NUT Carcinoma of Lung

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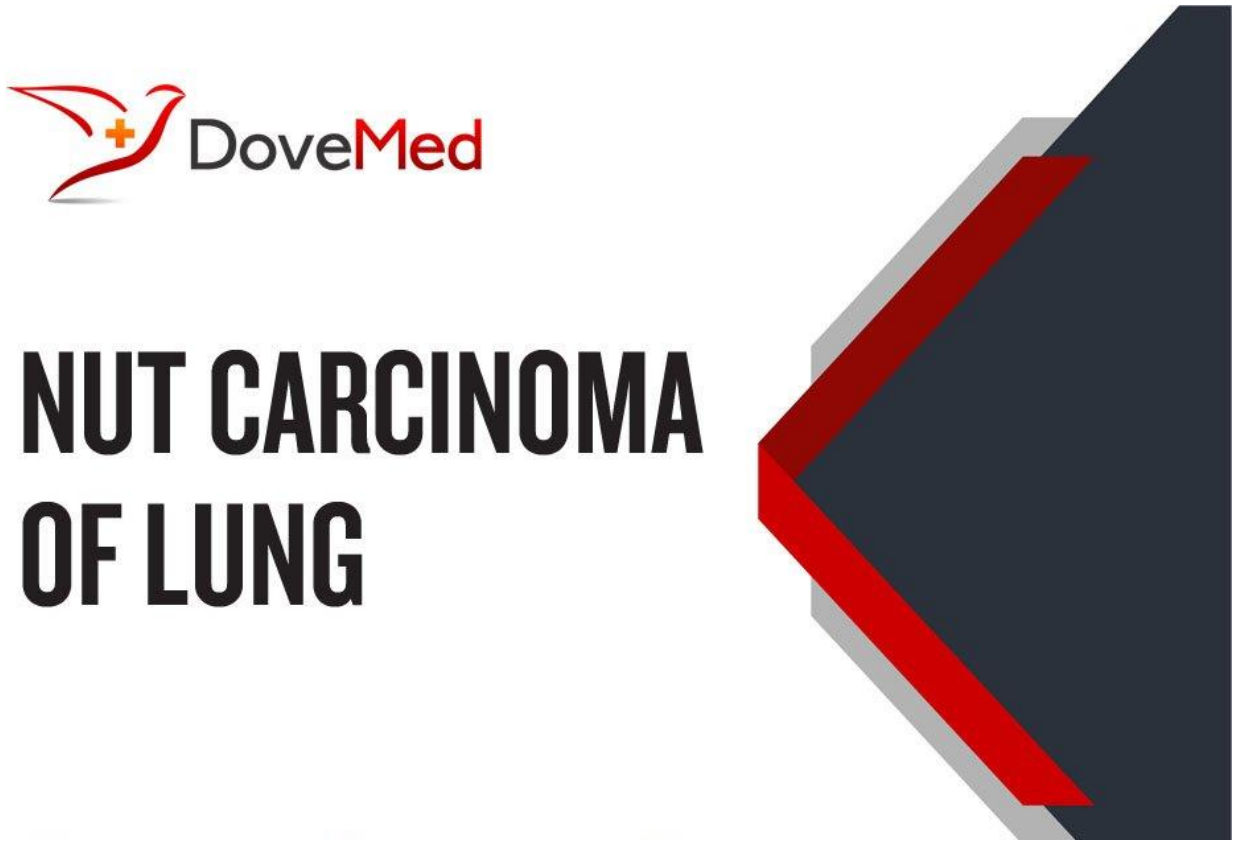

NUT Carcinoma of Lung is an extremely uncommon and aggressive malignancy that is named due to the presence of an abnormality involving the NUT gene (nuclear protein in testis).

What are the other Names for this Condition? (Also known as/Synonyms)

- Aggressive t(15; 19) Positive Carcinoma of Lung
- Midline Lethal Carcinoma of Lung
- Pulmonary Midline Carcinoma of Children and Young Adults with NUT Rearrangement

What is NUT Carcinoma of Lung? (Definition/Background Information)

- Lung cancer is a high mortality cancer that affects the lungs. Any individual can develop lung cancer, although individuals who smoke cigarettes remain at the highest risk for the condition. It is the most common cause of cancer-related death in the world
- NUT Carcinoma of Lung is an extremely uncommon and aggressive malignancy that is named due to the presence of an abnormality involving the NUT gene (nuclear protein in testis)

- It is a poorly-differentiated carcinoma of unknown cause. The influence of smoking or infection due to human papilloma virus or Epstein-Barr virus is not observed
- NUT Carcinoma of Lung can present with chest pain, breathing difficulties, and other general signs and symptoms, such weight loss and fatigue. The tumor is often diagnosed during advanced stages
- Chemotherapy, surgery, and/or radiation therapy, are generally not effective in treating NUT Carcinoma of Lung. The prognosis of the tumor is extremely poor, since it is a highly-aggressive malignancy

Who gets NUT Carcinoma of Lung? (Age and Sex Distribution)

- NUT Carcinoma of Lung is an extremely rare type of lung cancer with only about 100 cases being recorded in the medical literature
- A wide age range of individuals may be affected, although initially this cancer type was thought to be common among children and young adults
- In general, a male preference is noted for lung cancers. However, with NUT carcinoma, the male-female ratio is almost equal
- Current studies do not show any racial or ethnic predilection

What are the Risk Factors for NUT Carcinoma of Lung? (Predisposing Factors)

The risk factors that contribute towards NUT Carcinoma of Lung development are generally unknown. Although, in general, physicians believe that certain factors may increase an individual's risk for lung cancers and these include:

- Smoking: Smoking cigarettes, cigars, or pipes, increase the risk due to damaging chemicals being inhaled into the lungs. Prolonged smoking damages the lung, resulting in reduced clearance of the chemical carcinogens that accumulate in the lungs. This can lead to an increased risk of developing lung cancer
- Exposure to secondhand smoke: Individuals, who do not smoke, but live with smokers, also have an increased risk
- Air pollution: Exposure to polluted air may increase any individual's risk. This is true, especially in the case of smokers, who are exposed to air pollution, than non-smokers
- Exposure to asbestos and other harmful chemicals: Prolonged exposure to asbestos and other harmful chemicals including arsenic, chromium, nickel, and tar
- Individuals who are immunocompromised; those with weak immune systems
- Radon causing indoor air pollution: Radon, a colorless, odorless, and tasteless radioactive gas is produced by the natural breakdown of uranium in soil and rocks. In certain geographical regions, hazardous levels of radon gas can develop inside building or households. Individuals exposed to excessive amounts of radon gas are vulnerable to lung cancer
- Family history: Individuals with one or more immediate family members or relatives with a history of lung cancer
- Personal history: Individuals who have previously had lung cancer have an increased risk of its recurrence
- Certain longstanding lung diseases: Lung diseases, such as lung fibrosis, tuberculosis, bronchitis, or chronic obstructive pulmonary disease (COPD) over a prolonged period of time, may increase an individual's risk
- Radiation therapy to the chest: Individuals who had radiation therapy to the chest for another cancer are increasingly prone to lung cancer

- Working in mines
- The presence of alpha 1 antitrypsin deficiency disorder

Note:

- Pulmonary NUT Carcinomas are not known to arise in individuals who are smokers
- This cancer type is not associated with HPV or EBV infections

It is important to note that having a risk factor does not mean that one will get the condition. A risk factor increases ones chances of getting a condition compared to an individual without the risk factors. Some risk factors are more important than others.

Also, not having a risk factor does not mean that an individual will not get the condition. It is always important to discuss the effect of risk factors with your healthcare provider.

What are the Causes of NUT Carcinoma of Lung? (Etiology)

The exact cause of NUT Carcinoma of Lung is unknown. The development of this carcinoma is not associated with smoking, unlike most other types of lung cancer.

- A chromosomal translocation that is observed in all cases of NUT carcinoma involves the NUT gene on chromosome 15 along-with any of the following genes: (the NUT gene rearrangement defines the NUT carcinoma and is essential for a diagnosis)
    - In 70% of the cases, the BRD4 gene on chromosome 19 is involved
    - In 6% of the cases, the BRD3 gene on chromosome 9 is involved
    - In 24% of the cases, the gene remains unidentified
- In general, it is known that cancers form when normal, healthy cells begin transforming into abnormal cells - these cancer cells grow and divide uncontrollably (and lose their ability to die), resulting in the formation of a mass or a tumor
- The transformation of normally healthy cells into cancerous cells may be the result of genetic mutations. Mutations allow the cancer cells to grow and multiply uncontrollably to form new cancer cells
- These tumors can invade nearby tissues and adjoining body organs, and even metastasize and spread to other regions of the body

What are the Signs and Symptoms of NUT Carcinoma of Lung?

Early-stage lung cancer rarely causes any signs and symptoms and initially makes for a difficult diagnosis. Besides, several of the primary symptoms may result from non-malignant disorders too. The overlapping signs and symptoms may result in a delayed diagnosis of lung cancer in some cases.

NUT Carcinoma of Lung is an extremely aggressive malignancy and is most often diagnosed at an advanced stage. The signs and symptoms may include the following:

- Shortness of breath; difficulty in breathing
- Dry cough that may be persistent; blood in cough/sputum (hemoptysis)
- Chest pain, heaviness in the chest
- Sudden weight loss; unintentional weight loss; changes in appetite
- The individual is easily tired, resulting in fatigue even with minimal activity
- Pleural effusion or fluid in the chest
- Weight loss

Some features of the tumor include:

- These aggressive tumors may be present anywhere in the lung or thoracic region. They can invade into the pleura, the chest wall, and mediastinum
- They are often diagnosed through imaging studies (chest X-rays or CT scans) when rapid spread of the tumor to large portions of the lungs have taken place
- The tumor may appear as a poorly-defined large mass with infiltrating borders
- These carcinomas are known to disseminate/spread in the body through the blood and lymphatic system

How is NUT Carcinoma of Lung Diagnosed?

The following procedures and tools may be used in the diagnosis of NUT Carcinoma of Lung:

- Physical examination: During a physical exam, a physician will check the individual's overall health status, listen to their breathing, and check for possible fluid buildup in the lungs (auscultation)
- Pulmonary function tests can help determine the extent of lung damage; it can also help the healthcare provider assess the ability of lungs to deliver oxygen to the body
- Chest X-ray: Two-dimensional pictures using tiny amounts of radiation are taken, in order to detect any tumors or other medical issues associated with the lungs, such as pneumonia. Tumors inside the lung can be detected using a chest X-ray; although sometimes, these tumors are too small to visualize (tumors less than 1 cm in size may be missed on a chest X-ray)
- Computerized tomography (CT) scan: Also known as CAT scan, this radiological procedure creates detailed three-dimensional images of structures inside the body. CT scans may be helpful in detecting recurrences, or if the cancer has metastasized to the surrounding lymph nodes of the lungs
- Magnetic resonance imaging (MRI) scan: An MRI scan uses magnetic fields that create high quality pictures of certain body parts, such as tissues, muscles, nerves, and bones. These high-quality images may indicate to a physician, if any tumor is present
- Positron emission tomography (PET): A PET scan is a nuclear medicine imaging technique that uses three-dimensional images to show how tissue and organs are functioning. A small amount of radioactive material may be injected into a vein, inhaled or swallowed. A PET scan is also helpful in detecting recurrences, or if any metastasis (to the surrounding lymph nodes of the lungs) has occurred
- Sputum cytology: Sputum cytology is test that involves the collection of mucus (sputum), coughed-up by a patient. After the mucus is collected, a pathologist examines it in an anatomic pathology laboratory, to see if any cell abnormalities are present indicative of Pulmonary NUT Carcinoma
- Bone scan: A bone scan is a nuclear imaging test that involves injecting a radioactive tracer into an individual's vein. Bone scans are primarily used to detect if the cancerous cells have metastasized to the bones and formed secondary tumors
- Bone marrow biopsy: Bone marrow is a soft tissue found within bones. Occasionally, with NUT Carcinoma of Lung, a bone marrow biopsy is used to detect blood abnormalities, or if a physician believes that metastasis to the bone marrow may have occurred

A biopsy refers to a medical procedure that involves the removal of cells or tissues, which are then examined by a pathologist. Different biopsy procedures include:

- Tissue biopsy from the affected lung:
    - A biopsy of the tumor is performed and sent to a laboratory for a pathological examination. A pathologist examines the biopsy under a microscope. After putting together clinical findings, special studies on tissues (if needed) and with microscope findings, the pathologist arrives at a definitive diagnosis. Examination of the biopsy under a microscope by a pathologist is considered to be gold standard in arriving at a conclusive diagnosis
    - Biopsy specimens are studied initially using Hematoxylin and Eosin staining. The pathologist then decides on additional studies depending on the clinical situation
    - Sometimes, the pathologist may perform special studies, which may include immunohistochemical stains, molecular testing, flow cytometric analysis and very rarely, electron microscopic studies, to assist in the diagnosis
- The biopsy may be performed through any of the following procedures:
    - Bronchoscopy: A special medical instrument, called a bronchoscope, is inserted through the nose and into the lungs to collect small tissue samples
    - Thoracentesis: During thoracentesis, physicians use a special medical device called a cannula, to remove fluid between the lungs and the chest wall for examination
    - Thoracoscopy: A medical instrument called a thoracoscope is inserted into the chest through tiny incisions, in order to examine and remove tissue from the chest wall, which is then analyzed further
    - Thoracotomy: Thoracotomy is a surgical invasive procedure with special medical instruments to open-up the chest and remove tissue from the chest wall or the surrounding lymph nodes of the lungs
    - Mediastinoscopy: A medical instrument called a mediastinoscope is inserted into the chest wall to examine and remove samples
    - Fine needle aspiration biopsy (FNAB) or transthoracic needle biopsy: A device called a cannula is used to extract tissue or fluid from the lungs, or surrounding lymph nodes
    - Open lung biopsy

A differential diagnosis with respect to other lung cancer types/conditions may be necessary prior to establishing a definite diagnosis, by excluding the following cancers:

- Any type of poorly-differentiated carcinoma including squamous cell carcinoma (and its variants)
- Acute leukemia
- Adenosquamous carcinoma
- Ewing's sarcoma
- Germ cell tumors that have metastasized from other locations to the lung
- Small cell carcinoma
- Undifferentiated carcinoma

Many clinical conditions may have similar signs and symptoms. Your healthcare provider may perform additional tests to rule out other clinical conditions to arrive at a definitive diagnosis.

What are the possible Complications of NUT Carcinoma of Lung?

The complications of NUT Carcinoma of Lung can include:

- Dyspnea (shortness of breath): If the cancerous tumor expands to block important, large, or small airways of the chest or lung
- Hemoptysis (coughing-up blood): Individuals may cough-up blood, due to excessive amounts of blood in the airways
- Pain: Advanced stages that has metastasized to the pleural cavity (lining surrounding the lungs), invaded the chest wall, or other areas of the body may cause excessive pain
- Irreversible lung damage such as due to lung fibrosis
- Development of pneumothorax (collapsed lung)

Involvement of local and distant organs in lung cancer:

- Most cases are diagnosed during advanced stages when aggressive local invasion has also taken place. The tumor progression, initial diagnosis to complete tumor spread, within the chest may occur within 2 to 8 weeks
- The tumor spreads through the lymphatic or circulatory system: When the spread occurs through lymph, often the mediastinal lymph nodes are affected. When through blood, other regions such as the brain, liver, ovaries, and other parts of the lungs are affected
- Loss of function of the organ/area to which cancer has spread due to systemic involvement, which includes frequent sites such as brain, ovary, bone, and liver

There may be complications related to the methods used in treating the condition and may include:

- Side effects of radiation therapy that may include sunburn-like rashes, where radiation was targeted, red or dry skin, heaviness of the breasts, and general fatigue
- Side effects of chemotherapy, which may include nausea, vomiting, hair loss, decreased appetite, mouth sores, fatigue, low blood cell counts, and a higher chance of developing infections
- The treatment can also cause infertility in men and women. Hence, measures to protect the individual's fertility must be considered, before starting chemotherapy

How is NUT Carcinoma of Lung Treated?

Treatment options available for individuals with NUT Carcinoma of Lung are dependent upon the following:

- The staging of the cancer: If lung cancer is diagnosed, staging helps determine whether it has spread and which treatment options are best-suited for the individual
- Overall health status of the individual
- Type of gene mutation involved: This factor can determine the treatment possibilities or relative treatment resistance

NUT carcinomas are highly-aggressive that are typically diagnosed in the later stages of its growth. Thus, a systemic involvement is noted in most cases, which can be established through a PET scan. Due to this extensive tumor growth and spread, surgery may not be a treatment option in a majority of the patients.

A combination of chemotherapy and radiation therapy is also known to be ineffective in treating NUT Carcinoma of Lung. However, currently the use of bromodomain inhibitors (via clinical trials) is being investigated.

How can NUT Carcinoma of Lung be Prevented?

Currently, there is no known prevention method for NUT Carcinoma of Lung. Although there are no preventable measures for lung cancer, in general, various steps can be taken to help decrease the risk of its formation. These measures include:

- Complete smoking cessation and avoiding exposure to secondhand smoke: The risk for lung cancer decreases drastically following quitting or giving up smoking
- Physical activity: Individuals, who participate in a moderate amount of physical activity, may decrease their risk
- Adequate consumption of fruits and vegetables: A healthy diet, low in saturated fats and rich in many fruits and vegetables, may help decrease one's risk for lung cancer
- Avoid exposure to certain materials and chemicals (including asbestos, arsenic, chromium, nickel, and tar): Individuals who work with such substances should follow proper usage principles and occupational safety instructions, since a prolonged exposure to harmful chemicals may increase the risk for lung cancer. This risk is multiplied in smokers who are exposed to these harmful chemicals
- Avoid exposure to radioactive gas: Radon, a radioactive gas, produced by the natural breakdown of uranium in soil and rocks, may develop to hazardous levels inside building spaces. Individuals exposed to excessive amounts of radon gas are vulnerable to lung cancer
- Limit alcohol consumption: Alcoholic beverages have been linked to increasing an individual's risk for certain types of cancers, such as those affecting the lungs, mouth, throat, esophagus, breast, colon, and liver
- CT screening in high-risk groups can decrease the incidence of lung cancer, or at least help detect such cancers early. A low-dose CT scan is good to identify the tumors early. It is generally known that CT scans are about 3-4 times better than X-ray studies

What is the Prognosis of NUT Carcinoma of Lung? (Outcomes/Resolutions)

- NUT Carcinoma of Lung is an extremely uncommon but highly-aggressive malignancy. The prognosis of the condition is extremely poor. The average survival period following diagnosis is 7 months
- Factors, such as age or gender of the individual, location of tumor in the lung or thoracic region, and the type of translocation involved, have no bearing on prognosis
- The prognosis of lung cancer, in general, depends upon a set of several factors that include:
    - The grade of the lung tumor such as grade1, grade2, and grade 3. Grade1 indicates a well-differentiated tumor, grade 2 a moderately-differentiated tumor, whereas grade 3 indicates a poorly-differentiated tumor. Grade 3 tumors are higher prone to metastasis to the lymph nodes and recurrence
    - Stage of lung cancer: With lower-stage tumors, when the tumor is confined to site of origin, the prognosis is usually excellent with appropriate therapy. In higher-stage tumors, such as tumors with metastasis, the prognosis is poor
    - Histological subtype of the tumor: Some subtypes have better prognosis than others

    - The size of the lung tumor: Individuals with small-sized tumors fare better than those with large-sized tumors
    - Overall health of the individual: Individuals with overall excellent health have better prognosis compared with those with poor health
    - Age of the individual: Older individuals generally have poorer prognosis than younger individuals
    - Individuals with bulky disease of the lung cancer have a poorer prognosis
    - Involvement of the lymph node, which can adversely affect the prognosis
    - Involvement of vital organs may complicate the condition
    - The surgical respectability of the tumor (meaning, if the tumor can be removed completely)
    - Whether the tumor is occurring for the first time, or is a recurrent tumor. Recurring tumors have worse prognosis compared to tumors that do not recur
    - Response to treatment of lung cancer: Tumors that respond to treatment have better prognosis compared to tumors that do not respond to treatment
    - Progression of the condition makes the outcome worse
- An early diagnosis and prompt treatment of the tumor generally yields better outcomes than a late diagnosis and delayed treatment
- The combination chemotherapy drugs used, may have some severe side effects (like cardio-toxicity). This chiefly impacts the elderly adults, or those who are already affected by other medical conditions. Tolerance to the chemotherapy sessions is a positive influencing factor

It is important to have follow-up appointments with a physician, to evaluate the effects of the current treatment method, and to monitor for any returning tumors.

Additional and Relevant Useful Information for NUT Carcinoma of Lung:

- The incidence of NUT carcinoma affecting the lung is unknown. However, it has been reported that between 4-18% of the poorly-differentiated or undifferentiated malignancies affecting sites outside the lungs may be of this carcinoma type
- Lung cancer incidence is around 35 cases per 100,000 populations: The incidence of lung cancer in non-smokers is 1-2 cases per 20,000 populations per year; its incidence in smokers is 20-30 times higher than that of non-smokers
- Smoking is highly-associated with squamous cell carcinomas and small cell carcinomas; nevertheless, for all lung cancer forms, smoking is the single most important risk factor
- Studies under WHO indicate that the number of Adenocarcinoma of Lung cases is increasing (or has increased) due to design changes to cigarettes, composition of certain contents, and even better filtration of smoke through the cigarette. This is researched to be due to increased nitrosamines being inhaled through tobacco smoke

What are some Useful Resources for Additional Information?

American Cancer Society (ACS)
1599 Clifton Road, NE Atlanta, GA 30329-4251
Toll-Free: (800) 227-2345
TTY: (866) 228-4327
Website: http://www.cancer.org

American Lung Association
55 W. Wacker Drive, Suite 1150, Chicago, IL 60601

Phone: (312) 801-7630
Toll-Free: 1-800-LUNGUSA
American Lung Association Lung Helpline, to speak with a lung health professional: 1 (800) 548-8252
Fax: (202) 452-1805
Website: http://www.lung.org

References and Information Sources used for the Article:

William D. Travis, Elisabeth Brambilla, Allen P. Burke, Alexander Marx, Andrew G. Nicholson (Eds.); WHO Classification of Tumours of Lung, Pleura, Thymus and Heart (4th edition), IARC; Lyon 2015

https://www.ncbi.nlm.nih.gov/pubmed/26001144 (accessed on 01/02/2017)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2783402/ (accessed on 01/02/2017)

http://www.archbronconeumol.org/en/nut-midline-carcinoma-lung-a/articulo/S1579212916302233/ (accessed on 01/02/2017)

Helpful Peer-Reviewed Medical Articles:

Harms, A., Herpel, E., Pfarr, N., Penzel, R., Heussel, C. P., Herth, F. J., ... & Warth, A. (2015). NUT carcinoma of the thorax: Case report and review of the literature. Lung Cancer, 90(3), 484-491.

Walsh, E., Kuhnle, S., Rahman, S., Lemieux, M., Howley, P., & French, C. (2014). A novel NUT translocation partner binds to BRD4 and is necessary for the blockade of differentiation in NUT midline carcinoma. Cancer Research, 74(19 Supplement), 2476-2476.

Copin, M. C. (2016, January). [Large cell carcinoma, lymphoepithelioma-like carcinoma, NUT carcinoma]. In Annales de pathologie (Vol. 36, No. 1, pp. 24-33).

Kuroda, S., Suzuki, S., Kurita, A., Muraki, M., Aoshima, Y., Tanioka, F., & Sugimura, H. (2015). Cytological Features of a Variant NUT Midline Carcinoma of the Lung Harboring the NSD3-NUT Fusion Gene: A Case Report and Literature Review. Case reports in pathology, 2015.

Gokhale, P. C., Palakurthi, S., Xu, M., Calles, A., Shah, S. D., O'Connell, A., ... & Tran, C. A. (2015). Modeling patient-derived lung cancer in mice: Preclinical tool for drug development. Cancer Research, 75(15 Supplement), 1451-1451.

Policarpio-Nicolas, M. L. C., de Leon, E. M. B., & Jagirdar, J. (2015). Cytologic findings of NUT midline carcinoma in the hilum of the lung. Diagnostic cytopathology, 43(9), 739-742.

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