Bronchioloalveolar carcinoma also known as BAC, is a type of NSCLC. Non-small cell alveolus carcinoma is a type of epithelial alveolus carcinoma. NSCLC cover almost 86% to 88% of all alveolus carcinoma. In some cases chemotherapy is also not so successful on NSCLCs even this therapy is not effective as compared to small cell carcinoma. NSCLC has a very unique features as compared to other in terms of the demographics of who gets it, how it appear when we scan, and how it behave and how it respond to treatment. In a way we can says that Bronchioloalveolar carcinoma (BAC) is nearly similar to the ‘adenocarcinoma’ because of some feature and function how it behaves. NSCLC clinical presentation spread the entire spectrum from the ‘asymptomatic solitary pulmonary cyst’ to the full appearance but some symptoms of cough, haemoptysis and dyspnoea. Clinical symptoms always analogue with the area of disease. There are some cases which are present and they are recorded from the patient who is in the last stage of disease, so there are some symptoms which present in later stage or last stage of patient and not present in early stage. But BAC definition is still evolving everyday whenever new case reported and some new symptoms reported or noted which are new as compared to those which we heard earlier, many scientists says that the ‘BAC is a evolving chapter of medical industry’.
INTRODUCTION:
The term bronchioloalveolar carcinoma (BAC) was first used by Dr. Averill Liebow in 1960. Liebow used BAC to depict surrounding, normal corpuscle alveolus tumors, this type of tumors grows without the distortion of lung architecture. If we see pattern of the growth that characterize BAC is also designate by a different name but the most common is lepidic (lepidic pattern can be exemplify as a tumor consist of neoplastic cells which are lining the alveolar lining but there is no architectural disruption, complexity, and no lymphovascular and or pleural maraud and it is also construe as the divulge to scales or scaly covering layer). To chronicle the augmentation of the malignant corpuscles along extant alveolar septae. There was a time, when many pathologist and clinicians applied for BAC label for case adenocarcinomas showing the importance degree of abnormal growth pattern with in the tumors. Because, of this event, the prevalence of the BAC expands consequential.

A revised classification system for lung tumors was published by WHO after some event, and after this event it help us to initiate a more prohibitory definition of BAC, this classification which is present by WHO only include those cysts, with a characteristic of “pure lepidic” growing pattern and they have no evidence of stromal reaction or nor have vascular/ plural incursion. The ubiquitous of pure BACBronchioloalveolar carcinoma) are among Non-small cell lung cancer case series which employing the new revised arrangement is not more than 8%. BAC is the topic or we can say that is a type of alveolus cancer so it is obvious prognostic and a therapeutic makes it more important from different point of view to distinguish pure bronchioloalveolar tumor which has different quirk. We all know that bronchioloalveolar is alveolus cancer, but what define alveolus cancer and why it is called as alveolus cancer. The term alveolus carcinoma is used when tumor start arising from the respiratory epithelium(1).

If we follow World Health Organization (WHO) classification, epithelial alveolus cancer consists of four major corpuscle types which are:-

- Small cell alveolus carcinoma
- Non-small alveolus carcinoma
  Than histologies including -:
- Adenocarcinoma
- Squamous cell
- Large cell carcinoma

Adenocarcinomas is type of carcinoma tumor which takes place in every part of body. It is basically defined as neoplasia of epithelial that has glandular origin, glandular features. WHO classification regarding BAC they report that there are 3 types of BAC which are:-

- Non-mucinous
- Mucinous
- Mixed mucinous and non –mucinous
  (Note that – Mixed mucinous is extremely rare)

According to many scientist and WHO, Bronchioloalveolar we can say is a subtype of adenocarcinoma of the alveolus with much better prediction, and they have the penchant to escalate locally through the peripheral air space using the alveolus structure as stroma. There are two cell type – one is cuboidal and other is columnar (the cuboidal type resembling type 2 pneumocytes and columnar type are somewhat very much alike to bronchial cells). and they can start spreading along to the alveolar walls and septa without disturbing the alveolus framework. Because bronchioloalveolar carcinoma can’t be always certainly recognize from metastatic adenocarcinoma.

Bronchioloalveolar carcinoma is always contemplate to be the most argumentative topic of all primary lung tumor. There is some clinical finding but they are nonspecific excluding bronchorhea which indicate extensive alveolus disease. There is one report which state that around 12-30% of patient, there are no sign and symptoms which are exist and on doing chest radiographs these symptoms can be detected by this procedure only, unlike other type of alveolus carcinoma a clear association of smocking has not been confirmed.
We can say that Radiographically on the basis of many cases that BAC may follow one of the three patterns. unaccompanied tumor or amassment, confine area of the parenchymal solidify, tumor with multiple centers or disperse disease. The true ‘cavitation’ in the BAC is very rare and only about 9% of the occurrence in the large corpuscle sequence .(2) It is note that primary bronchioloalveolar carcinoma is exceptionally uncommon in children . BAC can present as a unaccompanied pulmonary tumor.(3) There was a theory regarding goat of ‘Murciano-Granadiana’ which was 5-year-old narrates that there is only one theory, It state that the analytic signs of cachexia and tachypnoea were noticeable, when animal head was lowered than there will be a discharge of white mucous and foamy fluid from proboscis in an ample quantity. Throughout the histopathologic inquisition an alveolus cyst with the traits of the BAC was recognized. The cyst corpuscle shows decisive conclusion for the proteins B and C surfactant. form this result it is confirmed that the alveolar type 2 corpuscle were the commencement of the neoplasia, than with the help of the polymerase chain reaction the cyst again tested, immunoblotting and immunohistochemistry for the existence of the ‘jaagsiekte sheep retrovirus(JSRV)’ and ‘enzootic nasal tumor virus (ENTV)’ , there is another retrovirus intently chronicle to the JSRV , but the conclusion we get is adverse , it is also the introductory research illustration of unpremeditated ‘bronchioloalveolar carcinoma’ (BAC) ,not allied to JSRV and ENTV inflammation in a goat .(4) It has been reported that F-FDG PET can diminish delicate in recognizing ‘bronchioloalveolar carcinoma (BAC)’ versus alveolus carcinoma with other type of histologies .Whereas for BAC ,CT characteristic basically are suggestive and according to many report and study they are very beneficial to basically for rectify recognition benchmark so PET/CN method in diagnosis can be very useful and it can become more rigorous. We research on cyst subject and on doing CT what we obtained is called as density and when we do F-FDG PET than we
obtained glucose metabolism and we do this on patient who is suffering from BAC and adenocarcinoma with BAC composing to resolve the role of both functional and atomic component of ‘PET/CT’ in the investigation of the inflammation .It is also proclaimed that lower SUV is directly proportional to pure BAC, higher TDR and lower HU than does BAC+adeno .For resolving the pure BAC existence it is only feasible using PET/CT and by resolving SUV, TDR and HU , it only use in the suggestive pulmonary tumor.(5) Bronchioloalveolar carcinoma (BAC) is always be the one of the most enigmatic and controversial lung cancer, and it also has broad spectrum of radiographic appearance most commonly appear at the initial examination as a solitary peripheral nodule and sometime it also occurs as multinodular consolidation and lobar or diffuse consolidation, there are other atypical features such as lobar at elactasis and cavitation. The development process in the BAC happen in stepwise , and the earliest to be recognized is a adenomatous hyperplasia (AAH)(6).

The World Health Organization has subclassified alveolus cancer on the basis of predominant corpuscle morphology and also on the expansion arrangement such as ‘bronchioloalveolar carcinoma (BAC)’. Adenocarcinoma with mixed subtype (AC mixed) and homogenously invasive tumor with variety of histologic pattern .There is also some clinical importance of the alveolus adenocarcinomas invasion is now supported by many studies because the risk of death in the non-mucinous BAC is slightly lower than that of pure invasive cysts and if in the case of cyst size is greater than 0.5cm of fibrosis and linear invasion (7)(7). After decades of researches , the term bronchioloalveolar carcinoma has itself fallen victim to our better understanding of alveolus carcinoma . If we compare present time, then we understand alveolus neoplasia and preneoplasia much better. With the advancing understanding of lung adenocarcinoma and its precursor, the term bronchioloalveolar carcinoma (BAC) become increasingly recognized now days and then in recent time pulmonary pathologist have acknowledge for several year that “tumors showing a pure bronchioloalveolar or lepidic pattern are now best regarded as adenocarcinoma –in-situ.(8)

The International Lung Cancer Consortium (ILCCO) was established in 2004, ILCCO is based on the collaboration of research group leading large molecular epidemiology, studies of alveolus carcinoma that are ongoing or which are recently completed, this framework offered many opportunities to investigate the role tobacco smoking in the development of bronchioloalveolar carcinoma (BAC) a rare form of alveolus carcinoma. We all know tobacco smoking in the main cause of alveolus carcinoma, smoking is responsible for an estimate 75-92% of cases in most population of the world ,the carcinogenic effect of tobacco smoking on different histological type has been investigated in several studies ,which include the most frequent type : A stronger risk is reported for the squamous corpuscle carcinoma, and small corpuscle carcinoma than for adenocarcinoma ,risk of large corpuscle carcinoma is investigated less frequently, seems intermediate. Bronchioloalveolar carcinoma (BAC) of the lung is the form of adenocarcinoma, because it is characterized by growth of neoplastic cells along the alveolar structure with limited invasion of blood vessels. The difference between bronchioloalveolar carcinoma (BAC) and other form of alveolus adenocarcinoma is very much difficult. in particular those are of larger size. they frequently displaying mixed histologies (9).

Alveolus carcinoma is the dominant cause of carcinoma related death in the united states in both women and men. There were 163,100 new cases and 155,900 deaths estimated for 2000.Non-small corpuscle alveolus tumor accounts for 82% of the cases, with the remaining 18% presenting as small cell cancer. Adenocarcinomas is further divided into 4 subtypes - Papillary, Mucinous, Acinar, Bronchioalveolar carcinoma (BAC). The most controversial primary malignant pulmonary
neoplasm is bronchioloalveolar carcinoma but it is also least common. There are many types of lung cancer -:

- **Non-small cell lung cancer (NSCLC)**: NSCLC is the most common type of alveolus carcinoma, making up to approx. 79-88% of all cases. They typically develop and then they are escalate gradually as related to the SCLC. NSCLC basically a staged based on the basis of size of primary cyst and if and where the carcinoma has spread (Stages 1,2,3,4). There are different kind of NSCLC but the most commonly diagnosed are:
  - **Adenocarcinoma**—Begins in the cells that forms the lining of the lungs
    1. Has gland like properties
    2. Makes up just over 30% alveolus carcinoma diagnosis

**Adenocarcinomas in situ (AIS) (formerly BAC)**

1. Rare subset of adenocarcinomas that begin in the alveoli
2. They can escalate without destroying tissue
3. It makes up about 5% of alveolus carcinoma diagnoses

- **Squamous cell carcinoma**—(1) Begins in the thin, flat cells that line the passage of the respiratory tract
  2. Makes up just under 29% of alveolus carcinoma diagnoses

- **Large cell carcinoma**—(1) faster growing form of NSCLC
  2. Makes up about 9% of lung cancer diagnoses

- **Large cell neuroendocrine tumors**—(1) fastest growing type of NSCLC

(2) Makes about 2% of alveolus carcinoma diagnoses

- **Small Cell Lung Cancer (SCLC)**—SCLC
  Makes up about 15-20% lung cancer cases, its reported that SCLC is a type of neuroendocrine tumor. SCLC is the fast-growing carcinoma that spread rapidly to other part of the body.

If we go according to the strict definition of BAC than, it says that entire tumor be composed of lepidic growth pattern and we need to examine entire tumor to ruled out the invasive area. A definitive diagnosis of BAC is not being based upon the small biopsy and cytology specimen. Rather, embedding of the entire tumor from the resection specimen is required. Furthermore, according to this strict definition than there is no nodal disease or extra pulmonary metastasis, many invasive adenocarcinomas will exhibit a component of lepidic growth, especially around periphery. The main issue in making a definitive diagnosis of BAC is determine by that if there is true effected area is present. Radiologically, bronchioloalveolar carcinoma has a different appearance with the peripherally located. Lobulated or ill marginated solitary pulmonary cyst is the most common one. It may also present as solid or partly solid nodules with ground glass opacification. The mucinous form present radiologically that’s why it is difficult to tell difference between pneumonia of an infected origin. This is recorded that the consolidation in BAC may remain unchanged for month.

Source: https://en.wikipedia.org/wiki/Large-cell_lung_carcinoma
DIAGNOSIS
Bronchioloalveolar carcinoma (BAC) mostly present in the form of solitary nodule, but sometime they are present in the form of cyst basically numerous type of synchronous, or a different process for example diffuse parenchymal mechanism. On investigation BAC mostly asymptomatic; there is a data which state that almost 65% of the patient in their institution when we do chest radiography or CT on them it shows that patient is examined when they are in early stage of ‘BAC’ and the patient having advanced diffused BAC can present with severe bronchorhea and refractory hypoxemia from the intrapulmonary shunting( a pulmonary shunt often occurs when the alveoli fill with fluid ,it causes part of the lungs to be unventilated but they are still perfused). Sometime the pneumonia or pneumonitis got mistaken in place of diffuse parenchymal disease and it is more frequent with the mucinous subset of bronchioloalveolar carcinoma.

Unlike non-bronchioloalveolar carcinoma alveolus carcinoma, maximum patient is present with surgically resectable inflammation having bronchioloalveolar carcinoma also. Pure bronchioloalveolar carcinoma definition does not associate with the distant metastases or lymph tumor, Patient having BAC tumors especially mixed, 11-28% have mediastinal tumor entanglement and on presentation approx. 6-9% have distant metastases. With the aid of fine needle biopsy there are some patient recognized with the ‘advanced adenocarcinoma’ but there is one fact that Bronchioloalveolar carcinoma traits also been detected if a larger amount of tissue was investigated histologically. Cytology is not adequate to make the investigation of ‘BAC’, to find out the presence or absence of intrusion it need histologic examination. Specificity cytology for BAC was 99% the sensitivity was only 12% this was recently reported. They estimated this on the basis of cytologic diagnosis alone, adenocarcinoma or undifferentiated NSCLC can be classified as almost 81-82% in bronchioloalveolar carcinoma (BAC) cases.

RADIOGRAPHIC FINDING
Radiographic findings include ground glass opacities, there are some non–resolving consolidation, and satellite nodule can boost the conjecture regarding bronchioloalveolar carcinoma indifferent of cytologic autopsyresult. Alveolus cyst lesser than 2-3 cm with transparent turf glass obscenity on contradiction–intensify soaring resolution CT are commonly pure bronchioloalveolar carcinoma, whereas the nosy composing increase with the component which are solid increase . lesion shows ground glass opacity when the percentage is more than 50%, the liability of nodal entanglement and repetition become very limited .Bronchioloalveolar carcinoma is very arduous to categorize from epidemic and the profound finding on CT scan have been described to find out the difference in BAC from pneumonia whereas positron emission tomography has increased approval as an detailed imaging modality to comprehend from cancerous alveolus cyst, it is noted that positron –emission tomography is less susceptible for bronchioloalveolar carcinoma than other type of NSCLC self–reliant of cyst size .Only about half of the patient with bronchioloalveolar carcinoma have a maximum cyst can uptake value (SUV) of larger than 2-2.5, the frequently preferred brink categorizing benign from malignant alveolus neoplasm . BAC has the lesser subtlety toward positron – emission tomography as result it is presumed that it has the secondary to the slower rate of the procreation of bronchioloalveolar carcinoma relate with other alveolus tumor, it was recently reported that mortality among patients with node-negative BAC was powerful predictor if a preoperative SUV is greater than 2.5.

SURGICAL TREATMENT:
Surgical treatment is not the best way to treat or diagnosed a patient who is suffering from BAC. But there are some surgeons and they have endorsed finite resection for patient who is suffering from peripheral pure BAC smaller than 2cm, it is based on study that in patient the
long-term survival term is always larger than almost 85-90, ‘even with sub-lobar resection’. But there are some studies auxiliary this way are very less , and have short follow up period . Whereas tumor are usually pure bronchioloalveolar carcinoma when on high resolution CT having pure ground–glass opacity , but nowadays there is limited resection of BAC because it is restrained for patient who cannot tolerate lobectomy with poor pulmonary reserve and for patient who is suffering from multifocal BAC . Bronchioloalveolar carcinoma with dispersed mutual alveolus involvement huddle dismal prognosis with a median continuity of approx. 4-5 months.

**SYSTEMATIC TREATMENT:**
It is unresectable chemotherapy has no effect on bronchioloalveolar carcinoma . But there are not enough testimony to backing this notion . It is made complicated by the patient who is suffering from mixed BAC as having adenocarcinoma , so it is difficult to analyses the response of BAC to chemotherapy , by misclassification of bronchioloalveolar carcinoma when the examination is completed by cytology and in most chemotherapy trial there is a absence of independent pathologic review . There are two small expected trials of chemotherapy in patient who is suffering from with advanced bronchioloalveolar carcinoma reported partial response to paclitaxel of 11-15%(11)

**MEDICATION**

<table>
<thead>
<tr>
<th>S.No</th>
<th>Generic Name</th>
<th>Brand Name</th>
<th>FDA Approval</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bevacizumab</td>
<td>Avastin</td>
<td>14-11-2014</td>
<td>Bevacizumab is a recombinant humanised monoclonal antibody that blocks angiogenesis by inhibiting vascular endothelial growth factor (VEGF-A)</td>
</tr>
<tr>
<td>2</td>
<td>Carboplatin</td>
<td>Paraplatin</td>
<td>8-3-1994</td>
<td>There are two theories exist to explain the molecular mechanism of action of carboplatin with DNA’ Aquation or the like cisplatin, Activation</td>
</tr>
<tr>
<td>3</td>
<td>Cisplatin</td>
<td>Platinon</td>
<td>30-06-2001</td>
<td>Cisplatin interfere with DNA replication which kills the fastest proliferating cells, which in theory are carcinogenic</td>
</tr>
<tr>
<td>4</td>
<td>Crizotinib</td>
<td>Xalkori</td>
<td>26-08-2011</td>
<td>Crizotinib has an amino pyridene, and function as protein kinase inhibitor by competitive binding with in the ATP binding</td>
</tr>
<tr>
<td>5</td>
<td>Docetaxel</td>
<td>Taxotere</td>
<td>23-12-1999</td>
<td>Docetaxel binds to microtubules reversely with high affinity and has a maximum Stoichiometry of one mole docetaxel</td>
</tr>
<tr>
<td>6</td>
<td>Erlotinib</td>
<td>Tarceva</td>
<td>18-11-2004</td>
<td>Erlotinib is an epidermal growth factor, receptor, inhibitor (EGFR)</td>
</tr>
<tr>
<td>7</td>
<td>Etoposide</td>
<td>Etopophos</td>
<td>19-03-1998</td>
<td>Etoposide forms are ternary, complex with DNA and the topoisoasemase second enzyme which aid in DNA unbinding</td>
</tr>
<tr>
<td>8</td>
<td>Gemcitabine</td>
<td>Gemzar</td>
<td>14-07-2006</td>
<td>Gemcitabine is a hydrophilic and must be transported into the cells via molecular transporter for nucleoside, catalyse by enzyme deoxycytidine kinase</td>
</tr>
<tr>
<td>9</td>
<td>Irinotecan</td>
<td>Camptosar</td>
<td>24-06-2004</td>
<td>Irinotecan is activated by hydrolysis to SN-38 an inhibitor of topoisoasemase 1</td>
</tr>
<tr>
<td>10</td>
<td>Paclitaxel</td>
<td>Taxol</td>
<td>30-06-1998</td>
<td>Paclitaxel is cytoskeletal drug that target tubulin</td>
</tr>
<tr>
<td>11</td>
<td>Pemetrexed</td>
<td>Alimta</td>
<td>2-7-2009</td>
<td>Pemetrexed similar to folic acid works by inhibiting 3 enzyme purine and pyrimidine synthesis</td>
</tr>
<tr>
<td>12</td>
<td>Vinorelvin</td>
<td>Navelbine</td>
<td>6-8-2000</td>
<td>Cytochrome P450 are a group of hemithiolate monoxygenases in liver microchomes this enzyme is involved in NADPH</td>
</tr>
</tbody>
</table>
DISCUSSION

Cough, chest pain, dyspnoea, haemoptysis, and sputum production are the most common symptoms of BAC which are discovered till now.(12). BAC is less known chapter in the medical industry, it is not wrong if we can say that the BAC is mystery lung cancer because we know very less about this cancer (13). From current analysis it is clear and it also provide some strong evidence that there is some beneficial effect of quitting smoking (9). There is some difference in the BAC+Adeno for example BAC usually have more air space and have fewer cellular component as a result BACs have lower CT number than do the Adeno+BACs. Patient who is suffering from pure bronchioloalveolar carcinoma mostly has lower HU, higher TDR, and lower SUV as compare to the patient who is suffering from BAC+adeno.

CONCLUSION

It is proven that BAC is a somewhat similar to adenocarcinoma with some exclusive radiological, epidemiological, and clinical features. There are some hints that the BAC existence is recognized to be appear from findings of a cyst on a CT scan or pure ground-glass cyst. There are some changes in the classification of adenocarcinoma, this will be modified the view how we outlook bronchioloalveolar carcinoma, there is term which we use in situ called as adenocarcinoma and is used for the cysts which has pure lepidic growth. If we need to find out the optimum treatment for BAC than clinical trials are very important steps in this process. There are some possible way to find out the presence of pure BACs, it can be possible in ‘pulmonary nodule’ by using CT/ PET and by determining SUV, TDR, HU. There are many things about BAC to be accomplished for example- cysts biology, epidemiology and most importantly the analysis option. In response to the cysts of mixed , There is universal classified scheme of BAC which include mixed BAC for response to treatment of tumor with mixed BAC it is very important to assist the research into the biology, but for alveolus malignancy screening the use of chest CT scanning nowadays increasing, there is chances that in future more cysts with bronchioloalveolar carcinoma histology will recognized . There is some traits in BAC which predict the response to TKIs- EGFR, but right now there is no information to backing this therapy for advanced BAC. In future when we do more research into the biology of bronchioloalveolar carcinoma it can be helpful in improving the use of existing therapies and from this we can developed more novel targeted therapies(13).

REFERENCES:


How to cite this article:

Source of Support: Nil
Conflict of Interest: None declared.