



Common Problems are Common...

Acute Complications of Cancer

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Common Problems

- Spinal Cord Compression
- Hypercalcaemia
- Neutropenic sepsis
- Superior Vena Cava obstruction
- Tumour Lysis Syndrome
- Metastases - protean manifestations
 - Liver e.g. jaundice/ coagulopathy /pain
 - Lung e.g. SOB, Haemoptysis
 - Brain e.g. headaches, seizures
 - Bone e.g. pain

Spinal Cord Compression

- Most common in myeloma, prostate, breast and lung cancers
- The cause is important as may dictate therapy
- Usually a posterior extension of a vertebral body mass
- Although Intrathecal metastases cause similar symptoms
- Have a clear understanding of urgency- it is a medical emergency

Spinal Cord Compression - Clinical features

- **Back pain crucial** – coughing , lying flat
- **Sensory disturbance below level of compression**
- **Progressive weakness**
- Sphincter dysfunction

Usually upper motor neuron (UMN) signs

May be complex e.g. –Brown Sequard

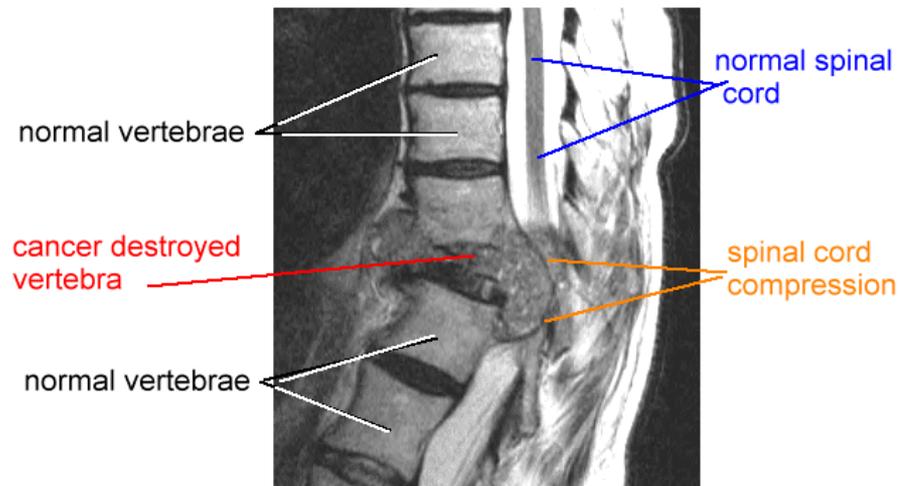
Or Conus Medullaris, Lhermitte's sign

- LMN signs may occur if:
 1. Nerve roots are involved
 2. Early in the clinical course of compression
 3. Lumbar spine can cause cauda equina syndrome



Management

- Confirm the diagnosis -Urgent MRI



- In Glasgow, close liason with Beatson Oncology centre – radiology team may be able to provide daily MRI service if problems at base hospital but must be referred early esp. at the weekend

Management

- Dexamethasone 10mg iv stat and 4 mg 6 hrly po
- Refer for urgent surgical decompression or radiotherapy
- Haematological cancers very radiosensitive while many solid organ metastasis do better with surgical decompression

- Radiosensitivity of tumours varies

Sensitive

Lymphoma

Myeloma

Breast

Prostate

Small-cell lung cancers

Resistant

Melanoma

Sarcoma

Renal cell carcinoma

Prognosis

- Depends on tumour type
- Degree of neurological compromise at presentation remains the single best predictor of outcome
- 80% of ambulatory patients will remain mobile with limited longterm dysfunction
- Once established paraplegia is difficult to reverse
- Aim to decompress ASAP certainly within 24-48h of presentation

Hypercalcaemia of malignancy

Cancer types:

Myeloma/Breast

> NSCLC

> other bony mets

- e.g small cell lung, colon, prostate

Pathogenesis multifactorial

- Humoral hypercalcemia of malignancy
 - Squamous (head and neck, esophagus, cervix, lung)
 - Renal
 - Ovarian
 - Breast
 - Endometrial
 - Human T-lymphotropic virus-associated lymphoma
- Local osteolysis from bone metastasis
 - Breast
 - Multiple myeloma
 - Lymphoma
- Calcitriol production
 - Hodgkin lymphoma
 - Non-Hodgkin lymphoma
- Ectopic parathyroid hormone secretion
 - Parathyroid
 - Ovary
 - Lung
 - Primitive neuroectoderm

Hypercalcaemia – Clinical Features

- Drowsiness, confusion,
- Nausea and vomiting
- Polyuria and Polydipsia
- Dehydration and constipation
- Renal impairment

- Diagnosis – think of it and test !
- Important to correct for albumin – Adjusted Ca²⁺
- In cancer patients Alb can be low avoid underestimating true Ca²⁺ level

Management

- High flow fluids – 3-4L 0.9% saline
- Intravenous bisphosphonate
 - Pamidronate 60-90mg iv or zoledronic acid 4mg iv
- Calcitonin
 - 100 U 8 hourly im/sc
- Corticosteroids
- Definitive and cancer therapy

Neutropenic sepsis

- Definitions vary – not helpful to be too rigid
- Fever $> 38^{\circ}\text{C}$ in an unwell cancer patient with low neutrophils: but hypothermia may occur in severe neutropenic sepsis so review all these patients who report feeling ill
- Level of neutropenia is crucial
 - $< 0.5 \times 10^9/\text{L}$ is severe neutropenia and effective phagocytic function is severely compromised
- Expected length/depth of neutropenia
 - Adjuvant chemo versus leukaemia induction

Guidelines

- NICE 2012
 - In the view of many Haematologists these are deeply flawed in treatment recommendations
 - Written by oncologists
 - The nature of adjuvant chemo versus aggressive therapy causing prolonged or profound neutropenia (often when BM is major organ involved e.g. leukaemia post transplant) is NOT properly addressed
 - Role of Tazocin as monotherapy and guidance on line removal most contentious
- ESMO 2010

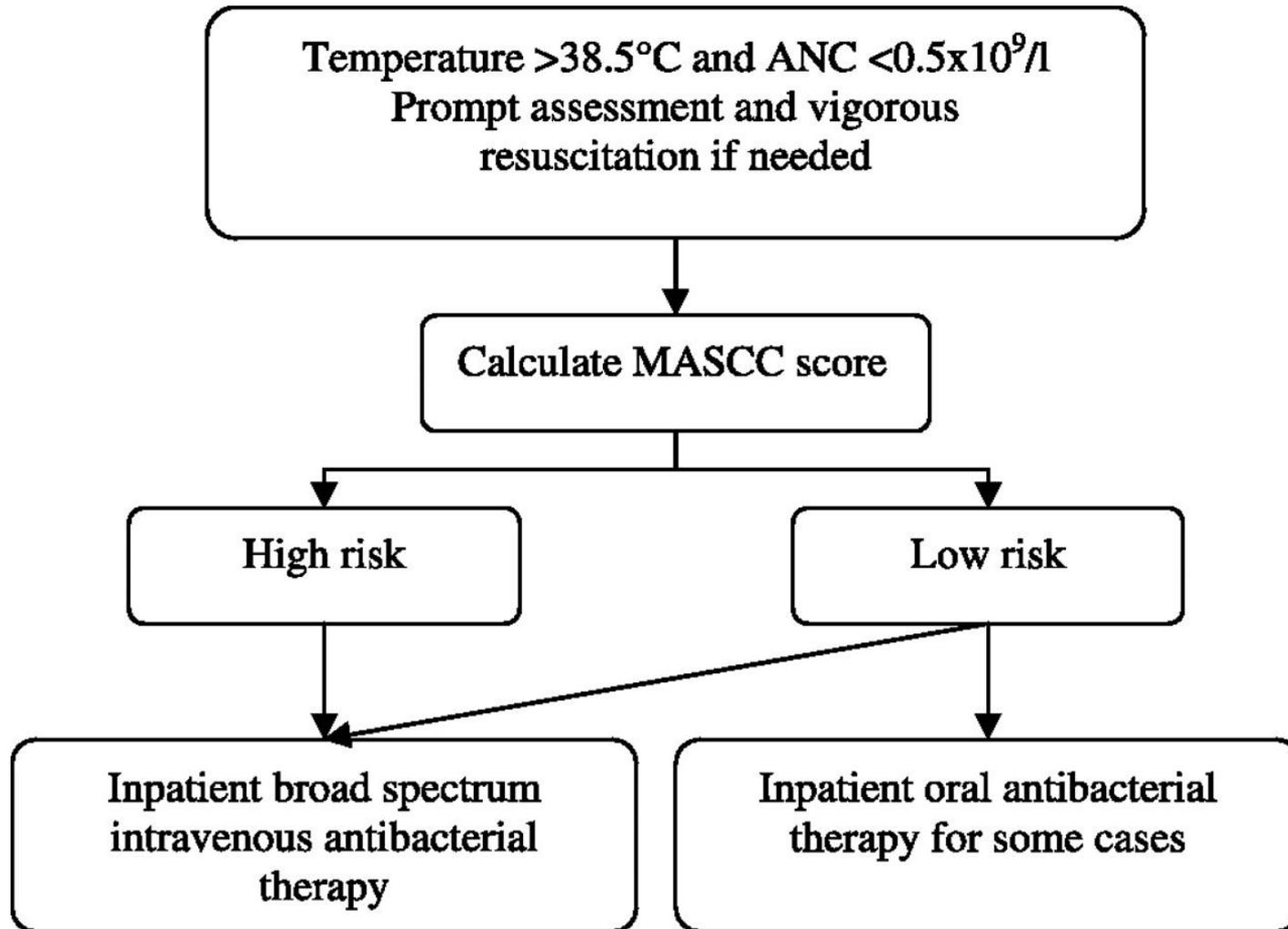
Multinational Association for Supportive Care (MASCC) index

Characteristic	Score	
Burden of illness: no or mild symptoms	5	
Burden of illness: moderate symptoms	3	
Burden of illness: severe symptoms	0	•Scores ≥ 21 are at low risk.
No hypotension (systolic BP >90 mmHg)	5	•Points attributed to the variable 'burden of illness' are not cumulative.
No chronic obstructive pulmonary disease	4	•The maximum theoretical score is 26.
Solid tumor/lymphoma with no previous fungal infection	4	•Can be used to assess severity before Neutrophil count is known
No dehydration	3	
Outpatient status (at onset of fever)	3	
Age <60 years	2	

Neutropenic sepsis – clinical features

- Often not an obvious source of sepsis
 - Always consider a hickman/PICC line if in situ
 - Look for femoral lines
- Neutropenic sepsis is a medical emergency
- High risk ‘disease’ can be rapidly progressive / fatal within 4-6 hours
 - Septic shock is usual cause of fatalities
 - Often gram negative sepsis / toxin producing MRSA

Initial management of febrile neutropenia.



de Naurois J et al. Ann Oncol 2010;21:v252-v256

Management - high risk (default)

- Culture all bodily secretions- peripheral/central bc
- Discuss patients with on call haem/oncology teams if unsure
- Supportive care
 - IV fluids
 - If systolic BP < 80 mmHg in my experience likelihood of requiring HDU/ITU support is high

Empirical HIGH DOSE IV antibiotic therapy

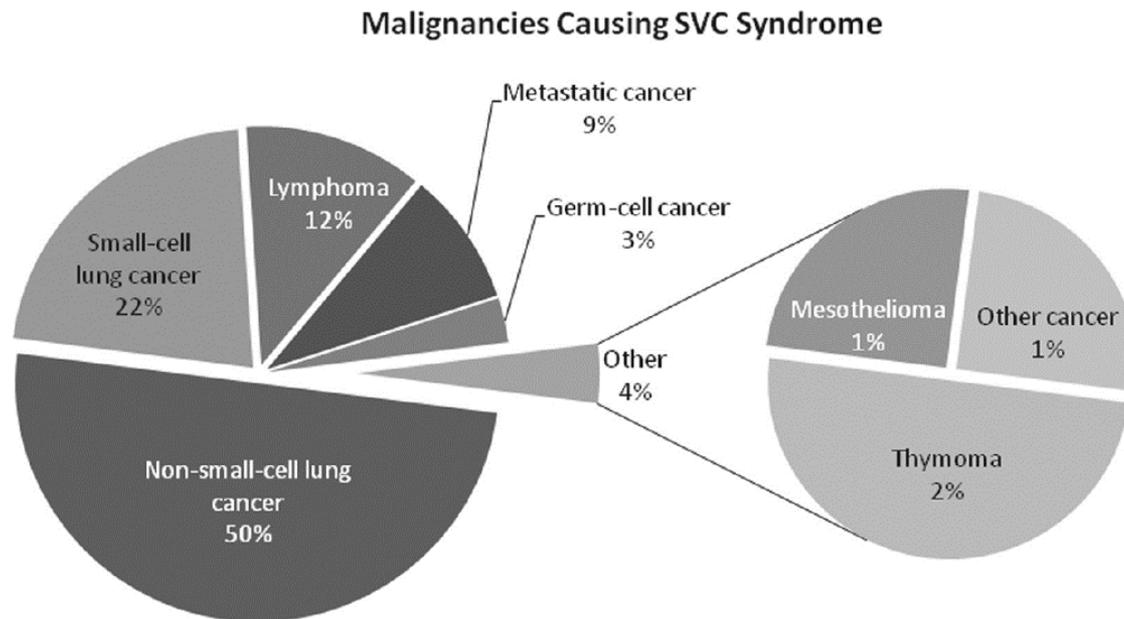
- Either single agent meropenem
Or/
- Broad spectrum penecillin and an aminoglycoside
e.g. Tazocin/ gentamicin

Management - 2

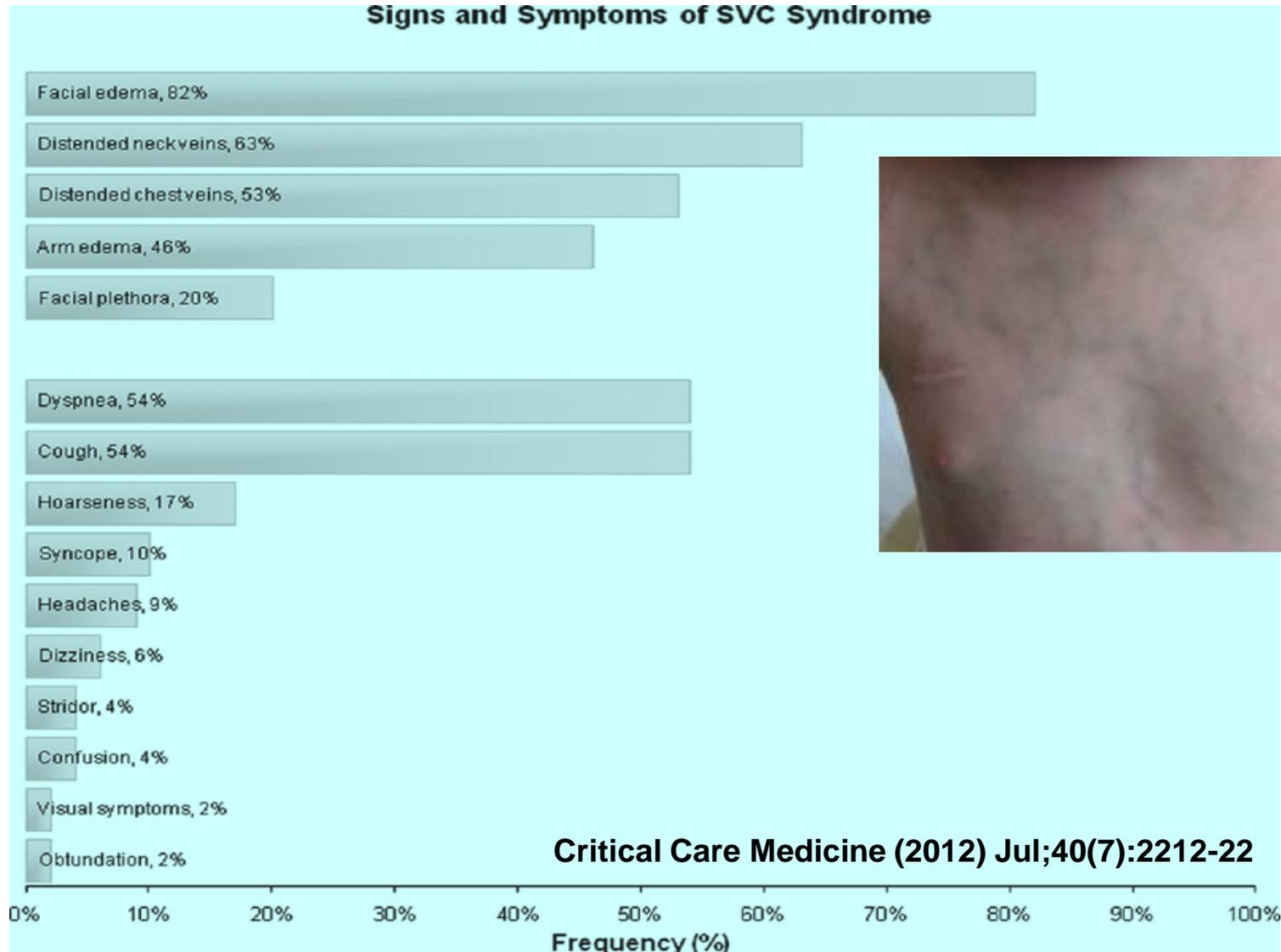
- If there is a central line or skin sepsis or known history of MRSA – add Vancomycin/Teicoplanin
- Remove ‘presenting’ central lines if severe sepsis
- If persistent hypotension unresponsive to aggressive fluid resuscitation 2-3 L ASAP
 - Contact ITU/HDU team – inotropes, catheterise
 - Consider hydrocortisone – hypoadrenalism
 - Use Meropenem and Amikacin to cover ESBL

Superior vena cava obstruction

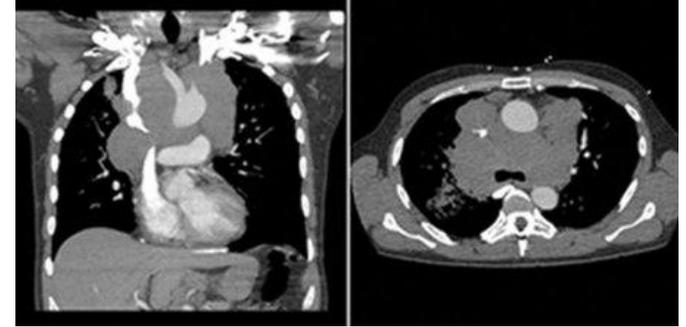
- Extrinsic compression
 - Lymphoma, Germ cell tumour, Lung cancer
- Intravascular occlusion
 - Thrombosis – secondary to central line or thrombophilia



Clinical features: inversely proportional to speed of occlusion



Management



Investigation

- CT thorax – chest/abdo/pelvis may give clues to primary pathology
- Biopsy is essential – prior to steroids when at all possible.
- History may help- e.g. previous diagnosis, smoker

Treatment

- Corticosteroids- Dexamethasone 16-24mg/24h
- Germ cell and lymphoma exquisitely sensitive to chemotherapy
- Other tumour types will need radiotherapy
- Stenting is increasingly popular – Interventional radiotherapy

Tumour Lysis syndrome (TLS)

- Medical emergency as a result of acute metabolic disturbances caused by rapid death of tumour cells
- Renal function is key factor
 - *TLS can cause AKI – usually due to urate production*
 - *(less commonly high phosphate)*
 - *TLS is made more likely if renal impairment*
- Most common- Aggressive Haematological malignancies (also: germ cell, nscc, breast)
- Usually precipitated by aggressive chemotherapy
- But...TLS may occur
 - *Spontaneously- part of presentation*
 - *With 'gentle' therapy – e.g. steroids , rituximab*

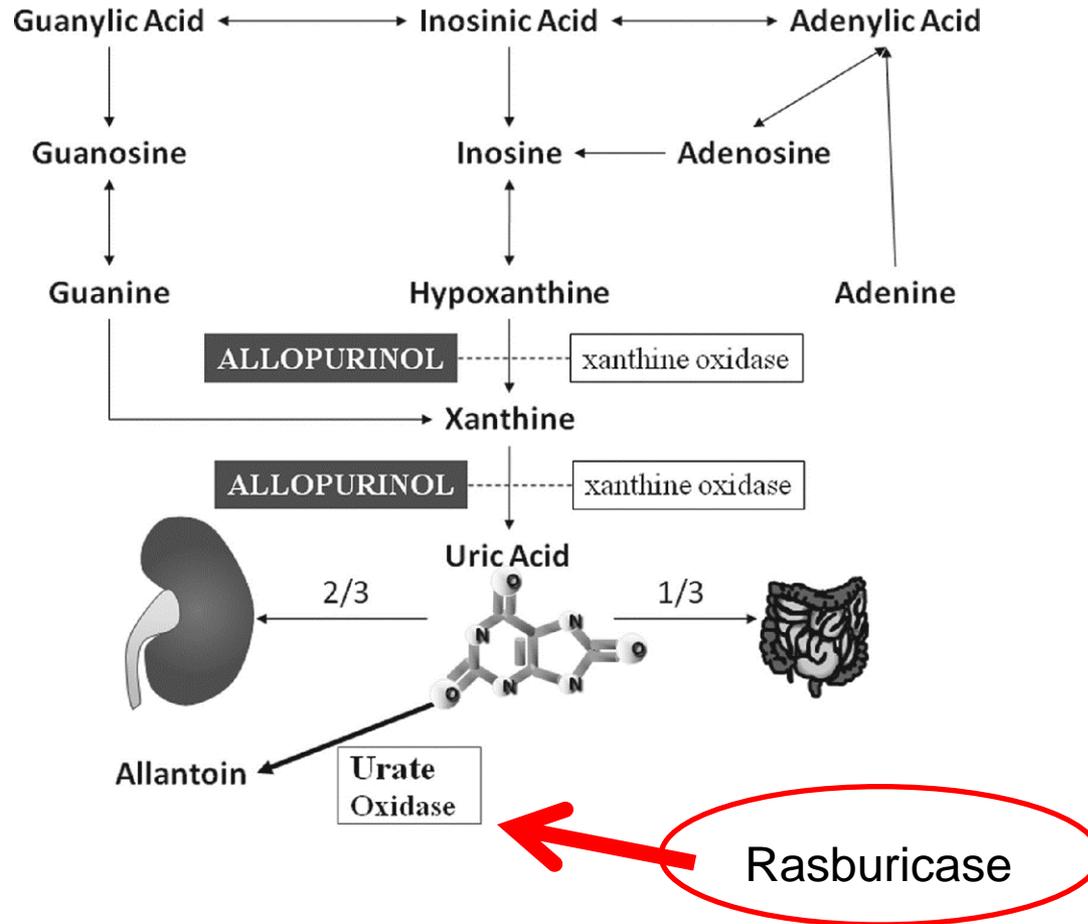
Tumour Lysis syndrome

Metabolic Abnormality	Value or Change From Baseline ^{124a}	Clinical Implications	Management
Hyperkalemia	≥ 6.0 mmol/L or 6 mEq/dL or 25% increase	Muscle cramps Paresthesias Dysrhythmias Ventricular fibrillation Cardiac arrest	Polystyrene sulfonate 1 gm/kg Insulin 0.1 unit/kg with dextrose 25% 2 mL/kg Sodium bicarbonate 1–2 mEq/kg IV push Calcium gluconate 100–200 mg/kg slow IV infusion
Hyperphosphatemia	≥ 2.1 mmol/L for children or ≥ 1.45 mmol/L for adults or 25% increase	Nausea Vomiting Diarrhea Lethargy Seizures Acute kidney injury	Volume loading Removal of phosphate from IV fluids Oral phosphate binders Hemodialysis
Hypocalcaemia	≤ 1.75 mmol/L or 25% decrease	Muscle cramps Tetany Hypotension Dysrhythmia	Calcium gluconate 50–100 mg/kg slow IV infusion with electrocardiogram monitoring. Give only if symptomatic.
Hyperuricemia	≥ 476 μ mol/L or 8 mg/dL or 25% increase	Acute kidney injury	Volume loading Rasburicase (see text for dosing) Allopurinol by mouth or IV

IV, intravenous.

^aCairo–Bishop definition requires two or more laboratory abnormalities within 3 days prior to or 7 days after initiation of cytotoxic therapy (124).

Prevention



Hydrogen peroxide is produced when uric acid is converted to Allantoin. This can cause methaemoglobin production and haemolysis so Rasburicase is C/I in G6PD deficiency

Management summary

- High flow fluids – twice maintenance 5-6 l/day
- Pragmatically may need diuretics
- Twice daily electrolyte and renal function
- Rasburicase in high risk/Allopurinol standard risk
- Standard management of hyperkalaemia
 - Ion exchange resins, Insulin/Dextrose, Ca gluconate
 - Possibly sodium bicarbonate – discussed with renal
- Renal Dialysis – haemofiltration if severe
 - hyperkalaemia, hyperphosphataemia, hyperuricaemia
 - NB Only replace Calcium if symptomatic as will ppt with phosphate in kidneys and worsen TKI

Short reference list

- Oncologic emergencies
Critical Care Medicine (2012) Jul;40(7):2212-22
- Haematological emergencies managing hypercalcaemia in adults and children with haematological disorders
British Journal of Haematology, 149, 465–477
- NICE guidance 2012 – neutropenic sepsis
- ESMO guidelines
de Naurois J et al. Ann Oncol 2010;21:v252-v256
- *Davidson's Principles and Practice of Medicine*