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Case Report

Unusual site of skin metastasis from lung adenocarcinoma: A case report

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Abstract

Background: Skin metastasis incidence is approximately 3,4% of lung cancer with highest incidence in man. It arises mostly in man from primary cancer of the lung (24%), colon (19%), melanoma (13%) and oral cavity (12%). In woman, it arises from breast (69%), colon (9%), melanoma (5%), ovaries (4%) and lung (4%) primary cancer. It may occur at the same time or before the primary cancer detected.
Case Illustration: Forty-sixth years old male referred with lesion found in chest x-ray during the medical check-up procedure. Nodules arose at parietal and abdomen region since three months prior. Chest CT scan revealed a solid 6,4 cm mass in long axis at the medial of left lung lobe. Head CT scan revealed subsolid nodule at cutaneous-subcutaneous of the left occipital attached to the periosteum without bone destruction and solid nodule at cortex-subcortex of right frontoparietal accompanied by perifocal edema. Bronchoscopy procedure found edematous mucosa of left B1 to B3 orificium. Histopathology and cytology examination confirmed adenocarcinoma with *wild-type* EGFR mutation.
Discussion: Preference site of lung cancer skin metastasis is at supra-diaphragm region. Nodules are usually firm, painless and appear as oval or round form. Ulceration may be seen. In our case, the lesion were ulcerate with granulation tissue at the edge and black scars form containing necrotic tissue. Adenocarcinoma is the most common type of lung cancer with skin metastases.
Conclusion: It is essential to consider any skin pathological form in patient with lung adenocarcinoma as skin metastases.

***Keywords*:** adenocarcinoma, lung cancer, skin metastasis

Abstrak

Latar belakang: Metastasis kanker paru ke kulit berkisar 3,4% dengan insidens tertinggi pada laki-laki yang umumnya berasal dari keganasan primer paru (24%), kolon (19%), melanoma (13%) dan rongga mulut (12%). Pada perempuan umumnya berasal dari keganasan primer payudara (69%), kolon (9%), melanoma (5%), ovarium (4%) dan paru (4%). Hal ini dapat terjadi pada saat yang sama atau sebelum kanker primer terdeteksi.
Ilustrasi kasus: Seorang laki-laki berusia 46 tahun datang dengan nodul pada foto toraks saat pemeriksaan kesehatan yang diawali kemunculan benjolan pada regio parietal dan abdomen tiga bulan sebelumnya. CT Scan toraks menemukan massa solid dengan ukuran terpanjang 6,4 cm pada lobus medius paru kiri. CT Scan kepala menemukan nodul subsolid pada lapisan kutis-subkutis di regio occipital yang melekat pada periosteum tanpa destruksi tulang dan nodul solid pada lapisan korteks-subkorteks di regio frontoparietal dengan edema perifokal. Pada bronkoskopi didapatkan mukosa edematosa di orifisium lobus atas kiri dengan stenosis kompresi pada sebagian orifisium B1 hingga B3 kiri. Pemeriksaan histopatologi dan sitologi menegakkan adenokarsinoma dengan mutasi EGFR *wild-type*.
Diskusi: Lokasi utama metastasis kulit pada kanker paru adalah regio supradiafragma dengan nodul yang keras, tanpa nyeri dan berbentuk oval atau bulat yang dapat disertai ulkus. Pada kasus ini, ditemukan lesi ulkus dengan jaringan granulasi pada tepi dan skar hitam yang mengandung jaringan nekrotik. Metastasis kulit pada kanker paru paling banyak ditemukan pada adenokarsinoma.
Kesimpulan: Lesi di kulit yang ditemukan pada pasien dengan adenokarsinoma paru harus diwaspadai sebagai metastasis.

Kata kunci: adenokarsinoma, kanker paru, metastasis kulit

Background

Skin metastases incidence is 3,4% of lung cancer with highest incidence in men that arise mostly from primary cancer of the lung (24%), colon (19%), melanoma (13%) and oral cavity (12%). In women, it arise from breast (69%), colon (9%), melanoma (5%), ovaries (4%) and lung (4%). In general, cutaneous metastasis from primary visceral malignancy is vary between 1-12%. It may occur at the same time or before the primary cancer detected. All histological types of lung cancer may develop metastases in the skin. Lung cancer is the fastest in developing skin metastases after initial diagnosis and a sign of poor prognosis, that combined with other extracutaneous metastases may decreases the survival time to approximately three months compared to ten months in skin metastases only. Preference site of lung cancer skin metastases is at supra-diaphragma region. Nodules are usually firm, painless and appear as oval or round form, adherent or mobile. Ulceration may be seen. Other form are plaque-like lesions, erysipelas-like papules, zosteriform lesions and scars. [1-5]

Case Illustration

A forty six-year-old male with history of smoking was referred to our hospital with lesion found in chest x-ray during the medical check-up before nodules biopsy procedure at the parietal and abdominal regions. Two months earlier, the nodules arised as tender and pain nodules that increasing in size. Blood streak and shortness of breath were sometimes occured accompanied by loss of body weight in three months. Pain also felt in right hand since year 2020 after ORIF procedure for right radius fracture caused by accident. Later on, several times seizures followed. Physical examination found mass at left parietal, left hypochondrium and suprapubic regions. Thoracic CT Scan procedure revealed solid 6,4 cm mass in long axis measured at the medial of the left lobe. The head CT Scan also revealed subsolid nodule at cutan-subcutaneous of the left occipital attached to the periosteum without any bone destruction ad solid nodule at cortex-subcortex of right frontoparietal accompanied by perifocal oedema that suggest a metastatic processes.

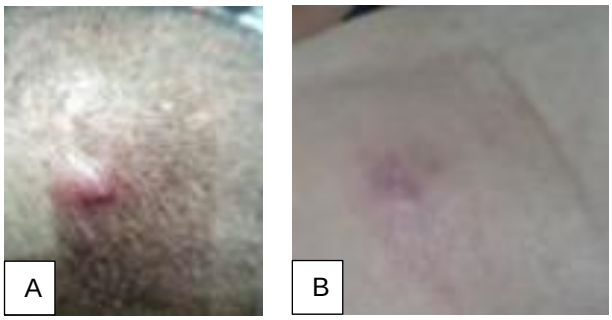

Figure 1. (A). Nodul in parietal region, (B). Nodul in abdominal region

Figure 2. (A). Nodul in parieto-occipital region**, (B).** Ulcerative mass in abdominal region, **(C).** Ulcerative mass in suprapubic region, **(D).** Masses in right hand.

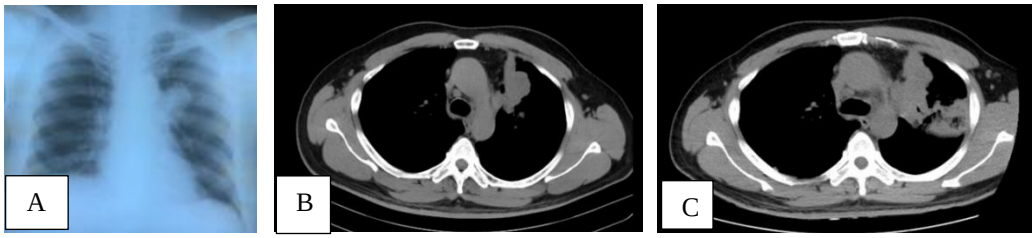

Figure 3. (A). Chest X-Ray prior to nodules biopsy, **(B).** Chest CT Scan following (A) **(C).** Chest CT Scan prior to diagnostic bronchoscopy procedure

Diagnostic bronchoscopy procedure found edematous mucosa at left upper lobe orificium with compression stenosis covering part of left B1, B2 and B3 orificium. Anatomical pathology result from histopathology examination from bronchial biopsy sample as well as cytology examination confirmed adenocarcinoma with wild type. The Epidermal Growth Factor Receptor (EGFR) mutation. Nodules biopsy from the chest wall, hand and inguinal confirmed metastases of adenocarcinoma. Bone scan concluded suspicion on osteoblastic metastatic lesion at right distal radius. In conclusion, the final diagnosis was left lung adenocarcinoma T4N2M1c (multiple subcutaneous nodules, brain, bones) stage IVB PS 2 wild type EGFR mutation, progressive disease. Patient underwent 5 cycles of external radiation continued with 10 cycles of whole brain radiotherapy and 6 cycles of chemotherapy with cisplatin and pemetrexate. Bondronat regiment also performed. As the disease progressed, new nodules found at occipital, femur and gluteus region.

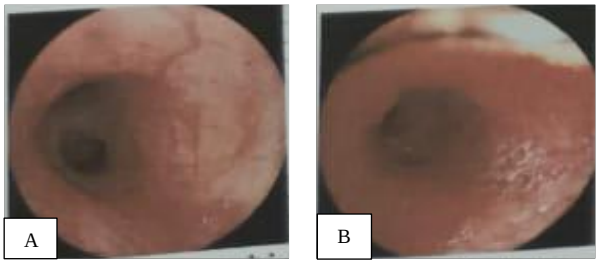

Figure 4. (A). Edematous hypervascularization and bumpy mucosa at left upper lobe orificcium, **(B).** Compression stenosis with edematous mucosa covering part of left B1+B2 and B3

Discussion

Lung cancer can metastasize to all organs with only 3,4% incidence at the skin. It is uncommon with poor prognostic indicator, one of which is due to poor response to chemotherapy. It becomes poorer with extracutaneous metastases and may be detected at the same time or before the primary cancer detected in 20-60% of cases that mostly occur in regions close to the primary site. The most common is adenocarcinoma, followed by squamous cell carcinoma, small cell and large cell carcinomas. The common sites of metastases from lung cancer are the head, neck, chest and abdomen, while skin metastasis is found mostly at supra-diaphragma region in single or multiple presentations. Cancer to the upper lobes of the lung also has a higher tendency to skin metastasis. The formation are firm, painless and appear as oval or round nodules. Some may mimic specific dermatological conditions such as cutaneous cyst, dermofibroma, pyogenic granuloma, hemangioma, papular eruptions, herpes zoster eruptions, rapidly infiltrating plaques, alopecic patches, cellulitis, erysipelas, bullae and vascular tumors with telangiectasis. Ulceration may be seen.[1-10] In our case, the lesions ulcerated with granulation tissue at the edge and black scars formed containing necrotic tissue. Patient also suffered with brain, bone, abdomen, wrist join and inguinal metastases. Seizure took place several times and pain was felt at metastatic site with easily bleed as well.

Pathogenesis of skin metastasis of lung cancer derived from lymphovascular invasion, that often limited to the dermis and subcutaneous layer with poor differentiation and upper lobe tumours increasing the risk of metastasis. Venous and arterial system may involve as the route of skin metastasis. Molecularly, skin metastasis is an organized, non-random and organ-selective process orchestrated by interaction among several heterogenous molecules which are largely unknown. The average time for lung cancer to metastasize to the skin is 5,7 months. [4,8-12]

The diagnosis is based on clinical information on respiratory and systemic complaints or a history of smoking, Physical examination finding is general as the skin metastasis may vary in form and location. The complementary examination is the chest X-ray followed by chest CT Scan that remains the best way to evaluate local extension. Diagnosis is confirmed by histopathological and immunohistochemistry (IHC) analysis, that often poorly differentiated.[5,11-14] In our case, diagnosis was confirmed by histopathological analysis from bronchial biopsy revealing malignancy with impression of adenocarcinoma. Biopsy from chest wall and right wrist and right inguinal also confirmed as metastases of adenocarcinoma. Cytology analysis were performed by bronchial washing and brushing that conclude a positivity of adenocarcinoma. The Epidermal Growth Factor Receptor (EGFR) mutation analysis was negative and patient then treated with chemotherapy. Bone survey was performed and stated no sign of metastases at the moment but as time goes by, there was suspicion on osteoblastic metastatic lesion at right distal radius found at bone scan.

Skin metastasis in lung cancer patients is associated with an aggressive tumor. Generally, only palliative chemotherapy is offered and radiotherapy to the cutaneous metastases is indicated associated with severe pain or bleeding for with survival times 3-6 months. Treatment for solitary cutaneous metastases

includes surgery, chemotherapy or radiotherapy. In case of multiple skin metastases, chemotherapy is the primary treatment. The respons is usually minimal due to poor blood supply to the skin. Resection of the skin lesion offers a better survival with three months of gain, but after all, the prognosis remains poor. Radiation therapy is indicated for pain and bleeding.[5,13-15] In our case, patient was treated with regiment of Cisplatin and Pemetrexate and 5 cycles of external electrone radiation continued with whole brain radiotherapy (WBRT) for the brain metastases, as radiotherapy is recommended for local palliation or prevention of symptoms such as pain and bleeding.[16] Response Evaluation Criteria in Solid Tumors (RECIST) after 4 cycles of chemotherapy was partial respons but came to progressive disease at the end of the cycle. Patient passed away 10 months after adenocarcinoma was confirmed and around 13 months after first nodul appearance at skin of abdomen and occipital region.

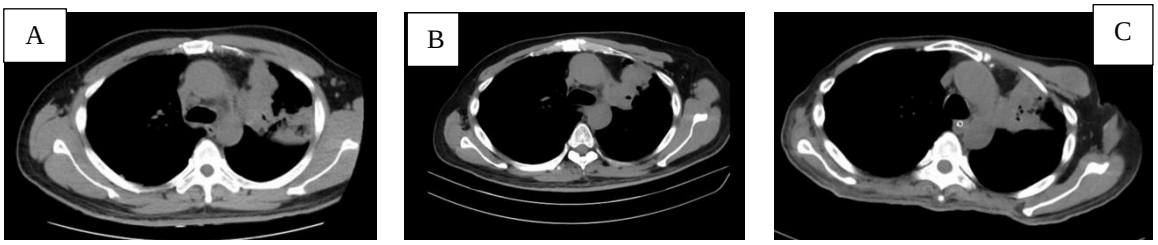

Figure 5. (A). Chest CT Scan prior to diagnostic bronchoscopy procedure, **(B).** Chest CT Scan after 4 cycles of chemotherapy – partial respons**, (C).** Chest CT Scan after 6 cycles of chemotherapy – progressive disease.

Conclusion

Skin metastases is an unusual form of lung adeno-carcinoma metastases. The lesion may be non-specific without any characteristic pattern and may be confused with other benign lesions. Therefore, it is essential to consider any skin pathological form in a patient with lung adenocarcinoma with suspicion to skin metastases as well as considering metastatic skin lesion in patient that leads to lung adeno-carcinoma diagnosis.

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