

Pulmonary Journal Club

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Articles for Discussion

Sugiyama M, et al. A distinctive cytomorphological feature of interstitial pneumonia-related lung adenocarcinoma: The potential issues and solutions in practical diagnosis. *Cancer Cytopathol.* 2023 Mar;131(3):198-206.

BACKGROUND:

- HNF4 α has recently been described in invasive mucinous adenocarcinoma of the lung (Sugano M, et al. *Am J Surg Pathol.* 2013 Feb;37(2):211-8).

OBJECTIVE:

- To describe cytomorphological features of interstitial pneumonia (IP)-related lung adenocarcinoma (LADC).

METHODS:

- Bronchial brushing cytology samples from 40 IP-related LADC cases (the IP group) and 110 control cases (LADC unrelated to IP; the non-IP group) were analyzed.
- All patients underwent surgery after brushing cytology, and their histopathological subtypes were determined.
- The authors reviewed the cytological features and focused particularly on cytoplasmic mucin production.

RESULTS:

- In the IP group, neoplastic cells with cytoplasmic mucin were detected at a significantly higher frequency (44.4% [8 of 18] vs. 6.3% [4 of 64]), and most of them were invasive mucinous adenocarcinomas (IMAs).
- Twenty-two of the 40 LADC cases in the IP group failed to be judged as "malignant/positive" (thus, they were judged to be "equivocal and/or negative").
- The frequency of equivocal and/or negative judgments was 55.0% (22 of 40) in the IP group and 41.8% (46 of 110) in the non-IP group.
- The cytological diagnosis of IMA was difficult because it showed only slight nuclear atypia.
- Therefore, the authors examined the immunocytochemical expression of hepatocyte nuclear factor 4 α (HNF4 α), a diagnostic marker for IMA.
- As a result, four of the six cases that were judged to be equivocal in the IP group showed positive signals and could be retrospectively judged as malignant/positive.

CONCLUSIONS:

- The cytological diagnosis of IP-related LADC may be more difficult because of the larger proportion of IMA.
- Immunocytochemistry for HNF4 α can be used to improve diagnostic confidence in IP-related LADC.

Brcic L, et al. A combination of MTAP and p16 immunohistochemistry can substitute for CDKN2A fluorescence in situ hybridization in diagnosis and prognosis of pleural mesotheliomas. Arch Pathol Lab Med. 2023 Mar 1;147(3):313-322.

BACKGROUND:

- Homozygous deletion (HD) of CDKN2A is one of the most frequent genetic abnormalities in pleural mesotheliomas.
- HD of CDKN2A by fluorescence in situ hybridization (FISH) is a reliable marker of malignancy in mesothelial proliferations; however, evaluation of CDKN2A deletion requires FISH.
- The 9p21 locus includes both CDKN2A and MTAP (methylthioadenosine phosphorylase); the latter is frequently codeleted with CDKN2A.

OBJECTIVE:

- To examine the question of whether immunohistochemistry for MTAP and p16, the protein product of CDKN2A, can serve as a surrogate for CDKN2A HD by FISH.

METHODS:

- A random selection of 125 pleural mesothelioma cases was divided into 3 groups for evaluation of p16 and MTAP expression compared with FISH for CDKN2A deletion:
 - 53 with HD,
 - 39 with heterozygous deletion, and
 - 33 without deletion.

RESULTS:

- By itself, loss of p16 nuclear expression (<1% staining) showed a high sensitivity (96%) but low specificity (43%) for CDKN2A HD by FISH.
- MTAP cytoplasmic expression loss ($\leq 30\%$ staining) showed a 97% specificity and 69% sensitivity.
- The combination of p16 nuclear (<1% staining) and MTAP cytoplasmic ($\leq 30\%$ staining) loss demonstrated both high specificity (96%) and high sensitivity (86%).
- Patients with retained p16 expression ($\geq 1\%$) had the best prognosis, whereas a p16 (<1%)/MTAP loss combination was associated with a dismal prognosis.

CONCLUSIONS:

- MTAP immunohistochemical staining is a valid surrogate marker for CDKN2A HD by FISH; however, to obtain the same accuracy as the FISH assay, a combination of nuclear p16 and cytoplasmic MTAP staining is recommended.
- These findings correlate with prognosis.

Rajan SK, et al. Progressive pulmonary fibrosis: an expert group consensus statement. Eur Respir J. 2023 Mar 30;61(3):2103187.

- Expert group consensus guidance is provided on the diagnosis, treatment and monitoring of fibrosing interstitial lung diseases (F-ILDs) with specific focus on the recognition of "progressive pulmonary fibrosis" (PPF).
 - It emphasizes the need for standardizing the definition of progressive F-ILDs, with an accurate initial diagnosis being of paramount importance in ensuring appropriate initial management.
 - Equally, case-by-case decisions on monitoring and management are essential, given the varying presentations of F-ILDs and the varying rates of progression.
 - The value of diagnostic tests in risk stratification at presentation and, separately, the importance of a logical monitoring strategy, tailored to manage the risk of progression, are also stressed.
 - The term PPF exactly describes the entity that clinicians often face in practice.
 - The importance of using antifibrotic therapy early in PPF (once initial management has failed to prevent progression) is increasingly supported by evidence.
 - Artificial intelligence software for high-resolution computed tomography analysis, although an exciting tool for the future, awaits validation.
 - Guidance is provided on pulmonary rehabilitation, oxygen and the use of non-invasive ventilation focused specifically on the needs of ILD patients with progressive disease.
 - PPF should be differentiated from acute deterioration due to drug-induced lung toxicity or other forms of acute exacerbations.
 - Referral criteria for a lung transplant are discussed and applied to patient needs in severe diseases where transplantation is not realistic, either due to access limitations or transplantation contraindications.

Lin S, et al. Digital quantification of tumor cellularity as a novel prognostic feature of non-small cell lung carcinoma. *Mod Pathol.* 2023 Mar;36(3):100055.

BACKGROUND:

- Non-small cell lung carcinoma is currently staged based on the size and involvement of other structures.
- Tumor size may be a surrogate measure of the total number of tumor cells.
- A recently revised reporting system for adenocarcinoma incorporates high-risk histologic patterns, which may have increased cellular density.
- Modern digital image analysis tools can be utilized to automate the quantification of cells.

OBJECTIVE:

- In this study, we tested the hypothesis that tumor cellularity can be used as a novel prognostic tool for lung cancer.

METHODS:

- Digital slides from The Cancer Genome Atlas lung adenocarcinoma (ADC) data set (n = 213) and lung squamous cell carcinoma (SCC) data set (n = 90) were obtained and analyzed using QuPath.
- The number of tumor cells was normalized with the surface area of the tumor to provide a measure of tumor cell density.
- Tumor cellularity was calculated by multiplying the size of the tumor with the cell density.
- Major histologic patterns and grade were compared with the tumor density of the lung ADC and lung SCC cases.
- The overall and progression-free survival were compared between groups of high and low tumor cellularity.

RESULTS:

- High-grade histologic patterns in the ADC and SCC cases were associated with greater tumor densities compared with low-grade patterns.
- Cases with lower tumor cellularity had improved overall and progression-free survival compared with cases with higher cellularity.

CONCLUSIONS:

- These results support tumor cellularity as a novel prognostic tool for non-small cell lung carcinoma that considers tumor stage and grade elements.

Wankhede D, et al. Prognostic impact of tumour budding in squamous cell carcinoma of the lung: a systematic review and meta-analysis. *Histopathology*. 2023 Mar;82(4):521-530.

BACKGROUND:

- Tumor budding is an established prognostic factor in various solid tumors, including colorectal cancers and oral squamous cell carcinomas.

OBJECTIVE:

- To investigate the prognostic role of tumor budding in lung squamous cell carcinoma (LSCC).

METHODS:

- The authors conducted a systematic review and meta-analysis.
- PubMed, Embase and Scopus were searched for peer-reviewed literature investigating the association between tumor budding and survival outcomes or clinicopathological variables in LSCC.
- The primary outcomes were pooled estimates for overall and recurrence-free survival with hazard ratio (HR) as the effect measure.
- The association between tumor budding and clinicopathological parameters was also investigated.

RESULTS:

- Of 243 studies, nine were included, comprising 2546 patients.
- An increased risk of death [HR = 1.76, 95% confidence interval (CI) = 1.50-2.05, $P < 0.00001$] and recurrence (HR = 1.37, 95% CI = 1.12-1.68, $P = 0.003$) was evident in patients with high-grade tumor budding.
- Sensitivity and subgroup analyses revealed consistent results.
- Pathological stage II, lymph node metastasis, lymphovascular and pleural invasion were associated with high-grade tumor budding.

CONCLUSIONS:

- Tumor budding is a new and promising prognostic factor in patients with LSCC.
- However, pervasive heterogeneity and publication bias reduces the credibility of these findings and the applicability of tumor budding in clinical practice.
- Future studies are required to standardize reporting on tumor budding in LSCC.

Articles for Notation – Neoplastic

Yang CY, et al. Genomic profiling with large-scale next-generation sequencing panels distinguishes separate primary lung adenocarcinomas from intrapulmonary metastases. *Mod Pathol.* 2023 Mar;36(3):100047.

OBJECTIVE:

- To investigate the value of large-scale next-generation sequencing (NGS) panels for distinguishing between separate primary lung cancers (SPLCs) and intrapulmonary metastases (IPMs).

METHODS:

- A total of 32 patients with 69 lung adenocarcinomas were included.
- Comprehensive histopathologic assessments of multiple pulmonary adenocarcinomas were performed independently by 3 pathologists.
- The consensus of histopathologic classification was determined by a majority vote.
- Genomic analysis was performed using an amplicon-based large-scale NGS panel, targeting single-nucleotide variants and short insertions and deletions in 409 genes.
- Tumor pairs were classified as SPLCs or IPMs according to a predefined molecular classification algorithm.

RESULTS:

- Using NGS and the authors' molecular classification algorithm, 97.6% of the tumor pairs could be unambiguously classified as SPLCs or IPMs.
- The molecular classification was predictive of postoperative clinical outcomes in terms of overall survival ($P = .015$) and recurrence-free interval ($P = .0012$).
- There was a moderate interobserver agreement regarding histopathologic classification ($\kappa = 0.524$ at the tumor pair level).
- The concordance between histopathologic and molecular classification was 100% in cases where pathologists reached a complete agreement but only 53.3% where they did not.

CONCLUSIONS:

- This study showed that large-scale NGS panels are a powerful modality that can help distinguish SPLCs from IPMs in patients with multiple lung adenocarcinomas and objectively provide accurate risk stratification.

Perez Holguin RA, et al. Outcomes after sublobar resection versus lobectomy in non-small cell carcinoma in situ. J Thorac Cardiovasc Surg. 2022 Jun 1:S0022-5223(22)00627-4.

OBJECTIVE:

- The aim of this study was to compare lobectomy and sublobar resection in patients with ≤ 2 cm pure non-small cell lung carcinoma (NSCLC) in situ.
- The relationship of these modalities with regional lymph node (LN) sampling was also investigated.

METHODS:

- The National Cancer Database was used to identify patients diagnosed with NSCLC clinical Tis N0 M0 with a tumor size ≤ 2 cm between 2004 and 2017.
- The χ^2 tests were used to examine subgroup differences by type of surgery.
- Kaplan-Meier method and Cox proportional hazard model were used to compare overall survival.

RESULTS:

- Of 707 patients, 56.7% (401 out of 707) underwent sublobar resection and 43.3% (306 out of 707) underwent lobectomy.
- There was no difference in 5-year overall survival in the sublobar resection group (85.1%) compared with the lobectomy group (88.9%; $P = .341$).
- Multivariable survival analyses showed no difference in overall survival (hazard ratio, 1.044; $P = .885$) in the treatment groups.
- LN sampling was performed in 50.9% of patients treated with sublobar resection.
 - In this group, LN sampling was not associated with improved survival (84.9% vs 85.0%; $P = .741$).

CONCLUSIONS:

- The authors observed no difference in overall survival between sublobar resection and lobectomy in patients with clinical Tis N0 M0 NSCLC with tumors ≤ 2 cm.
- Sublobar resection may be an appropriate surgical option for this population.
- LN sampling was not associated with improved survival in patients treated with sublobar resection.

Ernani V, et al. Cancer. Lobar versus sublobar resection for atypical lung carcinoid: An analysis from the National Cancer Database. 2023 Mar 15;129(6):860-866.

OBJECTIVE:

- To understand and analyze the outcomes of sublobar resection versus lobectomy in patients with atypical carcinoid (AC).

METHODS:

- A retrospective analysis using the National Cancer Database was performed to compare overall survival (OS) between patients treated with lobectomy and patients treated with sublobar resection for AC of the lung between the years 2004 and 2016.
- Patient characteristics were compared with χ^2 tests.
- The Kaplan-Meier method was used to estimate OS distributions, and the log-rank test was used to compare distributions by treatment strategy.
- A multivariable Cox regression model was used to assess associations between the treatment strategy and OS.
- A propensity score matching method was also implemented to further eliminate treatment selection bias in the study sample.

RESULTS:

- The database identified 669 patients with T1-T4 and N0-N3 lung ACs that were surgically resected.
- Unadjusted Kaplan-Meier survival curves did not demonstrate an OS difference between lobectomy and sublobar resection ($p = .094$).
- After propensity score matching, curves demonstrated a numerical improvement in OS with lobectomy; however, it was not statistically significant ($p = .5$).
- In a subgroup analysis, lobectomy and node-negative disease were associated with the best OS, whereas sublobar resection and node-positive disease were associated with the worst OS ($p < .0001$).
- Nodal involvement was associated with worse survival, regardless of surgical treatment ($p < .0001$).

CONCLUSIONS:

- In patients with T1-T4 and N0-N3 ACs of the lung, lobectomy was not associated with an improvement in OS in comparison with sublobar resection.

Mata DA, et al. Method of Tissue Acquisition Affects Success of Comprehensive Genomic Profiling in Lung Cancer. Arch Pathol Lab Med. 2023 Mar 1;147(3):338-347.

BACKGROUND:

- Comprehensive genomic profiling (CGP) is a next-generation sequencing approach that uses a single assay to analyze a broad panel of genes to detect the four main classes of genomic alterations known to drive cancer growth:
 - Base substitutions,
 - Insertions and deletions,
 - Copy number alterations, and
 - Rearrangements or fusions.
- Multiple procedural techniques can be used to obtain tissue to create a formalin-fixed, paraffin-embedded specimen for CGP in lung cancer.
- The literature is mixed on whether the procedure affects CGP success.

OBJECTIVE:

- To examine whether biopsy procedure affects lung cancer CGP success.

METHODS:

- This was a cross-sectional study of all patients with lung cancer whose specimens were submitted for CGP between January and February 2020.
- Multiple quality control metrics were used to determine whether cases were successfully profiled.

RESULTS:

- 3312 samples were identified.
 - 67.5% (2236 of 3312) of samples were obtained from biopsies,
 - 13.0% (432 of 3312) from fine-needle aspirations (FNAs),
 - 9.7% (321 of 3312) from resections,
 - 5.3% (174 of 3312) from fluid cytology cell blocks,
 - and 4.5% (149 of 3312) from bone biopsies.
- Overall,
 - 70.1% (2321 of 3312) of cases passed CGP,
 - 15.4% (510 of 3312) of cases were released as qualified reports, and
 - 14.5% (481 of 3312) of cases failed CGP.
- Resection samples were the most likely to be successfully sequenced, failing in only 2.8% of instances, while fluid cytology specimens were the least likely, failing in 23.0% of instances.
- Biopsy, FNA, and bone biopsy specimens failed at intermediate frequencies.
- Among patients with successfully sequenced samples, 48.0% were eligible for at least 1 therapy, based on a companion diagnostic or National Comprehensive Cancer Network biomarker.

CONCLUSIONS:

- The method of tissue acquisition was an important preanalytic factor that determined whether a sample would be successfully sequenced and whether a clinically actionable genomic alteration would be detected.

Articles for Notation – Non-Neoplastic

Borie R, et al. European Respiratory Society statement on familial pulmonary fibrosis. *Eur Respir J*. 2023 Mar 16;61(3):2201383.

- Genetic predisposition to pulmonary fibrosis is suggested by a 10-fold increase in disease prevalence in families of patients with a diagnosis of idiopathic pulmonary fibrosis.
- Initial studies of familial clustering of interstitial lung disease (ILD) led to the discovery of mutations in genes implicated in telomere homeostasis (telomere-related genes) and surfactant homeostasis (surfactant-related genes)
- Genetic predisposition to pulmonary fibrosis has been confirmed by the discovery of several gene mutations that cause pulmonary fibrosis.
- Although genetic sequencing of familial pulmonary fibrosis (FPF) cases is embedded in routine clinical practice in several countries, many centers have yet to incorporate genetic sequencing within ILD services and proper international consensus has not yet been established.
- An international and multidisciplinary expert Task Force (pulmonologists, geneticists, pediatrician, pathologist, genetic counsellor, patient representative and librarian) reviewed the literature between 1945 and 2022, and reached consensus for all the following questions:
 1. Which patients may benefit from genetic sequencing and clinical counselling?
 2. What is known of the natural history of FPF?
 3. Which genes are usually tested?
 4. What is the evidence for telomere length measurement?
 5. What is the role of common genetic variants (polymorphisms) in the diagnostic workup?
 6. What are the optimal treatment options for FPF?
 7. Which family members are eligible for genetic sequencing?
 8. Which clinical screening and follow-up parameters may be considered in family members?
- Through a robust review of the literature, the Task Force offers a statement on genetic sequencing, clinical management and screening of patients with FPF and their relatives.
- This proposal may serve as a basis for a prospective evaluation and future international recommendations.

Vietzen H, et al. The human cytomegalovirus-specific and UL40-mediated imprint in the natural killer cell repertoire is associated with antibody-mediated rejection in lung transplant recipients. *J Heart Lung Transplant*. 2023 Mar;42(3):305-314.

Comment in

J Heart Lung Transplant. 2023 Mar;42(3):315-316.

BACKGROUND:

- CD16+ natural killer (NK-) cells play, together with donor-specific antibodies (DSA) and via antibody-dependent cellular cytotoxicity (ADCC), an important role in the pathogenesis of antibody-mediated rejection (ABMR) in lung-transplant recipients (LTRs).
- Cytotoxic CD16+NKG2C+ NK cells proliferate in response to human Cytomegalovirus (HCMV) infections via the presentation of HCMV-encoded and highly polymorphic UL40 peptides.

OBJECTIVE:

- To clarify whether infections with HCMV-strains carrying different UL40 peptide variants are associated with the shift of the NK cell repertoire and the development of ABMR in LTRs.

METHODS:

- 30 DSA+ABMR+, 30 DSA+ABMR- and 90 DSA-ABMR- LTRs were included in the study.
- In all patients, 1 episode of high-level HCMV-replication occurred.
- In all DSA+ABMR+ LTRs, HCMV-replication occurred prior to ABMR diagnosis.
- The association of HCMV UL40 variants with the expansion of CD16+ NK cell subsets and ABMR was assessed in NK cell proliferation and ADCC assays.

RESULTS:

- The study revealed that the VMAPRTLIL and VMTPTLVL UL40 variants were significantly overrepresented in DSA+ABMR+ LTRs.
- Both peptides were associated with a pronounced proliferation of cytotoxic and proinflammatory CD16+NKG2C+ NK cells.
- The stimulation with both peptides led to a shift of the NK cell repertoire towards CD16+NKG2C+ NK cells, which was associated with strong ADCC responses after stimulation with endothelial cells and plasma from DSA+ABMR+ LTRs.

CONCLUSIONS:

- Distinct UL40 peptide variants of the infecting HCMV-strain are associated with the development of ABMR after lung transplantation, due to a shift towards a highly cytotoxic CD16+NKG2C+ NK cell population.
- These peptides are thus potential prognostic markers for ABMR.

Maron BA, et al. Evidence of Advanced Pulmonary Vascular Remodeling in Obstructive Hypertrophic Cardiomyopathy With Pulmonary Hypertension. *Chest*. 2023 Mar;163(3):678-686.

BACKGROUND:

- Elevated mean pulmonary artery pressure (mPAP) is common in patients with hypertrophic cardiomyopathy (HCM) and heart failure symptoms.
- However, dynamic left ventricular (LV) outflow tract obstruction may confound interpretation of pulmonary hypertension (PH) pathophysiologic features in HCM when relying on resting invasive hemodynamic data alone.

OBJECTIVE:

- To evaluate structural changes to the lung vasculature in patients with HCM with progressive heart failure.

METHODS:

- Clinical data and ultrarare lung autopsy specimens were acquired retrospectively from the National Institutes of Health (1975-1992).
- Patients were included based on the availability of lung tissue and recorded mPAP.
- Discarded tissue from rejected lung donors served as control specimens.
- Histomorphology was performed on pulmonary arterioles and veins.
- Comparisons were calculated using the Student t test and Mann-Whitney U test; Pearson correlation was used to assess association between morphometric measurements and HCM cardiac and hemodynamic measurements.

RESULTS:

- The HCM cohort (n = 7; mean \pm SD age, 43 \pm 18 years; 71% men) showed
 - Maximum mean \pm SD LV wall thickness of 25 \pm 2.8 mm, mean \pm SD outflow tract gradient of 90 \pm 30 mm Hg, median mPAP of 25 mm Hg, median pulmonary artery wedge pressure (PAWP) of 16 mm Hg, and median pulmonary vascular resistance of 1.8 Wood units.
- Compared with control samples (n = 5), patients with HCM showed
 - Greater indexed pulmonary arterial hypertrophy and arterial wall fibrosis, which correlated with mPAP, PAWP, and LV outflow tract gradient.
- Compared with control samples,
 - Pulmonary vein thickness was increased by 2.9-fold in the HCM group, which correlated with mPAP and LV outflow tract gradient.

CONCLUSIONS:

- These data demonstrate that in patients with obstructive HCM, heart failure is associated with pathogenic pulmonary vascular remodeling even when mPAP is elevated only mildly.

Ohya M, et al. Bystander CD8+T cells may be involved in the acute phase of diffuse alveolar damage. *Virchows Arch.* 2023 Mar;482(3):605-613.

BACKGROUND:

- Acute respiratory distress syndrome (ARDS) is a serious complication of systemic inflammatory response syndrome and diffuse alveolar damage (DAD) is a histological manifestation of ARDS.
- Endothelial cell injury is mainly responsible for ARDS.
- Many neutrophils and macrophages/monocytes, which are inflammatory cells that play a role in innate immunity, infiltrate the lung tissue in DAD.
- In recent years, it has become clear that CD8 plays an important role not only in the acquired immune system, but also in the innate immune system.
- Non-antigen-activated bystander CD8 + T cells express the unique granzyme B (GrB) + /CD25- /programmed cell death-1 (PD-1)-phenotype.
- The involvement of bystander CD8 + T cells in lung tissue in DAD is an unexplored field.

OBJECTIVE:

- To determine whether bystander CD8 is involved in DAD.

METHODS:

- Twenty-three consecutive autopsy specimens were retrieved from patients with DAD, and the phenotypes of infiltrating lymphocytes in the DAD lesions were evaluated using immunohistochemistry.
- In most cases, the number of CD8 + T cells was higher than that of CD4 + T cells, and many GrB + cells were also observed.
- However, the number of CD25 + and PD-1 + cells was low.

CONCLUSION:

- The authors conclude that bystander CD8 + T cells may be involved in cell injury during the development of DAD.

Borie R, et al. Pleuropulmonary manifestations of vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic (VEXAS) syndrome. *Chest*. 2023 Mar;163(3):575-585.

BACKGROUND:

- The vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic (VEXAS) syndrome is a newly identified autoinflammatory disorder related to somatic UBA1 mutations.
- Up to 72% of patients may show lung involvement.

OBJECTIVE:

- To investigate pleuropulmonary manifestations of VEXAS syndrome.

METHODS:

- 114 patients were included in the French cohort of VEXAS syndrome between November 2020 and May 2021.
- Patients who had chest CT scans available were discussed by a multidisciplinary team and were classified as showing pleuropulmonary involvement by the VEXAS syndrome or something else.

RESULTS:

- 51 patients had a CT scan available for review and 45 patients (39%) showed pleuropulmonary abnormalities on chest CT scan that were considered related to VEXAS syndrome.
 - Most of these 45 patients were men (95%) with a median age 67.0 years at the onset of symptoms.
 - 44% reported dyspnea and 40% reported cough.
 - All 45 patients showed lung opacities on chest CT scan (including ground-glass opacities [87%], consolidations [49%], reticulation [38%], and septal lines [51%]) and 53% of patients showed pleural effusion.
 - Most patients showed improvement with prednisone, but usually required > 20 mg/d.
 - The main clinical and biological features as well the median survival did not differ between the 45 patients with pleuropulmonary involvement and the rest of the cohort.

CONCLUSIONS:

- Pulmonary manifestations are frequent in VEXAS syndrome, but rarely are at the forefront.
- The initial outcome is favorable with prednisone and does not seem to lead to pulmonary fibrosis.

Review Article

Hung YP, Mino-Kenudson M. Beyond PD-L1: Assessment of LAG-3 and other predictive biomarkers in non-small cell lung carcinoma. *Cancer Cytopathol.* 2023 Mar;131(3):151-153.

Case Reports

Ghalib S, et al. A 52-Year-Old Man Who Smokes with Rapidly Progressive Respiratory Failure. *Chest.* 2023 Mar;163(3):e119-e123.

Diagnosis: Pneumonic type lung adenocarcinoma with lepidic growth.

Quigley N, et al. A 37-Year-Old Man with Right Lung Consolidation. *Chest.* 2023 Mar;163(3):e111-e114.

Diagnosis: Acute disseminated blastomycosis (pulmonary and cutaneous) in an immunocompetent host.

Palani P, et al. A 33-Year-Old Woman With Breathing Difficulty, Inspiratory Wheeze, and Hemoptysis. *Chest.* 2023 Mar;163(3):e141-e145.

Diagnosis: Synovial sarcoma of the trachea obstructing 70% to 80% of the lumen.