Oncology Emergencies

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GPO Systemic Therapy

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Disclaimer

- I have no competing interests
- and I receive no income from pharma.

Objectives

- To recognize common oncologic emergencies
- Institute appropriate initial management
- Refer appropriately

A word about emergencies

- Not all emergencies are created equal
- Response and definitive treatment may be required within short minutes, hours, ...or even the next day
- Treatment approach depends on the severity of the emergency and the prognosis of the disease
- Learn to recognize, stabilize, and ask for help
- Recognize which scenarios require immediate assessment and action

KEEP
CALM
AND
CARRY
ON

Febrile Neutropenia

Febrile neutropenia
Scenario

- 45 yr old woman, previously healthy, on adjuvant chemotherapy for breast cancer, arrives in Lady Minto Emergency Department with a letter saying she is on myelosupressive chemotherapy, and that she is to report for immediate medical assessment if she has a fever. Her temperature was 38.2 on arrival. She otherwise feels well.

Febrile neutropenia
Scenarios

- A 55 year old man on curative chemotherapy for lymphoma presents in Cowichan District Hospital Emergency semiconscious with a temp of 39, BP 80/40, P 120

- A 60 year old woman on palliative chemotherapy for lung cancer arrives in SPH emergency with a temp of 38 for most of the day, and a worsening cough.

Febrile neutropenia

- The definition
  - Febrile – oral temperature of 38° sustained over 1 hour or any single temperature =/over 38.2°
  - Neutropenia – Absolute neutrophil count (ANC) of less than 0.5 or expected to be less than 0.5 at nadir
  - Relative Neutropenia – ANC between 1.0 and 0.51
  - Profound neutropenia – ANC less than 0.1

IDSA Guidlelines 2002

Febrile Neutropenia: Definition

- OR: Any SIRS criteria, symptoms or signs, in an afebrile patient currently receiving chemotherapy.
- Some chemotherapy patients cannot mount a fever; eg. Long term use of corticosteroids. If hypotensive, tachycardic, unstable, and neutropenic, institute FN procedures.

SIRS criteria recognition

The Systemic Inflammation Response Syndrome (SIRS) is recognized by:

- *Temperature > 38° C or < 36° C*
- *Heart rate > 90 beats/minute (tachycardia)*
- *Respiratory rate > 20 breaths/minute (tachypnea)*
- *Systolic blood pressure ≤ 90 mm Hg (hypotension)*
- *Abnormally high or low white blood cells*

SIRS criteria (1 or more) predict serious infection and sepsis in a chemotherapy patient at time of ER presentation / triage

even in the absence of fever

Febrile neutropenia

- The cause
  - Chemo shuts down myelopoiesis until drug is excreted
  - Neutrophils have short life span
  - Most chemo protocols have nadir counts between at 1-2 weeks and ANC recovery between 3-4 weeks

Febrile neutropenia

- The problem
  - Infection can be documented in 1/3 of patients with fever and neutropenia.
  - Patients with fever and neutropenia will have bacteremia about 30% of the time
  - Bacteremia with neutropenia has a 8 - 23% short term mortality and is a true medical emergency.
  - Symptoms and signs of infection in neutropenic patients are often minimal to absent.

Paul, M. The Cochrane Library, 3, 2004

Febrile neutropenia

- The risk of infection increases with
  - Anticipated prolonged severe neutropenia(>/= 7 days)
  - Severity of neutropenia (ANC < .10)
  - Significant medical comorbidities, COPD, Diabetes
  - hepatic or renal insufficiency
  - Cancer not in remission, uncontrolled, progressive
  - Central lines
  - Mucosal disruption
  - Cancer diagnosis (CLL, Lymphoma, Myeloma)
  - Inpatient at time of development of fever

Febrile neutropenia

- Patient assessment
  - History
    - Type of cancer, status of their disease
    - Type and date of last chemo
    - Details of the fever – timing, severity, rigors
    - Particular attention to symptoms
      - Chest and sinuses
      - Dental
      - GI (mucositis occurs throughout GI tract)
      - Skin (HSV, lines, cuts/abrasions/disruptions,)
      - Steroid use (mask fever, adrenal suppression)

Febrile neutropenia

- Physical assessment
- How sick is the patient at presentation?
  - Hemodynamic status: clinical stablity
  - Hydration status
  - Mental Status
  - Particular attention to
    - Mouth (stomatitis)
    - Chest (findings minimal in dehydrated, neutropenic patient)
    - Abdominal, perineum, AVOID rectal exam
    - Skin (cellulitis, lines, HSV, perianal infections)
    - CVS signs of infection
    - Be aware of the possibility of meningitis, sinusitis, H zoster, H simplex, thrush

Febrile neutropenia

- Laboratory assessment
  - Required
    - CBC, diff stat
    - Blood culture X2 (one from line if present)
    - Urine culture, urinalysis
    - CXR (findings may increase with hydration and neutrophil recovery)
    - Lytes, urea, creat, glucose (esp. if on steroid)
    - Bilirubin, transaminases, alkaline phosphatase
  - Others as suggest by History and Physical
    - sputum, LP (not routine)
    - Consider monitoring procalcitonin (not yet on our protocols)

Febrile neutropenia

- Management
  - Where?
    - Hospital in most cases
    - Outpatient for low risk?
    - Call patient's medical oncologist
  - Fluid management – consider aggressive fluid resuscitation in septic patients with global hypoperfusion
  - Initial Antibiotics?

Pathogens of Febrile Neutropenia

Range of Pathogens Encountered in Febrile Neutropenic Patients

Commonly cultured organisms in febrile neutropenic patients

Gram negative	Gram positive	Other
Escherichia coli	Coagulase-negative staphylococcus	Clostridium difficile
Klebsiella	Staphylococcus aureus	Anaerobes
Pseudomonas	Streptococcus pneumoniae	Aspergillus
Enterobacter	Corynebacterium (JK)	Candida albicans
	Streptococci	Other Candida species
		Mycobacteria

Less commonly cultured organisms in febrile neutropenic patients

Gram negative	Gram positive
Proteus	Bacillus
Haemophilus	Listeria
Citrobacter	Stomatococcus
Serratia	Stomatococcus
Acinetobacter	
Neisseria	
Capnocytophaga	
Legionella	
Moraxella	
Stenotrophomonas	

Additional organisms in febrile neutropenic patients

Fungi	Viruses	Other
Cryptococcus	Herpes simplex virus 1,2	Babesia
Histoplasma	Varicella zoster virus	Toxoplasma
Coccidioides	Cytomegalovirus	Strongyloides
Zygomycetes	Epstein Barr virus	Nocardia
Pneumocystis jiroveci (formerly carinii)	Human herpesvirus 6	
	Enteroviruses	
	Respiratory syncytial virus	
	Influenza	
	(Live viral vaccines)	

PROTOCOL GOAL:

One Hour to Antibiotic

Febrile neutropenia

- Empiric Antibiotics
  - Need coverage for
    - Gram negative (not most common, but more lethal)
      - Pseudomonas, seeding of the bloodstream by endogenous GI bacteria
    - Gram positive (more common)
    - Anaerobes?
      - If sinus, dental, abdominal, pelvic source
    - Fungi (not routine)
    - Viruses (not routine)

Febrile neutropenia

- Antibiotics
  - Some good initial choices (choose one)

    Piperacillin/tazobactam 4.5g IV q6h*
    Imipenem/cilastatin 500mg IV q6h*
    Cefepime 2gm IV q8h
    Meropenem 500 mg IV q6h

    (yellow highlight =category 1, *= our local preference)

    - Penicillin allergy: Clindamycin 450 mg IV q8h plus Ciprofloxacin 400 mg IV q12h
    - Metronidazole if suspect anaerobes, C. difficile
  - Use Vancomycin initially if suspect MRSA, line infection, or patient in shock
    - 1g IV q12h, adjust for renal function

Febrile neutropenia

- IV Combination Therapy
  - Aminoglycoside plus antipseudomonal penicillin +/- betalactamase inhibitor category 1
  - Avoid aminoglycoside if platinum chemotherapy was given –nephrotoxic)

- Oral Therapy (low risk patients only)
  - For residents and FP's: designation of low risk should be discussed with the treating or on call oncologist.
  - Cipro plus amoxicillin/clavulanate
  - Cipro plus clindamycin if penicillin allergy
  - Not on prior quinolone prophylaxis, if pt was on quinolone prophylaxis, go to IV antibiotics

- Summary: initial antibiotics must be broad spectrum, consider local antibiotic susceptibility patterns, bactericidal, antipseudomonas coverage, recent antibiotic use.

- Goal: IV antibiotics within **one hour** of presenting with fever.

Requisite Factors for Outpatient FN Management ASCO 2013

- No prior fluoroquinolone
- Age less than 65
- ECOG 0 or 1
- Albumin > 35
- No previous FN episodes
- Not an advanced stage cancer
- Cancer in remission (CR not PR)
- No grade 3 mucositis or diarrhea
- Less than 2 co-morbidities
  (2 increases risk by 67%,
  3 increases risk 125%)
- ANC ≥ 0.2
- Daily clinic evaluation for 3 days
- Daily telephone contact
- Daily monitoring of ANC
- Return to hospital if recurrent fever or persistent fever after 48 hours
- Lives < 30 miles from the treating hospital
- Oncologist agrees
- Able to comply
- Family member at home 24/7
- Access to telephone 24/7

Febrile Neutropenia

- Use of G-CSF
  - Granulocyte colony stimulating factor
    - Speeds resolution of neutropenia
    - No change in mortality if used in FNP
    - Reduces hospital stay by 1 day
    - Local use is not consistent
    - Consensus is to use if
      - Profound neutropenia, shock, co morbidities
      - Worsening clinical course and expected prolonged neutropenia
      - Documented infection in neutorpenic patient not responding to antibiotics
    - Dose is 5µcg/kg SC daily (choose between 300 and 480µcg vials)

ASCO guidelines 2006

Febrile neutropenia

- Management in hospital
  - Daily site specific H&P, daily review of labs and cultures, evaluate response to therapy, fever trends, signs and symptoms of infection, fluid balance, drug toxicity (LFT, renal function).
  - If afebrile
    - Continue initial antibiotic until blood cultures available (~48 hrs)
      - Adjust antibiotic guided by culture/sensitivity
      - 5-7 days of IV antibiotic if blood culture positive, and repeat cultures are negative
    - If remain febrile
      - Stable, no new symptoms
        - Do not adjust antibiotic for 5 days
        - After 4 days reassess (fungal? disease related?)
      - Unstable, new symptoms
        - Broaden coverage to anaerobes, resistant gram neg and gram pos organisms, Candida coverage, add G-CSF
        - Infectious Disease consult

Febrile neutropenia

- Management in hospital
  - Criteria for discharge
    - Afebrile 24 hrs
    - Neutrophil recovery > 0.5 spontaneous, or > 1.0 if GCSF used
    - Negative cultures
  - Antibiotics duration
    - If all cultures negative, no focus of infection identified, and neutrophils recovered – stop
    - Complete a full antibiotic course for documented infections, appropriate to the source of infection.

Febrile neutropenia

- Fever in a neutropenic patient is life threatening.
- Prompt medical assessment and prompt aggressive broad spectrum antibiotic coverage is essential. One hour door to antibiotic
- Fever may be the only sign of impending septic shock in a neutropenic patient.
- Septic shock requires aggressive fluid management.

Guidelines: Monotherapy Choice

Cochrane database systematic review

Paul 2010

RCTs comparing effectiveness of anti-pseudomonal beta-lactams as empiric monotherapy for febrile neutropenia (n=44)

Pip-Tazo = Imipenem = Meropenem

(all cause mortality)

References

- NCCN Guidelines Version 2.2011

National Comprehensive Cancer Network

Prevention of Cancer-Related Infections

- BCCA Website-Supportive Care- Febrile Neutropenia

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Clinical Order Set

Demographics

Oncology – Fever and Neutropenia - Adult

Key: **Req** – Requisition **MAR** – Medication Administration Record **K** – Kardex **Dis** – Discontinued

KEY

Patient Population

– Fever (Temp 38.3°C or greater orally **Or** 38°C or greater tympanic x 1 reading **Or** 38°C or greater orally on 2 readings, 1 hour apart **And** Neutropenia (Absolute Neutrophil Count [ANC] less than 1 x 10^9/L)

– On Active Therapy: Chemotherapy, Radiation Therapy and/or Post-BMT for patients still on immunosuppression or within 1 year of BMT, and active blood cancers with cytopenias

Consults

- Oncology consulted - Dr _____ aware. Page Oncologist with ANC result and clinical assessment

Vitals/Monitoring

- HR, RR, BP, O_2 sats q8h and PRN **Or** _____
- Temp q8h and PRN **Or** _____
- If **UNSTABLE** (↓LOC, ↓BP, ↓Perfusion) HR, RR, BP, O_2 sats – every 15 minutes until stable and consider ICU consult
- No rectal temp, no rectal exam

Investigations

- Access Central line (all lumens/ports) and draw bloodwork. If no Central line then draw peripheral blood work with peripheral intravenous start
- Blood cultures x 2 (one from CVC, if present, plus peripheral blood, or 2 from separate peripheral sites)
- Hematology profile, sodium, potassium, chloride, carbon dioxide total, creatinine, glucose, bilirubin, ALT

☐ Lactate if unstable

- Urine Macroscopic; Urine Culture and Sensitivity
- Chest x-ray
- If Clinically indicated:
  - ☐ Throat swab Culture and Sensitivity
  - ☐ Stool Culture and Sensitivity
  - ☐ Procalcitonin
  - ☐ Sputum Gram Stain Culture and Sensitivity
  - ☐ Stool for C difficile toxin
  - ☐ Wound/Skin culture

Other: _____

IV Fluids

- Start 0.9% sodium chloride IV at _____ mL/h (maintenance)

☐ 0.9% sodium chloride IV bolus _____ mL over _____ minutes

Medications

- No rectal medications
- acetaminophen 500 to 1,000 mg PO q4h PRN FOR FEVER ONLY to a max of 4 g daily from all sources

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1

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Clinical Order Set

Demographics

Oncology – Fever and Neutropenia - Adult

Key: **Req** – Requisition **MAR** – Medication Administration Record **K** – Kardex **Dis** – Discontinued

KEY

Antibiotic Therapy – Goal: Within one hour of presentation at hospital

- 1st Antibiotic dose to be given STAT as soon as blood cultures drawn. Do not wait for ANC result

If ANC less than 1 x 10^9/L:

- ADMIT

☐ piperacillin/tazobactam 4.5 g IV q6h
Or
☐ imipenem/cilastin 500 mg IV q6h

For patients with severe beta-lactam (penicillin/cephalosporin) allergy (eg anaphylaxis, angioedema):

☐ clindamycin 600 mg IV q8h
And ☐ ciprofloxacin 400 mg IV q12h

For patients with possible central line infection or suspected MRSA or hemodynamic instability add:

vancomycin dosing guidelines – see Page 3 (dosed on total body weight [TBW])

☐ vancomycin _____ mg IV loading dose (25 mg/kg [TBW] round to nearest 250 mg) then

vancomycin _____ mg IV q _____ h

Subsequent vancomycin dosage adjustments

- As ordered by pharmacist. Target trough 10 to 15 mg/L

Investigations

- Further lab investigations for monitoring vancomycin therapy to be ordered by pharmacist/medical microbiologist

If C. difficile suspected:

☐ vancomycin 125 mg PO q6h x 10 days

Or Chemotherapy induced mucositis or typhlitis make patient NPO:

☐ metroNIDAZOLE 500 mg IV q8h x 10 days

Venous Thromboembolism (VTE) Prophylaxis

☐ dalteparin 5,000 units subcut once daily. Hold if platelets less than 50

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Dosing Guidelines for vancomycin	Clinical Decision Support

ACTUAL Body Weight (kg)	LOADING DOSE (25 mg/kg)	MAINTENANCE DOSE (15 mg/kg)
40 to 50	1250 mg	750 mg
51 to 60	1500 mg	1000 mg
61 to 70	1750 mg	1000 mg
71 to 80	2000 mg	1250 mg
81 to 90	2250 mg	1250 mg
91 to 100*	2500 mg	1500 mg

* For 100 kg and above obtain Pharmacy Consult. **Max 2500mg/dose**

- Algorithm to determine Vancomycin Target TROUGH and Initial Dosing INTERVAL
- For the following infections a higher trough should be targeted (**15 to 20 mg/L**): severe infections due to methicillin-resistant Staphylococcus aureus (MRSA) such as endocarditis, osteomyelitis/deep abscess, pneumonia, meningitis

LOW-TARGET 10 to 15 mg/L

INITIAL DOSING INTERVAL (hours)

SCr mcmol/L	Age Group (years)					
	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 - 79
40-60	8	8	12	12	12	18
61-80	8	12	12	12	18	18
81-100	12	12	12	18	18	18
101-120	12	12	18	18	18	24
121-140	12	18	18	18	24	
141-160	18	24	24	24		
161-180	24	24				
181-200	24					

HIGH-TARGET 15 to 20 mg/L

INITIAL DOSING INTERVAL (hours)

SCr mcmol/L	Age Group (years)						
	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 - 79	80-89
40-60	8	8	8	8	8 - 12*	12	12
61-80	8	8	8-12*	12	12	12	12-18*
81-100	12	12	12	12	12 - 18*	18	18
101-120	12	12	12 - 18*	18	18	18	18
121-140	12	18	18	18	18	18-24*	
141-160	18	18	18	18 - 24*	24		
161-180	18 - 24*	24	24	24			

* If more aggressive therapy is desired, select more frequent dosing interval

- Shaded boxes: patients have unstable and/or reduced renal function, and the nomogram may not be as predictive;
  For those with an interval stated, patients should receive a loading dose followed by 3 hour and pre-2nd dose serum levels to determine appropriate dosing
  For those with no dosing interval stated, patients should receive a loading dose followed by 3 hour and 24 hour post-dose serum levels to determine subsequent dosing
  A clinical pharmacist should be contacted for assistance with dosing and interpretation of levels

What's the diagnosis?

- 54 year old man, no known illnesses
- 6 week history of increasing back pain, upper lumbar area
- Makes appointment with his GP as the pain is getting his attention
- Distant history of smoking, quit 20 years ago

What's the diagnosis?

- The pain is fairly localized to the upper lumbar spine, seems worse when lying supine, or with coughing. He recently has felt some discomfort in his left leg. On questioning, bladder and bowel function are intact, but it feels a little funny when he wipes with toilet paper.
- You examine him and find:
- Mild bilateral leg weakness, slightly decreased pinprick sensation both feet, stocking distribution; plantar reflexes are upgoing; DTRs are brisk.

Clinical Presentation Spinal Cord Compression

- Pain is the commonest symptom
  - •Occurs in 80-90% of SCC
  - •Local and neuropathic pain often precedes other progressive symptoms by 2-3 months

- •Motor weakness
  - •Occurs in 50 to 60%
  - •Rapidity of onset variable, often sub acute over days –weeks, but can be very sudden and complete

Malignant Spinal Cord Compression

- Mechanism of cord damage

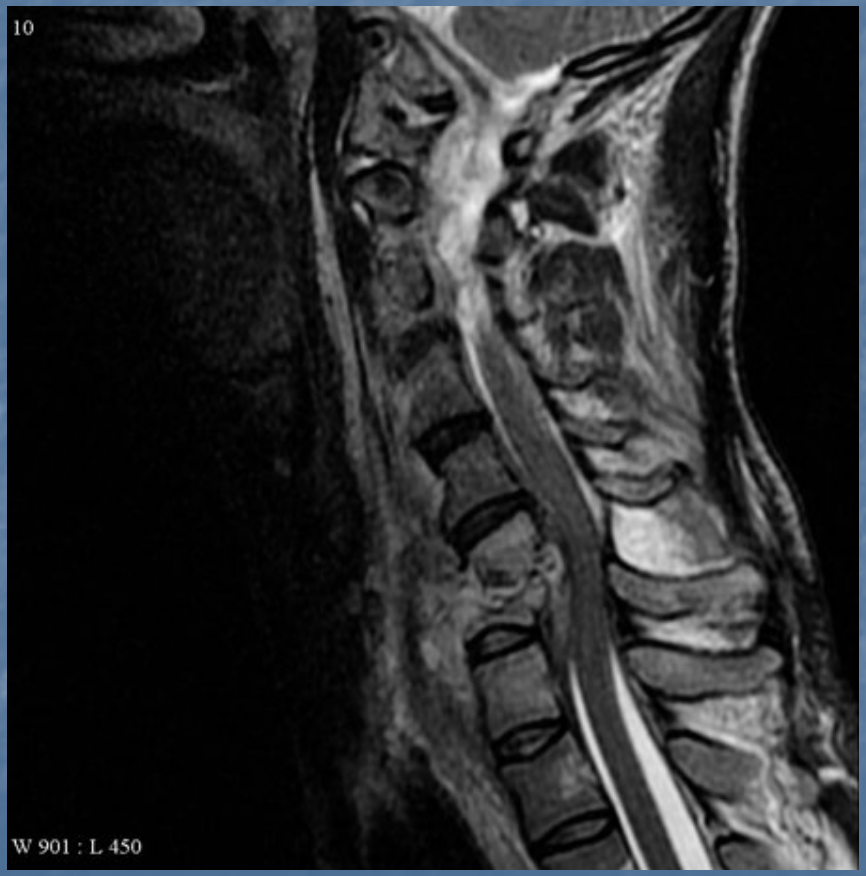
•Mechanical compression by tumor or bone resulting in demyelination

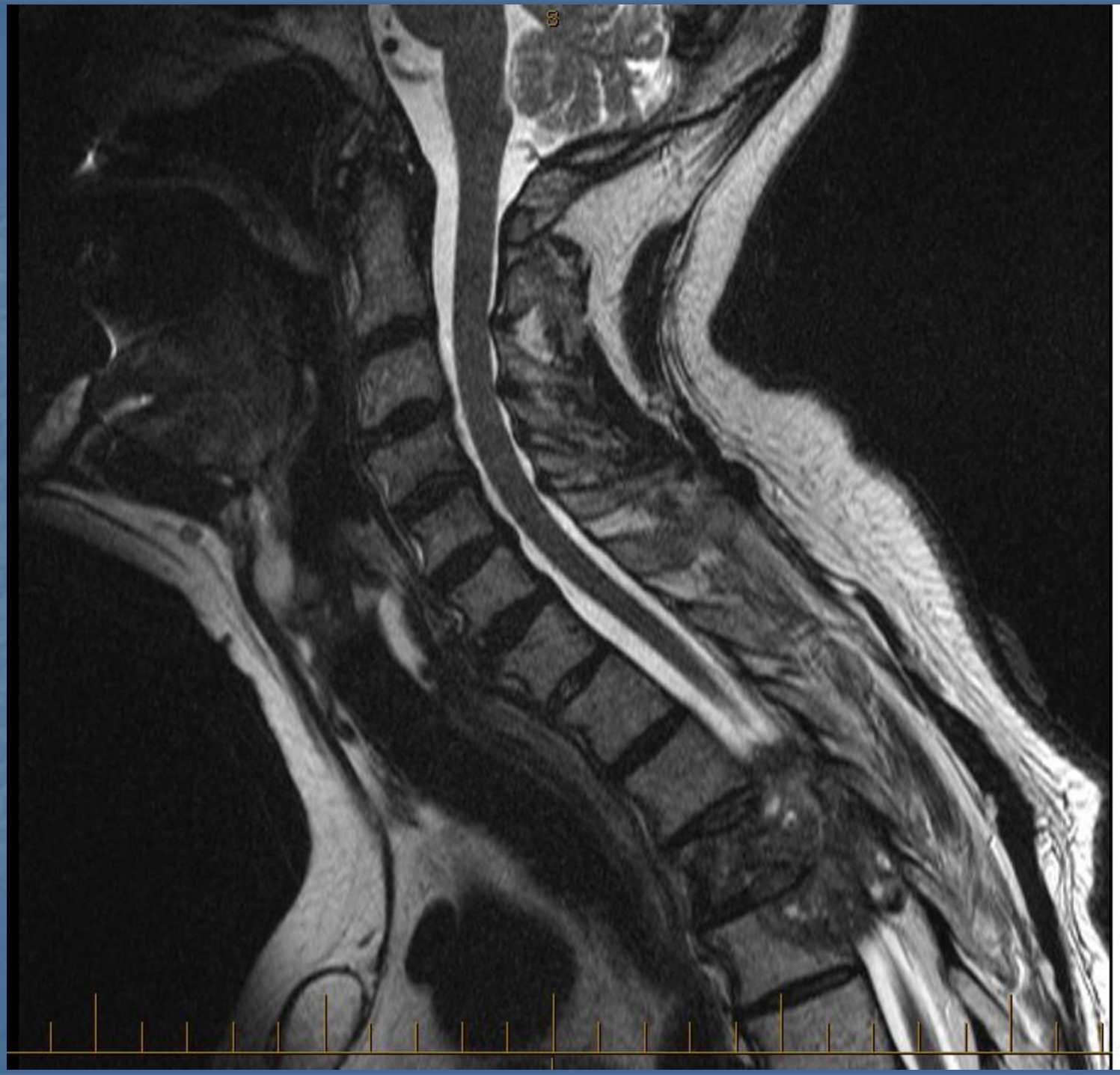
•Vascular Compression –arterial insufficiency and ischemia

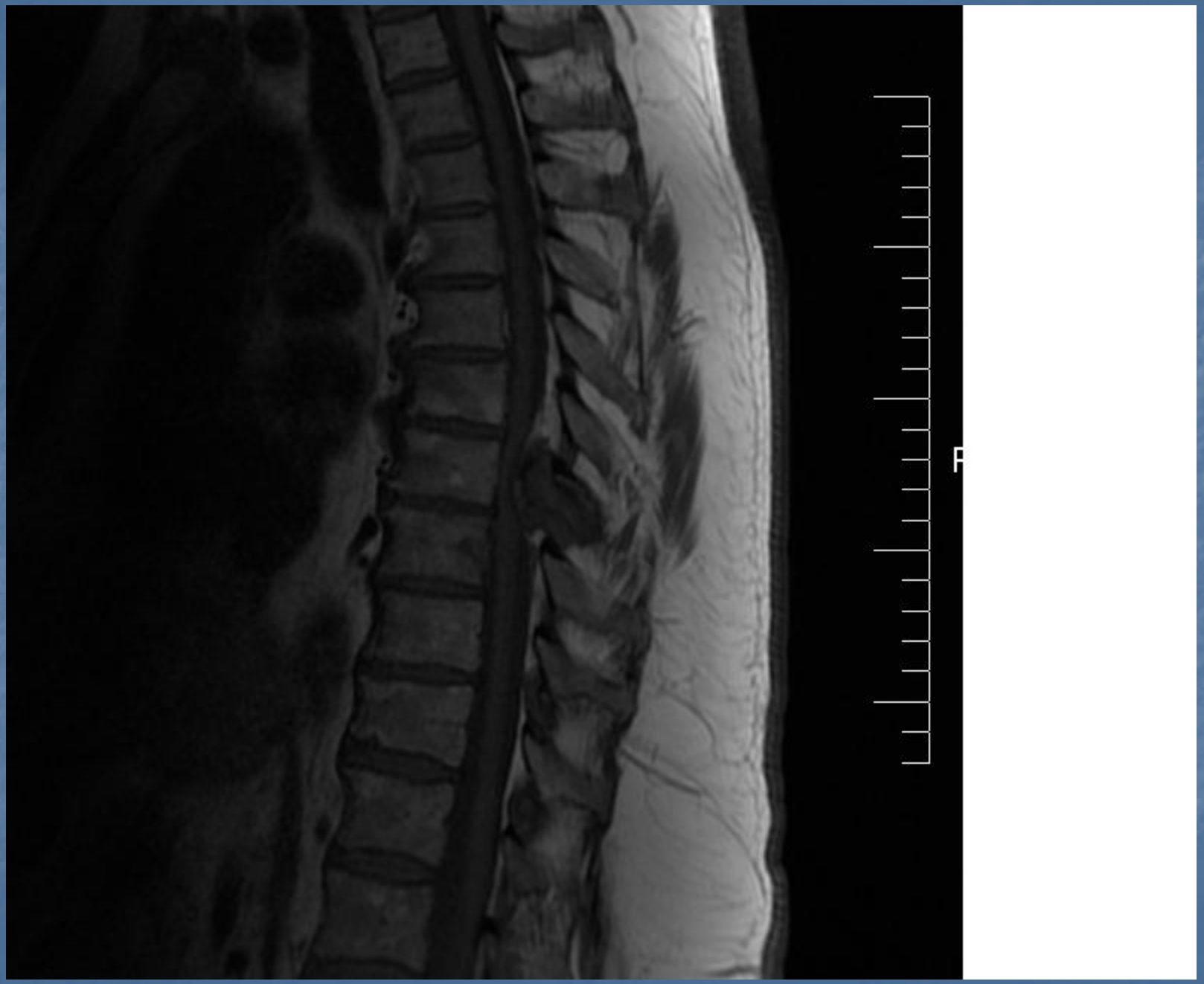
•Edema of neural tissue

•Direct tumour infiltration/invasion of neural tissue

Malignant Spinal Cord Compression







Malignant Spinal Cord Compression

- Urgent treatment to reduce incidence of parapelegia...very short time-line from onset of neurologic findings to irreversible cord damage.
- URGENT MRI- put the suspected diagnosis on the requistion, requires a phone consult with the radiologist. MRI entire spine: may have multiple lesions.
- One quarter of patients with SCC due to malignancy have no previous cancer diagnosis
- Occurs in 5 to 14 % of cancer patients

Malignant SCC

Prognostic Factors

Good prognostic factors:
Radio-or chemo-responsive tumour
Early detection
Gradual/slow onset
Ambulant
Good performance status

Poor prognostic factors:
Vertebral collapse
Acute onset with rapid progression
Flaccid paralysis
Autonomic dysfunction
Poor performance status

Malignant Spinal Cord Compression

- Metastatic prostate, breast and lung cancers most common
- Myeloma, lymphomas, melanoma
- Children: neuroblastomas and sarcomas

Malignant Spinal Cord Compression

- Treatment: high dose dexamethasone 8mg tid, tapering 2 weeks post RT completion
- Urgent Radiation Therapy - same day ideal and can prevent parapelegia, several fractions may be given over 1 to 2 weeks
- If no previous cancer history, histologic diagnosis is essential: attempt to biopsy the lesion, core, FNA, open

Hypercalcemia of Malignancy

- Definition: Corrected serum calcium > 2.67 mmol/L
- Paraneoplastic
  - Ectopic production of PTH related protein
  - Ectopic production of calcitriol
  - Ectopic PTH secretion (rare)
- Lytic: local release of cytokines (osteoclast activating factors)
- Unrelated –hyperparathyroidism etc….
- Most common malignant metabolic abnormality
- Consider this diagnosis in any confused patient

Clinical Presentation

Gastrointestinal

- Nausea
- Vomiting
- Constipation
- Abdominal pain

Neuromuscular

- Lethargy, fatigue
- Confusion, drowsiness
- Muscle weakness

Renal

- polyuria
- Dehydration
- Renal insufficiency

Cardiac

- Bradycardia
- Prolonged PR
- Shortened QT
- Wide T waves
- Arrythmias

Hypercalcemia Treatment

- Hydration: Normal saline
- IV Bisphosphonates
  - Pamidronate 60 to 90 mg IV over 60 min
  - Zoledronic Acid 4mg IV over 15 min (avoid if renal failure)
  - Denosumab 120 mg sc
  - Discontinue: Calcium, Vitamin D, thiazides, NSAIDs

Tumor Lysis Syndrome

- Metabolic complications which occur after treatment of bulky chemo-responsive neoplasias. Most common are high grade lymphomas and leukemias. Occasional spontaneous, or post radiation therapy.

Hyperphosphatemia

Hypocalcemia (due to precipitation of calcium phosphate)

Hyperkalemia

Hyperuricemia (breakdown of cellular RNA/DNA)

Acute renal failure

Tumor lysis Syndrome

- Prevention:
- Hydration N saline
- Allopurinol, pre and post chemotherapy
- Uric acid nephropathy :rasburicase rapid degradation of uric acid.

- Reference: The Tumor Lysis Syndrome NEJM 364;19 May 12 2011

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Clinical Order Set

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– On Active Therapy: Chemotherapy, Radiation Therapy and/or Post-BMT for patients still on immunosuppression or within 1 year of BMT, and active blood cancers with cytopenias

Consults

- Oncology consulted - Dr _____ aware Page Oncologist with ANC result and clinical assessment

Vitals/Monitoring

- HR, RR, BP, O_2 sats q8h and PRN **Or** _____
- Temp q8h and PRN **Or** _____
- If **UNSTABLE** (↓LOC, ↓BP, ↓Perfusion) HR, RR, BP, O_2 sats – every 15 minutes until stable and consider ICU consult
- No rectal temp, no rectal exam

Investigations

- Access Central line (all lumens/ports) and draw bloodwork. If no Central line then draw peripheral blood work with peripheral intravenous start
- Blood cultures x 2 (one from CVC, if present, plus peripheral blood, or 2 from separate peripheral sites)
- Hematology profile, sodium, potassium, chloride, carbon dioxide total, creatinine, glucose, bilirubin, ALT

☐ Lactate if unstable

- Urine Macroscopic; Urine Culture and Sensitivity
- Chest x-ray
- If Clinically indicated:
  - ☐ Throat swab Culture and Sensitivity
  - ☐ Sputum Gram Stain Culture and Sensitivity
  - ☐ Stool Culture and Sensitivity
  - ☐ Stool for C difficile toxin
  - ☐ Procalcitonin
  - ☐ Wound/Skin culture

Other: _____

IV Fluids

- Start 0.9% sodium chloride IV at _____ mL/h (maintenance)

☐ 0.9% sodium chloride IV bolus _____ mL over _____ minutes

Medications

- No rectal medications
- acetaminophen 500 to 1,000 mg PO q4h PRN FOR FEVER ONLY to a max of 4 g daily from all sources

1

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vancomycin dosing guidelines – see Page 3 (dosed on total body weight [TBW])

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	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 - 79	80-89
40-60	8	8	8	8	8 - 12*	12	12
61-80	8	8	8-12*	12	12	12	12-18*
81-100	12	12	12	12	12 - 18*	18	18
101-120	12	12	12 - 18*	18	18	18	18
121-140	12	18	18	18	18	18-24*	
141-160	18	18	18	18 - 24*	24		
161-180	18 - 24*	24	24	24			

* If more aggressive therapy is desired, select more frequent dosing interval

- Shaded boxes: patients have unstable and/or reduced renal function, and the nomogram may not be as predictive;
  For those with an interval stated, patients should receive a loading dose followed by 3 hour and pre-2nd dose serum levels to determine appropriate dosing
  For those with no dosing interval stated, patients should receive a loading dose followed by 3 hour and 24 hour post-dose serum levels to determine subsequent dosing
  A clinical pharmacist should be contacted for assistance with dosing and interpretation of levels