Cancer Biology Training Consortium
Example Lung Cancer Case
2018

CASE-BASED LEARNING
CBL CASE #1
John

FACILITATOR COPY

Case Goal: to enable students to apply their growing knowledge of basic physiology to the clinical presentation and understanding of non-small cell lung cancer.

Anatomy
1. Review the anatomy of the chest.
2. Correlate symptoms and physical findings with radiographic findings.

Biochemistry
1. Explain the concept of biological systems: not like light switches that turn on/off, but rather like seesaws with a balance point on which the system can be up- or down-regulated.

Cell Biology/Genetics
1. Explain how the expression of PDL1 affects cancer therapy treatment.

Physiology
1. Understand the process of pulmonary function testing and interpretation of the test results.

Clinical Decision-making and Biostatistics
1. Explain what risk factors are and how they are determined/defined.
2. Summarize how pre-test probability affects the interpretation of the test result.
3. Recognize when test sensitivity is of great importance.
4. Recognize when test specificity is of great importance.
5. Identify how considering patient-centered outcomes can improve clinical decision-making.

Health Economics
1. Discuss whether and when uncommon conditions which require expensive testing should be sought.

Learning issues will develop as the group decides what interests them and which direction they would like to proceed. It will be important to encourage students to focus not only on the facts of the case, but also on the physician-patient interactions.

Case 1 progress for All Groups:

Week 1	Lung mass work-up: History, physical exam, imaging, laboratory, pulmonary function testing, and biopsy	No Learning Issue
Week 2	NSCLC treatment: Lobectomy, alternative treatment options, treatment related toxicity, cancer follow up	Learning Issue due
Week 3	NSCLC recurrence: Genetic testing, EGFR, ALK, PD-1/PD-L1, chemotherapy, radiation therapy, treatment related toxicities	Learning Issue due
Week 4	No new information, discussion of learning issues only; feedback with students individually during 2nd hour	Learning Issue due

John-Segment 1

Inform students:

- Setting: Primary care office
- Patient is a 71-year-old male who presented to primary care office with a 3 month history of cough that is not improving with over the counter cold medicine, 20-pound unintentional weight loss, and a recent episode of coughing up a teaspoon of blood.

Synopsis: Patient was well until 3 months ago when he developed a non-productive cough. He tried multiple over the counter cold medicines without benefit. Over this time, he also noticed an approximately 20 pound weight loss despite not changing his eating habits or activity levels. Ten days ago, he experienced an episode of coughing up small flecks of dark blood mixed with sputum. No recent fevers or chills or chest pain. After the episode of coughing up blood, his wife scheduled a visit with his primary care provider.

Suggested questions to facilitate discussion:

- Identify possible causes of cough. What additional information from the patient history would be helpful in understanding the chief complaint?
- Identify possible causes of unintentional weight loss. What additional information from the patient history would be helpful in understanding the chief complaint?
- What is a pertinent positive?
- What is a pertinent negative?
- Which are the most important pertinent positives and pertinent negatives?
- Identify possible causes of coughing up blood. What additional information from the patient history would be helpful in understanding the chief complaint?
- What would you like to know regarding his past medical history, social history and family history?

Segment 2

Past Medical History: Prior fair to good health. He sees a physician regularly for ongoing health maintenance. Has history of hypertension and hyperlipidemia both controlled with medication, coronary artery disease with three stents placed 3 years ago. Past surgical history includes appendectomy as a child, inguinal hernia repair on left side, cataract surgery on both eyes.

Social History: He has smoked 2-3 packs of cigarettes per day for the past 40 years. He consumes a six-pack of beer per week. Denies any illicit drug use. He is married with 2 children. Retired factory worker with asbestos exposure approximately 20 years ago.

Family History: Both parents are deceased. Mother: heart disease, hypertension, stroke, diabetes. Father: hypertension and metastatic cancer of unknown origin. An older sister (80 years old) with COPD. Younger brother (67 years old): asthma and prostate cancer. Has two children both in good health.

Review of Systems:
General: feels well. Denies fever, chills, and night sweats.
Respiratory: positive for cough productive with clear sputum. Recent episode of hemoptysis. Negative for wheezing. Is able to climb one flight of stairs before becoming short of breath.
Cardiovascular: negative for chest pain
GI: denies changes in eating habits, abdominal pain, or changes in bowel movements.
Musculoskeletal: negative for muscle weakness
Neuro: denies headaches, vision changes, hearing changes, seizures, or coordination issues

Medications:
1) Losartan 100 mg daily
2) Hydrochlorothiazide 12.5 daily
2) Pravastatin: 40 mg daily

Sexual History: Monogamous with spouse

Physical Exam:

Vital signs: BP: 130/66. Pulse: 80, Temperature: 36.1˚C (Tympanic), Respiration: 20, Wt: 88.5 kg.

General appearance: alert, cooperative, no acute distress

Back: symmetric, normal curvature

Lungs: rhonchi in left and right upper lung zones.

Chest: Well healed thoracotomy scar

Heart: regular rate and rhythm, S1 and S2 normal, no murmurs, clicks, rubs or gallops

Lymphatics: negative for cervical, axillary, scalene or supraclavicular adenopathy

Abdomen: Flat with normal bowel sounds and no palpable hepato-splenomegaly or masses

Extremities: atraumatic, no cyanosis or edema, redness or tenderness in calves or thighs

Neurologic: alert and oriented x3. Normal strength, muscle tone, coordination and gait. Symmetric reflexes.

Remainder of physical exam non-contributory to the present illness.

Suggested questions to facilitate discussion:

- What is the significance of the past medical history, family history and social history? Does this change your differential diagnosis?
- What is the significance of the asbestos exposure?
- What is the significance of the breath sounds?
- How would you counsel the patient regarding his tobacco use?
- What is your differential diagnosis?

Segment 3

This segment includes: chest x-ray, laboratory, CT, pulmonary function testing, biopsy

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Laboratory Data

Na: 140 mEq/L (135-145 mEq/L)
K: 4.0 mEq/L (3.5-5.0 mEq/L)
Cl: 103 mEq/L (95-107 mEq/L)
CO_2: 24 mEq/L (24-32 mEq/L)
BUN: 13 mg/dL (10-20 mg/dL)
Creat: 0.7 mg/dL (0.7-1.4 mg/dL)
Gluc: 106 (65-99 mg/dL)

WBC: 9.6 K/mm^3 with normal differential (3.7-10.5 K/mm^3)
Hgb: 14.5 g/dL (11.9-15.1 g/dL)
Platelets: 210 K/mm^3 (150-400 K/mm^3)

Chest X-ray: (2cm nodule in the left upper lung zone. Thoracotomy changes).

Pulmonary function testing:
FVC: 5.47 L (139% predicted)
FEV1: 3.23 L (112%)
FEV1/FVC: 59%
TLC: 6.57 L (111%)
DLCO: 13.5 ml/min/mmHg (54%)

CT chest: (2cm nodule in the left upper lobe, central lobular emphysema).

Suggested questions to facilitate discussion:

- What is the significance of a 2cm nodule in a patient with a significant smoking history?
- Is screening recommended for individuals with a long smoking history?
- What is a "low dose CT scan?"
- For a screening test, which is more desirable: sensitivity or specificity? Why?
- What does pulmonary function testing evaluate?
- What are the different measurements of pulmonary function testing? Why are they needed in this case?

Segment 4

Synopsis: PET/CT scan, bronchoscopy

PET/CT scan: (intensely hypermetabolic, lobulated LUL lung nodule concerning for malignancy. No evidence of metastatic disease).

Left upper lobe transbronchial biopsy: Adenocarcinoma, poorly differentiated, TTF-1 positive, CK7 positive, CK20 negative.

Suggested questions to facilitate discussion:

- What is a PET scan? What does it assess?
- What regions are difficult to assess in a PET scan? Why?
- How is a bronchoscopy performed?
- What are the risks of bronchoscopy?
- What are TTF-1, CK7, and CK20? Why are these markers useful in a cancer work-up?
- What biochemical and oncogenic signaling pathways are involved in lung adenocarcinoma?
- How is lung cancer staged? What stage is the patient?
- Adenocarcinoma is a type of lung cancer. Are there additional types of lung cancer?
- What are the treatment options for this stage of non-small cell lung cancer? What should be considered when discussing treatment options?

Segment 5

Patient undergoes smoking cessation and cardiac evaluation. Patient is deemed to be low to moderate risk for surgical complications. He undergoes a left upper lobectomy.

Pathology: left upper lobectomy demonstrates poorly differentiated adenocarcinoma. Margins were negative. Fifteen lymph nodes were sampled from the left hilar and mediastinal lymph node stations; none were positive for malignancy.

Suggested questions to facilitate discussion:

- What is involved in a cardiac evaluation in preparation for a lobectomy?
- What is a mediastinoscopy? What mediastinal lymph node stations does it typically sample? When should a mediastinoscopy be performed?
- What is a lobectomy? How is it different than a wedge resection? How is it different than a pneumonectomy?
- How often and how long should the patient be followed? What imaging modalities should he be followed with?
- What is the difference between mediastinal and hilar lymph nodes?
- Should adjuvant treatment be considered? What does “adjuvant” mean? What do neoadjuvant, induction and consolidation therapy mean?

Segment 6

Synopsis: Two years later, he develops fullness in the left lower neck, worsening cough productive with clear sputum. CT scan was ordered followed by a PET/CT scan.

CT scan: (development of mediastinal, left hilar, and lower left cervical lymph nodes.).

PET/CT: Left lower neck and left supraclavicular hypermetabolic lymphadenopathy, likely representing metastases.

Suggested questions to facilitate discussion:

- How are consultants utilized in the care of patients? What is the role of a consultant?
- How accurate is a CT scan and PET/CT in establishing the diagnosis of recurrent lung cancer?
- What other diagnostic tests could be used to confirm or exclude a diagnosis of recurrent lung cancer?
- For a confirmatory diagnostic test, which is more important: sensitivity or specificity? Why?

Segment 7

Synopsis: Patient undergoes left supraclavicular lymph node biopsy. Molecular testing is ordered including: EGFR gene analysis, *ALK* FISH testing, PDL1 expression, *ROS1* rearrangement analysis, *BRAF*V600E mutation analysis.

Pathology: Adenocarcinoma, poorly differentiated, TTF-1 positive.

EGFR: normal nucleotide sequence of exons 18-21 of the *EGFR* gene
ALK rearrangement negative
PDL1 expression on tumor cells: 55%
ROS1 rearrangement negative
BRAFV600E negative

Suggested questions to facilitate discussion:

- How do you decide which site to biopsy?
- What is an endobronchial ultrasound and how is it performed?
- What is the *EGFR* gene? How does an *EGFR* mutation affect cancer treatment?
- What is PCR? Why only assess exons 18-21 of the *EGFR* gene?
- What is ALK? How is ALK assessed?
- What is FISH? How does an ALK rearrangement affect cancer treatment?
- What is PDL1? How is PDL1 expression assessed? How does PDL1 affect cancer treatment?
- What is *ROS1* and how is it detected? How does a ROS1 rearrangement affect cancer treatment?
- What does the stem *BRAF*V600E mean? How does this mutation affect cancer treatment?
- What are his treatment options? What treatment option would you recommend?
- What experimental therapeutics/clinical trials are currently enrolling subjects for lung adenocarcinoma?