PULMONARY PATHOLOGY JOURNAL CLUB
(April 2013 articles)
May 20, 2013

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I. Articles for Discussion

Rekhtman et al. Distinct profile of driver mutations and clinical features in immunomarker-defined subsets of pulmonary large-cell carcinoma. Mod Pathol 2013;26:511-522

Purpose: To establish the rate of targetable mutations in large cell lung carcinoma (LCLC), determine whether the distribution of these mutations can be predicted by immunophenotyping, and whether immunomarker-defined subsets of LCLC have distinct clinicopathologic characteristics.

Methods: TTF-1 and p40 (ΔNp63) staining was performed on 102 resected NSCLCs lacking morphologic evidence of glandular, squamous or neuroendocrine differentiation. Mucin stains were not used and sarcomatoid carcinomas composed entirely of spindle or giant cells were excluded. The resulting subtypes were correlated with nine therapeutically relevant genetic alterations characteristic of adenocarcinoma (EGFR, KRAS, BRAF, MAP2K/MEK1, NRAS, ERBB2/HER2 mutations and ALK rearrangements) or squamous cell carcinoma (PIK3CA and AKT1 mutations).

Results: Using immunohistochemistry, 62 (60%) LCLCs were reclassified as adenocarcinoma, 20 (20%) as squamous cell carcinoma, and 20 (20%) were marker-null. In 37% of cases, genetic alterations were found, most commonly KRAS (30 cases), followed by ALK (3 cases), BRAF (2 cases) and 1 each of EGFR, MAP2K1, and PIK3CA. Genetic alterations characteristic of adenocarcinoma occurred only in tumors with adenocarcinoma or marker-null immunoprofiles and the case with the PIK3CA mutation immunophenotyped as squamous cell carcinoma. Marker-null cases were associated with shorter overall and disease-free survival.
Figure 1  Immunohistochemistry-defined subtypes of large cell carcinoma. (a) Coexpression profiles of TTF-1 and ANp63 (p40). **TTF-1 and ANp63 labeled distinct cell populations. (b) Pie chart showing TTF-1/ANp63-based subtypes of large cell carcinoma. (c) Examples of microscopic findings. H&E shows morphologically indistinguishable non-small-cell carcinomas, all growing as entirely solid nests or sheets of tumor cells with no evidence of either glandular or squamous differentiation. Despite the lack of differentiating morphology, marker profiles provide evidence of submorphic differentiation as adenocarcinoma (A – C) or squamous cell carcinoma (D – F). (G – I) illustrates a marker-null large cell carcinoma. Benign pneumocytes (TTF-1+) are seen at the tumor periphery (black arrowheads) or entrapped within the tumor (blue arrowheads). Insets in a, d and g show higher power images. Abbreviations: ADC, adenocarcinoma; AD-SQC, adenosquamous carcinoma; LCC, large cell carcinoma; SQCC, squamous cell carcinoma.
Discussion: By applying TTF-1 and ΔNp63, 80% of LCLCs can be reclassified as adenocarcinoma or squamous cell carcinoma, which allows for triaging of specimens for molecular testing. It is speculated that at least some marker-null LCLCs represent TTF-1-negative adenocarcinomas, which is supported by the finding that these tumors have a mutation profile more similar to lung adenocarcinoma than squamous cell carcinoma, exhibiting high rates of KRAS and BRAF mutations.

Take Home Message: Marker-null LCLC should be tested for the same targetable mutations as pulmonary adenocarcinoma.


Purpose: To determine whether the pattern of fibrosis in chronic pulmonary sarcoidosis was non-specific, similar to other fibrosing lung diseases, or distinct enough to suspect sarcoid even in the absence of a clinical history.

Methods: The histologic sections from 9 lung explants from patients with a clinical diagnosis of end-stage sarcoid were retrospectively evaluated and correlated with CT findings.

Results: Explanted lungs from 7 females and 2 males were evaluated. In 8 of the 9 patients, the CT had shown either probable or definite sarcoid with perihilar fibrosis extending outward from the hilar regions into the upper lobes. Four patients had active granulomatous disease with non-fibrotic nodular granulomas in the interstitium. The other 5 had predominantly fibrotic lungs with thick hyalinized scarring, 3 of which showed areas of honeycombing. The honeycombing was predominantly central with prominent bronchiectasis. Granulomas were not identified in 2 of the predominantly fibrotic cases, but the CT findings were typical of sarcoid, and hilar nodal granulomas were seen in one. Patients with predominantly fibrotic lungs were significantly older.
Discussion: The 2 histologic patterns observed in the end-stage sarcoid lungs in this study (active granulomatous and fibrotic patterns) are distinct from that seen in UIP, as are the CT findings. Functionally end-stage pulmonary sarcoidosis may occur in the absence of massive scarring.

Take Home Message: End-stage pulmonary sarcoidosis appears not to bear as close a resemblance to UIP as was previously thought.

Purpose: To clarify the histologic features and correlate FISH and RT-PCR results of ROS1-rearranged lung cancers. ROS1-rearrangement has been shown previously to be associated with responsiveness to crizotinib.

Methods/Results: Of 799 resected NSCLCs evaluated by RT-PCR, 15 tumors harboring ROS1 fusion transcripts were identified. Most were from younger non-smoking females. Although overall survival of ROS1 fusion-positive tumors was similar to ROS1 fusion-negative tumors, none of the patients received crizotinib. All ROS fusion-positive tumors were adenocarcinomas except 1 adenosquamous carcinoma. Over half (53%) of cases showed at least focal solid growth with signet ring cells or cribriform architecture with abundant extracellular mucin, similar to the phenotype associated with ALK-rearranged lung cancers. All except 1 tumor showed TTF-1 staining. Using ROS1 break-apart probes, FISH detected positive rearrangement signals in 23-93% of tumor cells in ROS1 fusion-positive tumors, while ROS1 fusion-negative tumors showed only 0-6% rearrangement signals. None of the ROS1 fusion-positive tumors had EGFR, KRAS, KER2, ALK, or RET gene alterations.

TABLE 2. Clinicopathologic and Molecular Details of 15 Patients With ROS1 Fusion–Positive Lung Cancers

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>Smoking (pack-years)</th>
<th>Follow-up (mo)</th>
<th>Size (cm)</th>
<th>Diagnosis</th>
<th>Predominant Growth</th>
<th>Pattern</th>
<th>Pattern M</th>
<th>Fusion Gene</th>
<th>FISH Cell Rate (%)</th>
<th>FISH Patterns</th>
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<td>Ad</td>
<td>Lepidic</td>
<td>—</td>
<td>—</td>
<td>CD74-ROS1</td>
<td>63</td>
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<td>—</td>
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<td>&lt;5%</td>
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<td>&lt;5%</td>
<td>CD74-ROS1</td>
<td>53</td>
</tr>
</tbody>
</table>

* The percentage of "solid signet-ring-cell pattern."
† The percentage of "micronodular pattern."
‡ The percentage of tumor cells with rearrangement-positive FISH signals.
§ Predominant FISH signal pattern in rearrangement-positive cells.
FGR pattern with narrow spikes.

Ad indicates adenocarcinoma; Ad-Seq, adenocarcinoma with signet ring cell morphology; AWD, alive with disease; DOD, died of disease; FGR, fused, green, and red signals; FR, fused and red signals without green signals; GR, green and red signals without fused signals; NA, data not available; N/E, no evidence of disease.
Discussion: ROS1-rearranged lung cancers tend to affect younger never-smoking females and have a phenotypic resemblance to ALK-rearranged lung cancers. ROS1 break-apart FISH, using a 15% cutoff value and including isolated 3' signals as positive, is reliable for detecting ROS1 rearrangements.
Take Home Message: When you see a solid signet ring cell pattern or mucinous cribriform pattern, don’t forget to test for ROS1, as well as ALK.


Purpose: To report on the development of computer-aided nodule assessment and risk yield (CANARY) as an adjunct tool for characterizing and categorizing pulmonary nodules.

Methods: A training set of 54 pulmonary nodules, which had been diagnosed following resection as some form of adenocarcinoma, ranging from BAC to adenocarcinoma, was used to develop a tool to radiologically predict histopathologic tissue invasion and was subsequently validated in 86 consecutively resected nodules.

Results: CANARY successfully non-invasively characterizes pulmonary nodules along the adenocarcinoma spectrum non-invasively and accurately categorizes lesions as “aggressive” (invasive adenocarcinoma) or “indolent” (AIS and MIA). Sensitivity, specificity, positive predictive value, and negative predictive value were 98.7, 63.6, 94.9 and 87.5%, respectively, for the validation set.

Discussion: CANARY is a promising tool for non-invasive risk stratification of pulmonary adenocarcinomas.

Take Home Message: This technology seems like it will be well-suited to aiding in the management of patients who are marginal surgical candidates.
II. Articles for Notation

Original Articles

Neoplastic


Purpose: To assess the reliability of assessing molecular testing for EGFR and KRAS mutation on different types of cytological samples.

Methods: PCR followed by direct sequencing was performed on both scraped smears and needle washings from 32 FNA specimens of NSCLC.

Results: There was 100% concordance in the mutation status in 29 paired scraped smears and needle washings. Three scraped smears were uninformative due to poor DNA quality, but their paired needle washings were EGFR-mutated.

Discussion: Needle washings are a valuable source of material for mutational analysis.

Chen et al. Well-differentiated papillary mesothelioma: a clinicopathological and immunohistochemical study of 18 cases with additional observation. Histopathol 2013;62:805-813

Purpose: To present a single-institution experience with previously unpublished cases of well-differentiated papillary mesothelioma (WDPM) and explore the relationship to adenomatoid tumor and multicystic mesothelioma.

Methods/Results: Included in the series were 18 cases of WDPM (14 peritoneal, 2 pleural, 2 tunica vaginalis) from 14 females and 4 males with a median age of 37, the majority of which were discovered incidentally during surgery for other conditions. Classic histologic features of WDPM were seen in 13 cases, while 2 had a combined component of adenomatoid tumor and 3 showed areas more typical of multicystic mesothelioma. All cases of WDPM had an indolent course. Twenty cases of multicystic mesothelioma (MCM) were examined for comparison, 4 of which showed co-existing adenomatoid foci. WDPM was negative for both EMA and desmin.
Discussion: The occasional co-existence of WDPM with adenomatoid tumor or MCM suggests a histogenetic relationship.

Take Home Message: WDPM very occasionally shows adenomatoid or MCM-like foci and even more rarely has co-existing adenomatoid tumor or MCM. WDPM exhibits what could be considered an indeterminate immunophenotype with markers sometimes used to aid in the separation of benign and malignant mesothelial in that it is both EMA and desmin-negative.

Chung et al. Synaptonemal complex protein 3 as a novel prognostic marker in early stage non–small cell lung cancer. Hum Pathol 2013;44:472-479

Purpose: To investigate the potential correlation between synaptonemal complex protein 3 (SCP3), which is a marker for cell transformation, and clinicopathologic parameters in NSCLC.

Methods: Immunohistochemical expression of SCP3 in archival tissue from 258 cases of NSCLC was assessed and correlated with prognostic features.

Results: Staining was observed in 19.4% of cases and correlated with T status, nodal metastasis, tumor type (adenocarcinoma), and pleural invasion. In patients with pT1 tumors and early stage (I and II) disease, expression predicted worse overall survival.
Discussion: SCP3 expression portends a poor outcome in early stage NSCLC.

Take Home Message: This is a marker that along with a number of others may be used in the future to guide decisions about adjuvant therapy in early stage NSCLC patients.


Purpose: To develop a quality assessment process that ensures high-quality molecular testing in NSCLC.

Methods: FFPE NSCLC tumor sections were distributed to nearly 50 laboratories in the UK for routine EGFR molecular testing and the accuracy of reporting was assessed externally on 3 separate occasions (rounds) over 2 years. Participants received score reports with feedback following each round of quality assessment.

Results: Three rounds of assessment identified genotyping errors. In the first round, 24% of laboratories had at least one genotyping error (e.g. failure to detect exon 19 mutation). By the final round, the rate of genotyping errors decreased to 6.4%.

Discussion: Despite improvements over three rounds of external quality assessment, laboratories still demonstrated genotyping error rates that were characterized by the authors as “unacceptably high”, emphasizing the need for continued quality improvement and assessment.

Take Home Message: External quality assessment does improve performance across laboratories, but molecular testing is not infallible.

Esterbrook et al. Adequacy of endobronchial ultrasound transbronchial needle aspiration samples in the subtyping of non-small cell lung cancer. Lung Cancer 2013;80-30-34

Purpose: To evaluate the adequacy of material obtained by EBUS-TBNA for NSCLC subtyping.

Methods: All EBUS-TBNA procedures from a single teaching institution performed during a 2½ year period were analyzed. Procedures were performed using a 22-gauge needle with 2-3 punctures from each nodal station sampled and 6-10 passes per puncture and both cytospin cytologic preparations and cell blocks were prepared.

Results: Of 391 procedures, malignancy was diagnosed in 204 cases (53.7%), including 149 cases of NSCLC. Subtyping was possible in 79.2% of cases of NSCLC. Immunohistochemistry was performed in 73% of malignant cases and insufficient material was available in 1.5% of cases. Of cases in which EGFR testing was requested, sufficient material to obtain a result was available in 88.8% of cases.
Discussion: EBUS-TBNA samples, when made into cell blocks, are adequate not only for subtyping of NSCLC (only 20.8% NOS rate), but also for EGFR mutation analysis (88% success rate).

Take Home Message: EBUS-TBNA-derived cell blocks provide adequate tissue for appropriate patient management most of the time.


Purpose: To identify genetic alterations associated with crizotinib resistance.

Methods: Samples from 7 ALK-positive NSCLC patients showing acquired resistance to crizotinib were subjected to molecular analysis.

Results: Acquired crizotinib resistance developed after a median treatment duration of 6 months. Secondary ALK mutations were identified in 3 patients and one showed high ALK gene copy number and L858R in EGFR exon 21. Genetic alterations associated with acquired crizotinib resistance were not observed in 3 patients.

Discussion: Genetic alterations associated with acquired crizotinib resistance are heterogeneous.

Take Home Message: Newer techniques, such as next generation sequencing, will hopefully permit discovery of additional mechanisms by which ALK-positive NSCLC develop resistance to crizotinib.


Purpose: To correlate CT imaging characteristics to histologic findings of resected lung adenocarcinomas.

Methods: The CT findings and histologic growth patterns of 174 resected lung adenocarcinomas were analyzed.

Results: Margin configuration and solidity/ground glass opacity correlated with distinct histologies, with solid-predominant adenocarcinomas showing smooth margins on CT and lepidic-predominant tumors being peripheral, showing a positive bronchogram and an association with ground glass opacity. Non-spherical tumor growth negatively predicted overall and disease-specific survival.

Discussion: There are morphologic features on CT that are associated with specific histologic growth patterns.

Take Home Message: Not surprising that morphologic features on CT to some degree recapitulate what is seen on histologic examination.
Moskalev et al. Increased detection rates of **EGFR** and **KRAS** mutations in NSCLC specimens with low tumour cell content by 454 deep sequencing. *Virchows Arch 2013;462:409-419*

**Purpose:** To assess the performance of a 454 deep sequencing assay, a next-generation sequencing technique, to detect EGFR and KRAS mutations in NSCLC.

**Methods:** A total of 21 FFPE specimens of lung adenocarcinoma were tested, including cytologic cell block preparations, endoscopic biopsies, and resections using a novel two-step amplification protocol with 454 sequencing assay and Sanger sequencing.

**Results:** As compared to the 10-20% detection limit of Sanger sequencing, deep sequencing identified mutations down to an allele frequency of 0.2-1.5%. Additionally, of 16 samples with low tumor content that were EGFR wild-type status according to Sanger sequencing, deep sequencing identified EGFR mutations in seven.

**Discussion:** This novel method is superior to Sanger sequencing and allows detection of important mutations in samples with low tumor content.

**Take Home Message:** Next generation sequencing will hopefully allow mutational results to be achieved in all but the most scant of samples.

Ono et al. Podoplanin-positive cancer-associated fibroblasts could have prognostic value independent of cancer cell phenotype in stage I lung squamous cell carcinoma: usefulness of combining analysis of both cancer cell phenotype and cancer-associated fibroblast phenotype. *Chest 2013;143:963-970*

**Purpose:** To analyze prognostic significance of the tumor microenvironment in squamous cell carcinoma of the lung by studying the immunophenotype of both cancer cells and cancer-associated fibroblasts.

**Methods:** Expression of E-cadherin, laminin-5, podoplanin, c-MET, CA-IX, CD10 and CD44 in cancer cells and podoplanin, CA-IX, CD10, and CD44 in cancer-associated fibroblasts was evaluated in 142 patient with stage I squamous cell lung carcinoma and correlated with overall survival.

**Results:** Low E-cadherin expression in cancer cells correlated with poorer prognosis, as did high podoplanin expression in fibroblasts.

**Discussion:** The immunophenotype of cancer-associated fibroblasts appears to have prognostic significance independent of that of the tumor cells in squamous cell lung carcinoma.

**Take Home Message:** The tumor microenvironment becoming recognized as an important component of tumor behavior.

**Purpose:** To determine the prognostic value of metastatic lymph node ratio (LNR) in patients with radical surgery for NSCLC.

**Methods:** The prognostic value of multiple clinicopathologic parameters, including LNR was assessed from 480 consecutive resected NSCLC cases. LNR was defined as the ratio of positive nodes divided by the total number of retrieved nodes.

**Results:** The median number of nodes examined was 15. Higher LNRs (>0.35) were associated with worse overall and disease-free survival and was an independent prognostic factor by multivariate analysis.

**Discussion:** LNR is an independent predictor of survival, particularly in pN1 patients, but the results are not robust enough to conclude that LNR is superior to pN status.

**Take Home Message:** LNR is intriguing, but more data is necessary to determine if it will replace pN for lung cancer staging.

Russell et al. Correlation of mutation status and survival with predominant histologic subtype according to the new IASLC/ATS/ERS lung adenocarcinoma classification in stage III (N2) patients. J Thorac Oncol 2013;8:461-468

**Purpose:** To investigate the relationship between predominant histologic subtype, mutation status, and outcome in stage III (N2) lung adenocarcinoma.

**Methods:** Sixty-nine resected stage III (N2) lung adenocarcinomas were assessed and subjected to mutational analysis.

**Results:** Most tumors were acinar-predominant (38%). EGFR mutations were identified in 29% of tumors, most of which were either acinar or micropapillary-predominant, while 22% showed KRAS mutations, most of which were solid-predominant. Acinar-predominance was associated with improved overall survival. Survival was similar among patients with EGFR-mutated micropapillary-predominant and EGFR-mutated acinar-predominant tumors. The predominant pattern seen in nodal metastases did not always correspond to the predominant pattern of the primary tumor, particularly acinar-predominant primary tumors.
Discussion: Although EGFR mutations occurred more frequently in acinar-predominant tumors, improvement in survival was independent of mutational status. It is concluded that the predominant subtype of the primary tumor determines outcome in lung adenocarcinoma patients with N2 disease.

Take Home Message: At least according to this study, histologic subtyping does have prognostic value.


Purpose: To report on the safety and reliability of using image-guided small caliber percutaneous transthoracic core needle biopsy (PTCNB) to obtain tissue from NSCLC patients for molecular analysis as part of the BATTLE (biomarker-integrated approaches of targeted therapy for lung cancer elimination) trial.

Methods: The medical records of NSCLC patients undergoing PTCNB were reviewed for diagnostic yield of 11 predetermined molecular markers and procedural complications.

Results: PTCNB using 20-gauge needles was performed on 151 NSCLC patients yielding a total of 170 specimens. For 82.9% of patients, adequate tumor tissue was obtained for molecular analysis. In most of the cases in which inadequate tissue was obtained, the authors attributed the reason to lesion selection (e.g. large mass without recent PET-CT to assist in targeting the most viable region for biopsy). Metastatic lesions were 5.4 times more likely to yield diagnostic material than primary tumors. Pneumothorax complicated 15.3% of cases, requiring chest tube insertion in 9.4% of cases.
**Discussion:** PTCNB with image-guidance and 20-gauge needles is safe and provides adequate tissue for biomarker analysis in the majority of patients. The diagnostic yield of metastatic lesions is higher than primary tumors.

**Take Home Message:** PTCNB tissue samples that prove to be inadequate for mutational analysis most commonly reflect suboptimal lesion targeting, such as failure to biopsy the most viable and/or PET-avid region of a tumor.

**Yip et al. Patterns of DNA mutations and ALK rearrangement in resected node negative lung adenocarcinoma. J Thorac Oncol 2013;8:408-414**

**Purpose:** To identify patterns of mutations in early stage node negative lung adenocarcinoma.

**Methods:** Genotyping and FISH for ALK rearrangement was performed on resections from 204 stage IB chemotherapy-naïve lung adenocarcinoma patients.

**Results:** At least one mutation was detected in 54% of patients, including KRAS (37.7%), EGFR (14.2%), PIK3CA (1%), ALK (1%), and at a rate of 0.5% for each of the others (PDGFRA, AKT1, BRAF, FGFR1, and HRAS). Synchronous co- or double mutations were seen in 8.8% of patients. EGFR mutations were associated with well-differentiated tumors, while KRAS and PIK3CA were associated with poorly differentiated tumors. Mutations associated with EGFR-TKI resistance were identified in 5 tumors. KRAS, EGFR, and ALK mutations were mutually exclusive.

**Discussion:** A diversity of mutations was seen in this patient population, including mutations associated with EGFR-TKI resistance. The rate of ALK rearrangements was unexpectedly low.

**Take Home Message:** Mutational analysis is essential prior to instituting targeted therapies, as cases occasionally show mutations that would be unexpected based on the clinical features.

**Review Articles**


A review of the molecular pathogenic mechanisms in NSCLC. Although *sans* pictures and diagrams, does include a discussion of secondary resistance to EGFR inhibitors and emerging targets, including VEGF and MET inhibition.


A well-written review on the diagnostic tests that are currently available and those in the pipeline to identify patients with ALK-rearranged NSCLC. Includes a very nice depiction of the fusion gene and testing modalities (figure 1).
Case Reports


Case Summary: A 67-year-old female with a history of splenectomy for ITP developed ARDS after presenting with fever and myalgia. Imaging findings included pleural effusions, lower lobe consolidation, and a high-density lesion of the tracheal wall. Bronchoscopy disclosed an exophytic dense endotracheal lesion and ulcers and a bronchial aspirate grew A. niger. Biopsy of the bronchial lesion showed necrotic tissue with pigment and abundant polarizable crystals. Despite antifungal therapy, the patient expired.

Take Home Message: Tracheal oxalosis is extremely rare, but should be considered in the differential of endotracheal lesions in immunocompromised patients.


Case Summary: An 18-year-old previously healthy non-smoking female presented with fever, productive cough, pleuritic pain, painful pharyngitis, and increasing shortness of breath. There was a history of recent tick bite. Imaging showed pulmonary infiltrates and BAL showed numerous Tzanck cells with immunohistochemistry positive for HSV1. She was diagnosed with HSV1 pneumonia.

Take Home Message: Although unusual in an immunocompetent patient, HSV pneumonia sometimes occurs in young, otherwise healthy individuals with severe pharyngitis being a clue in the presented case.


Case Summary: A 58-year-old never-smoking male receiving long-term treatment with azathioprine and prednisolone for polymyositis was found to have a mass with eccentric cavitation (air crescent sign) on imaging. Biopsy showed grade 3 lymphomatoid granulomatosis (LYG).

Take Home Message: Air crescent sign is not specific for aspergillosis. Long-term immunosuppression should raise the clinical suspicion for LYG.

Popat et al. Transformation to “high grade” neuroendocrine carcinoma as an acquired drug resistance mechanism in EGFR-mutant lung adenocarcinoma. Lung Cancer 2013;80:1-4

Case Summary: A 46-year-old female with EGFR exon 19 deletion lung adenocarcinoma developed acquired resistance to EGFR-TKI therapy through transformation to a high grade
neuroendocrine carcinoma with SCLC and NSCLC components. The transformed tumor retained the original EGFR mutation. 

Take Home Message: Tumors can develop EGFR-TKI resistance not only through new mutations, such as exon 20 duplications, but also through transformation to high grade neuroendocrine carcinoma.


Case Summary: A 50-year-old male presented with pleuritic pain and dyspnea and was found to have a large pneumothorax and diffuse pulmonary nodules. VATS biopsy showed follicular bronchiolitis. The patient was subsequently confirmed to have HIV. Within 2 months of starting HAART, there was near complete resolution of the pulmonary nodules. A nice table comparing features of follicular bronchiolitis with other potential differential diagnoses (e.g. LIP, NLH, BALT lymphoma) is presented.

Take Home Message: The presence of follicular bronchiolitis should prompt consideration of HIV. Aggressive immunosuppressive therapy can induce remission of follicular bronchiolitis.

Weber et al. Primary pulmonary malignant meningioma with lymph node and liver metastasis in a centenary woman, an autopsy case. Virchows Arch 2013;462:481-485

Case Summary: At autopsy, a 108-year-old woman with no intracranial tumor and a long-standing history of a slowly growing pulmonary nodule was found to have an intrapulmonary meningioma (WHO grade III) with metastases to the hilar nodes and liver.

Take Home Message: Primary pulmonary meningioma is distinctly uncommon with most examples exhibiting benign behavior. Tumor cells are postulated to arise from multipotent cells or ectopic meningocytes.