

ONCOLOGY EMERGENCIES

I. METABOLIC EMERGENCIES

Tumour Lysis Syndrome

Introduction

- massive tumour cell death with rapid release of intracellular metabolites, which exceeds the excretory capacity of the kidneys leading to acute renal failure. Can occur before chemotherapy is started.
- more common in lymphoproliferative tumours with abdominal involvement (e.g. B cell/ T cell lymphoma, leukaemias and Burkitt's lymphoma)

Tumour lysis syndrome
Characterised by: hyperuricemia hyperkalemia hyperphosphatemia with associated hypocalcemia

Hyperuricaemia

- release of intracellular purines increase uric acid

Hyperkalemia

- occurs secondary to tumour cell lysis itself or secondary to renal failure from uric acid nephropathy or hyperphosphatemia.

Hyperphosphatemia with associated hypocalcaemia

Most commonly occurs in lymphoproliferative disorders because lymphoblast phosphate content is 4 times higher than normal lymphocytes.

Causes:

- tissue damage from CaPO_4 precipitation. Occurs when $\text{Ca} \times \text{PO}_4 > 60$ mg/dl. Results in renal failure, pruritis with gangrene, eye and joint inflammation
- hypocalcaemia leading to altered sensorium, photophobia, neuromuscular irritability, seizures, carpedal spasm and gastrointestinal symptoms

Renal failure

Multifactorial:

- uric acid, phosphorus and potassium are excreted by kidneys
- the environ of the collecting ducts of the kidney is acidic coupled with lactic acidosis due to high leucocyte associated poor perfusion will cause uric acid crystallization and then uric acid obstructive nephropathy. Usually occur when levels > 20 mg/dl.
- increased phosphorus excretion causing calcium phosphate precipitation (in vivo solubility dependant on $\text{Ca} \times \text{P} = 58$) in microvasculature and tubules.
- risk increases if renal parenchymal is infiltrated by tumour e.g. lymphoma or ureteral/venous obstruction from tumour compression (lymph nodes).

Table 1. Risk factors for Tumour lysis syndrome
Bulky disease
Rapid cellular turnover.
Tumour which is exquisitely sensitive to chemotherapy
Elevated LDH / serum uric acid
Depleted volume
Concentrated urine or acidic urine
Poor urine output

Management (Prevention):

To be instituted in every case of acute leukaemia or lymphoma prior to induction chemotherapy.

- **Hydration:** Double hydration - 125ml/m²/hr or 3000ml/m²/day. **No added potassium.**
- **Alkalinization of urine:** Adding NaHCO₃ at 150 - 200 mmol/m²/day (3 mls/kg/day NaHCO₃ 8.4%) into IV fluids to keep urine pH 7.0 - 7.5. Avoid over alkalinization as this may aggravate hypocalcaemia and cause hypoxanthine and xanthine precipitation. It can also cause precipitation of calcium phosphate if pH >8. Monitor urine pH and VBG 8 hourly. If urine pH < 7.0, consider increasing NaHCO₃ infusion. This can only be done if HCO₃⁻ in the blood is below normal range. Otherwise, have to accept that some patients just cannot alkalinise their urine.
- **Allopurinol** 10mg/kg/day, max 300mg/day.
- may have to *delay chemotherapy* until metabolic status stabilizes.
- **Close electrolyte monitoring-** BUSE, Ca²⁺, PO₄, uric acid, creatinine, bicarbonate
- **Strict I/O charting.** Ensure adequate urine flow once hydrated. Use diuretics with caution.

Management (Treatment)

- treat hyperkalaemia – resonium, dextrose-insulin, Consider dialysis.
- diuretics
- hypocalcaemia management depends on the phosphate level:
 - if phosphate is raised, then management is directed to correct the high phosphate
 - if phosphate is normal or if child is symptomatic, then give replacement IV calcium
 - if hypocalcaemia is refractory to treatment, exclude associated hypomagnesaemia
- dialysis if indicated. Haemodialysis most efficient at correcting electrolyte abnormalities. Peritoneal dialysis is not effective in removing phosphates.

Other Metabolic Emergencies:

Hyponatraemia

- usually occurs in acute myeloid leukaemia (AML)
- treat as for hyponatraemia.

Hypokalaemia

- common in AML
- rapid cellular generation leads to uptake of potassium into cells. (Intracellular potassium 30 - 40 X times higher than extracellular potassium). Therefore may hyperkalaemia may develop after chemotherapy.

Hypercalcaemia

- associated with Non Hodgkin lymphoma, Hodgkin lymphoma, alveolar rhabdomyosarcoma, rhabdoid tumours and others.

Management

- hydration.
- oral phosphate
- IV frusemide (which increases calcium excretion)
- mithramycin

II. HAEMATOLOGICAL EMERGENCIES

Hyperleucocytosis

- occurs in acute leukaemia. Defined as TWBC $> 100\,000 / \text{mm}^3$
- associated
 - in acute lymphoblastic leukaemia (ALL) with high risk of tumour lysis
 - in AML with leucostasis (esp monocytic)
 - affects the lungs due to pulmonary infiltrates. May cause dyspnoea, hypoxaemia and right ventricular failure
 - affects the central nervous system causing headaches, papilloedema, seizures, haemorrhage or infarct.
 - other complications: renal failure, priapism, dactylitis
- mechanism:
 - excessive leukocytes form aggregates and thrombi in small veins causing obstruction; worsens when blood is viscous.
 - excessive leukocytes competes for oxygen; damages vessel wall causing bleeding

Management

- hydration
 - to facilitate excretion of toxic metabolites
 - to reduce blood viscosity
- avoid increasing blood viscosity.
 - cautious in use of packed cell transfusion and diuretics.
- during induction in hyperleukocytosis, keep platelet $>20\,000/\text{mm}^3$ and coagulation profile near normal
- exchange transfusions and leukopheresis should not be used alone as rapid rebound usually occurs. Concurrent drug treatment should therefore be initiated soonest possible.

Coagulopathy

AML especially M3 is associated with an initial bleeding diathesis from *consumptive coagulopathy* due to release of a tissue factor with procoagulant activity from cells. However the use of all-trans retinoic acid (Atra) has circumvented this complication.

Management

- platelet transfusions – 6 units / m^2 should increase platelets by $50,000 / \text{mm}^3$
- fresh frozen plasma (FFP) or cryoprecipitate
- vitamin K
- +/- heparin therapy (10u/kg/hr) - controversial

Other haematological emergencies

- thrombocytopenia
- severe anaemia

III. SUPERIOR VENA CAVA OBSTRUCTION

Superior Vena Cava (SVC) Obstruction

- common in Non Hodgkin Lymphoma / Hodgkin Lymphoma / ALL .
- rarely: malignant teratoma, thymoma, neuroblastoma, rhabdomyosarcoma or Ewing's may present with anterior or middle mediastinal mass and obstruction.
- 50% associated with thrombosis.
- presentation: shortness of breath, facial swelling, syncope.

Management

- *recognition of symptoms and signs of SVC obstruction and avoidance of sedation and general anaesthesia*

Tissue diagnosis is important but should be established by the least invasive measure available. Risk of circulatory collapse or respiratory failure may occur with general anesthesia or sedation.

- BMA
- biopsy of superficial lymph node under local anaesthesia.
- measurement of serum markers e.g. alpha-fetoprotein

If tissue diagnosis is not obtainable, empiric treatment may be necessary based on the most likely diagnosis. Both chemotherapy and DXT may render histology uninterpretable within 48 hours, therefore biopsy as soon as possible.

- *avoid upper limb venepunctures*
 - bleeding due to increased intravascular pressure
 - aggravate SVC obstruction.
- primary mode of treatment is with steroids } if pathology due to Non-Hodkin
- chemotherapy. } Lymphoma
- +/- DXT.

IV. INFECTION

Febrile neutropenia

Febrile episodes in oncology patients **must** be treated with urgency especially if associated with neutropenia. Nearly all episodes of bacteraemia or disseminated fungal infections occur when the absolute neutrophil count (ANC) $<500 /\text{mm}^3$. Risk increases maximally if ANC $<100 /\text{mm}^3$ and greatly reduced if the ANC $>1000 /\text{mm}^3$.

Management (Follow Algorithm in Figure 1)

other considerations:

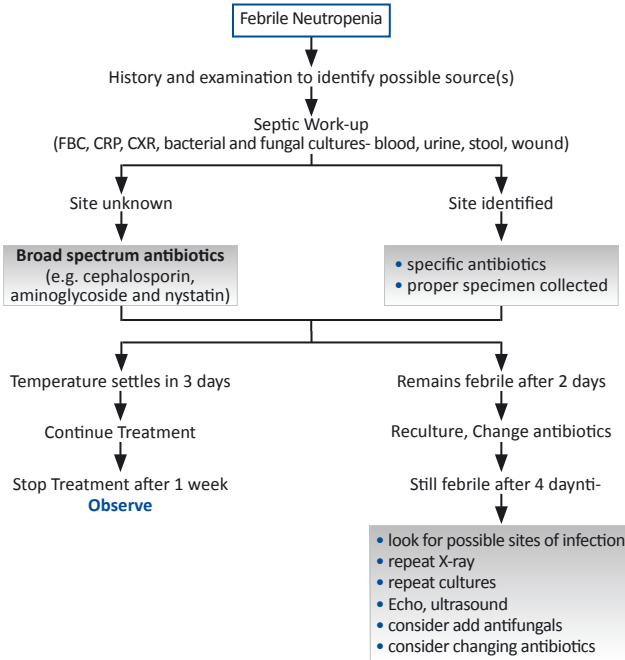
- if central line is present, culture from central line (both lumens); add anti-Staph cover e.g. cloxacillin
- repeated physical examination to look for new clues, signs and symptoms of possible sources
- close monitoring of patient's well-being
 - vital signs, perfusion, BP, I/O.
- repeat cultures if indicated
- investigative parameters, FBC, CRP, BUSE as per necessary.
- in presence of oral thrush or other evidence of candidal infection, start antifungals.
- try to omit aminoglycoside and vancomycin if on cisplatin - nephrotoxic and ototoxic. If required, monitor renal function closely.

Febrile neutropenia

Common organisms

Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae
Escherichia coli
Pseudomonas spp.
Klebsiella spp.
Candida spp
Aspergillus

Figure 1. Approach to a patient with febrile neutropenia



Abbreviations. FBC, full blood count; CRP, C-reactive protein; CXR, chest X-ray; CVL, central venous line.

Typhilitis

- a necrotizing colitis localised to the caecum occurring in neutropenic patients.
- bacterial invasion of mucosa causing inflammation - can lead on to full thickness infarction and perforation
- usual organisms are *Clostridium* and *Pseudomonas*
- X-ray shows non specific thickening of gut wall. At the other end of the spectrum, there can be presence of pneumatosis intestinalis +/- evidence of free gas

Management

- usually conservative with broad spectrum antibiotics covering gram negative organisms and anaerobes (metronidazole). Mortality 20-100%
- criteria for surgical intervention:
 - persistent gastrointestinal bleeding despite resolution of neutropenia and thrombocytopenia and correction of coagulation abnormalities.
 - evidence of perforation
 - clinical deterioration suggesting uncontrolled sepsis (controversial)

Shock

Table 2 lists the common causes of shock in child with cancer

Table 2. Common causes of shock in children with cancer		
Distributive	Hypovolaemic	Cardiogenic
<i>Sepsis</i>	<i>Haemorrhage</i>	<i>Myopathy</i>
<i>Anaphylaxis</i>	haemorrhagic cystitis	anthracycline
etoposide	gastrointestinal bleeding	high dose cyclophosphamide
L-asparaginase	ulcers	radiation therapy
anti-thymocyte globulin	typhilitis	<i>Cardiac tamponade</i>
cytosine	massive haemoptysis	intracardiac tumour
carboplatin	<i>Pancreatitis</i>	intracardiac thrombus
blood products	<i>Addisonian crisis</i>	pericardial effusion
amphotericin B	<i>Intractable vomiting</i>	constrictive pericarditis
<i>Veno occlusive disease</i>	<i>Diabetes mellitus</i>	<i>Metabolic</i>
	<i>Diabetes insipidus</i>	hyperkalaemia, hypokalaemia
	<i>Hypercalcaemia</i>	hypocalcaemia
		<i>Myocarditis</i>
		viral, bacterial, fungal

Management

Ascertain cause and treat accordingly

V. NEUROLOGICAL COMPLICATIONS

Spinal Cord Compression

- prolonged compression leads to permanent neurologic sequelae.
- epidural extension: lymphoma, neuroblastoma and soft tissue sarcoma
- intradural: Spinal cord tumour
- Presentation
 - back pain: localized or radicular, aggravated by movement, straight leg raising, neck flexion
 - later: weakness, sensory loss, loss of bladder and bowel continence
- diagnosed by CT myelogram/MRI

Management

- laminectomy urgent (if deterioration within 72 hours).
- if paralysis present > 72 hours, chemotherapy is the better option if tumour is chemosensitive, e.g. lymphoma, neuroblastoma and Ewing's tumour. This avoids vertebral damage. Onset of action of chemotherapy is similar to radiotherapy.
- prior IV Dexamethasone 0.5mg/kg 6 hourly to reduce oedema
- +/- Radiotherapy

Increased Intracranial Pressure (ICP) and brain herniation

Cause : Infratentorial tumours causing blockage of the 3rd or 4th ventricles such as medulloblastomas, astrocytomas and ependymomas.

Signs and symptoms vary according to age/site.

- infant - vomiting, lethargy, regression of milestones, seizures, symptoms of obstructive hydrocephalus and increased OFC.
- older - early morning recurrent headaches +/- vomiting, poor school performance
- cerebellar: ipsilateral hypotonia and ataxia

- herniation of cerebellar tonsil – head tilt and neck stiffness
- tumours near 3rd ventricle – craniopharyngioma, germinoma, optic glioma, hypothalamic and pituitary tumours
 - visual loss, increased ICP and hydrocephalus
 - aqueduct of Sylvius obstruction due to pineal tumour: raised ICP, Parinaud's syndrome (impaired upward gaze, convergence nystagmus, altered pupillary response)

Management

- assessment of vital signs, look for focal neurological deficit,
- look for evidence of raised ICP (bradycardia, hypertension and apnea)
- look for evidence of herniation (respiratory pattern, pupil size and reactivity)
- dexamethasone 0.5 mg/kg QID
- urgent CT to determine cause
- prophylactic antiepileptic agents.
- lumbar puncture is contraindicated
- decompression – i.e. shunting +/- surgery.

Cerebrovascular accident (CVA)

- can result from direct or metastatic spread of tumour, antineoplastic agent or haematological abnormality
- L-Asparaginase associated with venous or lateral and sagittal sinus thrombosis caused by rebound hypercoagulable state
- AML especially APML is associated with DVC and CVA, due to the release of procoagulant

Management

- supportive
- use of anticoagulant potentially detrimental
- in L-Asparaginase induced, recommended FFP bd

VI. MISCELLANEOUS EMERGENCIES

Pancreatitis

Should be considered in patients on L-Asparaginase and steroids and complaining of abdominal pain. Careful examination plus measurement of serum amylase and ultrasound abdomen.

ATRA (all-trans retinoic acid) syndrome

- characterised by: fever, respiratory distress, respiratory failure, oedema, pleural/pericardial effusion, hypotension
- pathophysiology: respiratory distress due to leukocytosis associated with ATRA induced multiplication and differentiation of leukaemic promyelocytes
- treatment: dexamethasone 0.5 – 1mg/kg/dose bd, maximum dose 20mg bd.