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Case Report

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Malignant Pleural Mesothelioma and Lung Cancer in a Very Young Age

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Abstract

The presence of cancer of the lungs is rare in adolescent patients, particularly in those under 20 years of age. A cancer that begins in the lungs is most often found in older patients with a history of tobacco use. In literature cancer in younger patients mostly meditational origins. Hence, we found two cases of lung cancer in a 15 and 17 years old male with different clinical presentation and history. In this paper, we hope to illustrate the unique challenges in diagnosing and treating young patients with lung cancer.

The third case is 29 years old young man with malignant pleural mesothelioma which is a rare, invasive and often fatal neoplasm that develops in the thin layer of tissue surrounding the lungs known as the pleura. Although rare, mesotheliomas do occur in the young; their characteristics are distinct from those of older patients.

Keywords: Lung Cancer, Mesothelioma, Adenocarcinoma, Young Age

Introduction

Lung cancer is the leading cause of death for men and women in the United States, surpassing deaths from breast, prostate, and colon cancer1. The age-adjusted incidence for 2006 reveals that lung cancer is the number one cause of death for men over the age of 40 and for women over the age of 60 [1]. The prevalence of lung cancer in young patients is 9.5%, as reported by Global Cancer statistic in 2006-2010. Increasing age and tobacco use constitute the strongest risk factors for lung cancer. Young patients under the age of 20 years of age without a history of tobacco use, environmental exposures, or genetic predisposition are rarely diagnosed with lung cancer, even those with history of tobacco use [2].

Malignant pleural mesothelioma (MPM) is a rare neoplasm, found in approx. 1 case/ million/year. It develops mainly in individuals over 60, men mostly, although it was also reported in children. Its main risk factor is asbestos. The incidence of mesothelioma in people exposed to asbestos is 300 times higher than in the general population. Other risk factors include erionite, radiotherapy and other surgeries causing pleural scarring. The most commonly reported symptoms include dyspnoea resulting from pleural effusion and pain in the chest. Diagnostic imaging involves: standard X-rays, CT, MRI, and PET. The best method for a final diagnosis seems to be video thoracoscopy. Treatment of mesothelioma includes chemotherapy, radiotherapy and surgical resections. The mortality is almost 100%. Recovery has been rarely reported, and only in cases of a very early diagnosis, subjected to adjuvant treatment. Malignant (MPM) is a very rare neoplasm; especially the local form. The diagnostics is difficult, the prognosis unfavorable, hard-to-treat. Commonly develops in pleura and peritoneum. Approximately 80% of MPM patients have a history of exposure to asbestos. However, it can take decades to develop and, as a result, is usually thought of as a disease of middle age and elder people. Patients with MPM frequently develop thoracic pain, dyspnea, weight loss and pleural effusion.

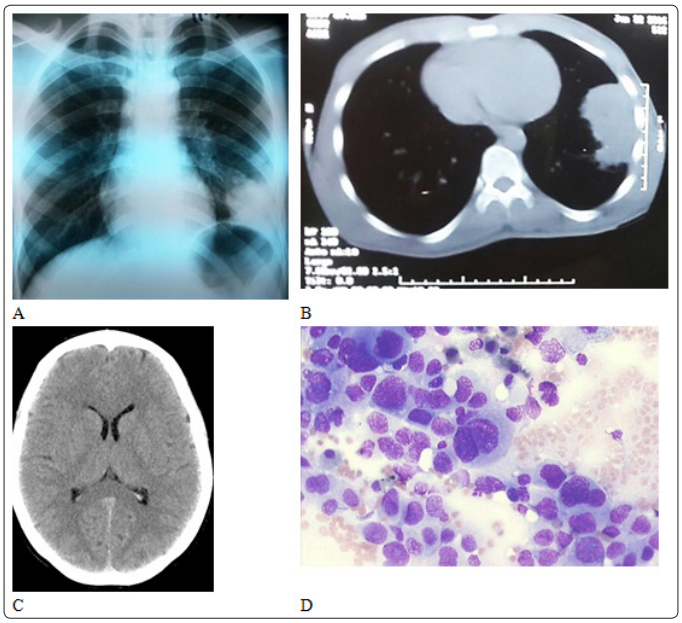
Case Reports

First Case Report

A 17 year old malereported to Hospital National Guido Valadares, Dili, Timor Leste, with a several-months history of cough, blood streakhemoptysis, and weight loss. The subject presented no shortness of breath, chest pain, headache, nausea or vomiting. He had an extensive history of tobacco smoking on average one pack of cigarettes a day since age 10 years old. He did not have a history of tuberculosis (TB) or TB contact or infectious disease. There was no family history of malignancy. The patient's general condition appeared to be moderate; however he was a bit malnourished, and in recent days had developed a mild fever. Respiratory symptoms such asdyspnea and cyanosis were not found. The neck region did not appear enlarged, and his supraclavicular lymph nodes appeared normal. Chest palpation was clear and no deformation was found. The subject's heart was not enlarged, and his heart beat and rhythm was normal. There was no abnormality of abdomen or extremities.

A posterior anterior chest radiograph revealed a multi lobular opacity at the left lower lobe lung (not the area adjacent to the chest wall). The hilus was not enlarged, the left diaphragm is elevated. The rest of the lung fields are clear. The patient was subsequently administered antibiotics for treatment of pneumonia. No clinical improvement resulted so a Computed Tomogram (CT) scan imaging was ordered.

CT scan imaging of the thorax revealed a 5x4x3 cm mass in the periphery of the left lower lobe and no destruction of the costae was found. Moreover, no meditational lymphadenopathy or pulmonary metastasis was discerned. The brain CT scan was normal; there was no sign of metastases. The abdominal ultrasonography (USG) and bone scans were also normal. Laboratory investigations revealed no abnormalities. Serological tests performed for infection(s) were negative. In due course, the decision was made to employ the use of a transthoracic needle aspiration, guided by CT scan. The resulting cytology report revealed the presence of malignant tumor formed from glandular structures in epithelial tissue (Adenocarcinoma). Unfortunately Epidermal Growth Factor Receptor (EGFR) mutation test was not performed due to the lack of facilities. The patient was subsequently diagnosed with Adenocarcinoma of the left lung, T2AN0M0 (stage IB). The subject was urgently referred to the thoracic surgeon for lower lobotomy. After the surgery the patient was well but unfortunately he didn't come for follow up examination.



The above images are from the 17 year old male diagnosed with adenocarcinoma. The descriptions are as follows:

a. Postero-anterior chest radiograph revealed a multi lobular opacity at the left lower lobe lung, not adjacent to the chest wall. The hilum is not enlarged, the left diaphragm is elevated. The rest of the lung fields are clear.
b. CT scan imaging of the thorax revealed a 5x4x3 cm mass in the periphery of the left lower lobe, not adjacent to the chest wall, with speculated. There is no destruction of the costae and no meditational lymphadenopathy or pulmonary metastasis is seen
c. CT Brain is normal, no metastasis were found.
d. Cytological specimen from transthoracic needle aspiration contains malignant cells of Adenocarcinoma

The Second Case

A 15 year old boy presented himself to Hospital National Guido Valadares, Dili, Timor Leste, with a several-months history of cough and weight loss. He has shortness of breath, chest pain, no headache, nausea or vomiting. He does not have a history of tobacco use and none of his family is smoker or has malignancy. No history of TB contact or any infectious disease. Patients were treated before admitted to the hospital at rural clinics with anti-tuberculosis drugs for one month. On physical examination, he appears with bad condition, malnourished, dyspnea, no cyanosis. Chest examination shows bulging, venectation, absent breath sound and stony dullness on the left side.

On chest x-ray shows total opacity on the left lung which pushed the heart to contra lateral side. He was treated for pneumonia after a chest radiograph showed total pacification of the left lung, after 10 days of antibiotic course shows no clinical improvement and no changed on chest radiograph. Thoracocentesis was done; approximately 500 milliliter serohemorrhagic color of fluid was drawn. The specimen was send to the laboratory and the results came out with no malignancy cells were found. There is no enlargement of neck or supraclavicular lymph nodes or any abnormality of abdomen or extremities. Abdominal ultrasound shows mild hepatomegaly and splenomegaly but no sign of metastases.

CT scan imaging was not performed due to technical issue. There is no destruction of the costae and no meditational lymphadenopathy or pulmonary metastases are seen on chest x-ray. Laboratory investigation shows moderate anemia, there is no sign of acute or chronic infection, infectious serologies were negative. Transthoracic needle aspiration guided by lung ultrasound was performed, the cytology report revealed adeno carcinoma, subtypebroncho alveolar carcinoma. The EGFR mutation test cannot be performed. The patient was diagnosed as primary adenocarcinoma of the left lung, T4N? M1a stage IVa (effusion) PS 3. He was urgently request referred to Sanglah hospital, Bali, Indonesia but it was cancelled on the day before the flight due to hypotension and hypoxemia and died the next day because respiratory failure.

The above images are from the 15 year old male diagnosed with Adenocarcinoma. The descriptions are as follows:

a. Postero-anterior chest radiograph revealed opacity which occupy all the left thorax cavity and pushed the heart to contra lateral
b. Cytological specimen from transthoracic needle aspiration contains malignant cells of Adenocarcinoma
c. Left hemi thorax bulge with venectation on the left chest
d. Brain is normal, no metastasis were found.

Third Case Report

A 29-year old male patient was admitted to our hospital on November 2018. He had smoked cigarettes for 15 years, 1 pack/day as well as moderate alcohol consumption. The patient was diagnosed with Tuberculosis at district Hospital and on Tuberculosis treatment for one week and 2 liter of hemorrhagic fluids was taken and referred to National Hospital. At hospital admission, he had 10 days with fixed moderate dyspnea, fever, left-sided pleurisy chest pain, headache, cough and no weight loss. Further questioning about asbestos exposure revealed nothing. Physical examination revealed a pleural effusion syndrome on the same side. No other associated clinical finding was described. Chest x-ray showed a homogenous opacity in left hemi thorax (Figure 1). Pleurasentesis was performed and 1200 ml of hemorrhagic/turbid pleural fluid was drained. Biochemical analysis of pleural fluid showed hemorrhagic/turbid effusion compatible with exudates. After we diagnosed complicated par pneumonic pleural effusion, Gentamycin and ceftriaxone were given. Several biochemical and microbiological analyzes were performed.

Chest CT was performed. It revealed a significant amount of fluid in the left pleural cavity and a poorly delineated, inhomogeneous mass lesion between the pleural layers in the base of the left lung in its largest dimension, the lesion measured 81 mm. The mass showed a slight enhancement after contrast medium administration. Above the tumour, there was a slight thickening of the pleura at some spots. USG of the chest was performed. It showed effusion in the pleural cavity and a poorly vascularised, hyperechogenic mass lesion between the layers of the thickened pleura. Within the tumour, there were hypo- and anechoic areas suggestive of haemorrhage. No neoplastic cells were found in cytological examinations of the fluid. Bronchoscopy was normal.

Pleura biopsy was performed that revealed a microscopic image and immunohistochemistry; we could diagnose that pleural thickening as mesothelioma.

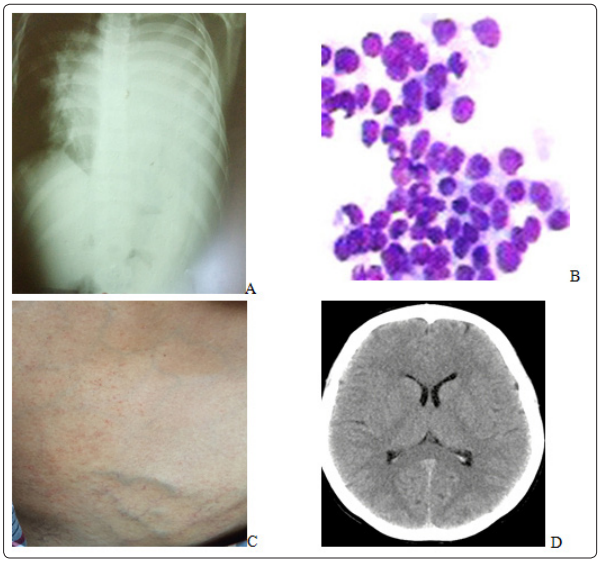


Figure 1 & 2: Initial Chest X-ray and lung window CT scan Thorax demonstrated a large right pleural effusion that occupies left hemi thorax which pushed the heart to the right side accompanied with chest pain

Fig 1,2 and 3 CT Scan Thorax demonstrate 51,2 X 35,7mm and 57,6 X 86,1 mm mass in pleura pars mediastinal with irregular border with significant amount of fluids.Fig.4 Pleural mesothelioma. Loosely combined multilateral cells imitate macrocellular cancer or lymphoma.

Conclusion

MPM is rare in young adults and its clinical presentation makes it different from mesothelioma in elderly patients, so it will be necessary to identify the new risk factors that can identify these patients.

Discussion

Lung cancer is the leading cause of cancer-related death worldwide, with non-small cell lung cancer (NSCLC) accounting for 85% of all lung cancers [3]. Lung Adenocarcinoma has the highest incidence among lung cancer patients, with a sex-specific incidence of about 30% in men and 37% in women in the United States [4]. The strongest risk factors for lung cancer are tobacco use and age. Notwithstanding, small-cell lung cancer and squamous cell lung cancer have a stronger association with tobacco use than Adenocarcinoma.4In Asian countries such as Thailand and Indonesia, lung cancers are rare among patients under the age of 40 [5, 6].

The most common type of cancers in the adolescent patients is pleural pulmonary blastoma, germ-cell tumors (teratocarcinoma), carcinoid, and metastatic cancer from non-lung primary, namely meditational tumors [7]. Data from Dharma is Cancer Hospital and Persahabatan Hospital in Jakarta shows only 5.9-15 patients are under 40 years old. In India, 40% of patients are under 50 years of age and only 11% are less than 40 years of age [8]. PIONEER Study, an Asian epidemiology study of Adenocarcinoma histology, reports the mean age of adenocarcinoma patients is 60 years of age, with youngest patients being around 17 years old [9]. Elhidsi et al in their retrospective and prospective cohort study reported in 218 Indonesian patients with lung Adenocarcinoma 65 of them were young patients. Most of the young patients are male (41.7%) and smokers (33.37%) [10]. In reference to NSCLC occurring in young people, a higher incidence of Adenocarcinoma is seen in female patients, and in the majority of these cases there is no history of tobacco use [11].

Tobacco smoking is by far the leading cause of lung cancer. About 80% of lung cancer deaths are caused by smoking, and many others are caused by exposure to secondhand smoke. Smoking is clearly the strongest risk factor for lung cancer, but it often interacts with other factors. Smokers exposed to other known risk factors such as radon and asbestos are at even higher risk. Not everyone who smokes gets lung cancer, so other factors like genetics likely play a role as well. Scientist's knowhow some of the risk factors for lung cancer can cause certain changes in the DNA of lung cells. These changes can lead to abnormal cell growth and, sometimes, cancer. DNA is the chemical in our cells that makes up our genes, which control how our cells function. We usually look like our parents because they are the source of our DNA. But DNA also can influence our risk for developing certain diseases, including various types of cancer.

Some genes help control when cells grow, divide to make new cells, and die:

- Genes that help cells grow, divide, or stay alive are called ontogenesis.
- Genes that help keep cell division under control or cause cells to die at the right time are called tumor suppressor genes.

Cancers can be caused by DNA changes that turn on ontogenesis or turn off tumor suppressor genes. Gene changes related to lung cancer are usually acquired during life rather than inherited. Acquired mutations in lung cells often result from exposure to factors in the environment, such as cancer-causing chemicals in tobacco smoke. But some gene changes may just be random events that sometimes happen inside a cell, without having an outside cause. Acquired changes in certain genes, such as the TP53 or p16 tumor suppressor genes and the K-RAS or ALK ontogenesis, are thought to be important in the development of non-small cell lung cancer. Changes in these and other genes may also make some lung cancers more likely to grow and spread than others. Not all lung cancers share the same gene changes, so there are undoubtedly changes in other genes that have not yet been found [12-17].

The first patient who is the subject of this report is an adolescent male (17 years old) with7 year's history of cigarette smoking, since

the age 10 years old. We do not know the EGFR or KRAS status for this patient's tumor due to the lack of facilities. These tests cannot be performed in our hospital yet. Elhidsi et al also report that EGFR mutation in younger patients are higher than elders (70.8% vs. 51.6%; p=0.007). It is our opinion that cigarette smoking, since a very young age, is the highest risk factor in this incident and, therefore, may have had the greater role in the development of cancer in our subject, combined with acquired gene changes due to exposure of tobacco use. The location of the tumor in this patient is peripheral, so it is not very difficult for us to perform biopsy using fine needle aspiration, to extract tissue from the chest wall. It is highly probable that it would have been very difficult to confirm the tumor using bronchoscopy. Since there was no clinical evidence of metastasis of brain, bones and other organs, we diagnose the patient as Adenocarcinoma of the left lung, stage IB (T2AN0M0) and suggest him to undergo surgery.

The second patient 15 years old with no history of cigarette smoking, Has a big solid tumor that growth very fast almost attach to chest cavity which is make easier to do Transthoracic needle aspiration for biopsy. We do not know the EGFR or KRAS status for this patient's tumor either due to the lack of facilities as previously stated these tests cannot be performed in our hospital yet. Elhidsi et al report that EGFR mutation in younger patients are higher than elderly (70.8% vs. 51.6%; p=0.007). In this case we assume that primary gene changes because of gene mutation plays a big role.

The Third case, a male 31 years old with malignant pleura mesothelioma, from literature reviews, Mesothelioma is a tumour causing many diagnostic difficulties. It, and especially its localized form, belongs to rare neoplasms. However, we should be aware of the presence of the localized form, due to the predicted incidence increase by the year 2020–2030.

Diffuse malignant mesothelioma is a once-rare primary neoplasm of the mesothelial tissues of the pleura, peritoneum, pericardium, and tunica vaginalis testis. Currently, approximately 3000 cases are reported annually in the United States, and approximately 80% of these lesions occur in individuals who have been exposed to asbestos [18-21]. The incidence of malignant mesothelioma is increasing because of the long latency period (≥30 years) from asbestos use and exposure before the 1960s [21].

The reported case illustrates quite common diagnostic difficulties found in mesothelioma. No cytological examinations of the pleural effusion showed the presence of neoplastic cells. They are found in only approx. 50% of patients with pleural effusion produced in the course of mesothelioma [21].

Conclusions

This is the first case report series of lung Adenocarcinoma in patients less than 20 years (17 and 15) of age from Timor Leste. Additional malignancies to be considered for thoracic masses in this age group include germ cell tumors (teratocarcinoma), lymphoma, carcinoid, and metastases from a non-lung primary cancer. The prognosis of Adenocarcinoma in young patients is meager. Survival in this group of patients remains highly variable. Mizushima et al found no difference in survival between lung Adenocarcinoma patients less than or more than 30 years of age [11].

Similarly, a retrospective study of patients younger than 50 years of age compared with those older than 50 found no difference in survival rates or in disease progression [12]. Nieder C et al in their studies found a worse prognosis for young patients with lung Adenocarcinoma than elder patients [13]. Overall survival (OS) in Indonesian young patient with EGFR mutation treated with Tyrosine kinas Inhibitor was 652 days (590-713 days; CI 95%) and OS young patient with wild type treated conventional chemotherapy 515 days (487-542 days) [10]. No differences were noted in 5 year disease-free survival between segmentectomy and lobotomy (70% vs. 71%; p=0.467) [14]. Because of the death rates of cases in youth under the age of 20 years of age, data evaluating the effectiveness of treatment for lung cancer in this age group, is limited [16]. Bourke et al. studied lung cancer in patients less than 45 years of age, comparing them with patients more than 45 years of age at three different geographic sites in the same study it has been reported lung cancer staging was demonstrated to be the factor most determinant for survival in patients less than 45 years of age [17].

The prognosis following a lobotomy depends on many different factors. Some of these include the stage of the lung cancer; that is, how far the cancer has spread—as well as the general health, and whether you have any other lung problems in addition to lung cancer. The overall mortality (risk of death) is less than 3 percent, yet many people do have temporary complications such as an air leak. When a lobotomy is successfully done for early stage lung cancer, it offers a chance for long-term survival without recurrence of cancer [18-21].

For the third case, as we know from the literature, malignant mesothelioma can be difficult to diagnose and is nearly untreatable. Asbestos exposure remains a major factor in the pathogenesis of this malignancy. Diagnosis requires recognition of patients at risk and knowledge of the clinical features of the disease. But in this case, the cause has not been determined.

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