INTRODUCTION:
Due to the progressive nature of the disease, symptom management is an integral part of heart failure (HF) treatment. Dyspnea is a prevalent symptom of left-sided HF. The etiology is thought to be from hypoxemia d/t increased pulmonary capillary wedge pressure as well as decreased pulmonary function and decreased respiratory muscle function. However, the etiology of dyspnea can be multifactorial and it is important to screen for other differential diagnoses, particularly when a HF patient “fails to thrive”.

CASE PRESENTATION:

Background Information:
• 74-year old, cachexic white male with refractory to treat/progressive dyspnea, despite HF treatment.
• History of:
  – Ischemic dilated cardiomyopathy, chronic atrial fibrillation, CABG, COPD, anemia, hyperthyroidism
  – Cardiac Resynchronization Therapy (CRT) placed 10 months ago. (AHA/ACC guidelines do not indicate CRT for HF pts with chronic –Fib d/t limited outcome data, but this pt received one anyway)
  – Remote smoking history- quit cigarettes 41 years ago
  – Echo - 4 chamber dilatation, severely reduced LV systolic function (LVEF <20%), Mild MR+TR, LA clot
  – Medications include ace-inhibitor (ACE-I), loop diuretic, thiazide diuretic for prn use, digitalis, anticoagulant, bronchodilator MDI, bronchodilator nebulizer treatments. (Pt not on beta-blocker (BB) d/t hx of bronchospasm with BB and he had refused rechallenge. Pt not on antithyroid agent d/t hx of adverse drug reaction of anxiety and he had refused rechallenge.)
• Chief Complaint:
  – Continues to c/o DOE, orthopnea, PND, and dry cough despite close follow-up/ interventions over 10-month period.
Denies chest pain, palpitations, anorexia. Stable mild fatigue. Gradual 10 lb wt loss in past 3 months, despite good appetite

Stable physical exam findings: BP 90/60. HR 72. Neck neg for goiter or nodules. Irreg, irreg rhythm. Soft S3. Mild TR. JVD at 5 cm with HOB elevated 45o. No ascites or hepatomegaly, NYHA IIIb.

Varied physical exam findings throughout the course of treatment:
- pt’s breath sounds ranged from clear to generalized scattered wheezes intermittently.
- pt developed continued diminished RLL breath sounds in the last 6 months.
- rest and ex O2 sat remained at 96% until 10th month- then dropped to 91%.
- pt had intermittent bilateral leg edema.

**Differential Diagnoses (for dyspnea):**
- CHF, angina, pulmonary embolus, COPD, asthma, anxiety, pneumonia, anemia, and lung cancer

**Labs/Confirmatory Evaluations:**
- Myoview showed dilated heart without focal perfusion defects, thus LHC was not done. (RHC to optimize medications were not done routinely at this facility.)
- PFT: moderate obstructive disease with FEV1/FVC 64%. No significant post-bronchodilator effect.
- INRs: remained stable throughout the course of treatment
- Thyroid function tests:
  - Baseline
    - TSH- 0.147 (0.465-4.68 WNL)
    - Free T4- 2.28 (0.78-2.19 WNL)
    - Free T3- 11.1 (2.77-5.77 WNL)
  - 8 months later
    - TSH- 0.302
    - Free T4- 2.11
    - Free T3 - 6.58
- BUN/Cr: WNL 10 months ago and as high as 40/1.4 within past 10 months with increased diuresis
• Pro-BNP: 5,368—Baseline when CRT placed  
  10,864—1 months later  
  10,179—6 months later  

(Normal Pro-BNP values: <125 pg/ml for pts <age 75, <450 pg/ml for pts >age 75 with >30,450 pg/ml as maximum range measured)

• CBC: H/H 10.1/30.2 with iron sat at 7% before IV ferrlicet.  
  H/H 10.8/32.9 with iron sat 9.5% after 8 treatments of IV ferrlicet.

• Intermittent hyperglycemia, yet hemoglobin A1C was 4.9 (Likely hemoglobin A1C slightly higher than this but anemia skews readings)

• Chest X-rays:  
  – Clear at baseline, prior to CRT placement  
  – Bilateral pleural effusions, 6 months later (despite aggressive diuresis)  
  – Increased R pleural effusion, R middle lobe atelectasis, worsening pulmonary venous congestion, 8 months later (despite aggressive diuresis)  
  – Greatly increased R pleural effusion, 10 months later (despite aggressive diuresis)

• Chest CT 10 months: Large R pleural effusion. Right middle bronchial lesion, enlarged precarinal lymph node concerning for malignancy

• Sputum cytology: neg

• Thoracentesis cytology: pos for squamous cell cancer

Review of Interventions/Treatments:

• ACE-I titrated to highest dose that pt could tolerate. Diuretics titrated to daily wts and monitored by clinical exams, serial BUN/CR/lytes, and BP’s. Pro-BNP remained elevated despite diuresis. Pt monitored daily with telehealth.  
  – Pt would intermittently report less dyspnea after diuresis, but it was never sustained.

• Spironolactone was started, but later dc’ed when pt noted tender right breast mass. Mass decreased in size (from 5 X 5 to 2x2 mm) and tenderness resolved. After washout period, Eplerenone was started. (In hindsight, digitalis should also have been dc’ed as it can also cause gynecomastia.)  
  – Pt would intermittently report less dyspnea after meds were adjusted, but it was never sustained.
• A thyroid scan/uptake was unremarkable.
  – HR remained controlled, despite untreated mild hyperthyroidism.

• 5 months after CRT placement, pt referred back to cardiologist for AV optimization – this particular cardiology dept did not have capability to perform AV optimization, but cardiologist said the pt had a high LV lead threshold. The pt’s output was increased and the plan was to have him return in 3 months and if the threshold was still high at that time, the LV lead would be repositioned.
  – Dyspnea was not any better after PM settings were changed.

• 6 months after CRT placement, pt referred to pulmonologist for refractory dyspnea. He said that COPD was treated appropriately but that dyspnea was related to CHF and anemia. He recommended treating anemia.

• Pt treated with 8 doses of IV ferrlicet without significant response (see lab values)
  – Dyspnea did not resolve after treatments.

• 10 months later, the pt was emergently admitted for “CHF exacerbation” and treated with thoracentesis. (See above chest CT/cytology results).
  – By the time this patient was diagnosed with squamous cell cancer, he died a few days later.

**SUMMARY:**

The pt had repeatedly denied anorexia or increased fatigue, but, in hindsight, this pt was stoic and had a very strong will to live, so he may have not wanted to admit that he was failing. In this case, cahexia and cough were caused from lung cancer, not end-stage heart failure. (It is doubtful that cahexia was from hyperthyroidism since difference in baseline and 8 month TFTs was minimal.) The pt’s intermittent wheezing was from bronchogenic restriction from the cancer and not “cardiac asthma”. The iron-deficient anemia was from cancer instead of chronic HF/COPD disease. The gynecomastia may have been a side effect of primary lung cancer rather than the aldosterone blocker or digoxin. Likewise, the intermittent hyperglycemia and even the fluid retention were likely other paraneoplastic syndromes of the cancer as well.

Multiple clinicians missed the diagnosis early on. In hindsight, had a RHC been done when the pt was refractory to medical therapy and the results not c/w congestion, this may have helped make an earlier diagnosis. Perhaps Max VO2 testing could have helped differentiate his pulmonary versus cardiac limitation of dyspnea. Given the pt’s remote smoking history and refractory to treat dyspnea, a chest CT could have been considered. It is clearly documented in the literature that chest x-rays are not sensitive for detecting lung nodules.

As clinical HF NP/RN specialists, we get very “keyed into the disease state” that we are treating. When HF patients continue to have dyspnea despite optimal medical therapy, it is important to “think outside of the box” and consider differential diagnoses before assuming worsening of the primary disease state.