CLINICAL CASE PRESENTATION

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- Patient is a 53 year never smoker female with a remote history of breast cancer. Treated by surgery, radiation and took hormonal therapy X 5 years.
- In 2020, reported irregular vaginal bleeding. Work up revealed an early-stage endometrial cancer. Incidentally, noted to have a lung nodule in that work up. Hysterectomy with BSO performed in 2020.
- The lung nodule turned out to be a right lower lobe adenocarcinoma at 2.6cm maximal size. Removed by lobectomy and LN dissection. Final pathology was pT1cN0 disease.
- She was being monitored by thoracic surgery service regularly.
- A follow up CT in 6/2023 showed mass effect near the right hilum and posterior to right mainstem bronchus. PET scan revealed a focus of soft tissue fullness at the surgical resection site near the hilum extending close to the proximal airway and a nodule in the lung parenchyma itself. Activity near a right paratracheal LN.
- EBUS biopsy shows hilar lymph nodes and RUL nodule to be positive for malignancy. Similar to prior lung tumor.
- Given prior history of surgery, further repeat surgical resection deemed not feasible by thoracic surgery service.
- Thyroid nodules also noted on further work up and assessed by biopsy.

Pathology Data

- Surgical pathology from the right lower lobe October 2020:
- Lung, right lower lobe, lobectomy:
  - Moderately differentiated adenocarcinoma, with papillary (80%) and acinar (20%) growth patterns (see comment).
  - 2.6 cm in greatest dimension.
- Histologic Grade: G2: Moderately differentiated
  - Spread Through Air Spaces (STAS): Not identified
  - Tumor Size: 2.6 cm x 2.5 cm x 1.6 cm
  - Tumor Focality: Single focus
  - Visceral Pleura Invasion: Not identified
  - Lymphovascular Invasion: Not identified

Pathology Data Continued

- PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th Edition)
  - Primary Tumor (pT): pT1c
  - Regional Lymph Nodes (pN): pN0
  - Napsin A: positive
  - TTF1: positive
  - CK7: positive
  - CK20: negative
  - GATA3: negative
  - PAX8: negative
  - NGS: *PTEN (c.331T>C, p.W111R) (VAF ~70%)*
  - TMB: Low
  - MSI: Stable
  - PD-L1 IHC (22C3): No expression, tumor proportion score (TPS): 0%
  - Pan-TRK: Tumor cells are NEGATIVE for TRK protein expression.

Pathology Data Continued

- RUL nodule in 6/28/2023:
  Adenocarcinoma
  TTF1: Positive (patchy weak to moderate nuclear staining)
  p40: Negative
- PAX8 negative in the tumor
- Lymph node, station 11R, fine needle aspiration:Positive for malignant cells-consistent with adenocarcinoma.
- NGS: Results Summary

  EGFR amplification

  PTEN W111R

  Tumor Mutation Burden (TMB): TMB- Low (9.2 Muts/Mb)

  Microsatellite Instability (MSI): MS-Stable

  Pertinent Negative Biomarkers: ALK, BRAF, EGFR, ERBB2, KRAS, MET, ROS1, RET,NTRK1, NTRK2, NTRK3

  Pan-TRK: Tumor cells are NEGATIVE for TRK protein expression

  PD-L1 Tumor Proportion Score (TPS): 1 %

  RNA (archer multiplex): negative

Pathology Data Continued

Thyroid nodule biopsy on 3/22/2024

- "Middle Left Thyroid Nodule," Fine Needle Aspiration: Benign. Consistent with benign adenomatoid nodule.
- "Upper Left Thyroid Nodule," Fine Needle Aspiration: Atypia of undetermined significance.

Pathology Data Continued

- Primary malignant neoplasm of female breast (disorder) (Stage Date: 04/22/2016 : B/l Mastectomy with DCIS in left breast and Pleomorphic LCIS in Right breast.
- BRCA1: Negative (mutation not present)
- BRCA2: Negative (mutation not present)
- Invitae; BRCA Panel: Gene sequencing: Negative
- MMR **(Mismatch Repair): Proficient;**

- Primary endometrioid carcinoma of endometrium of body of uterus (disorder)
- Stage Date: 08/03/2020, Stage IA (T1a, N0,cM0)

Genetic Testing Blood on 10/22/2020

- PTEN c 331T>C (p. Trp 111Arg): Heterozygous- Likely Pathogenic
- Additional VUS: MET c. 1450 C>T 9p.His484Tyr). Heterozygous - Uncertain significance
- (Interpretation: PTEN mutation is likely pathogenic but additional data are needed to prove conclusively)
- (Interpretation: MET: seen in population database 0.03%. Not been reported in individual in the literature affected with MET related conditions).

Questions

- In patients who have locally advanced NSCLC and are never or oligo smokers (low neoantigen load, low TMB etc) and with no AGA, would you use Immunotherapy consolidation after chemoradiation?

- What would you do for locally advanced NSCLC patients who are EGFR, ALK, ROS1, RET positive?