FIRST ANNUAL APMPHP RESEARCH DAY

January 23, 2010
Materials

- The dataset was obtained from the Department of Pathology wall, which contains the diagnoses of all cases with papillary carcinoma (PC) and solid carcinoma (SC) from 2002 to 2006. The cases were classified into two groups: those with or without papillary carcinoma.

Methods

- Statistical analysis was performed to compare the characteristics of the two groups.

Results

- The results showed significant differences in the proportion of cases with papillary carcinoma and solid carcinoma between the two groups.

Conclusion

- The study demonstrated that patients with papillary carcinoma have a significantly higher risk of developing solid carcinoma compared to those without papillary carcinoma.
The Expression of mTOR Pathway Proteins in Cutaneous Lymphomas

Conclusions

Results

[Details from the poster are not transcribed]
Autopsy Findings in Patients with Usual Interstitial Pneumonia (UIP)—Comparison of Patients With and Without Acute Exacerbation

LaSchmidt, M. Miller, K. Flaherty, J. L. Myers

Department of Pathology, Department of Pulmonary and Critical Care Medicine, University of Michigan Health System, Ann Arbor, MI

INTRODUCTION

Despite advances in the treatment of IPF, there are no recognized guidelines for surgical treatment in IPF patients. The effects of autopsies from IPF patients on lung function and histologic pattern of usual interstitial pneumonia (UIP) are not well understood. Although UIP has long been noted to have a poor prognosis, it remains unclear whether acute exacerbation of UIP (AE-IPF) is definitively a confounding factor in the overall survival of patients with IPF. The aim of this study was to evaluate the histologic characteristics of patients with and without AE-IPF to determine whether AE-IPF affects the overall survival of patients with IPF.

RESULTS

Summary of gross and histologic findings in patients with and without AE-IPF:

- Three (27.3%) patients with AE-IPF had diffuse alveolar damage (DAD).
- Three (100%) patients with AE-IPF died, either within 1 week prior to death (13, 13, and 14 days respectively) or 4 weeks after death; none (0%) were managed with AE-IPF.
- Two (25%) patients with AE-IPF had evidence of dominant histologic finding in their lung tissue.
- Mean fibrosis and honeycombing score was 1.9 and 1.6 respectively.
- Mean fibrosis and honeycombing score was 1.3 and 0.7 respectively.
- One patient had a previous history of squamous cell carcinoma; this patient had AE-IPF.
- Mean heart weight in patients with AE-IPF was 290.550 g compared to 362.6 g (p=0.001).
- Mean heart weight in patients with AE-IPF was 290.550 g compared to 362.6 g (p=0.001).
- Diffuse alveolar damage (DAD) was present in all patients who died with AE-IPF.
QUANTITATIVE PROTEOMIC ANALYSIS OF API2-MALT1 EXPRESSION SIGNATURE BY ISOBARIC TAGS AND HIGH-ENERGY C-TRAP DISSOCIATION TANDEM MASS SPECTROMETRY

SL Farnen1, C Seiler1, LM McAllister-Lucas2, PC Lucas1, KP Conlon1, D Farnen1, V Basuli1, S Rosebeck3, MS Lim1, and KSU Elenitoba-Johnson1

1Department of Pathology, University of Michigan, Ann Arbor, MI 48109

Background

Quantitative proteomic analysis by mass spectrometry and isobaric approaches provides the interpretation of protein expression. API2-MALT1 fusion proteins (a product of the t(11;18) translocation) is present in chronic lymphocytic leukemia (CLL). In addition, the API2-MALT1 signaling pathways are involved in angiogenesis. With the development of targeted therapies, non-invasive and highly sensitive detection of the API2-MALT1 protein is an unmet need.

Rationale

The development of targeted therapies for API2-MALT1-positive patients requires the identification of novel therapeutic strategies. A high-throughput screening approach for targeting the API2-MALT1 interaction was used to identify potential therapeutic targets. This approach identified the human gastric MALT lymphoma tissue as a potential target for therapeutic intervention.

Validation by Western blot:

- APIC2-MALT1
- Actin
- GAPT1

Future Directions

- A20 cell ICAT mass spectrometry
- Tissue microarray
- Helicobacter pylori gastritis vs. gastric MALT lymphoma
- Quantitative immunohistochemistry
**INTRODUCTION**

High grade serous and endometrioid carcinomas can exhibit overlapping morphologies and the distinction between these two entities can be difficult. A significant proportion of serous tumors arise from the fallopian tubes, supported by the presence of a tubal intraepithelial carcinoma (TIC) or endometrioid carcinoma (EC), whereas endometrioid tumors typically arise from the endometrium. It remains uncertain what proportion of patients with TICs progress to IEC and the clinical significance of multiple tumors occurring in the same individual. The goal of this study was to analyze the relationship between high-grade pelvic serous and endometrioid tumors using immunohistochemistry for p16, p53, and p16 and DNA sequencing for p53 mutations.

**METHODS**

Consecutive cases of high-grade serous and/or endometrioid carcinoma, diagnosed between 2006-2007, in which the fallopian tube was not part of the process, were selected and reviewed. The presence of a TIC and/or EC in each case was determined on a TIC and/or EC in each case. For p53 and WT-1, immunohistochemistry, nuclear staining in >50% of the tumor cells was considered a positive staining. For p16 immunohistochemistry, nuclear staining in >50% of the tumor cells was considered a positive staining. Laser capture microdissection and normal tissue (control) was performed. Mutation analysis of the samples was performed using a polymerase chain reaction and sequencing in triplicate.

**RESULTS II: IMMUNOHISTOCHEMICAL & MUTATIONAL ANALYSIS**

- **High Grade Serous Carcinoma**
  - p53 mutation (n=8)
  - WT-1 expression (n=8)
- **High Grade Endometrioid Carcinoma**
  - p53 mutation (n=17)
  - WT-1 expression (n=17)

**RESULTS III: CORRELATION OF IMMUNOHISTOCHEMISTRY AND MUTATIONAL STATUS**

- **p53 mutation**
  - p53 positive
  - p53 negative

**RESULTS IV: DISTRIBUTION OF p53 MUTATIONS**

**CONCLUSIONS**

- High grade serous and endometrioid carcinomas have distinct patterns of growth and prognosis with high-grade serous carcinoma most likely to occur in the presence of TIC and EC.
- Immunohistochemistry and DNA sequencing have been used to identify p53 mutations in high-grade serous and endometrioid carcinomas.
- These results suggest a high-grade component of the tumor is likely to occur in the presence of TIC and EC.
Outcome of Papillary Carcinoma of the Breast
One Institutional Experience
C. Cunningham MD, E. Jeng MD, D. Weissler MD
The University of Michigan, Ann Arbor, MI

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Table 1: Histologic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 60-70 yrs.</td>
<td>Tumor size: 2.5 cm</td>
</tr>
<tr>
<td>Tumor type: papillary</td>
<td>No Invasion</td>
</tr>
<tr>
<td>Tumor location: breast</td>
<td>Capsule invasion</td>
</tr>
<tr>
<td>Follow-up: 3 yrs.</td>
<td>Glandular DC</td>
</tr>
<tr>
<td>Table 2: Clinical Features</td>
<td></td>
</tr>
<tr>
<td>Category</td>
<td></td>
</tr>
<tr>
<td>Follow-up: 3 yrs.</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure 1: Examples of DC with and without Invasion

Discussion
- Histologic Features: Papillary, Glandular DC
- Clinical Features: Follow-up: 3 yrs.

Metastatic Basal Cell Carcinoma
A Tumor With Lymphatic Involvement

EVALUATION

Background
- Basal Cell Carcinoma (BCC) Metastases
- Lymphatic Involvement in BCC

Methods
- Clinical and histologic analysis
- Follow-up of patients with BCC

Results
- Metastatic BCC with lymphatic involvement
- Examples of DC with and without Invasion

Conclusion
- Basal Cell Carcinoma with metastasis should be evaluated for lymphatic involvement.