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Derivation of Lung Epithelium from Human Cord Blood-derived Mesenchymal Stem Cells (Sueblinvong V et al; Am J Respir Crit Care Med 2008; 177:701-711)

Background: In 1999 a national PAP registry was established in Japan.

Objective: To describe the epidemiology and baseline clinical and laboratory features of primary PAP in a large contemporaneous cohort of patients at the time of enrollment into the registry.

Methods: This study was conducted by the Japanese PAP Research Network through multiple referral centers encompassing all of Japan. Between July 1999 and July 2006 248 individuals diagnosed with PAP were enrolled in the study. All individuals with previously diagnosis of PAP were included in the study to assess prevalence. Diagnostic criteria included characteristic findings on HRCT of the chest, confirmed by cytology or pathology specimens (BAL fluid alone (58.7%), BAL plus transbronchial biopsy (34.1%), VATS biopsy (7.2%)). Patients were assessed for multiple parameters including pulmonary function tests, GM-CSF autoantibody level and arterial blood gas measurement. Disease severity was scored from 1 (asymptomatic with PaO2at or above 70 mmHg) to 5 (severe, PaO2 less than 50 mmHg).

Results:

- Of 248 patients enrolled in the PAP registry, 90% had auto-antibodies to GM-CSF and were considered as primary autoimmune PAP.
- The estimated incidence and prevalence of autoimmune PAP in Japan is 0.49 and 6.2 cases per million respectively.
- Two thirds of patients were men.
- Mean age at diagnosis 51 years.
- The disease is rare in children.
- Mean duration of symptoms at enrollment was 10 months.
- One third of individuals were asymptomatic (equal gender distribution). These individuals were picked up on routine health screening programs in which chest radiographs were performed (school entry, government employees and registered corporations).
- 43% of individuals were never smokers (24% of men, and 83% of women).
- Dust exposure reported in 26% (32% of men, and 13% of women).
- No familial cases.
- There was no correlation between disease severity and anti-GM-CSF antibody titer.
- Lung volumes (FVC% and VC%) and airflow (FEV1/FVC) were normal in all patients except those in disease severity category 5.
- Gas transfer (diffusing capacity of carbon monoxide) was the only significantly abnormal pulmonary function test.
- Intercurrent medical illness in 35% (see table 4 in paper).
• Concomitant pulmonary infection uncommon (4 pulmonary aspergillosis, 3 AMB, 2 MTB, no cases of Norcardia identified).

Conclusion: A lot of data on PAP in the Japanese population packed into this paper!


Background: Mutations in the ABCC3 gene (which codes a lipid transporter on the limiting membrane of lamellar bodies in alveolar type II cells) are a cause of fatal surfactant deficiency in newborns and chronic interstitial lung disease in children.

Methods: Review of the medical records of nine children with ABCC3 gene mutations evaluated at Texas Children’s Hospital between 1992 and 2005. Clinical data on each patient was extracted, and all radiology studies and pathology specimens were re-examined.

Characteristics of the nine children with ABCC3 mutations:

Pathology of the biopsy specimens:

3. Surfactant in Airway Disease (Goran Enhorning, Chest 2008; 133: 975-980)

Overview: Who remembers the Law of Laplace? This paper reviews the physical properties of surfactant, reiterating in glorious detail how surfactant prevents alveolar collapse by decreasing surface tension at the air-moisture interface as alveolar radius diminishes with exhalation. But wait! … there’s more … surfactant appears to play a significant role in maintaining small airway patency as well.

If surfactant phospholipids are deficient in the small conducting airways, the pressure of moisture in the narrow airway section will be less than what it is in the wide section. This will cause moisture to move from the wide airway to the narrow airway, which eventually might become blocked. If enough surfactant is present, the molecules come into close approximation at end-expiration, which lowers surface tension and will prevent liquid from moving into narrow airway sections.

Conventional treatments for asthma (B adrenergic agonists and steroids) accelerate surfactant synthesis in addition to relaxing smooth muscle and modulating inflammation. This action may be a significant but underappreciated effect. The article highlights how surfactant research may reap future benefits in asthma therapy.

Objective: To compare proliferation markers Ki-67 and repp86 in benign versus malignant mesothelial proliferations.

Method: 36 cases of proven malignant mesothelioma (25 epithelioid, 10 mixed and 1 sarcomatoid) and 22 cases of reactive mesothelial proliferation from the files of a respiratory referral hospital in Tehran from 1999 to 2004.

Results:

Comments:


Background: A series of basaloid carcinomas (BC) comparing the survival and clinical features with non-basaloid NSCLC (non-BC).

Method: Of a total of 1418 NSCLC resected at a single institution over a 24 year period (January 1979 to December 2003) 90 were diagnosed as basaloid carcinomas (Drs Brambilla and Lantuejoul), for an overall prevalence of 6.3%. 36 of the 90 were previously reported in their 1992 paper. 46 of the 90 were large cell basaloid carcinomas, and 44 were basaloid variants of squamous carcinomas. Large cell neuroendocrine carcinomas were excluded from the control group of NSCLC. Comparison was made on a number of parameters including tumour stage, age, sex, procedure type, and survival.

Results: There was no significant difference between basaloid and non-basaloid NSCLC groups for sex, tumour laterality, type of operation, T stage or Charlson comorbidity index. Median survival for BC was 36 months, and for non-BC was not reached at 5 years, with % survival over 5 years 33% for BC and 51% for non-BC. BC was associated with greater tobacco consumption. There was no difference in survival between basaloid large cell carcinoma and basaloid squamous carcinoma. (see Tables 1 and 2 in the paper).

Conclusion: This study supports basaloid NSCLC as more aggressive neoplasms compared to non-basaloid NSCLC (excluding LCNEC).

Articles for Brief Mention
Thyroid transcription factor-1 expression in ovarian epithelial neoplasms (Kubba LA, et al. Modern Pathology, 2008; 21, 485-490)

Serous, endometrioid and clear cell ovarian carcinomas may be nuclear TTF positive.

TTF-1 immunoreactivity evaluated in primary ovarian epithelial neoplasms using:

Microarrays (MD Anderson Cancer Center);
- 138 ovarian serous carcinomas (none positive)
- 65 endometrioid carcinomas (2/65 positive - one case diffusely positive)
- 35 mucinous adenocarcinomas (none positive)
- 30 mucinous neoplasms of low malignant potential (none positive)
- 10 clear cell carcinomas (none positive)

Whole tissue sections (34 consecutive cases, Royal Group of Hospitals Trust, Belfast);
- 19 serous carcinomas (7/19 positive - 6 focal only, 1 diffusely positive)
- 5 endometrioid carcinomas (1/5 focally positive)
- 7 mucinous carcinomas (none positive)
- 3 clear cell carcinomas (1/3 diffusely positive).

Pulmonary Manifestations in Patients with POEMS Syndrome (Allam, JS, et al. Chest, 2008;133:969-974)

The range of pulmonary manifestations of POEMS syndrome includes respiratory muscle weakness/restrictive lung disease, pulmonary hypertension and low DLCO.

A retrospective medical record review of 137 patients with POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) from Mayo Clinic Rochester over a 28 year period between 1975 and 2003. Respiratory symptoms identified in 28%. 32/137 pts had PTFs in the first 2 years of diagnosis, of which 75% were abnormal, the most common abnormalities being a restrictive pattern and decreased diffusion capacity (DLCO). 59% of pts tested for maximal respiratory pressure were found to have significant respiratory muscle weakness, which was correlated with decreased survival. History of cough also correlated with decreased survival. None of 50 patients having CT scans of “chest of abdomen” were reported to have any parenchymal lung abnormalities (CT resolution and number with chest exams not stated). Pulmonary hypertension was demonstrated in 12 of 25 patients who underwent echocardiogram within the first two years of diagnosis (none with pulmonary embolism).


Langerin was focally positive in 2/10 histiocytic sarcomas. Langerin appears to be slightly more sensitive and less specific than CD1a in the setting of Non-pulmonary LCH.
17 cases of LCH (including one from the lung) and 64 cases of various non-Langerhan’s histiocytic disorders (files of City of Hope National Medical Center and consultation files of Lawrence Weiss) were immunostained for Langerin and CD1a. All of the LCH cases were positive for Langerin (membrane and granular cytoplasmic staining of over 75% of lesional cells in all cases) and CD1a, with the exception of one case that was negative for CD1a but demonstrated Birbeck granules on EM. Of the 64 non-Langerhans histiocytic disorders (7 monocyte/macrophage hemophagocytic syndrome, 4SHML, 8 AML, 7 AMML, 10 CMML, 10 histiocytic sarcoma, 5 juvenile xanthogranuloma, 5 interdigitating dendritic cell tumour and 8 follicular dendritic cell tumour) 2 of the histiocytic sarcomas stained for Langerin (in less than 5% of the lesional cells), and all cases were negative for CD1a. The authors note that CD1a is not entirely specific for LCH as other investigators have observed positive reactions in JXG, SHML, and histiocytic sarcoma.

Serodiagnosis of Mycobacterium avium-Complex Pulmonary Disease Using an Enzyme Immunoassay Kit (Kitada S, et al. Am J Respir Crit Care Med 2008; 177:793-797)

The authors have developed an immunoassay for serological diagnosis of MAC based upon an IgA antibody to a glycoprotein core antigen on the MAC cell wall. A Japanese multicenter study testing serum from 70 confirmed cases of fibrocutaneous or nodular-bronchiectatic MAC pulmonary disease, 18 with MAC contamination (defined as a single positive sputum with no radiological evidence of disease), 36 pulmonary tuberculosis, 45 other pulmonary diseases, and 65 healthy subjects. Based on results of this study at a cut off set at 0.7 U/ml, the assay sensitivity was 84% and specificity was 100%. Such an assay may prove useful as an adjunct to biopsy cases where the morphology suggests MAC but sputum and/or bronchoscopic cultures are negative. The current data does not address other MAC related disease that may come to the attention of the Pathologist, such as equivocal cases of hypersensitivity pneumonitis.


The title of this paper caught my eye, so I had to read it! To me, the two images of urine cytology that were provided are largely unconvincing. There are no ancillary studies to support the contention that the atypical cells identified in the urine derive from metastatic lung carcinoma, and the clinical and pathological work ups in the five cases are incomplete as described. In four of five cases, a history of chemotherapy preceeding the abnormal urine cytology is described.

A Comparison of Survival and Disease-specific Survival in Surgically Resected, Lymph Node–positive Bronchioloalveolar Carcinoma Versus Nonsmall Cell Lung Cancer (Varlotta JM, et al. Cancer 2008; 112:1547-54)
This study finds that BAC patients with either N1 or N2 lymph node status are significantly less likely to have poorly differentiated or undifferentiated tumors than patients with non-BAC cancers with comparable lymph nodes status. *How can we expect our clinical colleagues to understand current terminology of lung cancer pathology if it is seemingly beyond the editors of “Cancer”?*


* A high degree of genetic concordance is found between the two components of five out of six cases of combined small cell carcinoma/large cell neuroendocrine carcinoma.*

In this study (University of Parma and Milan School of Medicine Italy) the authors microdissect the phenotypically distinct small cell carcinoma and large cell neuroendocrine carcinoma components of 6 cases of combined SCLC/LCNEC for DNA extraction and genetic analysis. Details of the genetic analysis and interpretation of the data are beyond my ability to comment upon. According to the authors, there was a high degree of genetic concordance between the two components in five of six cases, ranging from 82 to 100% of all informative chromosomal regions investigated, supporting the hypothesis of a monoclonal carcinogenesis mechanism, with tumor cells of the two components deriving from a common precursor undergoing divergent differentiation.