., 2019. Miliary metastases in lung cancer. *QJM*. pii: hcz156. doi: 10.1093/qjmed/hcz156. [Epub ahead of print] [1<sup>st</sup> November 2019]
- Prajapat, D.K., Khanna, A., Tawar, D. 2015.

- Adenocarcinoma of the lung masquerading as miliary mottling: A rare presentation. *Egypt J Intern Med* 27(3): 118-20.
- Schaller, A., Beau-Faller, M., Mennecier, B., Renaud-Picard, B., Weingertner, N., Massard, G., Quoix, E. 2014. Lung adenocarcinoma with pulmonary miliary metastases and complex somatic heterozygous EGFR Mutation. *Case Rep Oncol* 7(3): 769-73
- Wu, C.Y., Hu, H.Y., Pu, C.Y., Huang, N., Shen, H.C., Li, C.P., Chou, Y.J. 2011. Pulmonary tuberculosis increases the risk of lung cancer. A population-based cohort study. *Cancer* 117(3): 618-24
- WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries. 2018 [WHO website] Generated: 2019-11-18. <https://www.who.int/tb/data/en/> [1<sup>st</sup> October 2019]
- Zhao, W., Tian, Y., Peng, F., Long, J., Liu, L., Huang, M., Lu, Y. 2017 Differential diagnosis of acute miliary pulmonary tuberculosis from widespread-metastatic cancer for postoperative lung cancer patients: two cases. *J Thorac Dis.* 9(2): E115-E120.

Received: 7 Sept 2018

Accepted: 5 Dec 2019