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ARTICLES FOR NOTATION – NONNEOPLASTIC


ARCHIVES SPECIAL SECTION - 2016 MAYO CLINIC PATHOLOGY UPDATE: A TRIBUTE TO THE CAREER OF THOMAS V. COLBY, MD


CASE REPORTS


ARTICLES FOR DISCUSSION


Background:
- Severe asthma (SA), also referred to as therapy-resistant asthma, as defined by the European Respiratory Society/American Thoracic Society guidelines is asthma
  - that requires high-dose inhaled/oral corticosteroids (CS) with an additional controller medication to maintain control, or
  - that remains uncontrolled despite exhaustive therapy
- The histologic changes, particularly at the level of the distal airways are unknown

Methods
- This study describes the clinical, radiologic, and histologic characteristics of 29 SA patients who underwent video-assisted thoracoscopic surgery lung biopsy
- Pathologic observations were correlated with clinical features, especially the presence of autoimmune disease (AID) (15/29, 51.7%)

Results
- Ten biopsies (34.5%)
  - small airway manifestations of asthma
- Nineteen biopsies (65.5%)
  - asthmatic granulomatosis
    - asthmatic bronchiolitis and
    - alveolar septal mononuclear infiltrates with non-necrotizing granulomas
- SA patients without asthmatic granulomatosis
  - showed more striking small airway injury, subbasement membrane thickening, and neutrophilic infiltrates
- Cases with concurrent AID
  - had a tendency to more parenchymal eosinophilic inflammation,
  - more bronchiolocentric granulomas, and
  - a suggestion of increased responsivity to nonsteroidal immunosuppressive therapy

Discussion
- Histologic examination of video-assisted thoracoscopic surgery lung biopsies in SA demonstrates diverse pathologies including
  - cases associated with granulomatous inflammation
  - in addition to eosinophilic infiltrates
FIGURE 2. SA manifesting as AG (SA-AG) showing patchy mononuclear cell infiltrates associated with an ill-defined, poorly formed non-necrotizing granulomas, containing lymphocytes, histiocytes, and giant cells, located in the interstitium (A, B) and with bronchiolocentric in SA-AG with concurrent AID (SA-AG-AID) (C, D) (hematoxylin and eosin).
Objective:
- To report 12 lung NE tumors
  - with morphologic features of carcinoid tumor but
  - with mitotic count >10/2mm² are reported

Results:
- Clinical features
  - 7 males and 5 females
  - Age ranging from 56 to 78 years
  - 4 never-smokers
- Histologic findings
  - All tumors showed architectural and cytomorphologic features of carcinoid tumor
  - Mitotic count ranged from 11 to 61/2mm²
  - Punctate-type necrosis was present in 8 tumors
  - One tumor occurred in the background of DIPNECH
- Treatment and prognosis
  - All tumors were treated by resection
  - All but 1 patient subsequently developed metastasis
  - 7 died of the tumor
  - For metastatic tumors
    - 4 patients were treated by platinum-based chemotherapy with no apparent response, whereas
    - 3 other patients were treated by combined capecitabine and temozolomide - novel chemotherapy for well-differentiated neuroendocrine tumor/carcinoid tumor - 2 of them responded

Discussion
- This subset of tumor would be classified as large cell neuroendocrine carcinoma according to the current WHO classification scheme, but their clinical and pathologic features appear to have more in common with the carcinoid tumor group than large cell neuroendocrine carcinoma
- Identification of this subset may be relevant for further therapeutic management.
FIGURE 1. Predominantly endobronchial tumor (case 5) (hematoxylin and eosin stain).

FIGURE 2. Uniform polygonal cells with abundant amphophilic granular cytoplasm, round nuclei, and salt and pepper chromatin. Two mitotic figures are seen (hematoxylin and cosin stain).

Background:
- The current WHO classification of lung cancer states that a diagnosis of SCLC can be reliably made on routine histological and cytological grounds but immunohistochemistry (IHC) may be required, particularly
  - In cases in which histologic features are equivocal and
  - In cases in which the pathologist wants to increase confidence in diagnosis
- However, reproducibility studies based on hematoxylin and eosin–stained slides alone for SCLC versus large cell neuroendocrine carcinoma (LCNEC) have shown pairwise k scores ranging from 0.35 to 0.81
- This study examined whether judicious use of IHC improves diagnostic reproducibility for SCLC.

Methods:
- Nineteen lung pathologists studied interactive digital images of 79 tumors, predominantly neuroendocrine lung tumors
- Images of resection and biopsy specimens were used to make diagnoses
  - solely on the basis of morphologic features (level 1)
  - morphologic features along with requested IHC staining results (level 2), and
  - all available IHC staining results (level 3)

Results:
- Rate of agreement for 19 pathologists reading all 79 cases:
  - level 1 - 64.7%
  - level 2 - 73.2%
  - level 3 - 77.5%
- With IHC, k scores for four tumor categories (SCLC, LCNEC, carcinoid tumors, and other) increased in resection samples from 0.43 to 0.60 and in biopsy specimens from 0.43 to 0.64.

Conclusions:
- Diagnosis using hematoxylin and eosin staining alone showed moderate agreement among pathologists in tumors with neuroendocrine morphology, but agreement improved to good in most cases with the judicious use of IHC, especially in the diagnosis of SCLC
- An approach for IHC in the differential diagnosis of SCLC is provided.
### Table 4. IHC Stains in Differential Diagnosis of SCLC

<table>
<thead>
<tr>
<th>Differential</th>
<th>IHC (types)</th>
<th>SCLC</th>
<th>Other Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pro-SCLC</td>
<td>Cytokeratin</td>
<td>Dotlike cytoplasmic staining in SCLC</td>
<td>Diffuse cytoplasmic staining does not exclude SCLC but is also found in LCNECs and otherSqCCs, crushed carcinoids, metastatic carcinoma</td>
</tr>
<tr>
<td></td>
<td>MB1/Ki67</td>
<td>50% of the nuclei are positive</td>
<td>&gt;50% also in LCNEC, e.g. metastases CRC; &lt;25% in carcinoid</td>
</tr>
<tr>
<td></td>
<td>TTF1</td>
<td>Positive in 90% of SCLCs$^a$</td>
<td>Lack of TTF1 may be present in LCNEC and in many carcinoids</td>
</tr>
<tr>
<td></td>
<td>CD56</td>
<td>Membranous abundant staining in 98%</td>
<td>Lack of membranous staining fits with many other Dx (e.g. LCNEC)</td>
</tr>
<tr>
<td></td>
<td>Chromogranin A</td>
<td>Focal positivity in occasional tumor cell, sensitivity 46%-90%</td>
<td>If strong diffuse staining, consider carcinoid; if focal or diffuse staining, few NSCLCs, nonepithelial tumors; negative staining fits with many other Dx</td>
</tr>
<tr>
<td></td>
<td>Synaptophysin</td>
<td>Focal or diffuse staining, sensitivity 100%</td>
<td>Focal or diffuse staining, few NSCLCs, nonepithelial tumors; negative staining fits with many other Dx</td>
</tr>
<tr>
<td></td>
<td>p16</td>
<td>Nuclear staining 95%-100%</td>
<td>Nuclear staining in LCNEC in 95%. Lack of p16 positivity fits with many other Dx (e.g., NSCLC [also with NE staining])</td>
</tr>
<tr>
<td></td>
<td>pRb</td>
<td>Negative in SCLC</td>
<td>LCNEC positive or negative, AC positive</td>
</tr>
</tbody>
</table>

Differential diagnostic stains depending of cytokeratin

**Negative cytokeratin stain result**

- Vimentin: Negative in SCLC
  - Positivity supports Dx other than carcinoma but also sarcomatoid carcinoma
- CD45: Negative in SCLC
  - Positivity supports non-Hodgkin’s lymphoma$^a$
- CD99: Negative in SCLC
  - Positivity supports Ewing sarcoma
- S100: Negative in SCLC
  - Positivity supports melanoma

**Positive cytokeratin result**

- p40: Negative in SCLC
  - Positivity supports$^b$ (basaloid) SqCC, metastases of SqCC
- ER, PR: Negative in SCLC
  - Positivity supports metastatic breast carcinoma
- PSA: Negative in SCLC
  - Positivity supports metastatic prostate carcinoma
- p63: Occasionally focally positive in SCLC
  - Focal positivity may be present in LCNEC, carcinoid; positivity in >80% of nuclei favors SqCC.
- OTP: Negative in SCLC
  - Positive in typical carcinoid
Flow Diagram Neuroendocrine Lung Cancer

Tumor fields

Cytoplasm

Minimal

In between

Moderate / Abundant

Nucleus

Moulding ++
Dense chromat	n
Nucleoli -/±

Pleomorphic nuclei
Vesicular chromat	n
Nucleoli ++ / ±

Monotonous nuclei
Dense chromat	n
Nucleoli -/±

Architecture

High cell density
Necrosis ++/±

Yes

Yes

Yes

Yes

Carcinoid

Dot necrosis

No

No

No

No

No

Mitoses

Mitoses ++
Ki67 high

Mitoses high
Ki67 >25

Mitoses high
Ki67 >25

<2

2-10

>10

SCLC

LCNEC

SCLC

LCNEC

SCLC

SCLC

SCLC

SCLC

SCLC
Background:
- High-grade neuroendocrine carcinomas and carcinoids can arise in different sites such as lung, gastrointestinal tract, prostate, and skin
- Classic neuroendocrine markers such as CD56, synaptophysin, and chromogranin cannot distinguish carcinoids from high-grade neuroendocrine carcinomas
- Recently, mouse monoclonal mASH1 has been shown to help discriminate carcinoids from high-grade neuroendocrine carcinomas in various neoplastic sites
- To date, there have been no comprehensive immunohistochemistry studies with mASH1 on nonneuroendocrine neoplasms.

Objective:
- To evaluate the specificity and sensitivity of mASH1 in various normal and neoplastic tissues, including lung cancers.

Design:
- Formalin-fixed, paraffin-embedded tissue microarrays consisting of normal tissues and various neoplastic tissues were immunohistochemically evaluated with mASH1.

Results:
- In lung cancers, mASH1 stained
  - 1.1% (1 of 93) of adenocarcinomas,
  - 0.9% (1 of 111) of squamous cell carcinomas,
  - 0% (0 of 30) of large cell carcinomas,
  - 66.7% (6 of 9) of large cell neuroendocrine carcinomas, and
  - 82.5% (94 of 114) of small cell carcinomas.
- In various other neoplastic tissues (n = 1114), mASH1 was expressed in thyroid medullary carcinomas, thymic carcinomas, and brain cancers; mASH1 was also expressed in a very low percentage of breast carcinomas, ovarian cancers, and pancreatic neuroendocrine tumors
- All typical carcinoids of various sites were negative (0 of 11), however, in lung atypical carcinoids, mASH1 was expressed in 42.9% (9 of 21).

Conclusions:
- Although not organ specific, mASH1 is highly specific for high-grade neuroendocrine carcinomas versus carcinoids and other non-neuroendocrine neoplasms.
Figure 1. mASH1 staining in lung cancers. A, Large cell neuroendocrine carcinoma. B, Stage 4 small cell lung cancer (original magnification x20).

Table 3. mASH1 Staining in Non–Small Cell Lung Carcinoma (n = 268)

<table>
<thead>
<tr>
<th>Lung Cancer</th>
<th>No. Positive/Total</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>1/93</td>
<td>1.1</td>
</tr>
<tr>
<td>Squamous cell</td>
<td>1/111</td>
<td>0.9</td>
</tr>
<tr>
<td>Classic large cell</td>
<td>0/30</td>
<td>0.0</td>
</tr>
<tr>
<td>Large cell neuroendocrine carcinoma</td>
<td>6/9</td>
<td>66.7</td>
</tr>
<tr>
<td>Typical carcinoid</td>
<td>0/4</td>
<td>0.0</td>
</tr>
<tr>
<td>Atypical carcinoid</td>
<td>9/21</td>
<td>42.9</td>
</tr>
</tbody>
</table>

Table 4. mASH1 Staining in Small Cell Lung Cancer (n = 114)

<table>
<thead>
<tr>
<th>Stage</th>
<th>No. Positive/Total</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–4</td>
<td>94/114</td>
<td>82.5</td>
</tr>
<tr>
<td>1–3 (limited stage)</td>
<td>63/79</td>
<td>79.7</td>
</tr>
<tr>
<td>4 (extended stage)</td>
<td>31/35</td>
<td>88.6</td>
</tr>
</tbody>
</table>

Background:
- The Blueprint Programmed Death Ligand 1 (PD-L1) Immunohistochemistry (IHC) Assay Comparison Project
  - is an industrial-academic collaborative partnership
  - to provide information on the analytical and clinical comparability of four PD-L1 IHC assays used in clinical trials

Methods:

Analytical Performance Comparison
- A total of 39 NSCLC tumors were stained with four PD-L1 IHC assays (22C3, 28-8, SP142, and SP263), as used in the clinical trials
- Three experts in interpreting their respective assays independently evaluated the percentages of tumor and immune cells staining positive at any intensity

Clinical Diagnostic Performance Comparison
- No actual patient clinical outcome data were available for these 39 cases
- Clinical diagnostic performance was assessed through comparisons of patient classification above and below a selected expression cutoff
- Although several cutoffs relating to levels of PD-L1 expression have been used in clinical trials, for this study the companies submitted a single clinical cutoff for inclusion in this comparative analysis
  - 1% TC staining for the 28-8 and 22C3 assays
  - 25% TC staining for the SP 263 assay
  - 1% TC staining and/or 1% tumor area infiltrated by PD-L1–positive ICs for the SP142 assay

| Table 1. PD-L1 Assay Systems Used in the Blueprint Project |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Agent                           | Nivolumab       | Pembrolizumab   | Atezolizumab    | Durvalumab      |
| Primary antibody clone used in the assay system | 28-8 (Dako) | 22C3 (Dako) | SP142 (Ventana) | SP263 (Ventana) |
| Interpretive scoring            | Tumor cell membrane | Tumor cell membrane | Tumor cell membrane | Tumor cell membrane |
| Instrument and detection systems required | EnVision Flex on AutostainerLink 48 | EnVision Flex on AutostainerLink 48 | OptiView detection and amplification on Benchmark ULTRA | OptiView detection on Benchmark ULTRA |
| Therapeutic developer           | Bristol-Myers Squibb | Merck | Genentech | AstraZeneca |
Results:

**Analytical Performance Comparison**
- Analytical comparison demonstrated that the percentage of PD-L1–stained tumor cells was comparable when the 22C3, 28-8, and SP263 assays were used, whereas the SP142 assay exhibited fewer stained tumor cells overall.
- The variability of immune cell staining across the four assays appears to be higher than for tumor cell staining.

**Clinical Diagnostic Performance Comparison**
- Nineteen of the 38 cases (50.0%) were above the cutoffs utilized by all four assays, meaning that clinical PD-L1 positivity would be concordant regardless of the assay used.
- Five of 38 (13%) samples were determined to be below the cutoff regardless of the assay used.
- Fourteen cases (37%) showed discordance between clinical levels of PD-L1 expression, so a different PD-L1 classification would be made depending on which assay/scoring system was used.
Conclusions:

Analytical Performance Comparison
- The Blueprint PD-L1 IHC Assay Comparison Project revealed that three of the four assays were closely aligned on tumor cell staining whereas the fourth showed consistently fewer tumor cells stained.
- All of the assays demonstrated immune cell staining, but with greater variability than with tumor cell staining.

Clinical Diagnostic Performance Comparison
- By comparing assays and cutoffs, the study indicated that despite similar analytical performance of PD-L1 expression for three assays, interchanging assays and cutoffs would lead to “misclassification” of PD-L1 status for slightly more than a third of patients.

Introduction:
- Spread through air spaces (STAS) has not yet been characterized in squamous cell carcinoma (SCC).

Methods:
- The authors reviewed 445 resected stage I to III lung SCCs and investigated the clinical significance of STAS.
- Cumulative incidence of recurrence and lung cancer–specific death were evaluated b

Results:
- Of the total 445 patients, 336 (76%) were older than 65 years.
- Among the 273 patients who died, 91 (33%) died of lung cancer whereas the remaining ones died of competing events or unknown cause
- STAS was observed in 132 patients (30%) and the frequency increased with stage
- The cumulative incidences of any, distant, and locoregional recurrence as well as lung cancer–specific death were significantly higher in patients with STAS compared with in those without STAS, whereas there was no statistically significant difference in overall survival.
- In multivariable models for any recurrence and lung cancer–specific death, STAS was an independent predictor for both outcomes

Conclusion:
- STAS was present in one-third of resected lung SCCs
- In competing risks analysis in a cohort in which three fourths of the patients were elderly, STAS was associated with lung cancer–specific outcomes
- Our findings suggest that STAS is one of the most prognostically significant histologic findings in lung SCC

Background:

- BRCA1-associated protein 1 (BAP1) is a tumor suppressor gene involved in regulation of the cell cycle, cellular differentiation, repair of DNA damage, and apoptosis
- In the distinction of malignant mesothelioma from benign mesothelial proliferations, immunohistochemical loss of BAP1, the protein expressed by the BAP1 gene, has proven highly specific for malignant mesothelioma
- However, few studies have investigated the rate of BAP1 loss in tumors that commonly metastasize to the pleura
- The authors’ objective was to determine the rate of BAP1 loss in non–small cell lung cancer (NSCLC)

Methods

- Immunohistochemistry for BAP1 was performed using tissue microarrays containing 133 confirmed cases of NSCLC (80 of lung adenocarcinoma and 53 of squamous cell carcinoma)
- Cases were interpreted as showing BAP1 loss if nuclear staining was completely absent in all tumor cells and present in stromal and inflammatory cells that served as internal controls
- Cases showing no BAP1 staining in the internal controls were excluded

Results

- After exclusion of 32 cases for technical reasons, only 1 case of pulmonary adenocarcinoma of 101 cases of NSCLC (69 adenocarcinoma and 32 squamous cell carcinoma; 1.0% of cases) showed BAP1 loss

Conclusion

- The authors conclude that loss of BAP1 expression is a rare event in NSCLC
- Therefore, BAP1 is a potentially useful addition to the immunohistochemical markers used to distinguish mesothelioma from pleural metastasis of NSCLC

Background:

- BRCA-associated protein 1 (BAP1) immunohistochemistry (IHC) and CDKN2A (p16) fluorescence in situ hybridization (FISH) have shown clinical utility in confirming the diagnosis of malignant pleural mesothelioma (MPM), but the role for using these 2 markers to guide clinical management is not yet clear.
- Although p16 loss is predictive of poor prognosis, there is controversy as to whether BAP1 loss is predictive of a more favorable prognosis.

Methods:

- The authors performed CDKN2A FISH on a previously published tissue microarray on which they had performed BAP1 IHC, revealing combined BAP1/p16 status for 93 MPM cases.

Results:

- As expected, BAP1 IHC in combination with CDKN2A FISH resulted in high sensitivity (84%) and specificity (100%) for MPM, and p16 loss was an independent predictor of poor survival.
- There was no association between BAP1 loss and p16 loss, as 26%, 28%, 30%, and 16% of overall cases demonstrated loss of BAP1 alone, loss of p16 alone, loss of both BAP1 and p16, or neither abnormality, respectively.
- Although multivariate analysis demonstrated that BAP1 IHC is not an independent predictor of prognosis, when viewed in combination with homozygous CDKN2A deletion, risk stratification was evident.
- More specifically, patients with CDKN2A disomy and loss of BAP1 expression had improved outcomes compared with those with CDKN2A disomy and retained BAP1 expression, and this finding was notably evident among epithelioid cases.

Conclusion:

- The authors conclude that BAP1 IHC provides prognostic information within the context of CDKN2A FISH that may have clinical utility beyond diagnosis.

Background:

- BRCA1-associated protein 1 (BAP1) is a tumor suppressor gene involved in regulation of the cell cycle, cellular differentiation, repair of DNA damage, and apoptosis
- In the distinction of malignant mesothelioma from benign mesothelial proliferations, immunohistochemical loss of BAP1, the protein expressed by the BAP1 gene, has proven highly specific for malignant mesothelioma
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Conclusion

- The authors conclude that loss of BAP1 expression is a rare event in NSCLC
- Therefore, BAP1 is a potentially useful addition to the immunohistochemical markers used to distinguish mesothelioma from pleural metastasis of NSCLC

Background:

- The authors evaluated glucose transporter type 1 (GLUT1) and carbonic anhydrase IX (CAIX) expression, together with volume-based 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) parameters, in non-small cell lung cancer (NSCLC) patients, and examined the prognostic significance of those parameters according to its histologic subtype.

Method:

- A total of 269 patients, who underwent surgical resection for NSCLC, were reviewed retrospectively.
- Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) values were measured by preoperative 18 F-fluorodeoxyglucose positron emission tomography computed tomography. GLUT1 and CAIX expression was evaluated using immunohistochemical method.

Results:

- The mean MTV and TLG values were 30.0 ± 57.1 and 165.4 ± 361.3, respectively, and were significantly higher in patients with squamous cell carcinoma than with adenocarcinoma.
- GLUT1 expression was identified in 99% of squamous cell carcinoma and 50% of adenocarcinoma patients.
- MTV and TLG values were significantly higher in GLUT1-positive than GLUT-negative adenocarcinomas.
- However, CAIX expression did not show this pattern.
  - GLUT1-positive adenocarcinoma patients had a lower OS than GLUT1-negative patients, whereas CAIX-positive and
  - CAIX-negative patients showed similar OS rates.
- Patients with high MTV and TLG values showed lower OS rates than those with low MTV and TLG values.
- Multivariate analysis showed that GLUT1 positivity was an independent risk factor for a lower OS rate in lung adenocarcinoma patients.
- GLUT1 expression was associated with micropapillary/solid histology, lymphovascular invasion, and advanced pTNM stage.

Conclusions:

- MTV and TLG values, and GLUT1 expression, significantly differed between patients with squamous cell carcinoma and adenocarcinoma.
- High GLUT1 expression levels were significantly associated with MTV and TLG values and adverse clinical outcomes in patients with adenocarcinoma.
Background:

- Optimal histopathological analysis of biopsies from metastases of neuroendocrine tumor (NET) of the lung requires more than morphology only
- Additional parameters such as Ki-67 labeling index are required for adequate diagnosis, but few studies have compared reproducibility of different counting protocols and modalities of reporting on biopsies of lung NET
- The authors compared the results of four different manual counting techniques to establish Ki-67 LI

Methods

- On 47 paired biopsies and surgical specimens from 22 typical carcinoids (TCs), 14 atypical carcinoids (ACs), six large cell neuroendocrine carcinomas (LCNECs), and five small cell carcinomas (SCCs) immunohistochemical staining of Ki-67 antigen was performed
- The authors counted, in regions of highest nuclear staining (HSR), a full ×40-high-power field (diameter = 0.55 mm), 500 or 2000 cells, or 2 mm² surface area, including the HSR or the entire biopsy fragment(s)
- Mitoses and necrosis were evaluated in an area of 2 mm² or the entire biopsy fragment(s)

Results

- Between the four counting methods, no differences in Ki-67 LI were observed
- However, a Ki-67 LI higher than 5% was found in only four cases when in an HSR, 500 cells were counted (18%), five (23%) when in an HSR 2000 cells were counted, four (18%) when 2 mm² were counted, and one (5%) TC case when the entire biopsy was counted
- A 20% cutoff distinguished TC and AC from LCNEC and SCC with 100% specificity and sensitivity, while mitoses and necrosis failed to a large extent
- Ki-67 LI in biopsy samples was concordant with that in resection specimens when 2000 cells, 2 mm², or the entire biopsy fragment(s) were counted.

Conclusion

- The authors believe that their results are important for clinical management of patients with metastases of a lung NET

Background:

- Malignant pleural mesothelioma shows marked cytoarchitectural diversity
- The aim of the study was to evaluate how morphological phenotype impacted upon overall survival

Methods:

- 191 cases of malignant pleural mesothelioma with available follow-up were identified, examined and classified according to histological types
- The epithelioid mesotheliomas were further subdivided according to morphological subtypes: myxoid, microcystic, tubulopapillary, solid epithelioid, micropapillary and pleomorphic; biphasic mesotheliomas were divided into epithelioid component dominant and sarcomatoid component dominant; pure sarcomatoid mesotheliomas were divided into not otherwise specified, leiomyoid, desmoplastic and heterologous.
- All cases were confirmed by two experienced observers

Results

- Myxoid variant malignant pleural epithelioid mesothelioma was observed to have a favorable overall survival compared with pleomorphic form
- Pleomorphic phenotype had the worst overall survival

Conclusion

- Morphological phenotype is an important histological factor that should be included in pathology reports to convey potential favorable prognostic subgroups of patients with mesothelioma

Background:

- Programmed cell death-1 (PD-1)/programmed cell death-ligand 1 (PD-L1) pathway-targeted immunotherapy has become the standard option of care in the management of lung cancer
- The expression of the PD-L1 protein in lung cancer is expected to be a prognostic factor or to predict the response to PD-1-blocking antibodies
- However, the association between PD-L1 positivity and the clinicopathological features and patient outcomes in lung squamous cell carcinoma (SCC) remains unclear because the definitive cut-off value for the expression of PD-L1 protein remains to be established.

Materials and methods:

- The expression of PD-L1 protein in 205 surgically resected primary lung SCC patients was evaluated by immunohistochemistry with the antibody clone SP142
- The authors generated a histogram to show the proportion of PD-L1-positive carcinoma cells, and set the cut-off values as 1%, 5%, 10% and 50%.
- Moreover, they examined the proliferative capacity of these tumors using Ki-67 immunohistochemistry.

Results:

- The samples from 106 (51.7%), 72 (35.1%), 61 (29.7%) and 37 (18.0%) patients were positive for the expression of PD-L1 protein at cut-off values of 1%, 5%, 10% and 50%, respectively
- Fisher’s exact test showed that, for almost all of the factors, PD-L1 positivity was not associated with the clinicopathological features with any of the four cut-off values
- Univariate and multivariate survival analyses revealed that the PD-L1-positive patients only had a poorer prognosis than the PD-L1-negative patients at the 1% cut-off value
- The Ki-67 labeling index in the PD-L1-positive patients was higher than that in the PD-L1-negative patients

Conclusions:

- The expression of PD-L1 protein was associated with a poor prognosis in lung SCC patients
- The 1% cut-off value for PD-L1 might become a better predictive marker than the other cut-off values
ARTICLES FOR NOTATION – NONNEOPLASTIC


Background:

- Surgical lung biopsy remains the gold standard for histopathologic diagnosis of idiopathic interstitial pneumonias
- Emerging data suggest an increasing role for transbronchial cryobiopsy (TBC) in DPLD evaluation.

Methods:

- The authors retrospectively reviewed medical records of patients with radiographic features of DPLD who underwent TBC at Mayo Clinic in Rochester, Minnesota from June 2013 to September 2015

Results:

- Seventy-four patients (33 women [45%]) with a mean age of 63 years (SD, 13.8) were included
- The mean maximal diameter of the samples was 9.2 mm (range, 2-20 mm)
- The median number of samples per procedure was three (range, one to seven)
- Diagnostic yield was 51% (38 of 74 specimens)
- The most frequent histopathologic patterns were
  - granulomatous inflammation (12 patients) and organizing pneumonia (OP) (11 patients)
- resulting in the final diagnoses of
  - hypersensitivity pneumonitis (six patients)
  - cryptogenic OP (six patients)
  - connective tissue disease-associated OP (three patients)
  - drug toxicity (three patients)
  - infection-related OP (two patients)
  - sarcoidosis (two patients), and
  - aspiration (one patient)
- Other histopathologic patterns included respiratory bronchiolitis (three patients, acute fibrinous and organizing pneumonia (two patients), desquamative interstitial pneumonia (1 patient), diffuse alveolar damage (one patient), pulmonary alveolar proteinosis (one patient), amyloidosis (one patient), eosinophilic pneumonia (one patient), necrotizing vasculitis (one patient), bronchiolitis with food particles (one patient), and malignancy (three patients).
- Pneumothorax developed in one patient (1.4%), and bleeding occurred in 16 patients (22%).

Conclusions:

- Our single-center cohort demonstrated a 51% diagnostic yield from TBC
- The rates of pneumothorax and bleeding were 1.4% and 22%, respectively

Background:

- Surgical lung biopsy (SLB) is invasive and not possible in all patients with undiagnosed interstitial lung disease (ILD)
- The authors hypothesized that transbronchial biopsy (TBB) findings combined with clinical and high-resolution CT (HRCT) data leads to a confident diagnosis congruent to SLB and therefore avoids the need for SLB in some patients

Methods:

- The authors evaluated 33 patients being investigated for suspected ILD who underwent HRCT, TBB, and SLB.
- First, clinicians, radiologists, and a pathologist reviewed the clinical information and HRCT and TBB findings
- Clinicians were asked to provide a diagnosis and were also asked if SLB was needed for a more confident diagnosis
- Subsequently, the clinical, HRCT, and SLB data were reviewed, and the same participants were asked to provide a final diagnosis
- Clinician consensus and overall agreement between TBB- and SLB-based diagnoses were calculated.

Results:

- Four patients had definite usual interstitial pneumonia (UIP) on HRCT and would not be considered for biopsy using current guidelines
- Of the 29 patients without a definitive HRCT diagnosis, the clinicians felt confident of the diagnosis (ie, would not recommend SLB) in six cases
- In these cases, there was 100% agreement between TBB and SLB diagnoses
- UIP was the most common diagnosis (n 1/4 3) and was associated with an HRCT diagnosis of possible UIP/nonspecific interstitial pneumonia-like
- Agreement was poor (33%) between TBB and SLB diagnoses when confidence in the TBB diagnosis was low

Conclusions:

- Information from TBB, when combined with clinical and HRCT data, may provide enough information to make a confident and accurate diagnosis in approximately 20% to 30% of patients with ILD
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CASE REPORTS


- Diagnosis: Relapsed classical Hodgkin’s lymphoma