

# A Case Report of Wild Type Adenocarcinoma

Anak Agung Bagus Bramardipa<sup>1\*</sup>, Anak Agung Gde Upeksha<sup>2</sup>

<sup>1</sup>Internship Doctor at Pulmonology and Respiratory Medicine Departement, Bali Mandara Hospital, Denpasar, Bali, Indonesia  
bramardipa[at]gmail.com

<sup>2</sup>Pulmonologist at Pulmonology and Respiratory Medicine Departement, Bali Mandara Hospital, Denpasar, Bali, Indonesia  
upekshagde[at]gmail.com

**Abstract:** ***Background:** Lung cancer is placed in the first place as the most cause of cancer death in men and third in women in Indonesia, and are highly linked with smoking habit. Adenocarcinoma is the most common non-small cell carcinoma and divided into adenocarcinomas with mutations and adenocarcinomas without mutations which lead to different treatment option. **Case:** A male patient in his 60s was come with chief complaint pain sensation in his right chest wall along with breath difficulty. A solid mass was found from CT-Scan. He then undergo trans-thoracic needle aspiration biopsy and the result was suggesting to non-small cell lung carcinoma, gene mutation test using Next-generation sequencing (NGS) then done with no mutation were found from the sample. **Conclusion:** Multiple genes alteration can be detected at once by using NGS, this test helps in a condition where minimal tissue sample were obtained. Chemotherapy is therapeutic choice in wild-type adenocarcinoma.*

**Keyword:** Cancer, Non-Small Cell Lung Cancer, Wild Type Adenocarcinoma

## 1. Introduction

Lung cancer globally has been the most cause of cancer burden and death. In 2018, lung cancer contribute up to 12% of total cancer cases, around 2.1 million new cases<sup>1</sup> and estimated for 1.76 millions death or 18.4% of cancer death<sup>2</sup>. In Indonesia, lung cancer placed first as the most cause of cancer death in men and third in women.<sup>3</sup> Environmental and life style especially smoking have been associated with the lung cancer incidence estimated around 85-90% of lung cancer, other factors include genetics, chronic lung disease, and exposure to hazard such as radon.<sup>4,5</sup> Lung cancer is categorized into two major groups: non-small cell lung carcinoma (NSCLC) which account for 85% of total lung cancer cases, and small cell lung cancer (SCLC) that contribute to 15% cases. Non-small cell lung carcinoma are divided into adenocarcinoma (35-40%), squamous cell carcinoma or SqCC (25-30%) and large cell carcinoma (10-15%)<sup>6</sup>.

Adenocarcinoma is the most common non-small cell carcinoma, this carcinoma grows from alveolar cells from the small airway epithelium and located mostly in peripheral.<sup>4,7</sup> Based on genetic drive, adenocarcinoma can be divided into Adenocarcinoma with mutations and adenocarcinomas without mutations or wild type this mutation will lead to different therapy.<sup>3</sup> Cough, dyspnea and chest pain are common symptoms of lung cancer, usually present in late stage, other symptoms may related to location of metastasis or tumor location.<sup>4</sup>

In managing patient with lung cancer, multidisciplinary approach are essential, locating tumor position and spread using imaging modalities are needed to determined staging and choose what procedure will be used to obtain a tissue samples, transthoracic needle aspiration biopsy with CT guiding usually used if the tumor is located in the peripheral. Histopathological examination and molecular testing are essential to establish the diagnosis and choosing the treatment.<sup>4,8,9</sup>

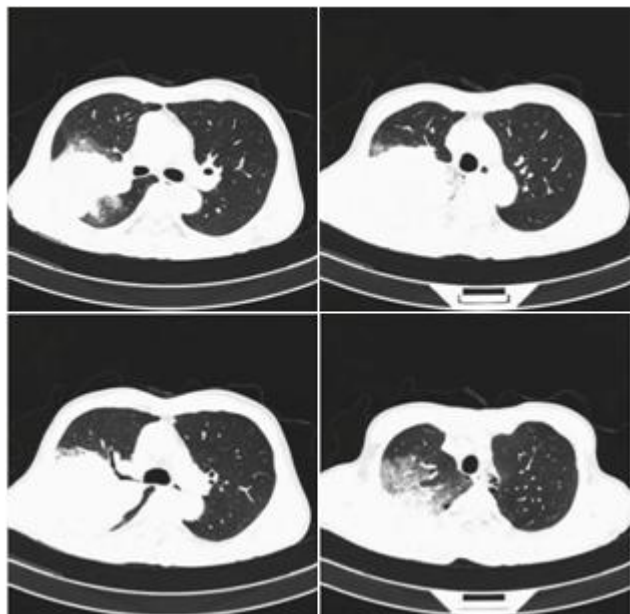
Epidermal Growth Factor Receptor (EGFR) gene mutation status had an essential prognostic in Adenocarcinoma patient as patient with EGFR mutation are sensitiv to targeted therapies and longer their progression free survival compared to thus in patient without EGFR mutation.<sup>10</sup> This report will discuss about patient with adenocarcinoma without EGFR mutation.

## 2. Case Report

A male patient in his 60s was come after referred from secondary-care hospital with chief complaint pain sensation in his right chest wall along with breath difficulty, this complain was started since three months before he came. He also complained a general weakness with decreased body weight and appetite. From history taking, there was no similar symptoms on family, patient denied any past history of diseases, he was a smoker since 40 years ago. Patient still able to do daily activities but limited because of the pain (performance score: 1). On general examination, patient was compos mentis, respiratory rate was 22 times per minutes, heart rate showed 96 times per minutes, blood pressure was 136/88 mmHg and oxygen saturation on 96% room air, the pain scale was 7/10.

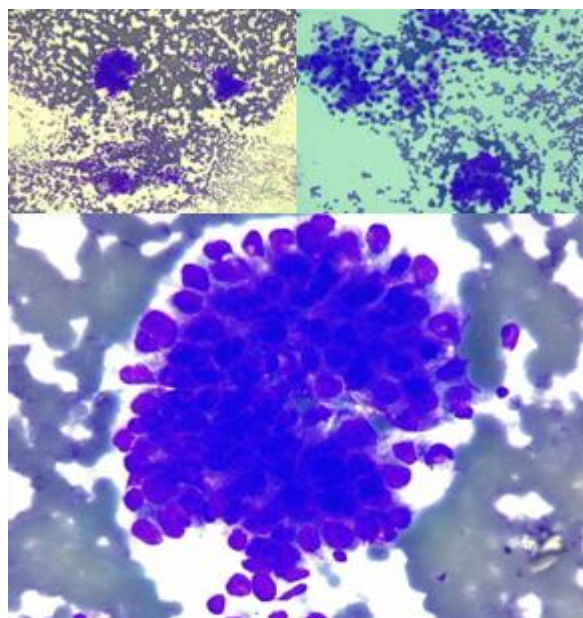
A Thorax CT-scan with contrast were ordered (**Figure 1**) and showed an irregular speculated solid mass with central necrotic 7.8 x 8.4 x 7.4 cm in size on the superior lobe of right lung attached on parietal part of pleura and superior mediastinum surrounded by pneumonitis reaction. There are also multiple lymphadenopathy on the paratrachea and paraaortic 1.2 x 4 cm in size with no lesions in bones and hepar. The staging based on the result suggestive to T4N3M0 (IIIC).

After the size and location of mass were found, trans-thoracic needle aspiration biopsy was prepared to earn sample for histopathological examination in order to establish the diagnosis, the biopsy was done under CT-guiding and the result was suggesting to non-small cell lung carcinoma likely an adenocarcinoma (**Figure 2**).



**Figure 1:** Thorax CT-Scan

Molecular testing then ordered after the adenocarcinoma diagnose were established to find out if there any genes mutation that could differ the treatment planning, Next-Generation Sequencing (NGS) were used to detect any mutation in ALK, KRAS, BRAF, RET, EGFR, ROS1, NRAS, ERBB2, TP53 and the result was No Mutation were detected from the sample.



**Figure 2:** The biopsy sample's smear

While waiting for the molecular testing result, patient received symptomatic medicine including double combination of pain killer. The patient then referred to quaternary-leveled care hospital to received chemotherapy after the molecular result was done.

### 3. Discussion

Most of lung cancer patient are diagnosed in late stage where available therapeutic option is narrow and metastasis process may have been spread so it does have a poor

prognosis.<sup>1,9</sup> Adenocarcinoma is estimated dominating the total cases of lung cancer with 40% of the cases, it originate from alveolar cells from smaller airway lining cell.<sup>4</sup> The treatment of adenocarcinoma is depend on its stage and driver mutations status,<sup>4</sup> the staging was determine using the new eight (8<sup>th</sup>) edition of TNM classification.<sup>9,11</sup> In the cases, a solid mass 7.8 x 8.4 x 7.4 cm sized was found which is classified as T4, there are also multiple lymphadenopathy on the paratrachea and paraaortic 1.2 x 4 cm in size on both lungs and count for N3 with no sign of lytic or blastic in bones and no seen new lesions in liver. Based on 8<sup>th</sup> of TNM staging, this patient is grouped as IIIC.<sup>11</sup>

Adenocarcinoma was divided into adenocarcinoma with mutation and without mutations.<sup>3</sup> Therefore, in handling adenocarcinoma patient, clinically significant biomarker should be tested as it does affect the treatment,<sup>9</sup> this make tissue availability is fundamental in diagnostic process as a lot of biomarker needed to be tested within a minimal sample from biopsy, therefore proper tissue sample handing is critical.<sup>12</sup> Next-Generation Sequencing or NGS is a molecular diagnostic tools which can detect multiple alteration of relevant genes at once and could helped in a condition where minimal tissue were earned.<sup>13</sup> Based on NCCN guidelines, EGFR mutation along with ALK, KRAS, ROS1, BRAF, RET, ERBB2, PD-L1, METex14, NTRK1/2/3 are tested in Adenocarcinoma advanced stage which were tested by using NGS in the case with the result were no mutation were found.

Most common mutation faced in adenocarcinoma is EGFR mutation, this mutation is mostly found in asian female with no smoking history,<sup>6</sup> while wild type adenocarcinoma or adenocarcinoma without EGFR mutation are mostly in men with smoking history<sup>3</sup> just like patient in the case.

EGFR or epidermal growth factor receptor is a protein that plays important role in tumorigenesis as it taking role in cell growth and death. The new modalities that target this gene (EGFR-TKI) shows a great progress of treatment, however, in wild type patient, they are not sensitive to EGFR-TKI.<sup>10</sup> Chemotherapy is therapeutic choice in wild-type patient, platinum based in combination with antimetabolites such as perimetrexed and pembrolizumab are the first line of chemotherapy.<sup>3,4,14</sup> Patient was referred to quaternary-care hospital to seek for chemotherapy.

### 4. Conclusions

The treatment of adenocarcinoma is depend on its stage and driver mutations status, the 8<sup>th</sup> edition of TNM staging were used to determine stage of cancer while molecular testing need to be done to find out mutation status of patient. Chemotherapy is therapeutic choice in wild-type adenocarcinoma, where platinum based combined with perimetrexed and pembrolizumab are the first line of chemotherapy.

### Acknowledgements

None declared.

**Conflict of Interest**

The research was carried out independently without involving the interests of other parties in this research.

**Funding**

The authors received no financial support for the case report, authorship, and/or the publication on this article.

**References**

- [1] Schabath MB, Cote ML. Cancer progress and priorities: Lung cancer. *Cancer Epidemiol Biomarkers Prev* [Internet].2019; 28 (10): 1563–79. Available from: <https://pubmed.ncbi.nlm.nih.gov/31575553/>
- [2] Bade BC, Dela Cruz CS. Lung Cancer 2020: Epidemiology, Etiology, and Prevention. *Clin Chest Med* [Internet].2020; 41 (1): 1–24. Available from: <https://doi.org/10.1016/j.ccm.2019.10.001>
- [3] Agus Setyawan U, Yudhanto HS, Madarina A. One Year Survival of Wild-Type Adenocarcinoma Lung Cancer Patients Receiving Chemotherapy at dr. Saiful Anwar Hospital, Malang. *Respir Sci* [Internet].2022; 2 (3): 148–55. Available from: <https://respiratoryscience.or.id/index.php/journal/article/view/47>
- [4] Duma N, Santana-Davila R, Molina JR. Non-Small Cell Lung Cancer: Epidemiology, Screening, Diagnosis, and Treatment. *Mayo Clin Proc* [Internet].2019; 94 (8): 1623–40. Available from: <https://doi.org/10.1016/j.mayocp.2019.01.013>
- [5] de Groot PM, Wu CC, Carter BW, Munden RF. The epidemiology of lung cancer. *Transl Lung Cancer Res* [Internet].2018; 7 (3): 220–33. Available from: <https://pubmed.ncbi.nlm.nih.gov/30050761/>
- [6] Inamura K. Lung cancer: understanding its molecular pathology and the 2015 WHO classification. *Front Oncol* [Internet].2017; 7 (AUG): 1–7. Available from: <https://www.frontiersin.org/articles/10.3389/fonc.2017.00193/full>
- [7] Travis WD. Lung Cancer Pathology: Current Concepts. *Clin Chest Med* [Internet].2020; 41 (1): 67–85. Available from: <https://doi.org/10.1016/j.ccm.2019.11.001>
- [8] Planchard D, Popat S, Kerr K, Novello S, Smit EF, Faivre-Finn C, et al. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* [Internet].2018; 29 (January): iv192–237. Available from: <https://doi.org/10.1093/annonc/mdy275>
- [9] Padinharayil H, Varghese J, John MC, Rajanikant GK, Wilson CM, Al-Yozbaki M, et al. Non-small cell lung carcinoma (NSCLC): Implications on molecular pathology and advances in early diagnostics and therapeutics. *Genes Dis* [Internet].2022; (xxxx). Available from: <https://doi.org/10.1016/j.gendis.2022.07.023>
- [10] Zheng H, Zhang Y, Zhan Y, Liu S, Lu J, Feng J, et al. Prognostic analysis of patients with mutant and wild-type EGFR gene lung adenocarcinoma. *Cancer Manag Res* [Internet].2019; 11: 6139–50. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6613610/>
- [11] Dettnerbeck FC. The eighth edition TNM stage classification for lung cancer: What does it mean on main street? *J Thorac Cardiovasc Surg* [Internet].2018; 155 (1): 356–9. Available from: <https://doi.org/10.1016/j.jtcvs.2017.08.138>
- [12] Zacharias M, Absenger G, Kashofer K, Wurm R, Lindenmann J, Terbuch A, et al. Reflex testing in non-small cell lung carcinoma using DNA-and RNA-based next-generation sequencing-a single-center experience. *Transl Lung Cancer Res* [Internet].2021; 10 (11): 4221–34. Available from: <https://pubmed.ncbi.nlm.nih.gov/35004252/>
- [13] Drilon A, Wang L, Arcila ME, Balasubramanian S, Greenbowe JR, Ross JS, et al. Broad, hybrid capture-based next-generation sequencing identifies actionable genomic alterations in lung adenocarcinomas otherwise negative for such alterations by other genomic testing approaches. *Clin Cancer Res* [Internet].2015; 21 (16): 3631–9. Available from: <https://pubmed.ncbi.nlm.nih.gov/25567908/>
- [14] Gómez-López A, Revuelta-Salgado F, García-Luján R. Non-small cell lung cancer. *Med*.2022; 13 (67): 3933–41.