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BRONCHO ALVEOLAR CARCINOMA (B.A.C.)

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Bronchoalveolar carcinoma (BAC) is a clinicopathologic entity of adenocarcinoma with a pure bronchioloalveolar growth pattern and appears as an in situ alveolar adenocarcinoma. It arises from type II pneumocytes or Clara cells and grows along alveolar septa. BAC occurs more frequently in women and in younger patients. BAC presents with distinct clinical features, such as endobronchial spread and bronchorrhea in advanced stages. Intrapulmonary spreading and rare systemic metastatic potential is the hallmark of this tumour.

Although it seems to be less dependent on tobacco exposure, smoking cannot be excluded as a risk factor.

It may arise in-patient with prior history of lung disease. The cancer theory suggests that BAC can develop in previously scarred lung parenchyma. Tuberculosis is a very common disease worldwide and the scar of this chronic inflammatory process could be the inciting factor for BAC.

Regarding molecular mechanisms underlying BAC it has been found that p53 and ras genes are less often mutated than in other pulmonary adenocarcinomas, suggesting the cellular mechanisms.

NATURAL HISTORY:

Clinical presentation is quite variable ranging from asymptomatic solitary nodule to mucous bronchorrhea in extensive disease.

Classically BAC produces copious mucoid sputum, which leads to frequent severe dyspnea with frothy sputum in end-stage disease.

A unique attribute of BAC is its aerogeneous spread. Lymphatic spread is not the favoured route. Regional and distant metastasis occurs less commonly in BAC.

A rare presentation of lung cancer as ovarian metastasis has been reported [2]
It is quite likely that clinical pattern and pathologic stage are the most important prognostic factor. Degree of invasion on histological examination does not predict survival.

DIAGNOSIS:

HISTOPATHOLOGY:

It presents in three different pathological forms

- 1) solitary peripheral nodule (most frequent)
- 2) multifocal disease (favourable survival, particularly in women)
- 3) rapidly progressive pneumonic form (spreading from lobe to lobe)

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The histological criteria defining bronchioloalveolar carcinoma (BAC) were recently revised; tumors were classified as pure BAC, BAC with focal invasion, and adenocarcinoma with BAC features. Correlation between histopathological form and clinical behaviour is not clear.

Atypical adenomatous hyperplasia (AAH) is a probable forerunner of bronchioloalveolar carcinoma (BAC) and pulmonary adenocarcinoma (AC) of mixed type. A high degree of overlap of genetic changes was found in high-grade AAH, BAC, and AC within individual patients. The high number of aberrations and the degree of shared aberrations found in high-grade AAH and AC raises questions about the separation of these two entities. In addition, in view of the monoclonal origin of multiple foci within the same patient, AAH may not be a precursor of AC in some cases, but may represent intraepithelial spread.

IMAGING:

CT scanning

BAC presents as ground glass appearance on computed tomography scanning. One study [3] measured localized ground-glass attenuation-(GGA) in the peripheral lung on thin-section computed tomography (CT) and assessed any relationship between the attenuation and lesion. The contrast index correlated histological findings of the tumor growth in BAC. The contrast index may be a useful and objective measurement for determining surgical treatment for localized BAC. It can be used as a tool for the preoperative assessment.

On HRCT, the presence of an air bronchogram may have an independent prognostic significance in lung adenocarcinoma with BAC components to analyze the internal and peripheral textures of small peripheral bronchogenic carcinomas (<2 cm).

PET scanning

Focal bronchioloalveolar cell carcinoma (BAC) has been reported as often being negative on 2-[fluorine-18] fluoro-2-deoxy-D-glucose (FDG-PET) scans. However, in the presence of multifocal disease, FDG-PET seems to be highly sensitive[4].

TREATMENT:

SURGICAL OPTIONS:

Surgical resection has a fundamental role in management of BAC because of its intrapulmonary spreading and being infrequently systemic...

CURATIVE SURGRY

Unilateral multinodular or pneumonic forms:

BAC is unique in its alveolar spread that results in multifocal pulmonary recurrences. This characteristic of BAC and resultant disease has led to maximal parenchyma saving approach. In some retrospective studies [6] [7] survival was found to be better for lobectomy than for pneumonectomy, combined with lymphadenectomy. Complete resection of multifocal non-small cell lung cancer when bronchioloalveolar carcinoma is a component may achieve survivals similar to that of stage I and II unifocal non-small cell lung cancer. When bronchioloalveolar carcinoma is believed to be one of the cell types in multifocal disease without lymph node metastases, first line of management should be the surgical resection [1].

Solitary BAC nodules:

Limited resection could be considered, as a suitable substitute to lobectomy for the treatment of solitary lung nodules with pure pathological BAC patterns, provided specific conditions based upon computed tomography scan findings are present. These specific types of BAC have been described by Noguchi et al. [7] as Type A and B adenocarcinomas. However, wedge resection has to be avoided in other cases of BAC as well as all other types of lung cancer as is demonstrated in several studies [9] [10].

The fact that mediastinal lymph nodes are very infrequently involved in peripheral small sized BAC and especially in Noguchi's type A and B evoke the interest in mediastinal node dissection. In BAC <2 cm without foci of active fibroblast proliferation in histology, mediastinal lymph node dissection would be unnecessary. One study has emphasized the importance of it even in <1 cm non-small cell lung cancer (NSCLC) [9].

COMBINED THERAPY

Neoadjuvant or adjuvant chemotherapy or radiotherapy in treatment of BAC is a less explored area. However, it has been shown that use of postoperative thoracic radiotherapy can reduce the loco-regional recurrences [10].

BAC patients in advanced stages do poorly with conventional chemotherapy as is the case for patients with other non-small-cell lung cancer (NSCLC) types.

New Pharmacological (Targeted) Therapy:

Recently, an orally active, quinazoline-derived selective epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (EGFR-TKI), ZD1839 ("Iressa"), has been investigated in phase II clinical studies (IDEAL 1 and IDEAL 2) as monotherapy against chemotherapy-refractory Non Small Cell Lung Cancer, and there is some evidence that it has provided clinically significant antitumor activity.

In this study serous sputum production was dramatically reduced within 3 days of starting the treatment, and hypoxia and radiographic signs of bilateral lung consolidation were visibly improved within 7 days. This improvement in symptomatology remains stable over a period of months with no evidence of recurrence or severe adverse events. The side effects of dry skin and acne over the face, trunk, and periungual areas have been noted.

PROGNOSIS

The overall survival rate is 48 to 69% [1]. There are significant differences in 5-year survival rate between men (37%) and women (74%). The 5-year survival rate for patients with mixed type BAC is 20% that is significantly worse than that for non-mucinous (62%) and mucinous (59%). As concern the survival rate after different types of surgeries, it has been observed that lobe or complete lung resections have better 5-year survival than wedge resections.

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