Northwestern Medicine®

Case Presentation

- Elizabeth Kudlaty, MD, MS
- ISAAI Meeting, January 23, 2022
- Fellow, Division of Allergy and Immunology, Northwestern University McGaw Medical Center

Chief Complaint

- 19 y.o. female presents to her PCP's office c/o progressive DOE which started 8 months prior

HPI

- 19 y.o. female with progressive DOE
  - Admitted 12/2020 at an outside hospital for severe DOE (unable to go up 1 flight of stairs)
    - Workup included CT PE notable for diffuse ground glass opacities (GGOs)
    - 5x negative covid tests, based on CT findings diagnosed with Covid-19 PNA
    - Vaping nicotine/ marijuana daily prior to admission, stopped following discharge
    - Respiratory status improved with 1 week of prednisone, Breo Ellipta and albuterol
    - Diagnosed with **presumptive** asthma exacerbation 2/2 vaping in addition to covid 19

HPI, continued

- Symptom free until 5/2021
  - Worsening DOE
  - Productive cough of yellow sputum
  - Wheezing
  - Albuterol use 20x/ day, +nighttime symptoms
  - +PND, congestion/ rhinorrhea
  - Ran out of Breo Ellipta with associated worsening respiratory status
  - Resumed vaping to help manage anxiety
- Seeing PCP in 8/2021

ROS

- General: denies fevers, chills, **+ 8lb weight loss (trying to lose weight)**
- HEENT: no vision changes, eye pain, dry eyes, dry mouth, oral/ nasal ulcers; **+sinus pressure, +nasal crusting**
- Lungs: **+SOB, +DOE, +wheeze, +cough**
- Chest: no cp, palpitations, arrythmia, LE edema
- Abd: no abd pain, **+nausea, +vomiting, +constipation**
- Ext: no LE edema
- Neuro: no numbness, weakness, tingling
- Psych: **+anxiety, depression**
- Skin: no rashes

PMHx, etc

- **Pmhx:**
  - Depression/ anxiety
  - Seasonal rhinitis/ sinusitis
  - Recent dx of asthma (no PFTs, spiro etc)
- **Past surg hx:** None
- **Home medications**
  - OCP
  - Duloxetine 60mg QHS
  - Breo Ellipta (100-25mcg)
  - Albuterol inhaler PRN
- **Allergies:** Bactrim (nausea)

Medical history continued

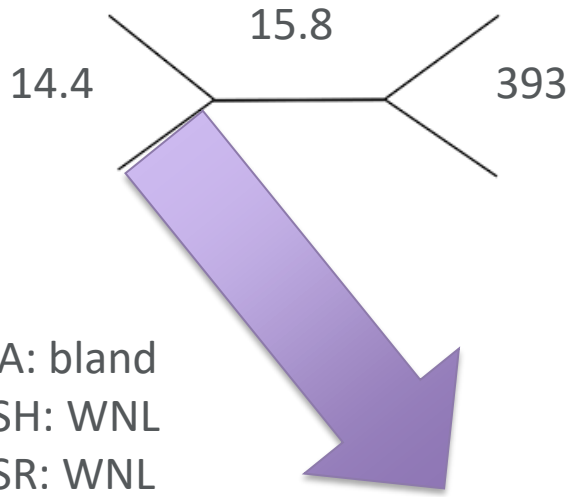
- **Family history**
  - Father, paternal grandfather: asthma
  - Mother: SAR, ovarian cancer
  - Great aunt: Lupus
  - Great uncle: RA
- **Social history**
  - Pharmacy student
  - Daily vaping of nicotine, smokes marijuana (sometimes w/ vape pen) x4 years
  - Etoh on weekends
  - Pet rabbit
  - Eats raw seafood weekly
  - No international travel

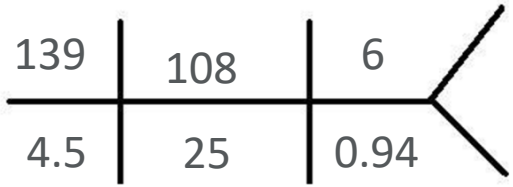
Vitals/ Physical exam:

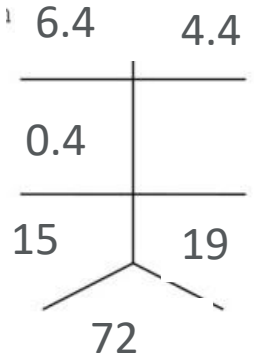
- Temp 98.1 F, HR 71, RR 18, BP 119/61, SpO2 95%

- Gen'l: young woman in NAD
- Skin: no rash or urticarial eruption
- HEENT: MMM, anicteric sclera, no conjunctival injection
- Lymph: No LAD
- Lungs: **normal WOB on RA, conversant in full sentences. Diffuse inspiratory and expiratory wheezes, fair to poor air movement**
- Cardiac: RRR no mrg, no elevated JVP, no LE edema
- Abd: soft, non-distended, non-tender, no organomegaly
- Ext: warm well perfused, no edema
- Neuro: AOx4, no focal deficits

Initial labs



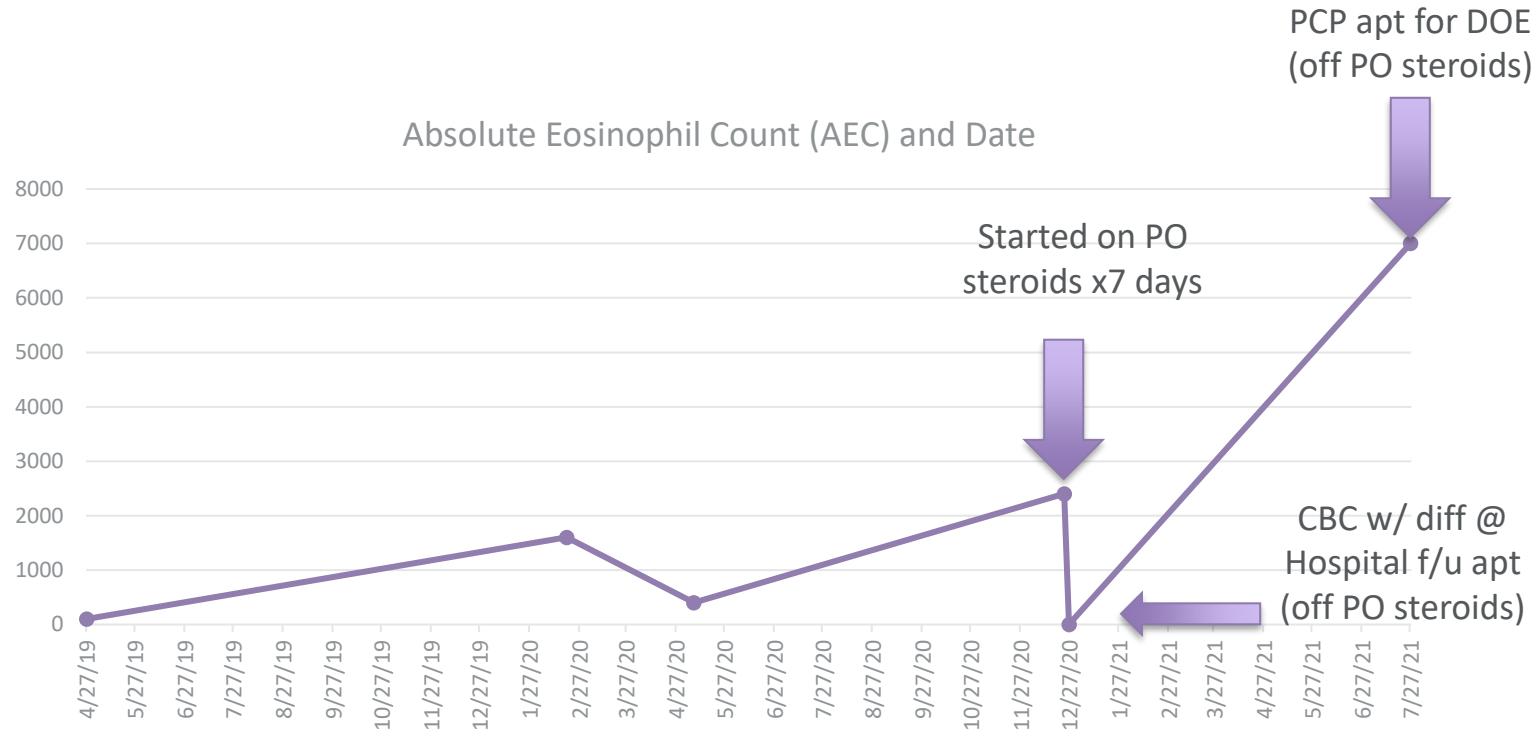




UA: bland
TSH: WNL
ESR: WNL

AEC: 7,000

CBC w/ diff trend



Northwestern Medicine®

Differential diagnosis: 19 y.o. female with pmhx of SAR, asthma who presents w/ several month h/o respiratory symptoms found to have peripheral eosinophilia, thrombocytosis, erythrocytosis

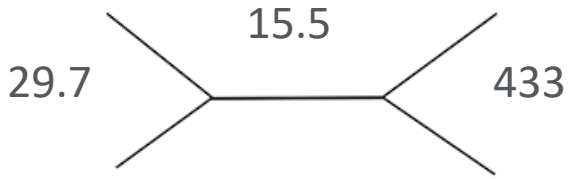
- Infectious
  - Helminth/ fungal (cocci)
- Allergy/ atopy
- Asthma
- [illegible]
- Primary HES/ neoplalstic
- Secondary (reactive) HES
- Familial HES
- Idiopathic HES

- Acute Eosinophilic Leukemia
- Chronic myeloid or myelomonocytic leukemia
- Systemic mastocytosis with
- [illegible]
- [illegible] significance
- Medication related
- Connective tissue disorders
- Adrenal insufficiency

We need more information to determine the etiology of this patient's eosinophilia

Northwestern Medicine®

Triage—where should patient be managed?



AEC 18,700

Sent to NMH ED by PCP given progressive peripheral eosinophilia consistent with hypereosinophilia (HE) → **told she has acute leukemia**

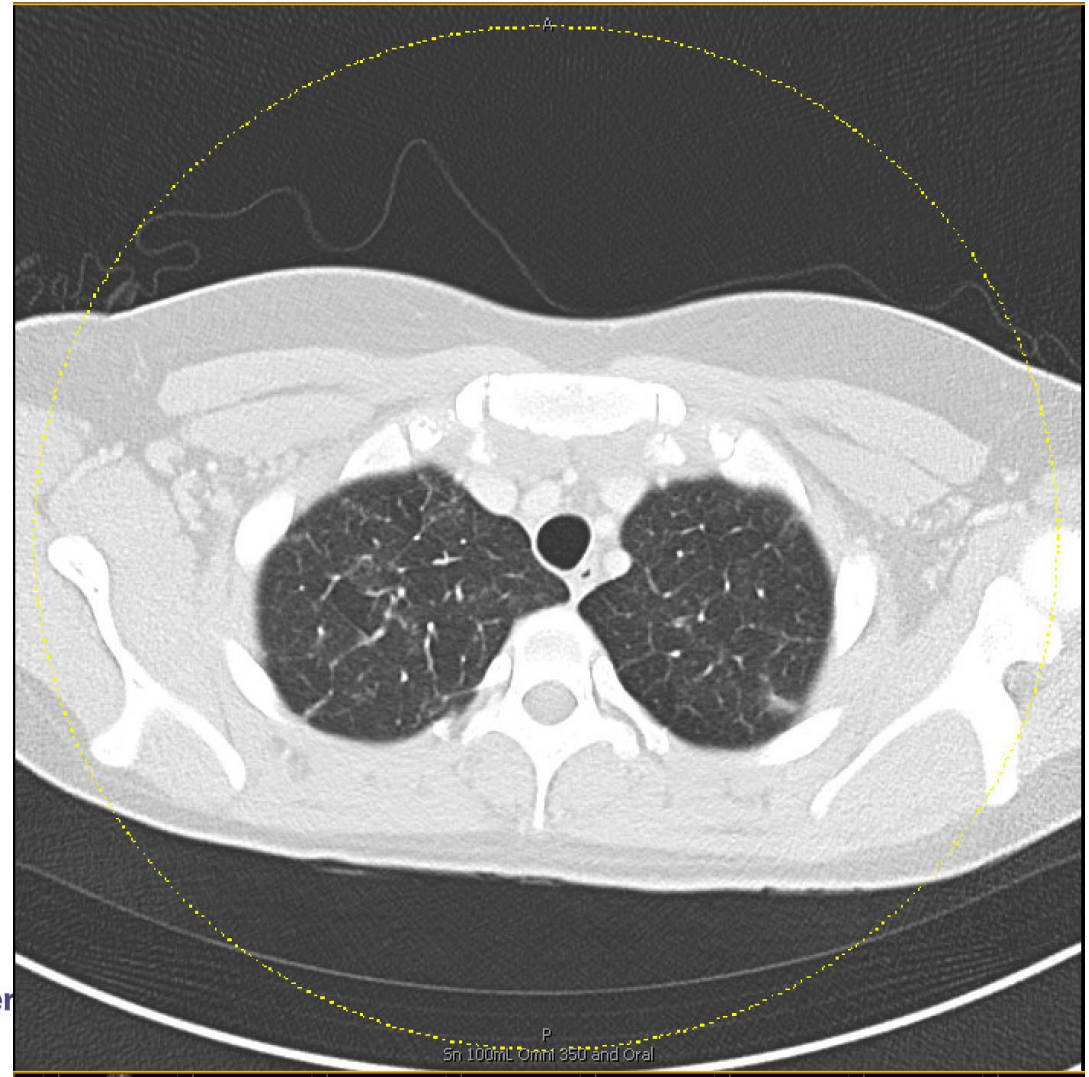
Admitted to Liquid Tumor Service

Acute Eosinophilic Leukemia

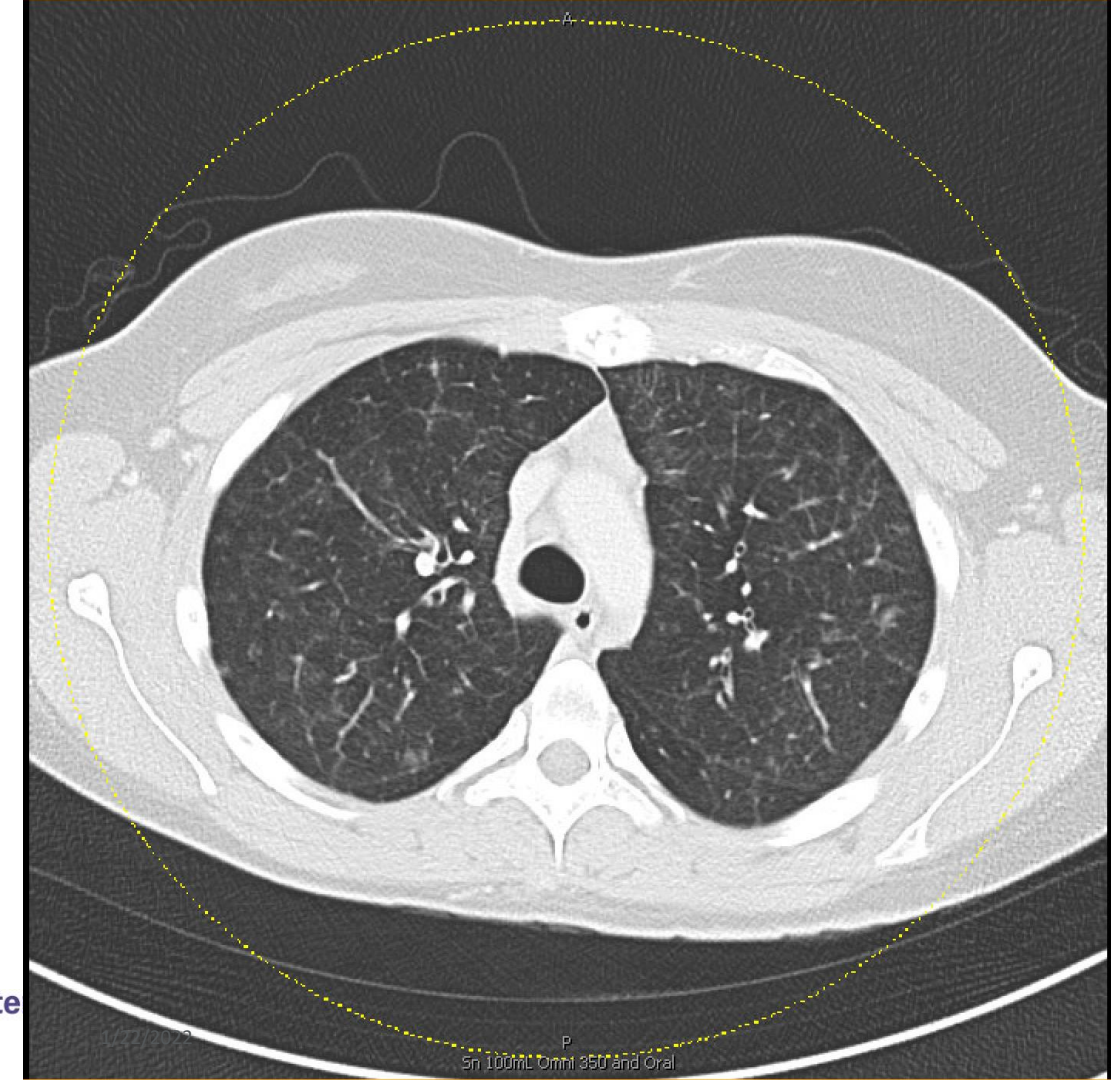
- Rare subtype of acute myeloid leukemia
- Classically described as increase in immature eos; >10% blasts in marrow
- Commonly w/ infiltration of tissue (ie: CNS and bones) w/ immature eos
- Similar clinical course to acute leukemia
- Typically see anemia, thrombocytopenia, susceptibility to infection

Hospital workup

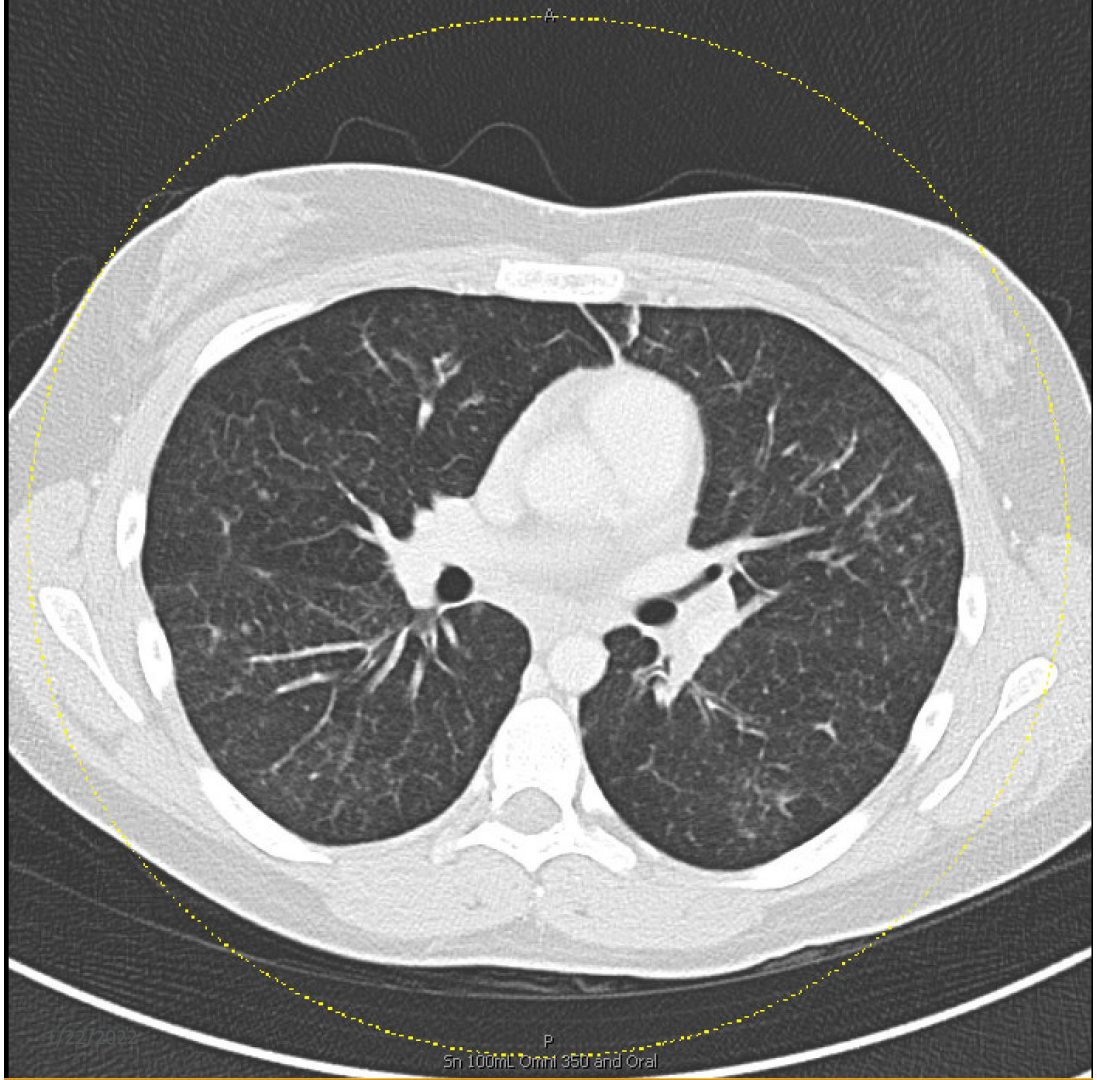
- B12
- Tryptase
- Troponin
- BNP
- ANCA
- Stool culture, O and P
- Strongyloides IgG
- Fungal studies (histo/blasto, aspergillus, sputum AFB, sputum fungal cx)
- HIV
- Quant Gold
- IgE
- PDGFRA PCR
- BCR-ABL
- FLT3
- Bone marrow
- CT Chest/Abdomen/Pelvis w/ contrast



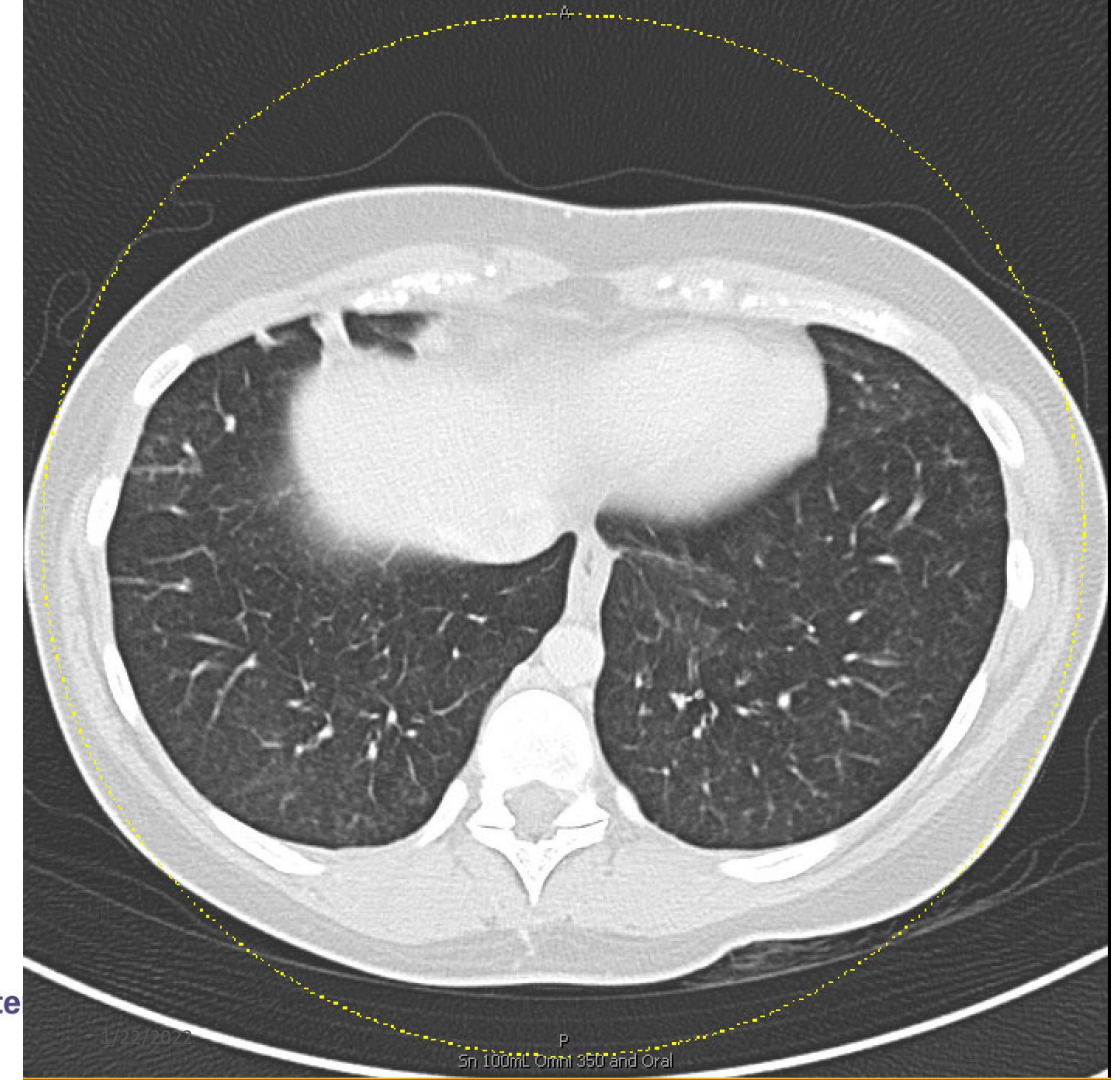
Northwestern Medicine®



Northwestern Medicine®



Northwestern Medicine®



Northwestern Medicine®

Imaging Read

- IMPRESSION:

- Prominent mediastinal and hilar lymph nodes. Numerous tiny pulmonary nodules scattered throughout both lungs and within mid and upper lung zone perilymphatic distribution. Findings are most suspicious for sarcoidosis. Consider correlation with serum ACE levels and lymph node biopsy for further evaluation.

Sarcoidosis and Peripheral Eosinophilia

- Peripheral Blood Eosinophilia in association with sarcoidosis
  - Renston et al. 2000, Mayo Clinical Proceedings
  - Retrospective chart review of 140 cases of sarcoidosis who underwent bronch
    - 41% had peripheral blood eosinophilia (PBE)
    - 3% had >10% PBE (mean 1396, SD 952 cells/mL)
    - Highest count occurred in 1 patient, 21% of diff
- A case of sarcoidosis with eosinophilia in peripheral blood and bronchoalveolar lavage fluid
  - Takahashi et al. 2013, Resp Med Case Rep
  - Retrospective review of 178 patients with sarcoidosis who underwent bronchoscopy
    - PBE observed in 35.4% of patients (many of which had other atopic comorbidities), range 0-1038 cells/mL

Hospital workup: results

- B12 127, Folate 8.9
- Tryptase 5.2
- Troponin negative
- BNP 27
- ANCA negative
- HIV negative
- Quant Gold negative
- Histo/ Blasto negative
- Ferritin/ Iron, transferrin/ TIBC: 10/ 72/ 400/ 560
- Aspergillus negative

The issue is tissue

- ANA: 1:320, speckled, reflex autoimmune panel neg
- Stool culture, O and P negative
- Flow cytometry: negative for clonal population
- [illegible]yloides IgG negative
- IgE 216
- BCR-ABL negative
- FLT3 negative
- Bone marrow pending

Northwestern Medicine®

Clinical update

- GI is consulted for nutritional deficiencies, GI symptoms
- Pulm is consulted for bronchoscopy
- Allergy-Immunology is consulted
- Rheum is consulted
- Onc is primary

Trans-bronchial biopsy

- Lung, right upper lobe, transbronchial biopsy:
- Lung parenchyma with diffuse eosinophilic infiltrate.
- Histologic sections show multiple alveolated pieces of lung parenchyma with diffuse eosinophilic infiltrate, including within alveolar septae, around blood vessels, and within blood vessel walls. No granulomas or parasites are seen. The differential diagnosis includes but is not limited to a vasculitic process (including eosinophilic granulomatosis with polyangiitis), infection, drug related reaction, and hematopoietic neoplasm.

EGD

- Impression:
  - Z-line irregular. Biopsied.
- Erythematous mucosa in the stomach. Non specific finding. Biopsied to evaluate for eosinophilic involvement.
- Normal upper/middle third esophagus and duodenum. Biopsied
- Path report:
  - **A. Duodenum, biopsy:** Duodenal mucosa with eosinophils **(up to 28 eosinophils per high-power field).**
  - **B. Stomach, biopsy:** Oxyntic and antral mucosa with mild reactive features and up to **10 eosinophils per high-power field.** No *Helicobacter pylori*-like microorganisms identified.
  - **C. Gastroesophageal junction, biopsy:** Squamous and gastric-type mucosa with mild chronic inflammation and up to **19 eosinophils per high-power field.** Negative for intestinal metaplasia and dysplasia.
  - **D. Esophagus, biopsy:** Squamous epithelium with mild reactive features, mild chronic inflammation, and occasional intraepithelial eosinophils (**up to 2 eosinophils per high-power field).**

Bone Marrow Biopsy

- **Normocellular bone marrow with increased eosinophils, multilineage hematopoiesis, and no increased blasts**.
- Flow cytometric immunophenotyping performed on the bone marrow aspirate reveals **a polytypic B-cell population and a T-cell population** without evidence of immunophenotypic abnormality based on the markers assayed.
- Comment: The etiology of the patient's hypereosinophilia is unclear. There is no definitive morphologic evidence of a hematologic malignancy in this sample; however correlation

DDx updated

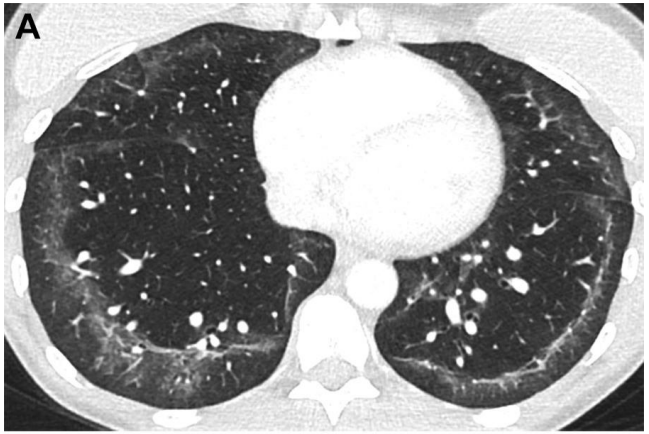
- **HE with primary organ involvement**
  - **EGPA**
- **Sarcoidosis**
  - **No granulomas on biopsy**
- **Fungal**
  - **Studies negative**
- **Primary HES (neoplastic/ myeloid)**
  - **Bone marrow/ molecular testing negative**
- **Drug/ medication induced**
  - **EVALI**

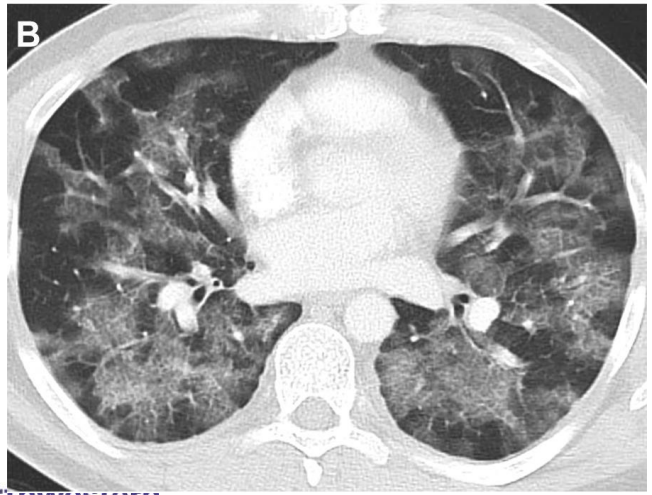
Poll Question:

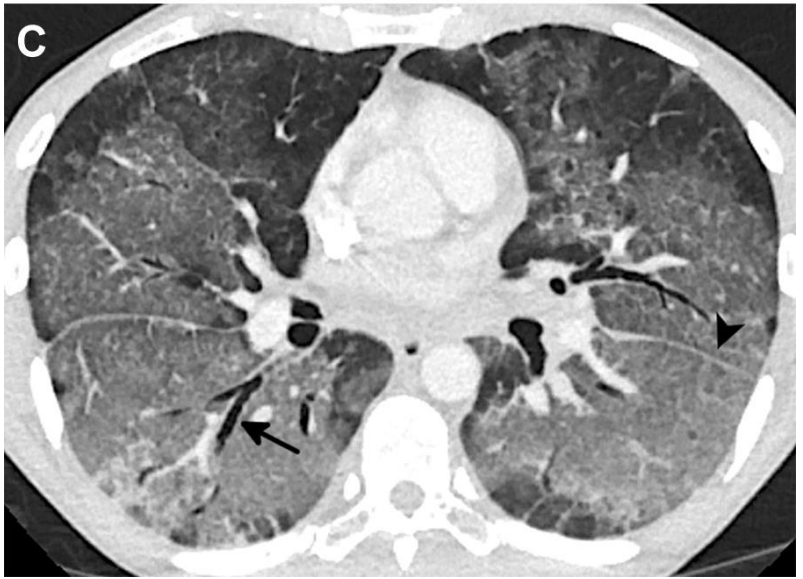
- What is the most common CT finding in E-cigarette (or vaping) use associated lung injury (EVALI)?
  - A) Crazy paving (ground glass opacities with superimposed interlobular/ intralobular septal thickening)
  - B) Diffuse bilateral ground glass opacities with peripheral sparing
  - C) Fibrosis
  - D) Atoll/ reverse halo sign

Poll Question:

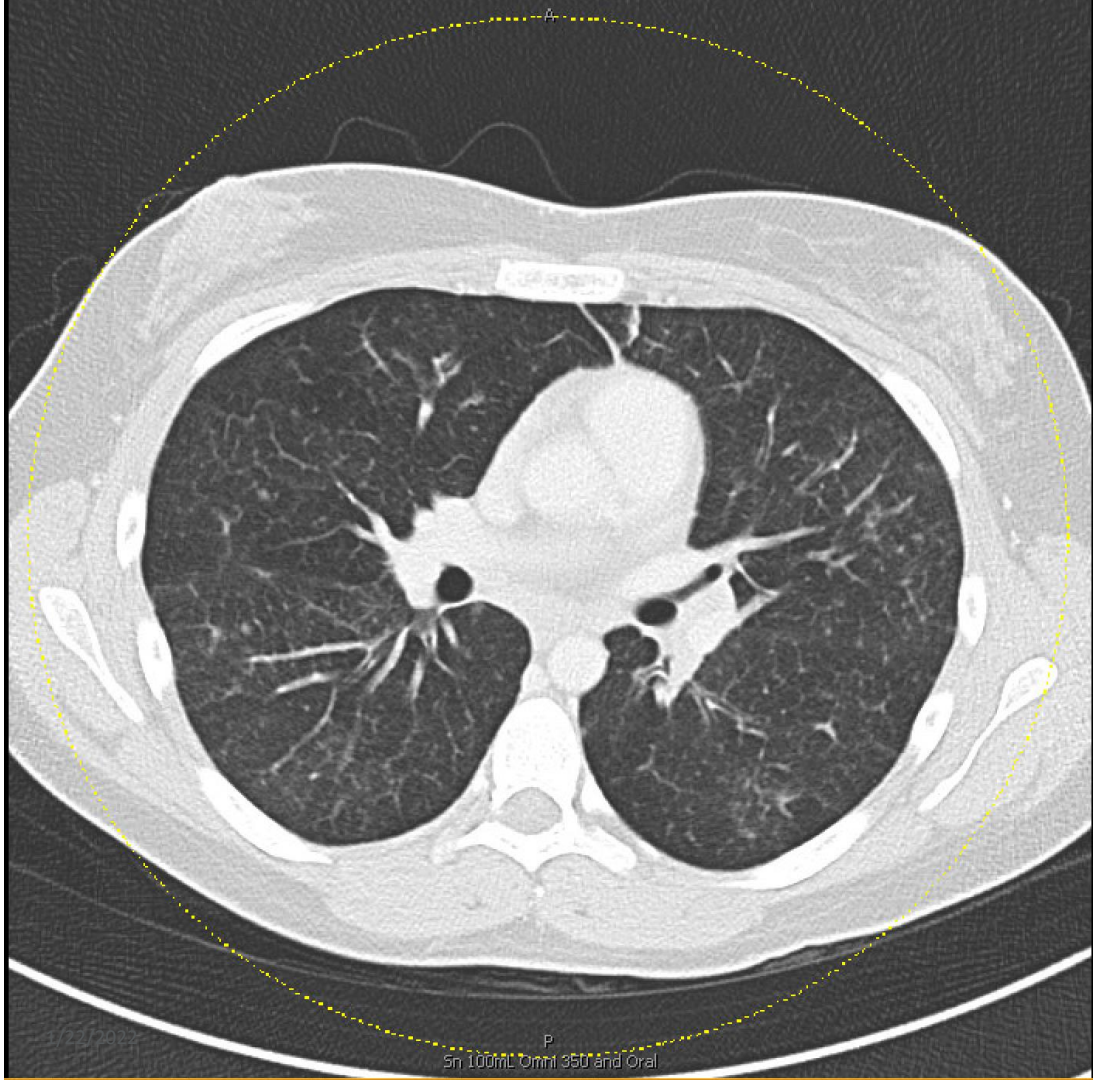
- What is the most common CT finding in E-cigarette (or vaping) use associated lung injury?
  - A) Crazy paving (ground glass opacities with superimposed interlobular/ intralobular septal thickening)
  - **B) Diffuse bilateral ground glass opacities with peripheral sparing**
  - C) Fibrosis
  - D) Atoll/ reverse halo sign







Northwestern Medicine®



Northwestern Medicine®

E-cigarette product use associated lung injury (EVALI)

- EVALI is an acute or subacute respiratory illness, typical onset 6 days, range 0 days to 2 months. GI symptoms common (n/v/d/ abd pain)
- Risk factor: e-cigarette use (THC, vitamin E acetate in 75-80%) nicotine/ other additives have also been reported
- Case definition criteria
  - Use of e-cigarette/ related product within 90 days
  - Lung opacities on CXR or CT
  - Exclusion of lung infection
  - Absence of likely alternative diagnosis
- Treatment:
  - Empiric abx to cover pathogens
  - **Routine use of steroids not recommended (?utility in worsening sx, hypoxemia)**
  - Supportive care

EVALI and Lab Evaluation

- Bronchoscopy finding in EVALI: lipid laden macrophages with red oil staining (Maddock et al 2019)
  - Thought to be 2/2 carrier oils used to dissolve THC
- Leukocytosis observed in 83%
- Neutrophilia observed in 91%
  - Layden et al. 2020
- Eosinophilia is not commented on in reports

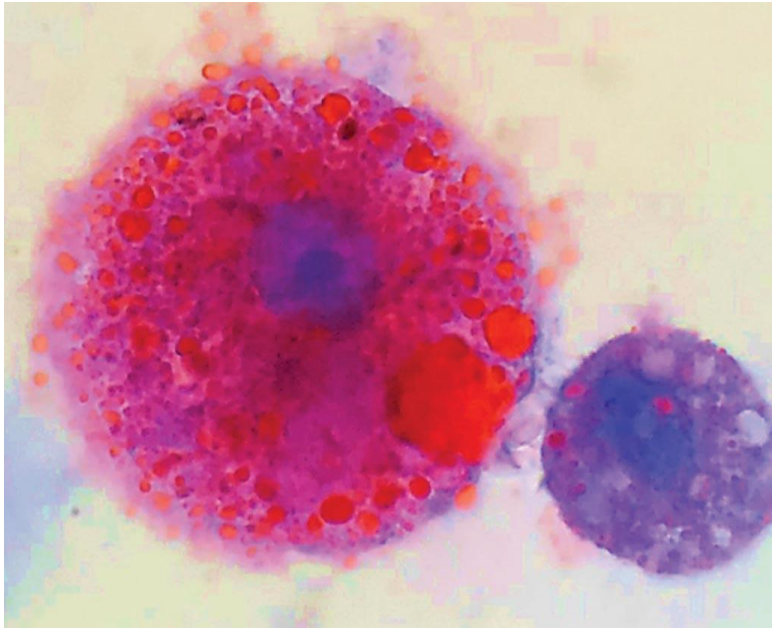


Figure: Labmedica.com

EVALI and acute eosinophilic pneumonia (AEP)

- AEP is a rare condition, 2:1 male prevalence, ages 20-40, ~200 cases reported (febrile illness <4 wks, hypoxia, diffuse pulmonary infiltrates, BAL w/ >25% eos, absence other causes eos)
- AEP has been reported in several cases of EVALI (Arter et la. 2019, Thota et all. 2014, Wolf et al. 2020)
  - Treatment: high dose IV steroids until resolution of respiratory failure followed by oral steroid taper
- PBE rarely elevated on initial presentation of AEP, mild PBE seen in later disease course (Jhun et al. 2014)

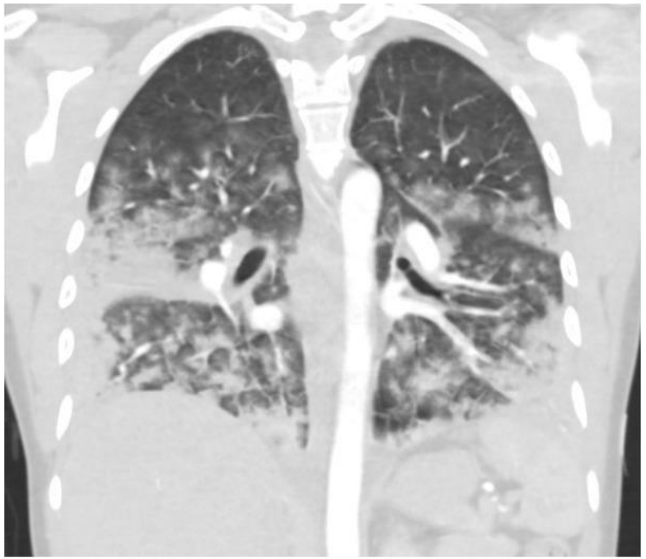


Figure credit: Wolf et al. 2020, J Crit Care Med

Eosinophillic Granulomatosis with Polyangitis (EGPA)

- Multisystem disorder (CRS, asthma, prominent PBE)
- Vasculitis of small/ medium sized arteries (often not apparent in initial stages of disease); commonly ANCA negative
- Lung involvement most common, skin second most. Can involve any organ
- Neuropathy common feature, seen in up to 75% of pts
- Stages: prodromal/ allergic→ eosinophilic→ vasculitic
- Transbronchial biopsy is not preferred (sampling issues)
- Major histopathologic findings: (not all findings may be present, esp if treated)
  - Eosinophilic infiltrate
  - Prominent necrosis
  - Eosinophilic/ giant cell vasculitis
  - Interstitial/ perivascular necrotizing granuloma

EGPA: 1990 ACR criteria

- Asthma (history)
- Peripheral eosinophilia (>10% of peripheral blood)
- Mono/ polyneuropathy
- Pulmonary infiltrates (non-fixed)
- Paranasal sinus abnormality
- Extravascular eosinophils on histology

4 items or greater are met
Sensitivity 85.0%
Specificity 99.7%

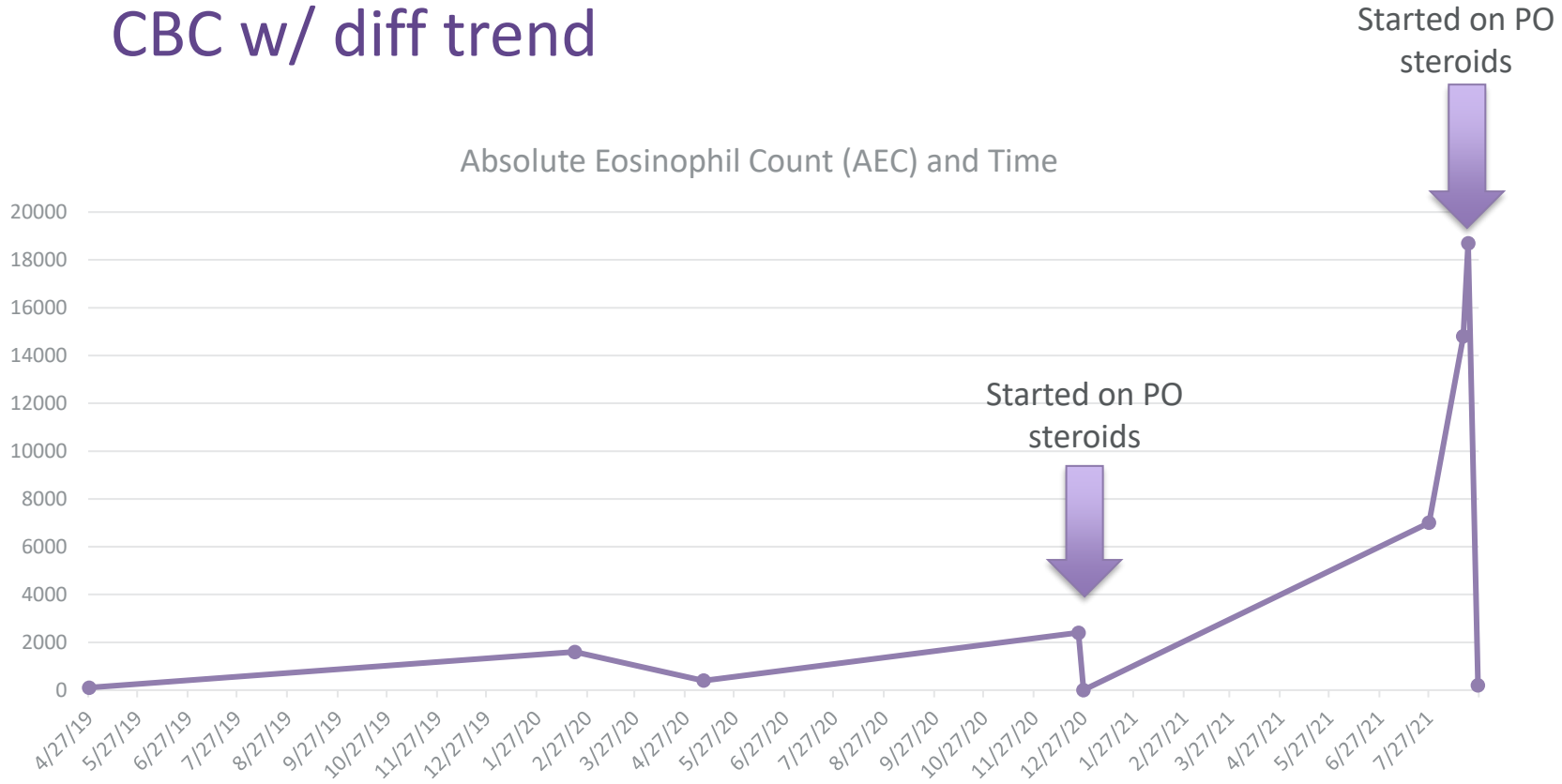
DDx updated

- HE with primary organ involvement
  - EGPA—likely diagnosis
- Sarcoidosis
  - No granulomas on biopsy
- Fungal
  - Studies negative
- Primary HES (neoplastic/ myeloid)
  - Bone marrow/ molecular testing negative
- Drug/ medication induced
  - EVALI: labs and clinical course not consistent

Case Resolution and Update

- Diagnosis of EGPA is made (4/6 ACR criteria)
- Started on prednisone taper 40mg→ 20mg until follow up
- Plan to start mepolizumab 300mg qmonthly (awaiting insurance)
- Patient seen in Allergy/ Immunology clinic ~1 month following hospitalization
- Transferred care closer to where she attended school, following with Rheumatology there
- Near totally cut out vaping

CBC w/ diff trend



Northwestern Medicine®

Take Home Points

- Importance of taking a detailed history
- Eosinophilia often requires multi-disciplinary team
- Keep a broad differential, do not anchor
- EVALI is an important differential consideration
- EGPA can have varied histology, ACR criteria have high sensitivity/ specificity
- Sarcoidosis is associated with PBE, although usually mild

Thank You

Northwestern Medicine®

Questions?

Northwestern Medicine®