Pleuropulmonary Neoplasia

APPROVED

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Robbins Questions w/ tumors/cancers:
#14, 18, 23, 24, 25, 29, 33, 37, 40, 47, 49, 57,
Common Cancers and Cancer Deaths
Three Most Common Cancers among Men

- Prostate: (157/100,00)
- Lung/Bronchus: (80/100,00)
- Colorectal: (53/100,00)
Three Most Common Cancers among Women

- Breast: (120/100,000)
- **Lung/Bronchus:** (55/100,000)
- Colorectal: (41/100,000)

*in the last decade, lung cancer has become this common in women*
Lung Cancer and Women

- Estimated 72,000 lung cancer deaths among women in the USA in 2010
- Leading cause of cancer death in both sexes, more deaths from lung cancer than all the other most common solid tumors combined, women achieved equity with men in 2005
Carcinoma of the Lung

• **Leading cause of cancer death IN THE WORLD** - 1990 data
  1 million cases worldwide, 1 million deaths, accounts for nearly 13% all cancers globally.

• **Most** who develop lung cancer **DIE FROM IT**
"The roles I play in movies are far from easy on my voice—
I can’t risk throat irritation.
So I smoke Camels—they’re mild"

John Wayne, an American icon, unfortunately died from lung cancer.
Lung Cancer killed them too

Paul Newman, Joe Dimaggio, Walt Disney, Duke Ellington, George Harrison, Nat King Cole, Yul Brynner, Suzanne Pleshette, Vincent Price, Desi Arnaz, John Updike, Ayn Rand as well as 90,139 and 69,078 less famous men and women in 2005 alone
Lung cancer - risk factors

- Tobacco usage, esp. cigarette smoking, accounts for up to 90% of all lung cancer deaths. Fewer than 20% of smokers get cancer.
- ETS/ cigars
- Radon
- Asbestos
Who painted this? Van Gogh, late 1870s. Surgeon General warning came out in 1960s. Van Gogh painted this just to annoy his instructor.
Lung cancer risk - gender

- 1950-1990, 600% rise in lung cancer mortality in women
- ? Increased biologic susceptibility suggested in case control studies
- Female smokers have 2-3 x risk of developing small cell carcinoma
increase in lung cancer in women is due to their increase in smoking in the 1960s which was due to new cigarettes such as Virginia Slims that were advertised to women
these days, cigarette companies still target young women and he says there should be more public outcry on this. I agree

these has been decrease in death rate for breast cancer in the last couple decades but this is not true for lung cancer

- Highest: Kentucky > Arkansas > W. Va
- New England: ME #8, RI#22, NH# 23, VT # 29,
- North Carolina #16
- Lowest= Utah. Mortality patterns generally reflect prevalence of smoking
It is always better to quit smoking. The earlier the better. However, even if you quit, your risk will not come back down to normal.

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Figure 8. Effects of stopping smoking at various ages on the cumulative risk for death from lung cancer up to age 75 at death rates for men in the United Kingdom in 1990. Nonsmoker risks are taken from a US prospective study of mortality. (From Peet R, Darby S, Deo H, et al: Smoking, smoking cessation, and lung cancer in the UK since 1950: Combination of national statistics with two case-control studies. BMJ 321:323–329, 2000; with permission.)
Classification

- Small cell vs Non-small cell carcinoma (bronchogenic ca)
- Bronchial tumors, salivary gland-like tumors
- Malignancies of the pleura

*bronchogenic carcinoma is synonymous with cancer of the lung, strictly speaking this term is for cancer arising from within the bronchi, but it is a little bit of a misnomer*
W.H.O. CLASSIFICATION OF LUNG CANCER

- Adenocarcinoma
- Squamous cell carcinoma
- Large cell carcinoma
- Small cell carcinoma

4 basic types
BRONCHOGENIC CARCINOMA

- SMALL CELL 20-25%
- NON-SMALL CELL
  SQUAMOUS CELL - 25-40%
  ADENOCARCINOMA - 25-40%
  LARGE CELL - 10-15%

This is the most common lung cancer of the non-small cell cancers
most of these cancers have strong association with smoking

Subtype by smoker status

- Squamous cell: 98% vs 2%
- Adenocarcinoma: 82% vs 18%
- BAC: 70% vs 30%
- Small cell: 99% vs 1%
- Large cell: 93% vs 7%
Biology of lung cancer

- Local growth, local invasion of bronchi, vasculature and pleura
- Spread via lymphatics: peribronchial, hilar and mediastinal lymph node groups
- Distant hematogeneous metastases—bone, liver, adrenal glands and CNS

Spreads first via the lymphatics. It is very bad once it gets into the mediastinum. These are the common sites of metastases.
Staging: TNM system

- T = features of primary tumor: size, relationship to carina, mediastinal structures, chest wall
- N = nodes: peribronchial, hilar, mediastinal
- M = metastases: lung, adrenals, bones, brain.
Non-small cell carcinomas

- Squamous
- Large cell
- Adenocarcinoma
- Mixed
- Behavior primarily a function of clinical stage, more than type.
- Surgical approach

- there are some with mixed histologies
- behavior depends on the stage of the cancer
- usually with non-small cell carcinoma.
Signs and Symptoms

- Local direct effects from endobronchial growth, obstruction
- Direct extension into mediastinum and chest wall, nerve entrapment syndromes, superior vena cava syndrome
- Paraneoplastic/endocrine syndromes

beneath the bronchi or in the mucosa itself
may see recurrent pneumonias, cough, spitting up blood (hemoptyysis)
may see chest pain
congestion of the upper extremities
a lot of these cancers may secrete hormones
see a mass that is not aerated
see it in this view, this is a typical local lung cancer
malignant cells

from sputum, malignant cells are pleomorphic, have multiple nuclei, and are larger than normal

normally sized cell

can make diagnosis on this cytology
can do needle aspiration and do stain
we usually use these noninvasive means to diagnose
Squamous Cell Ca

- 30% of all primary lung malignancies
- Central, involve large airways, endobronchial growth
- Strong association with cigarette smoking
Squamous cell ca: morphology

- Differentiating features of squamous epithelium; keratinization (pearls) and intercellular bridges
- likely to cavitate: 70% cavitary lung ca are squamous

kind of looks like skin histologically
CT scan

large squamous cell carcinoma with an air fluid level in it
Peripheral squamous cell carcinoma

Airway and pulmonary artery

Tumor here with center being necrotic
cytologically, squamous cell carcinoma cells like to wrap around each other
in sputum can see the elongated cells and also see keratin (pink) within the cytoplasm of the cells
can see some intercellular bridges here

so, keratin production and intercellular bridges are hallmarks of squamous cell differentiation
because these tumors grow endobronchially, behind the obstruction there may be filling of air spaces with debris and lipid and there may be post obstructive pneumonia, so on the radiograph, not all of it may be tumor, you may also find some post obstructive pneumonia
Bronchogenic ca: small cell carcinoma

- 20-25% all lung cancers
- aggressive, responsive to chemo
- central tumor, staged as limited (30%) vs extensive (70%)
- Distinctive clinical manifestations: Eaton-Lambert syndrome, SIADH, ACTH

- inappropriate ACTH
- proximal muscle weakness
- small cell ca is most likely to have paraneoplastic syndromes
- inappropriate ADH

- most lethal form of lung cancer
- cures are generally less than 10%
- may be quizzed about these on the wards
SYMPTOM COMPLEXES

- CENTRAL/ENDOBRONCHIAL GROWTH
- PERIPHERAL GROWTH
- REGIONAL SPREAD
- PARANEOPlastic SYNDROMES
small cell ca tends to be central tumor, you can see that it is central
small cell ca tends to compress bronchus from the outside, and does not so much go into the bronchus
Small cell CA often metastasizes to the liver as can be seen here.
The image shows a medical specimen, specifically a view of the lungs and surrounding tissue. The annotation indicates that there is a tumor in the central part and it is in the upper lobe and into the lymph nodes.
small cell ca tends not to grow discrete masses but grows out via the airways into the periphery
Small cell carcinoma: morphology

- Small cells, (1-1.5 x lymphocyte)
- Hyperchromatic nuclei, molding and crush
- necrosis
nuclear molding seen here where the nucleus is sort of molded by its neighbors above and below
island of tumor cells in a background of necrotic debris
the surface epithelium

tumor is not growing through the lumen but undermining the wall of the bronchus
small angulated hyperchromatic nuclei with almost no cytoplasm
Adenocarcinoma

- 35% primary lung malignancies
- most common type involving the non-smoker
- typically peripheral, subpleural
- heterogenous morphology; acinar, papillary, solid, bronchiolo-alveolar cell (BAC) types

most common form of primary lung cancer
not central but tend to be in periphery
Adenocarcinoma, morphology:

- Acinar/glandular
- Papillary
- Solid with mucin production
- BAC
tumor cells form glands

so know that adenocarcinomas form glands and make mucin
Bronchiolo-alveolar cell carcinoma

- Unusual and by definition non-invasive variant of adenocarcinoma, least strong association with smoking or extrapulmonary manifestations
- Non-invasive, but aerogenous spread in the lung makes them frequently inoperable owing to multifocality
- Mucinous and non-mucinous variants
at late stage you will see a lung that is completely consolidated
mucin

BAC cells, basally oriented nuclei, mucin in the cytoplasm

BAC cell can become detached from other cells and spread to other parts of the lung
BAC does not metastasize but it can become multifocal in the lung.
Large cell carcinoma

• Lacks glandular differentiation or mucin production (adenocarcinoma)
• Lacks intercellular bridges or cytoplasmic keratinization (squamous cell)
• May have neuroendocrine features
large cell carcinoma, cannot tell by gross exam that this is large cell carcinoma, need to do microscopic exam

if see peripheral nodules more likely to be adenocarcinoma but do not know for sure
histologically we see that the cells are pleomorphic but do not have characteristics of adenocarcinoma or squamous cell carcinoma so we call it large cell carcinoma
Pulmonary carcinoid tumors

• Generally **low grade** neuroendocrine malignancies classically presenting in the airways, often in **younger patient population and unrelated to smoking**

• **Unlike gastrointestinal carcinoid tumors** unlikely to result in the carcinoid syndrome which has to do with catecholamine production and flushing in the patients
tend to have nested pattern of small low grade tumor cells, these cells derive from neuroendocrine cells in the walls of the bronchus
patients may develop cough or wheeze or pneumonia due to obstructed bronchus
BRONCHIAL TUMORS

• Same histologic classification as tumors of major and minor salivary glands, but are arising in bronchi
• Adenoid cystic carcinoma
• Mucoepidermoid carcinoma
• Acinic cell carcinoma
• Younger patient population with symptoms relating to endobronchial obstruction
example of adenoid cystic carcinoma, take home point is that any tumor that can arise in the major and minor salivary glands in the head and neck can arise in the bronchi
Asbestos-associated diseases

- benign pleural disease: effusions, plaques, fibrosis
- pulmonary fibrosis (asbestosis)
- mesotheliomas
- cocarcinogen with cigarette smoke in the development of bronchogenic carcinoma

asbestos and smoking work synergistically to produce cancer, 55 fold increase in risk

no role of smoking in mesothelioma
Malignant Mesothelioma

- Rare tumor, increasing incidence
  3000-4000 new cases/year
- Tumor grows along serosal surfaces:
  pleura, pericardium, peritoneum,
  tunica vaginalis testis
- Strong association with asbestos
  exposure, NOT tobacco
Pleural Mesothelioma

• Grows as rind around lung along fissures, invades chest wall and mediastinum

• approach is surgical. Rad Extrapleural pneumonectomy, poor response to therapy.

(can look this up on google if interested, unfortunately most ppl with this cancer succumb to the disease)
cancer growing down the fissures

diffuse rind of mesothelioma surrounding the lung
Ribs up here

Mesotheliomas tend to originate in the parietal pleura

Tumor on pleura

Lung down here
excision of pleura, tumor tends to form a carpet of nodules all over the surface
metastases into lymph nodes

rind of tumor around the lung
Mesothelioma, role of asbestos:

- Plaques: hallmark of asbestos exposure in over 70%
- Asbestosis in 20% (increased tissues asbestos levels with associated interstitial fibrosis)
80% of mesotheliomas associated with asbestos

mesothelioma cells

macrophage with asbestos body
nodule of tumor on the surface of the lung
mesotheliomas can form gland like structures and papillae and can look like adenocarcinomas
Diagnostic Elements in Malignant Mesothelioma

- Gross distribution of tumor
- H&E
- Histochemistry: mucins and glycoproteins
- Immunohistochemistry
- Electron microscopy
mesotheliomas will have these long surface microvilli, this is a diagnostic feature
mesothelioma can occur anywhere there is a serosal membrane, this is late stage peritoneum mesothelioma, see gut epithelium trapped by the tumor, this type of mesothelioma is associated with high exposure to asbestos.
The lung and metastatic disease

- Metastasizes to: lung, regional nodes, sbones, brain, liver, adrenals
- Receives hematogenous and lymphatic metastases from breast, GI, sarcomas, H/N melanoma
- Mucinous lung primaries also spread aerogenously within lung
this is probably from metastasis rather than infiltrative lung cancer

hematogenous metastases often favor the lower lobes because of more perfusion
late stage metastases from the colon

breast, melanoma, and gastrointestinal metastases are most common seen at Duke
Benign tumors

- Most common in the lung is the hamartoma; a benign but abnormal proliferation of mesenchymal elements (cartilage, connective tissue and fat) normally present within that particular site.
completely benign, just abnormal growth
not cancer, a piece of fly ash