01/10/25 Morning Report with @CPSolvers

"One life, so many dreams" Case Presenter: Lea Bischof (@xLea_B) Case Discussants: Rabih (@rabihmgeha), Ethan Chiu (@e_chiu17)

CC: 56yM w/ dyspnea & spine pain

HPI: Cough w/ whitish sputum, dyspnea for **10 days**, unintentional weight loss 8 kg past year, increased fatigue and sacral pain.
Presented in heme clinic **3 months ago:** thrombopenia 31k (termed as ITP) and isolated Alk-Phos elevation, concern for malignancy, therefore received **PAN-Imaging**: sacral bone osteo-destructive space occupying lesion 6x5cm, osteolytic lesions, prostate inhomogeneous and enlarged.

PMH:
COPD
Thrombocytopenia

Meds:
Hydromorphone
Sultanol
Lorazepam

Soc Hx:
From Austria
No travels
Office worker

Health-Related Behaviors:
Active smoker
50py, alcohol occasionally

Allergies:
None

Vitals: T: 38.4°C BP:120/60 **HR**: 108 **Sat:** 98%
Exam: Gen: AxOx3
HEENT: pupils nl, no jaundice; **CV:** nl heart auscultation
Pulm: dry rales on auscultation; **Abd:** unremarkable
MSK: Hematoma left upper thigh; painful palpation upper lumbar spine + sacrum, no edema, palpable pulses

Notable Labs & Imaging:
Hematology:
WBC:12 (Diff **Erythro- and Normoblasts)** Hgb:**9** (MCV:98), Plt: **35k**
INR 1.4, aPTT 31, CRP: 88, ESR: nl
Chemistry
AST:nl ALT: slightly elevated ALP: **2103** TBili:1.9 Total Protein: nl
Albumin 3.9, LDH: 384; PSA: wnl, Retic Index: hypoproliferative, SPEP: wnl, kappa/Lambda nl, Flow Cytometry: myeloid precursors of unknown origin
PBS: L shift to precursor cells to blasts, discrete signs of dysplasia of granulocytes
Started on ABx → cough + pulm sx improved, CRP decreased.
BM aspirate: Leukoerythroblastosis, **CT puncture iliac crest: formation of adenocarcinoma w/ partial signet ring cell morphology**
Syphilis, Quantiferon, Folate: unremarkable
Imaging:
PAN-Imaging: sacral bone osteo-destructive space occupying lesion 6x5cm, osteolytic lesions, **prostate inhomogenous + enlarged**
US abdomen: spleen 11cm (nl), no metastases in spleen or liver
PET CT: signs of central + peri bone activation (sacrum, rips, femur) consistent w/ **mixed osteolytic + osteoblastic**, **RLL lung consolidation**, no mediastinal or hilar lymph nodes; **Bronchoscopy:** unremarkable; **Upper endoscopy:** no clear malignant lesion;**Rectosigmoidoscopy**: nl

Dx: CUP w/ BM carcinomatosis (non-hematologic malignancy that invades to bone marrow)
→ further increase of myeloid precursors in blood, PBS showed schistocytes ("BM MAHA"); BM mets: (suspected) tumor patients, unexplained cytopenias, Leukoerythroblastosis in PBS, abnormal LDH; all solid cancers that can spread hematogenously (most common: breast, stomach, lung, prostate)

Problem Representation: A 56yM active smoker (50py) p/w dyspnea, spine pain, bicytopenia (macrocytic anemia, thrombopenia), Leukoerythroblastosis on PBS, ALK-Phos elevation, enlarged and inhomogeneous prostate, osteolytic lesions on sacrum, elevated LDH, imaging notable for mixed osteolytic & osteoblastic lesions.

Teaching Points (Khashayar):
Dyspnea pyramid -> start from the lungs and move outwards from there -> cardiovascular -> anemia etc.
The combination with spine pain -> brings out other causes into play -> bone marrow, anemia,
Cough -> usually very unspecific -> thinking about what's causing the stimulation of cough receptors -> complication of underlying disease leading to coming to surface
 # Osteolytic Lesions
Usual thoughts -> myelomas, breast cancers, renal carcinomas, pagets, metastatic cancer (prostate), osteosarcoma, chondrosarcoma, and hyperparathyroidism (brown tumor)
P's of Bone lesions -> PTH, paraprotein, RPR(syphilis leading to osteitis), alk phos, PSA
ALKp rise due to bone lesions -> osteoblastic lesions cause a rise which is interesting because in myelomas we expect a lytic lesion
Pure blastic disease -> prostate cancer (sometimes mixed)
Pure lytic disease -> Multiple Myeloma (without a pathologic fracture)
Osteomyelitis -> Alkp rise is usually not seen because bone formation is suppressed
Approach -> Multiple vs single , bone disease vs distant disease (sarcoid, TB, cancer metastasis) -> Biopsy is usually disappointing so we're looking for external focus of disease -> in this patient specifically -> lungs, prostate, bone marrow*(not part of bone disease!!!)*
 # Cancer of unknown primary
Thrombocytopenia -> subacute isolated thrombocytopenia ->Portal hypertension, single cell getting hit in the marrow -> Anemia is complicating picture -
Erythroblastosis -> production of immature RBCs -> significant stress on the bone marrow
Hematoma -> spontaneous hemorrhage in the muscles -> coagulopathies usually present this case but as of now can be attributed to the thrombocytopenia
the three Ms -> Macroangiopathic hemolytic anemia, TTP(microangiopathic), *Marrow(ineffective erythropoiesis)* -> Marrow + DIC -> APML -> is there a chronic form of DIC? -> Low-grade, compensated DIC can occur in clinical situations including giant hemangioma, metastatic carcinoma, or the dead fetus syndrome
Bone marrow disease + bone lesions + coagulopathies(+subacute DIC) ->
Blasts -> baby RBCs -> points to extensive peripheral destruction, mutations in the cell leading to monoclonal proliferation (pushed out baby RBCs due to mutations and infiltration vs Space occupying lesion) -> combine the findings with extra marrow disease findings & no crying of the marrow(tear drop cells) -> metastatic cancer
Cancer of unknown primary -> In spite of the increasingly sophisticated diagnostic workup, detailed investigations fail to reveal a primary site of origin for about 3–5% of metastatic tumors. The most commonly reported subtype in cancer of unknown primary origin is adenocarcinoma. Signet ring cell carcinoma (SRCC) is a rare poorly differentiated aggressive subtype of adenocarcinoma that most commonly arise from the gastrointestinal tract. It usually presents late and is associated with poor prognosis -> cancer of unknown primary -> with aggressive signet ring cell carcinoma often arising late from the gastrointestinal tract -> a sign of poor differentiation -> basically any cancer with metastatic potential -> breast, stomach, prostate(can be present with normal PSA due to dedifferentiation and lung)
When should we consider metastasis -> patients with unexplained or progressive cytopenias, leukoerythroblastic cells, consider in tumore or suspected, rise in alkP and/or LDH