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THE COLLEGE OF FAMILY PHYSICIANS OF CANADA
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IMMUNOTHERAPY-RELATED ADVERSE EVENTS: CLINICAL PEARLS FOR FAMILY PHYSICIANS

Genevieve Chaput: MD, MA, CAC (PC), FCFP
Ovie, Albert: MD, MSc, CCFP
Schiff, Benjamin: MD, FCFP

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LEARNING OBJECTIVES

At the conclusion of this activity, participants will be able to:

- Identify common and severe adverse events associated with cancer treatments
- Differentiate between cancer treatment-related adverse events and other causes of patient deterioration
- Apply evidence-based guidelines for the diagnosis and management adverse events due to cancer treatments

COMPLICATIONS OF CHEMOTHERAPY:

PNEUMONITIS

Schiff, Benjamin: MD, FCFP

FMF
Family Medicine Forum
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PRESENTER DISCLOSURE

Presenter: Benjamin Schiff

Any direct financial relationships, including receipt of honoraria:

Not applicable

Membership on advisory boards or speakers' bureaus:

Not applicable

Patents for drugs or devices:

Not applicable

Other:

Not applicable

LEARNING OBJECTIVES

- Appreciate the different forms of Drug Induced Interstitial Lung Disease (DI-ILD)
- Recognize the broad DDx for respiratory decline in cancer patients
- Develop an approach to investigating and managing DI-ILD

CASE PRESENTATION

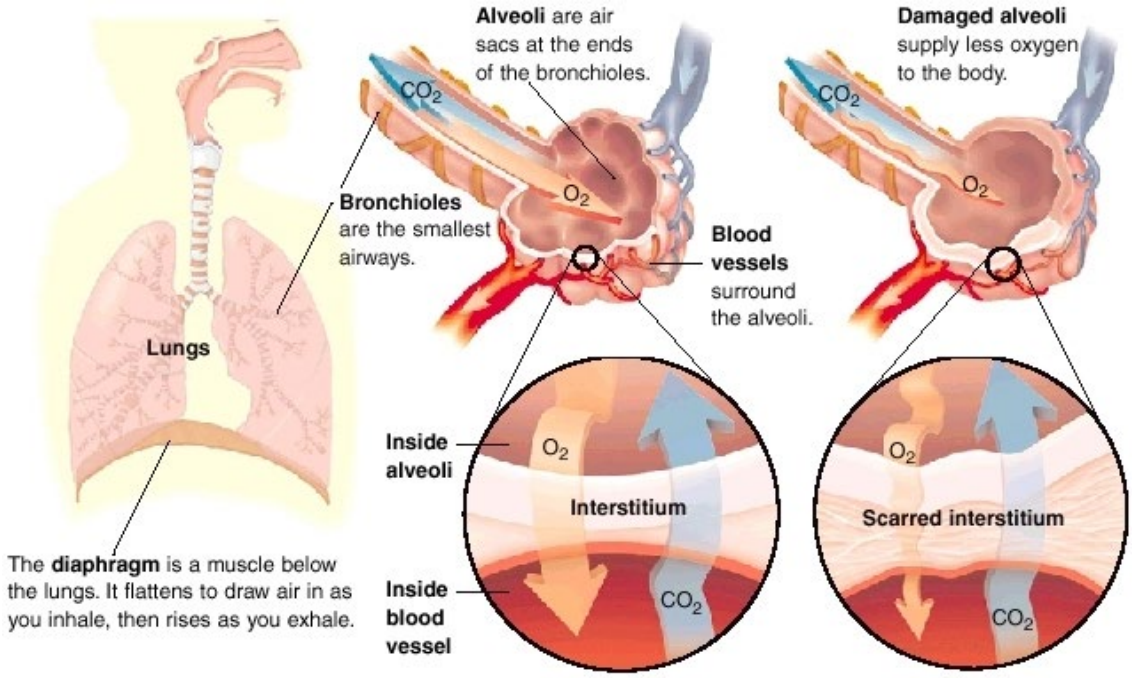
- 75 y/o Female with metastatic lung cancer, ex smoker
- Recent admission for anemia related to colonic angiodysplasia
- At that time found to have brain lesions of uncertain significance
- Was treated for a few weeks with decadron 8 mg BiD which was then tapered
- Had been receiving pembraluzimab (Pembro) which was stopped on discharge 2 weeks ago
- Presents with marked increase in baseline dyspnea with dry cough
- No clear fever, sick contacts, chest pain
- O2 Saturation 79% on room air in er

CASE PRESENTATION

- CXR shows bilateral mixed air space and reticular pattern
- CT shows diffuse ground glass pattern
- Normal CBC
- Normal Troponin
- NT-BNP 3200 (previous 4500)
- No sputum obtained
- BIO-FIRE done
- Nasal swab PCP done

ILD/PNEUMONITIS IS A BROAD TERM FOR A GROUP OF INFLAMMATORY LUNG DISORDERS

- Pulmonary disorders of ILD/pneumonitis include idiopathic pulmonary fibrosis (unknown cause) but do not include infection or cancer
- ILD/pneumonitis is marked by the presence of inflammation or scarring of the lung interstitium



Adapted from: Harvard University. Available at: https://acil.med.harvard.edu/interstitial-lung-disease. Accessed October 2022.

Kreuter M, et al. BioMed Res Int 2015;2015:123876

NOVEL CANCER THERAPIES WITH INCREASED RISK OF LUNG TOXICITY

- Historically, some chemotherapies increase risk of lung toxicity (eg.bleomycine, gemcitabine, oxaliplatin, taxanes/paclitaxel)
- New targeted and precision oncology has led to development of many new anti-cancer treatments with diverse side effects
- Pulmonary toxicities (eg. bronchospasm, pleural effusions, pneumonitis) are important complications from many novel agents, with pathophysiology and management that differ per offending drug

DRUG INDUCED INTERSTITIAL LUNG DISEASE

- ILD resulting from exposure to drugs, causing inflammation and possibly interstitial fibrosis
- Most common causes are anti-cancer drugs:
  - Chemotherapeutic agents (e.g., bleomycin, taxanes [paclitaxel], oxaliplatin)
  - CDK4/6 inhibitors (e.g., palbociclib, abemaciclib)
  - EGFR inhibitors (e.g., erlotinib)
  - mTOR inhibitors (e.g., everolimus)
  - Immune checkpoint inhibitors (PD-1 and PD-L1 inhibitors, and combination PD-1 and CTLA-4 inhibitors)
  - Anti-HER2 (e.g, trastuzumab deruxtecan [T-Dxd], lapatinib)

INCIDENCE OF ILD VARY BY CLASS OF DRUGS

Mechanism	Drug	Tumour types	Any grade ILD, %	Grade 5 ILD, %
TKI and/or EGFR inhibitor	Gefitinib[1]	EGFR-mutated NSCLC	5.0	1.0
	Gefitinib[2]	NSCLC	2.4	1.8
	Erlotinib[3]	Recurrent/advanced NSCLC	4.5	1.6
	Cetuximab[4]	Head and neck squamous cancer	4.5	0.5
	Osimertinib[5]	EGFR-mutated inoperable or recurrent NSCLC	6.5	0.8
Immune checkpoint inhibitor	Nivolumab[6]	Recurrent or advanced NSCLC	7.2	0.9
	Nivolumab + ipilimumab[7]	Advanced NSCLC	6	0
	PD-L1 inhibitors[8]	Melanoma, NSCLC, or renal cell carcinoma	2.7	NR
CDK4/6 Inhibitors	Abemaciclib[9]	Metastatic breast cancer	3.2	0.4
	Palbociclib[10]	HR+ HER2- advanced breast cancer	0.69	0
	Ribociclib[11]	HR+ HER2- advanced breast cancer	1.6	0.1
Anti-HER2	Lapatinib[12]	HER2-positive advanced or metastatic breast cancer	0.2	0
mTOR inhibitors	Everolimus[13]	HR-positive HER2-negative advanced breast cancer	19	0
	Trastuzumab deruxtecan(T-DXd)[14]	**Breast 44.3%; gastric 25.6%; lung 17.7%; colorectal 9.3%; other cancer 3.0%**	**15.4**	**2.2**

CDK4/6 Cyclin-dependant kinase 4/6
HER2 Human epidermal growth factor receptor
mTOR mammalian target of rapamycin **NR** Not reported
PD-L1 Programmed death-ligand

1. H, et al. Jpn J Clin Oncol 2013;43:664-8 **2.** Hotta K, et al. J Thorac Oncol 2010;5:179-84 **3.** Nakagawa K, et al. J Thorac Oncol 2012;7:1296-303
4. Nakano K, et al. Head Neck 2019;41:2574-80 **5.** Gemma A, et al. J Thorac Oncol 2020;15:1893-906 **6.** Kato T, et al. Lung Cancer 2017;104:111-8
7. ESMO Open 2021;6:100273 **8.** Nishino M, et al. JAMA Oncol 2016;2:1607-16 **9.** Verzanio (abemaciclib) Product monograph. April 2019
10. Finn RS, et al. Oncologist 2021;26:e749-e755 **11.** Kisqali (ribociclib) Product Monograph. November 2012 **12.** Hackshaw MD, et al. Breast Cancer Res Treat 2020;183:23-39
13. Affinitor Product Monograph. Nov 2021 **14.** Powell CA, et al. ESMO Open 2022;7:100554

A NUMBER OF FACTORS ARE KNOWN TO BE LINKED TO THE RISK OF DEVELOPING DRUG INDUCED-ILD (DI-ILD)

General risk factors[1-6]

- Hx of pre-existing lung disease/reduced lung function
- Poor performance status
- Smoking
- Age > 60 years
- Japanese or African American ethnicity
- Male sex

Risk factors in oncology[1,4,5]

- Prior Tx with multiple chemo regimens or thoracic RT
- Hx of radiation recall pneumonitis
- Lung cancer (*squamous) or lung metastases
- Prior drug-induced pneumonitis
- Ongoing Tx with multiple molecularly targeted agents (MTAs) or combo MTAs + cytotoxic agents

Hx History; **RT** Radiation therapy; **Tx** Treatment

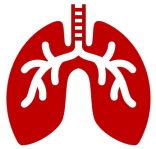
However, many people who develop DI-ILD have no risk factors – highlighting the need for vigilance

CLINICAL AND RADIOLOGICAL PRESENTATION(S)

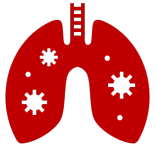
- Asymptomatic (ie. incidental finding of CT imaging)
- Dyspnea, Cough, Hypoxemia, Fever
- In my experience, hypoxemia is the most common initial presentation
- Typically occur within weeks to months, but quite variable
- Concomitant AEs (Adverse Events) may be also be present depending on drug class (eg rash with TKI (Tyrosine Kinase Inhibitors), colitis with immunotherapies, etc)

DIAGNOSIS OF DI-ILD REQUIRES RULING OUT A NUMBER OF DIFFERENTIAL DIAGNOSES

Opportunistic infections (e.g., PCP)



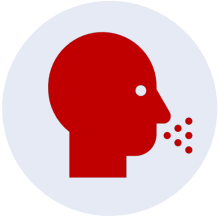
Alveolar hemorrhage



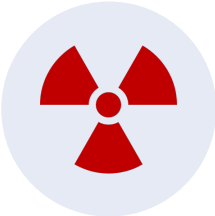
Metastatic involvement of the lung

Systolic or diastolic heart failure

Bacterial, viral, or fungal infections



Aspiration pneumonia



Radiation induced lung injury

Pulmonary embolism

PCP Pneumocystis pneumonia

Müller NL, et al. Br J Cancer 2004;91 (Suppl 2):S24-30

DIFFERENTIAL DIAGNOSIS

- Progression of cancer in the lungs (lymphangitic disease, volume loss/ collapse, pleural effusion)
- Pre-existing ILD (NSIP, new exposures)
- Airways disease (COPD, asthma)
- Infections (including opportunistic, funga)
- CHF/Volume overload
- Toxicity from other drug exposures (chemo, Abx nitrofurantoin, MTX, amiodarone)
- Intercurrent illness/ new exposures

INVESTIGATIONS AND MANAGEMENT

- Multi-disciplinary approach
- Complete history and physical including drug exposure
- Labs; including CBC, extended ‘lytes, VBG, Blood cultures, NT BNP, sputum culture, nasopharyngeal swabs (VIRAL, PCP)
- Consider special testing for fungal diseases (e.g. galactomannan for aspergellosis)
- Imaging
- Bronchoscopy (BAL)
- Lung biopsy

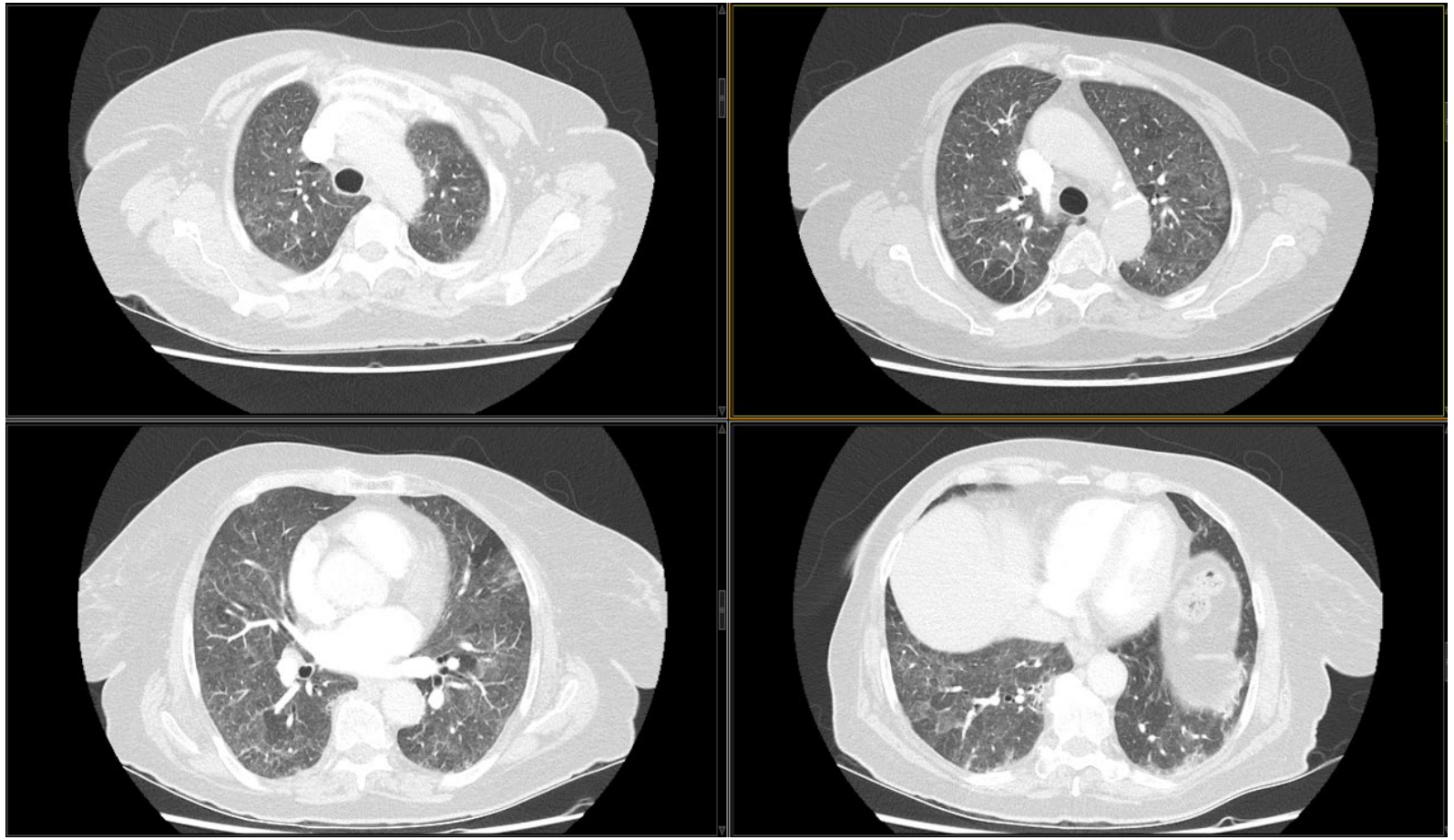
ALTHOUGH THE IMAGING PRESENTATION OF DI-ILD IS OFTEN NONSPECIFIC, THERE ARE COMMON PATTERNS

- Ground glass opacities (GGO)
- Organizing pneumonia (OP)
- Non-specific interstitial pneumonia (NSIP)
- Hypersensitivity pneumonitis (HP)
- Diffuse alveolar damage (DAD)
  - Most aggressive presentation AIP (acute interstitial pneumonia) – usually grade 4 DI-ILD

Conte P, et al. ESMO Open 2022;7:100404

HYPERSENSITIVITY PNEUMONITIS (GGO)

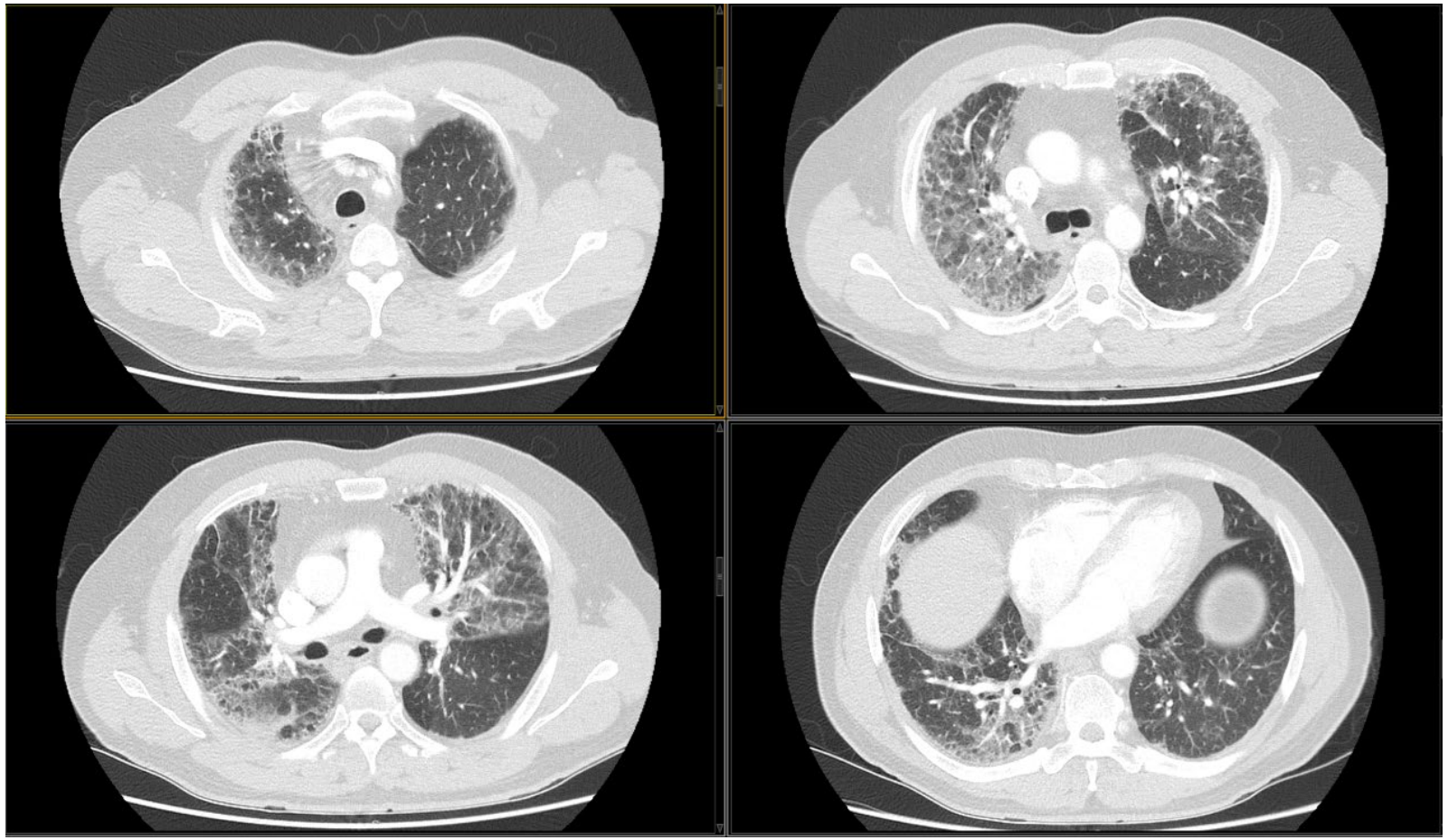
- Often presents in its non-fibrotic form – seen here as subtle but diffuse ground glass opacity (GGO), sometimes with an aspect of centrilobular nodularity.
- While GGO is nonspecific, mosaic lung attenuation with patchy spared lobules is typical of the air trapping seen in HP.



Conte P, et al. ESMO Open 2022;7:100404
Images provided by Dr. Micheal McInnis

DIFFUSE ALVEOLAR DAMAGE

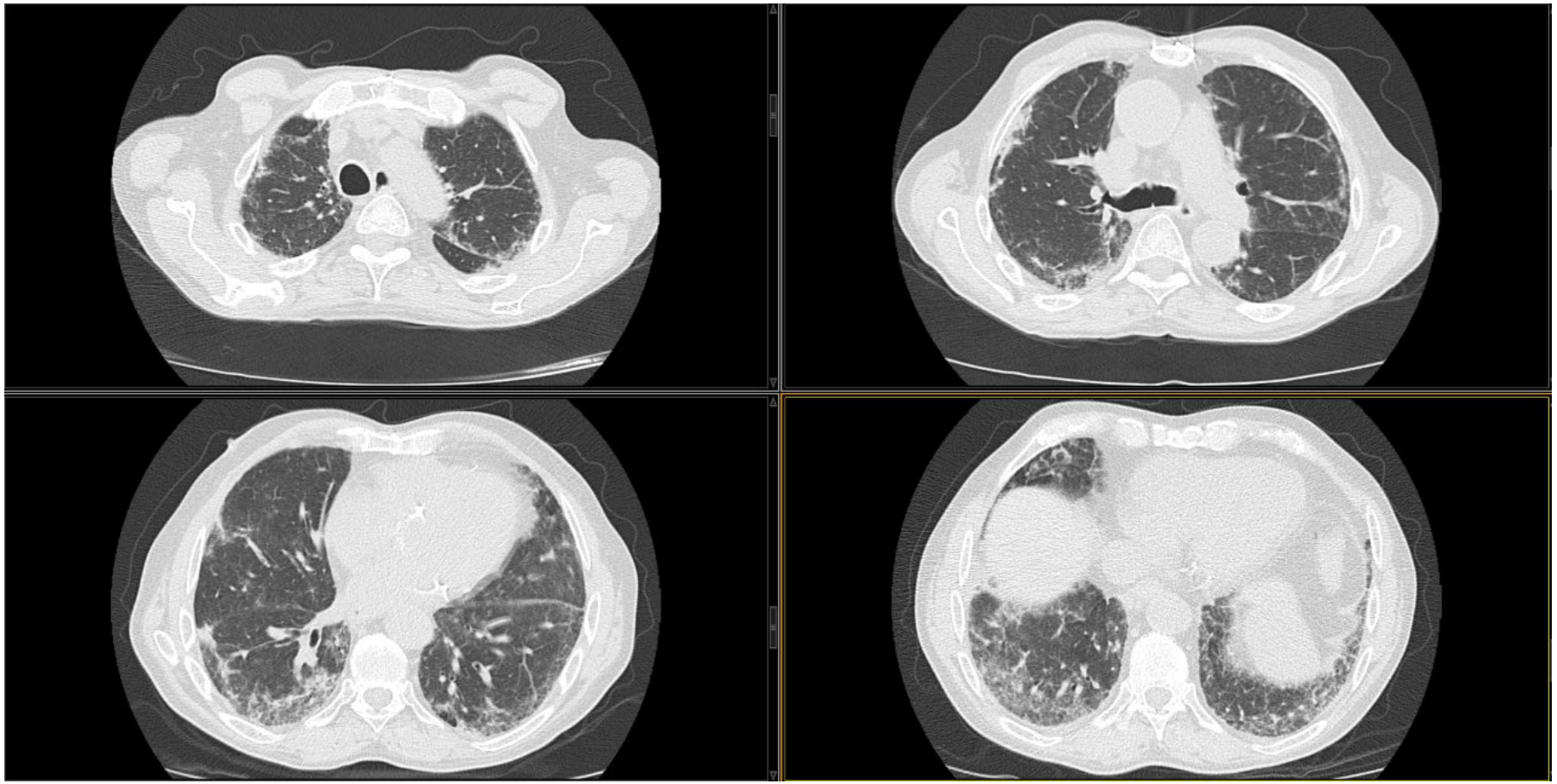
Characterized by broad areas of ground glass opacity (GGO), often with a geographic distribution (bottom left image – contrasting regions of abnormal and normal lung.



Conte P, et al. ESMO Open 2022;7:100404
Images provided by Dr. Micheal McInnis

NON-SPECIFIC INTERSTITIAL PNEUMONIA (NSIP)

- Characterized by ground glass opacity, which tends to be basal with peripheral reticular opacities
- Note sparing of the immediate subpleural lung in the top right and bottom left image which is a hallmark of NSIP.

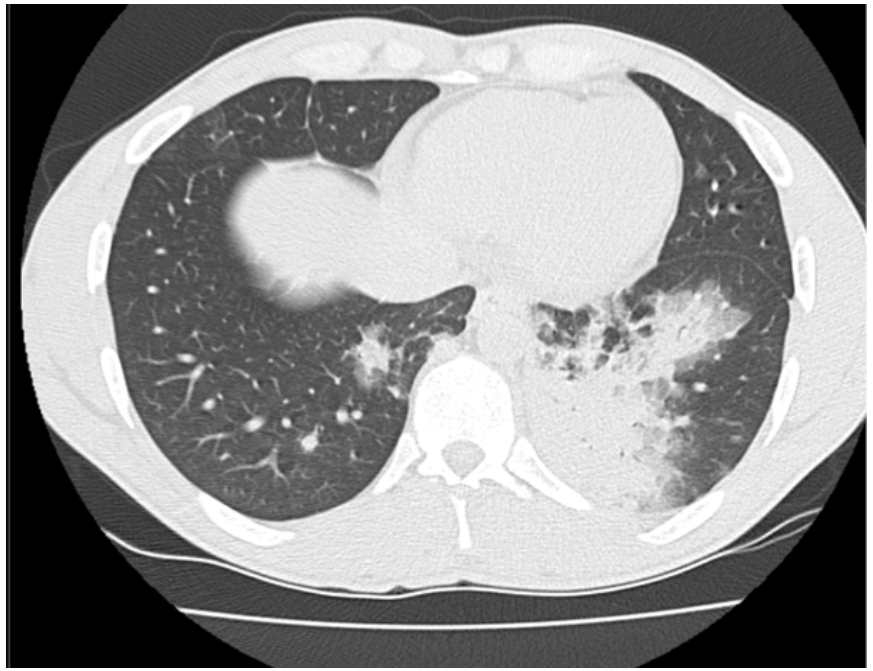


Conte P, et al. ESMO Open 2022;7:100404
Images provided by Dr. Micheal McInnis

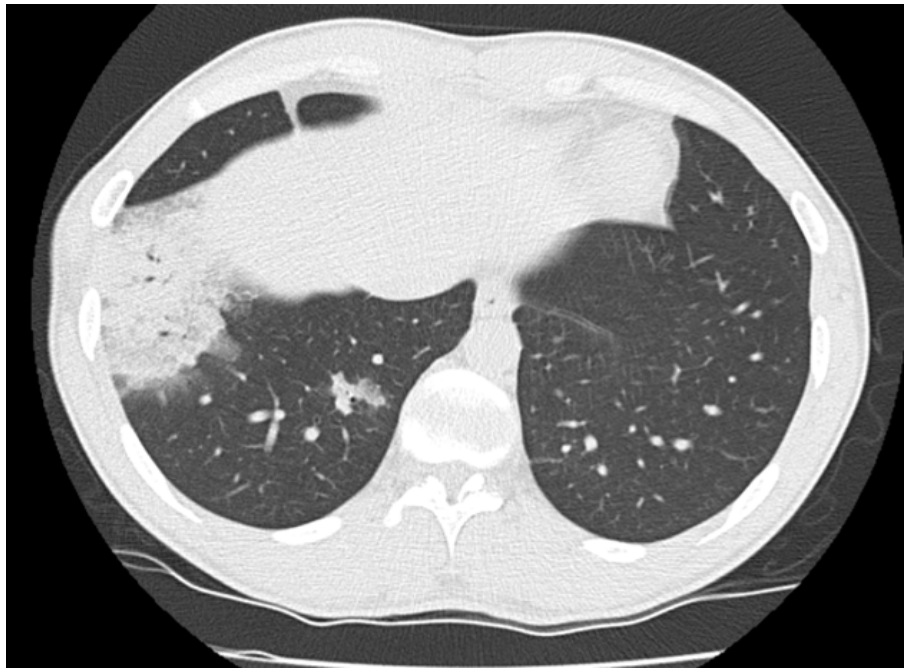
ORGANIZING PNEUMONIA

- Characterized by multifocal areas of ground glass opacity (GGO) and peripheral consolidation
- Reversed halo/atoll signs may be seen
- OP often fluctuates (as shown on the right)

Typical OP at baseline: Large volume of consolidation, predominantly in the LL lobe, and mild surrounding GGO



Follow-up image 3 months later shows complete resolution of LL lobe findings and new RL lobe consolidation



LL Left lobe **RL** Right lobe

Conte P, et al. ESMO Open 2022;7:100404
Images provided by Dr. Micheal McInnis

TREATMENT PRINCIPLES

- Early initiation of treatment proportional to degree of illness
- Treat for multiple causes simultaneously when very sick pending results of investigations (often these patients at risk for chf; trial of lasix)
- **Frequent reassessments** with labs and imaging
- Oxygen requirements excellent marker of disease progression/regression
- Respiratory support as needed (high flow, bipap, intubation)

MANAGEMENT OF DI-ILD IS DEPENDENT ON THE GRADE OF CTCAE PNEUMONITIS

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
CTCAE def'n	Asymptomatic with radiological findings only	Symptomatic: medical intervention indicated and instrumental ADL are limited	Symptoms are severe Self-care ADLs are limited Supplemental oxygen is indicated	Life-threatening respiratory compromise Urgent intervention needed (e.g. tracheotomy or intubation)	Death related to AE

CTCAE; COMMON TERMINOLGY CRITERIA FOR ADVERSE EVENTS

Radiologist collaboration with the MDT after DI-ILD identification is key for monitoring and management until resolution

1. National Cancer Institute, CTCAE Version 5.0, November 27, 2017. Available from: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf. Accessed January 2023.

MANAGEMENT INDIVIDUALIZED DEPENDING ON OFFENDING AGENT

- HOLD drug
- Initiate steroid treatment (eg 1mg/kg starting dose) SLOOOW TAPER..
- Monitor response clinically and radiographically
- In general, recommended to discontinue TKI, though re-challenge and dose reduction is often considered
  - Cancer response to targeted treatment, lack of alternative treatment, grade of severity and resolution on steroids are clinical factors that enter into decision-making about re-challenge (case-by-case, depending on tumor, degree of pulmonary risk and cancer therapy)

ESCALATION OF IMMUNOSUPPRESSIVE TREATMENT (GRADE 3/4) FOR IMMUNOTHERAPY RELATED ILD

- Escalate steroid treatment
- Infliximab 5 mg/kg IV, repeat in 2 weeks PRN
- Ig IV 2g/kg over 2-5d
- Tocilizumab 4-8 mg/kg IV, repeat in 2 weeks PRN
- Cyclophosphamide

- If chronic/refractory pneumonitis: mycophenolate mofetil (MMF) 1-1.5g BID as tolerated
- Start 500 BID, ↑ by 250 BID q weekly with labs

BACK TO THE CASE

- Initially managed with IV solumedrol, but further clinical decline requiring OPTIFLOW
- Nasal swab positive for PCP; given risk of PCP in context of previous steroid use and clinical decline; SEPTRA started
- Over 1 week significant improvement
- Eventually back on room air with improvement (though not complete resolution) of CT findings
- Eventually d/c to residence

TAKE HOME MESSAGES

- More common with newer generations of chemotherapy
- Vigilance required; high index of suspicion especially with unexplained hypoxia
- Understand the often broad DDX
- Step-wise approach to investigations, multi-D approach
- Initial management may require multiple simultaneous strategies depending on severity of illness

COMPLICATIONS OF CHEMOTHERAPY: FEBRILE NEUTROPENIA

Ovie, Albert: MD, MSc, CCFP, ABPM (AM)

PRESENTER DISCLOSURE

Presenter: Ovie Albert

Any direct financial relationships, including receipt of honoraria:

Not applicable

Membership on advisory boards or speakers' bureaus:

Not applicable

Patents for drugs or devices:

Not applicable

Other:

Not applicable

Learning Objectives — Febrile Neutropenia

At the end of this session, participants will be able to:

1. **Appreciate** the clinical significance, morbidity, and mortality associated with febrile neutropenia.
2. **Recognize** febrile neutropenia as an urgent complication in patients receiving chemotherapy.
3. **Understand** the fundamental principles of assessment, risk stratification, and management.
4. **Apply** a practical, patient-centered approach to optimize outcomes.

Febrile neutropenia is associated with in-hospital mortality rates of 5–11% in adults, with higher rates (>20%) in those with sepsis, hemodynamic instability, or comorbidities; up to 50% of patients require hospitalization, and complications occur in 15–25%.

FN = medical emergency • Follow local protocols & adjust for renal function

CASE PRESENTATION

- 56-year-old man with diffuse large B-cell lymphoma, day 9 post-R-CHOP (Cyclophosphamide, Doxorubicin,Vincristine and Prednisone) cycle 2
- ex-smoker, currently 10 cigarettes/day despite chemo. Interested in quitting
- Presents with fever 38.5 °C at home, mild fatigue, “feels like a flu”
- In ED: HR 112, BP 102/66, Sat 95% RA, afebrile now, appears only mildly ill
- On exam: no obvious source, central venous port in place
- CBC: ANC 0.2 × 10^9/L
- → “He looks okay—can this wait?”

WHY THIS MATTERS

- High early complication risk; fever may be the only sign of infection
- Any recent-chemo patient with fever = FN until excluded
- Goal: antibiotics started within 60 minutes of triage
- Ex-smoker, currently 10 cigarettes/day; NRT discussed at triage as patient interested in quitting.

GP Red Flags
Temp ≥38.3 °C once OR ≥38.0 °C for ≥1 h
Appears well? Still treat as FN

FN = medical emergency • Follow local protocols & adjust for renal function

FEBRILE NEUTROPENIA (FN)

Definition:

- **Fever:** single oral ≥38.3 °C or ≥38.0 °C sustained ≥1 h
- **Neutropenia:** ANC <500/ML, or <1000 with expected decline <500 in 48h
- Inflammatory signs often **muted**; fever may be **only clue**
- FN is a **medical emergency**: mortality up to 10% if delayed
- **GP Red Flag box:**
- Do not delay antibiotics while waiting for labs or imaging

GP Red Flags
Recent chemo + fever ⇒ act now
Consider FN even without localizing symptoms

RISK STRATIFICATION

- Febrile neutropenia most commonly occurs in cancer patients receiving cytotoxic chemotherapy and affects:
  - 10%-50% of patients with solid tumor malignancies
  - > 80% of patients with hematologic malignancies
- To help determine the approach to evaluation and treatment,
  - careful patient risk assessment should classify patients as either
  - low-or high-risk

COMPLICATIONS OF CHEMOTHERAPY - FEBRILE NEUTROPENIA

Practical red flags & first-line management for GPs and ED clinicians

Family Medicine Forum 2025 • Febrile Neutropenia • Presenter: Ovie

Definitions:

- Fever: single oral ≤38.3 °C or ≥38.0 °C sustained for at least
- **Neutropenia** : ANC ≤500/ ML, or <1000 with expected decline <500 in 48 hours
- Hypotention, isgns, often muteid ; fewer may be only clue

GP RED FLAGS

- Any fever after **recent** chemo = FN until proven otherwise
- Do not delay antiobotics for tests

Antibiotics within 60 minutes

First — hour: or

1) Sepsis-risk triage → IV x2 → focused history
2) Labs → cultures (each CVC lumen + peripheral), lactate
3) Start IV antipseu domonal β-lactam ≤50 min, vancomycin only if indicated
4) Risk-stratify (MASCC; +CISNE if applicable)
5) Disposition: low-tisk oral pathway with ≥4 h observation vs admit
6) Persistent fever day 4–7 + prolonged neuttopenia → consider antifungal with ID/Onc
7) Document return precautions & follow-lip

Febrile Neutropenia is a Medical Emergency—Immediate Recognition & Action Save Lives

HIGH RISK DEFINED BY EITHER:

- Anticipated prolonged (> 7 days duration) and profound neutropenia (ANC ≤ 100 cells/mm^3 following cytotoxic chemotherapy)

OR

- Significant medical comorbid conditions, including hypotension, pneumonia, new-onset abdominal pain, or neurologic changes

Low risk defined as:

- Anticipated brief neutropenic periods (≤ 7 days) and no or few comorbidities

EVALUATION

- Perform a thorough **history and physical examination**, noting that a typical inflammatory response may be blunted in immunocompromised patients.
- When taking a history, consider:
  - chemotherapy regimen used
  - Use of other immunosuppressive medications
  - Prior antibiotic exposures
  - History of prior infections including colonization with multidrug resistant organisms
  - Comorbidities

ASK AND RESEARCH CHARTS FOR

- Ask about prior latent infections known to reactivate (such as, tuberculosis, herpes simplex, and hepatitis B virus), ill contacts, unusual exposures, and the receipt of blood transfusions.

FIRST 10 MINUTES: ESSENTIALS

- Sepsis-risk triage; IV access ×2
- Focused history: last chemo, regimen, FQ prophylaxis, central line, allergies
- Order now: CBC/diff, CMP, lactate;2 sets of blood cultures (each line lumen + 1 peripheral)
- Chest imaging for patients with signs or symptoms of lower respiratory tract infection
- Do not delay antibiotics while perfecting tests/imaging

GP Red Flags
Antibiotics within 60 minutes
If unstable → call for senior/ICU early

FN = medical emergency • Follow local protocols & adjust for renal function

Chest Imaging for Patients with Signs or Symptoms of Lower Respiratory Tract Infection

- Note: CXR can be normal in neutropenia - infiltrates may be absent because neutrophils are required for visible inflammation
- Targeted imaging if focal symptoms (e.g., abdominal, sinus, CNS)
- Consider LP if meningitis features or unexplained delirium

IMMEDIATE EMPIRIC THERAPY (IV)

- Choose one antipseudomonal β-lactam:
- Piperacillin–tazobactam 4.5 g IV q6–8h
- Cefepime 2 g IV q8h
- Meropenem 1 g IV q8h (institutional choice)
- Add vancomycin only if: instability, pneumonia, skin/soft-tissue or catheter-related infection, known MRSA

GP Red Flags

Do not give routine vancomycin
True β-lactam anaphylaxis? → aztreonam + vanco (per local policy)

FN = medical emergency • Follow local protocols & adjust for renal function

Risk stratification: who is low-risk?

- Use **MASCC (Multinational Association for Supportive Care in Cancer)** score
  → **≥21 suggests low-risk** and supports outpatient management when clinically stable.
  → Considers burden of illness, hypotension, dehydration, COPD, age, and outpatient status.

- For stable solid-tumor outpatients, add **CISNE (Clinical Index of Stable Febrile Neutropenia)**
  → **0 = low**, **1–2 = intermediate**, **≥3 = high risk** (predicts complications in stable patients).

- Low-risk patients may be candidates for **outpatient oral therapy** with **close follow-up** (observe ≥4 h after first oral dose).

GP Red Flags

Any instability OR MASCC <21 OR CISNE ≥3 → admit
Anticipated prolonged severe neutropenia (≥7 d) → admit

OUTPATIENT-SAFE CHECKLIST

- Clinically stable; no pneumonia or deep focus
- Short expected neutropenia; no severe mucositis
- Reliable supports; 24/7 contact; return within 24–48 h
- Observe ≥4 h after first oral dose before discharge

GP Red Flags

Poor supports or barriers to meds → do NOT discharge
New focal pain (abdomen/perianal) → image & admit

FN = medical emergency • Follow local protocols & adjust for renal function

OUTPATIENT ORAL REGIMENS (EXAMPLES)

- Ciprofloxacin 750 mg PO q12h + amoxicillin–clavulanate 875/125 mg PO q12h
- If true penicillin allergy: ciprofloxacin + clindamycin (local dosing)
- Avoid oral FQ regimens if on prior FQ prophylaxis

GP Red Flags
Ensure first dose given before discharge
Clear 24–48 h follow-up plan

FN = medical emergency • Follow local protocols & adjust for renal function

WHEN TO BROADEN OR ESCALATE

- Clinical deterioration or site-specific source: ensure anaerobic coverage (piptazo or carbapenem)
- Persistent fever after 4–7 days + prolonged neutropenia: consider antifungal (per ID/Onc)
- Suspected catheter infection: cover MRSA; consider line management

GP Red Flags

Rising lactate, hypoxia, altered mentation → escalate level of care

New chest findings → early imaging + broaden

FN = medical emergency • Follow local protocols & adjust for renal function

SPECIAL CASE: TYPHLITIS (NEUTROPENIC ENTEROCOLITIS)

- Triad: fever + abdominal pain + bowel-wall thickening on imaging
- High mortality if missed—consider CT to define extent
- Management: broad IV with anaerobic coverage, fluids, avoid rectal procedures, early surgical/ID input

GP Red Flags
RLQ or perianal pain in FN → image & admit
Do NOT perform rectal exam/thermometry

FN = medical emergency • Follow local protocols & adjust for renal function

WHAT NOT TO DO

- Do not delay antibiotics for complete work-up
- Do not default to vancomycin without indications
- Do not rely on appearance—FN can look deceptively well
- Avoid rectal temperatures/exams

💡 **G-CSF Pearl**
Use for prophylaxis in high-risk chemotherapy or prolonged neutropenia—not as first-line FN therapy.

GP Red Flags
'Looks okay' ≠ safe to observe without treatment
If in doubt, treat as FN and reassess

FN = medical emergency • Follow local protocols & adjust for renal function

FIRST-HOUR ALGORITHM (PRACTICAL)

1. Sepsis-risk triage; IV ×2; brief history (chemo date, regimen, FQ prophylaxis, line, allergies)
2. Labs + cultures (each line lumen + peripheral) if feasible
3. Start IV antipseudomonal β-lactam within 60 min; add vanco only if indicated
4. Risk-stratify (MASCC; add CISNE if applicable)
5. Disposition: low-risk oral pathway with ≥4 h observation vs admit
6. Persistent fever day 4–7 + prolonged neutropenia → consider antifungal with ID/Onc
7. Document return precautions and follow-up

GP Red Flags

Antibiotics FIRST; tests must not delay therapy

Any instability → admit/ICU consult

FN = medical emergency • Follow local protocols & adjust for renal function

BACK TO THE CASE

- Sepsis-risk Triage; IV ×2; labs sent; **blood cultures** drawn from **each CVC lumen + one peripheral**
- **Piperacillin–tazobactam within 60 minutes**; **vancomycin deferred** (no instability or clear MRSA/line indications)
- **No focal source** (CXR/UA unremarkable); close observation
- **Afebrile by 24 h**; hemodynamically stable; **MASCC 23 (low-risk)**
- **Blood cultures no growth** at 48 h; **ANC rising** to 0.6 × 10^9/L
- * NRT patch initiated on admission; brief cessation counselling provided. (Teachable moment for Nicotine USE Disorder.
- **Step-down to oral** ciprofloxacin + amoxicillin-clavulanate; **observed ≥4 h** pre-discharge
- Completed **7-day** total course; counts **recovered**; **no readmission** at follow-up

* Why? FN hospitalization is a **“teachable moment”** for smoking cessation. NRT is safe, avoids withdrawal

TAKE-HOME MESSAGES

- Recognize fast, treat fast: IV anti-pseudomonal within 60 minutes
- Risk-stratify smartly (MASCC/CISNE); observe if discharging on oral pathway
- Watch for exceptions: typhlitis, line infection, pneumonia
- Always document allergies, return precautions, and follow-up
- *Early antibiotics save lives; G-CSF may reduce duration of neutropenia in selected high-risk patients—follow oncology guidance.*

GP Red Flags
Fever + recent chemo = FN until proven otherwise
Do not delay antibiotics

FN = medical emergency • Follow local protocols & adjust for renal function

REFERENCES (SELECTED)

- ASCO/IDSA Guidelines on Outpatient Management of FN (2018, with updates)
- IDSA Guidelines for FN in Adults (core principles)
- NICE: Neutropenic Sepsis—recognition and early management
- Local institutional protocols and antibiograms
- DyNAMED - https://www-dynamed-com.ezproxy.shirp.ca/approach-to/febrile-neutropenia

FN = medical emergency • Follow local protocols & adjust for renal function

MANAGING CANCER TREATMENT–RELATED DIARRHEA

Genevieve Chaput: MD, MA, CAC (PC), FCFP

PRESENTER DISCLOSURE

Presenter: Genevieve Chaput

Any direct financial relationships, including receipt of honoraria:

Not applicable

Membership on advisory boards or speakers' bureaus:

Not applicable

Patents for drugs or devices:

Not applicable

Other:

Chair of the Cancer care Member Interest Group (MIG); Member, CFPC MIG Council Committee

LEARNING OBJECTIVES

- Recognize causes of diarrhea in patients undergoing cancer treatment
- Apply evidence-based management strategies in primary care
- Identify red flags that require urgent referral or hospitalization
- Support patient self-management and monitoring

CLINICAL CASE – INTRODUCTION

- Mr. A, a 54-year-old man with metastatic colorectal cancer on FOLFIRI (Folinic acid, Fluorouracil (5-FU) and Irinotecan), presents with 5 days of watery diarrhea following his third chemotherapy cycle.

- How should you approach assessment and management of this patient?

ASSESSMENT – KEY QUESTIONS

- Onset: When did it start? Is it cyclical with treatment?
- Provoking/Palliating: Any triggers?
- Quality/Quantity: Watery, bloody, mucous? Tenesmus?
- Related symptoms:
  - Pain? Bloating? Gas?
  - Nausea? Fever? Thirst? Weakness?

ASSESSMENT – KEY QUESTIONS

- Severity:
  - Frequency per day?
  - Nocturnal symptoms?
  - Incontinence?
  - Intermittent bouts of constipation?
- Exploring patient's needs and values
  - Assess impact on quality of life, explore if concerns that will cause treatment delays, offer support

PHYSICAL EXAM

- General appearance and mental/cognitive status
- Vitals, volume assessment
- Weight
- Abdominal exam
- Rectal exam, if indicated
- PPS score (functional assessment score)

INVESTIGATIONS

Patient's goals of care = front and center, serves as guide to extent of investigations

- Lab panel, as indicated (especially for renal function, WBC, potassium and magnesium)
- Abdominal x-rays, to eliminate potential obstruction or overflow constipation
- CT scan to assess for enteritis/colitis or other causes
- C. difficile, stool cultures (bacterial, O & P)
- May need C Scope
- If immune-mediated colitis is suspected: consider further work-up

COMMON ETIOLOGIES OF DIARRHEA in CANCER PATIENTS

- **Chemotherapy-induced mucosal injury (5-FU, irinotecan)**
  - Incidence: ranges between 50-90%
- **Radiation enteritis (radiotherapy to pelvic or abdominal fields)**
  - Frequent, up to 70% of patients
- **Immunotherapy-related colitis +/- enteritis**
  - Associated with high morbidity: importance of early detection and prompt management
- Antibiotic-associated or infectious (C. difficile)
- Malabsorption (bile salt diarrhea, pancreatic insufficiency)
- Overflow diarrhea due to constipation

NON-PHARMACOLOGIC MANAGEMENT

- Diet
  - To avoid:
    - Limit caffeine
    - Avoid sorbitol and insoluble fibre
    - Avoid hyper-osmotic beverages
  - To promote:
    - Small frequent meals
    - High soluble fibre foods

NON-PHARMACOLOGIC MANAGEMENT

- Skin care considerations
  - Promote good skin hygiene (sitz baths, fragrance-free and mild soaps)
  - Apply skin barriers (zinc compounds, Ihle's paste)
  - Adequate hygiene care of stoma
  - If anal fissures: topical calcium channel blockers (nifedipine, diltiazem)
  - Skin breakdown: consider topical opioids

SUPPORTIVE CARE

- IV fluids (type depends on volume status, PO intake, electrolyte results
- Frequent lab monitoring (usually daily)
- Consider antibiotics for fever

PHARMACOLOGIC MANAGEMENT – STEPWISE

- **First line**:

  Loperamide 2 mg after each loose stool (max 16 mg/day)

- **Second line**:

  Diphenoxylate/atropine (Lomotil) 1–2 tabs q4h prn, max 4 times/day

- **Third line**:

  Octreotide: typically reserved for refractory cases

PHARMACOLOGIC MANAGEMENT

- **Pharmacological management to be tailored to underlying tumor/clinical presentation:**
  - Bile salt diarrhea: Cholestyramine
  - Pancreatic insufficiency: Creon
  - Neuroendocrine tumors: Tryptophan hydroxylase inhibitors (Xermelo)

BACK TO OUR CLINICAL CASE: MR. A

- Mr. A, a 54-year-old man with metastatic colorectal cancer on FOLFIRI, presents with 5 days of watery diarrhea following his third chemotherapy cycle.
- Additional details:
  - Pattern of diarrhea: during and for approximately one week after chemotherapy cycles
  - Denies fever, pain, bleeding, n/v, or symptoms suggestive of infection
  - No diarrhea outside of these timeframes, rather constipated
  - On Hydromorphone Contin 3mg po BID for pain management
  - States QOL still good, chief concerns is delay in treatments

MR. A: APPROACH AND MANAGEMENT

- Vitals and physical exam
- Abdominal x-ray series

All: normal findings and nil acute

Management:

- Counseling on non-pharmacological self-management + refer to dietician for assessment and more thorough expert counseling
- Prescribe Loperamide prn, Sennokot scheduled off chemotherapy days/week after chemotherapy
- Teaching and support to patient, including when to seek urgent care **(⚠ Red flags)**

WHEN URGENT CARE REQUIRED

- ⚠️ **Red flags:**
- >6 watery stools/day or nocturnal diarrhea
- Blood/melena, fever >38°C, severe abdominal pain
- Orthostatic hypotension, confusion, dehydration
- Immunotherapy-induced colitis (suspect if bloody)
- Inability to maintain oral hydration

CLINICAL PEARLS FOR FAMILY PHYSICIANS

- Patient education is key:
  - Monitor stool frequency
  - Reinforce hydration and diet strategies
  - Teach patient when to seek care (red flags)
- Immunotherapy colitis: urgent referral; hold treatment; corticosteroids ± infliximab
- Chemotherapy-induced: may require dose reduction
- Avoid antimotility drugs in suspected infectious or bloody diarrhea
- Assess for overlapping constipation (‘overflow’)

RESOURCES FOR FAMILY PHYSICIANS

- BC Cancer Symptom Management Guidelines (2023)
- Cancer Care Ontario. Symptom Management – Diarrhea (2022)
- ASCO Guidelines: Management of Cancer Therapy–Induced Diarrhea, JCO 2021
- UpToDate: Evaluation and management of chemotherapy-induced diarrhea

Thank you for your attention!

Questions?

Scan the QR code to join the
Member Interest Groups Discussion Forum
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THE COLLEGE OF FAMILY PHYSICIANS OF CANADA
LE COLLÈGE DES MÉDECINS DE FAMILLE DU CANADA

Files Discussion Events

https://timedright.link/cfpc-migs-hub

- **Diverse:** 23 discussion groups
- **Popular:** Over 5,000 members
- **Private:** A secure platform where CFPC members connect based on their area of interest

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Lisez le code QR pour vous joindre aux **groupes d'intérêt des members Discussion** sur la plateforme MiGroups

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