Emergencies in cancer patients

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Overview

- Cancer related
- Treatment related

- Medical emergencies
- Surgical emergencies

- Unrelated to cancer, though with increased incidence in cancer patients

Cancer related

- **Local (mechanical) effect of cancer**
  - Vena cava syndrome
  - Intracranial hypertension
  - Compression of pericardium/airways
  - Effusions – pericardial, pleural, ascites
  - Spinal cord compression
- **Metabolic**
  - SIADH, hypercalcemia, hyperviscosity syndrom, re-feeding syndrome, diabetes decompensation due to cancer/treatment, spontanious tumor lysis syndrom
- **Thrombembolic disease -** PE

Treatment related and medical emergencies

- **Febrile neutropenia/neutropenic sepsis**
- Thrombocytopenia
- **Tumor lysis syndrome**
- **Chemotehrapy associated diarrhea – colitis**
- AKI (acute kidney injury)
  - Cisplatin, TLS, posterenal, dehydration, interstitial nephritis)
- Liver failure
- Congestive heart failure (acute, deterioration of chronic HF)
  - Tachyarhytmias due to side effects/electrolyte imbalance
- Acute coronary artery disease (5-FU, cDDP)
- Alergic reactions/anaphylaxis
- Increased risk of PE
- Deterioration of medical conditions

Surgical

- GI obtsruction, urinary tract obstruction (postrenal AKI)
- Pneumothorax – spontanious/complication of procedures (central line, tapping effusions)
- Cancer bleeding– melanoma, GI cancers, lungs cancer..
- Acute abdominal
- Spinal cord compression

Neutropenic sepsis

febrile neutropenia

Introduction

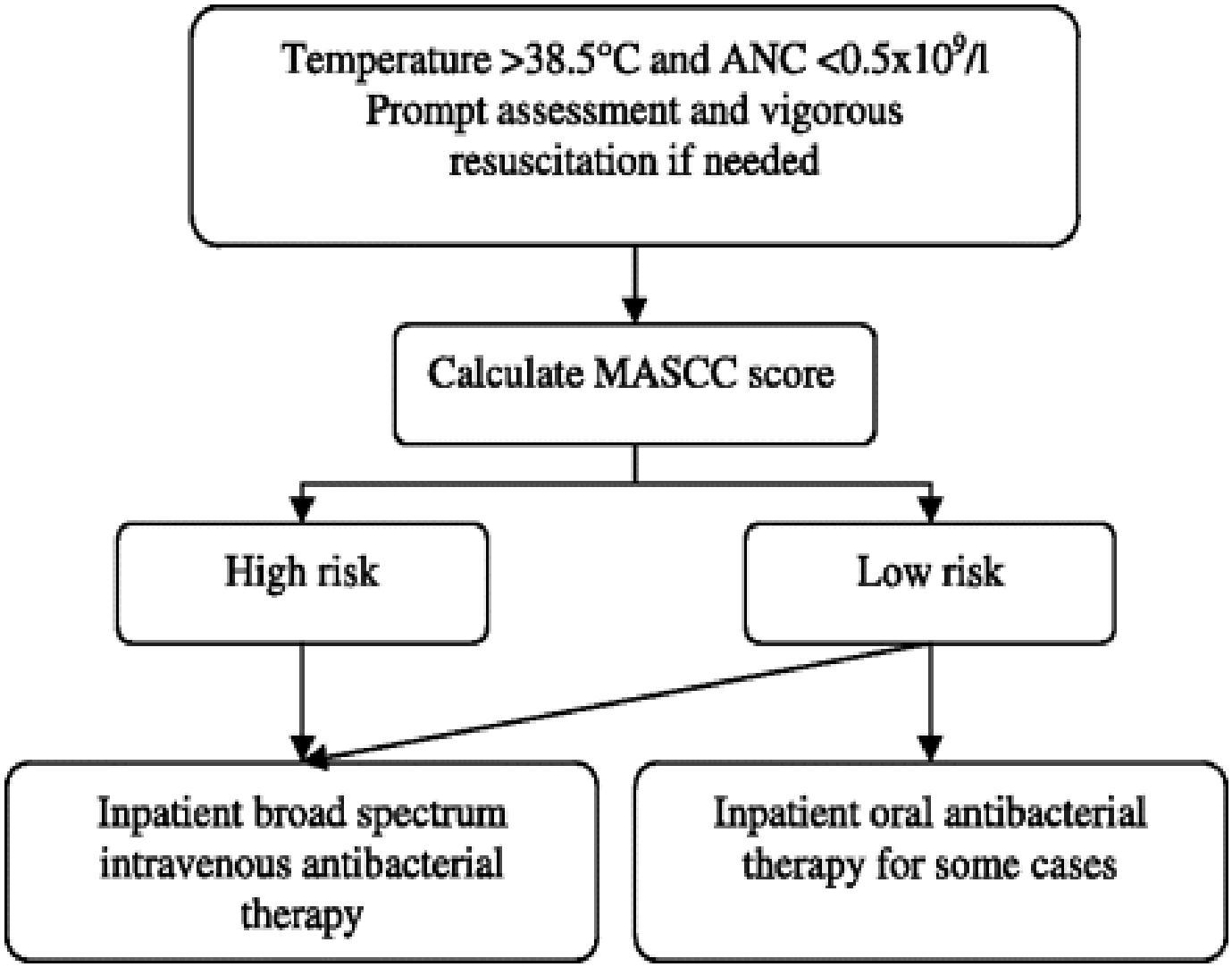
- **FN definition** – TT >38.5°C* or 2 episodes of TT >38.0°C for 2h** and ABC count <0.5 × 10^9/l or expected fall < 0.5 × 10^9/l
- Potential lifethreatening condition

* or 38,3 pending source

** or 1 hour pending source

Risk factors

- MASCC (symptoms of underlying disease, COPD, age, hematol. Malignancies, mycotic infection, dehydration, BP<90, inpatinet onset)
- https://www.qxmd.com/calculate/calculator_134/mascc-febrile-neutropenia-risk
- Time of neutropenia
- GIT toxicity
- Other medical conditions (CHF, CAD, DM, CKD, COPD)
- Known colonisation with MRSA/VRE/ESBL
- Onset during G-CSF profylaxis


Temperature >38.5°C and ANC <0.5x10⁹/l
Prompt assessment and vigorous resuscitation if needed
Calculate MASCC score
High risk
Low risk
Inpatient broad spectrum intravenous antibacterial therapy
Inpatient oral antibacterial therapy for some cases

Management

- C/E incl. PR
- ECG
- Lung X ray +/- abdomen
- BC+coag, electrolytes, RFT, LFT, CRP, prokalcitonin
- BC– central line + peripheral line, urine, (C. diff, stool, throat, tonsills…)

Management

- Broad spectre antibiotics incl. anti pseudomonas aeruginis activity
- History of MRSA/VRE/ESBL?
- Up front G-CSF up are not generally recommended
- Antimycotics – pending of mycotis infection risk

Management

- Tazocin (piperacilin/tazobactam) 4,5g i.v. a 6 h till neu >1,0, then a 8h
- Gentamycin 240-320mg in septic patients
- Antimycotics – pending on mycotic infection risk
- Metronidazol in pts with S/O collitis
- G-CSF up front in pts with pneumonia, GI toxicity and severe comorbidities (CHF, CAD, DM, CKD, COPD)

Vena Cava Syndrome (VCS)

- **Superior vena cava obstruction account for 99 % of VCS cases**
  - **Anatomy of the mediastinum + Thin-walled vein filled at relatively low pressure → any significant compression can result in obstruction to blood flow**
    - **External compression by tumour or lymphadenopathy**
    - **Internal compression by thrombosis or catheter**
- **The severity of the resulting syndrome depends on the rapidity of onset and level of the obstruction**
- **Despite the sometimes dramatic and distressing clinical picture, VCS is usually not lethal complication**

Vena Cava Syndrome (VCS)

- **Symptoms and Signs**
  - **Cough and dyspnea**
  - **Facial, cervical and arms edema**
  - **Venous dilatations (chest and upper extremities)**
  - **Headache**
  - **Dysphagia**
  - **Symptoms worse by bending or lying down**

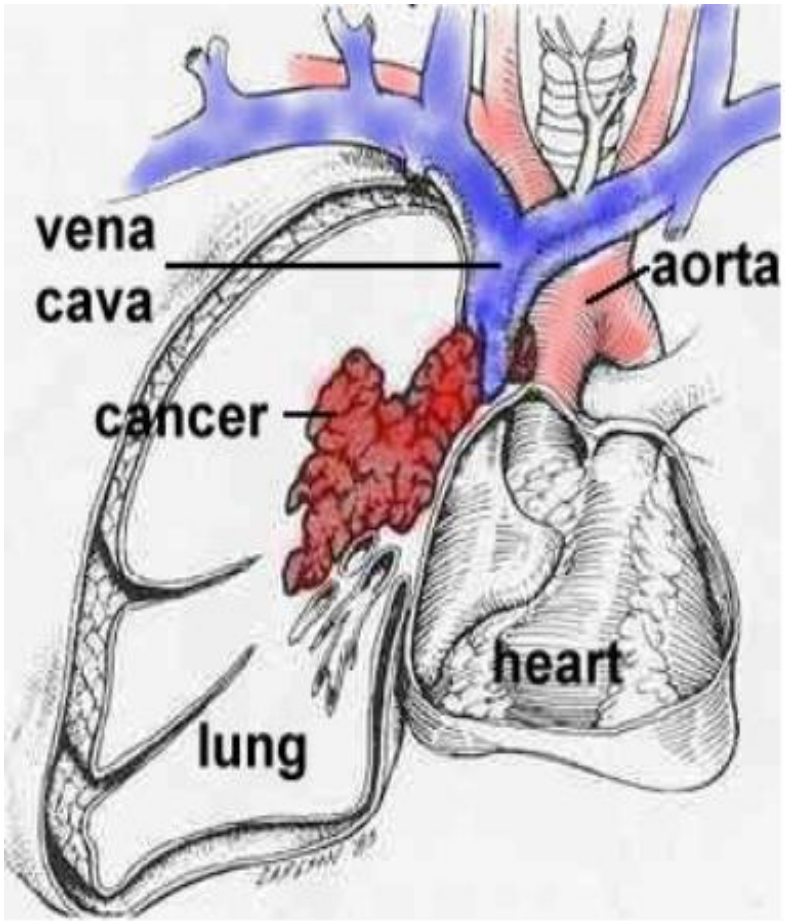
Vena Cava Syndrome (VCS)

- **Causes**
  - **Malignant (85 – 95 %)**
    - Lung cancer, Non-Hodgkins lymphoma, Germ cell neoplasms, Metastatic breast cancer, Oesophageal carcinoma, others
  - **Non-Malignant**
    - Mediastinal fibrosis, VC thrombosis, Indwelling central lines (catheters), Sarcoidosis, TBC, others
- **Differential diagnosis: Heart failure, Cardiac tamponade**
- **Diagnosis**
  - Chest X-ray (mediastinal widening, mass, pleural effusion, … normal X-ray in < 20 %)
  - CT of the thorax with contrast or CT/MRI venography

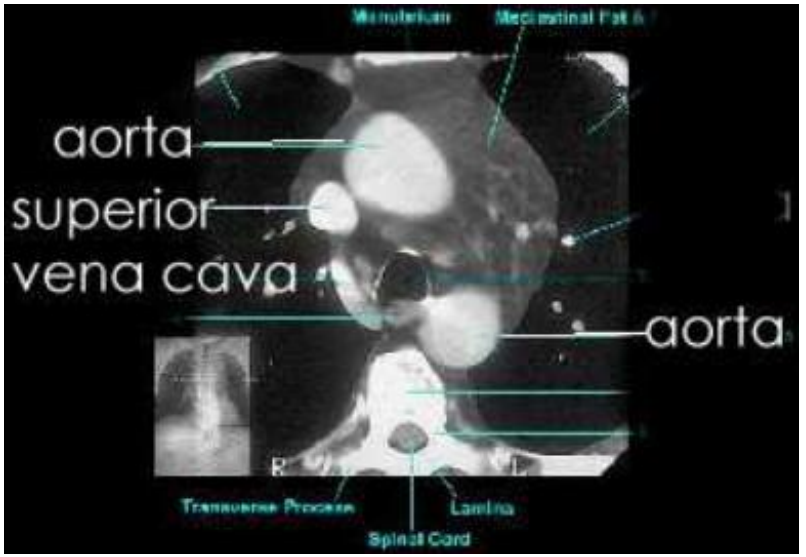
Vena Cava Syndrome (VCS)

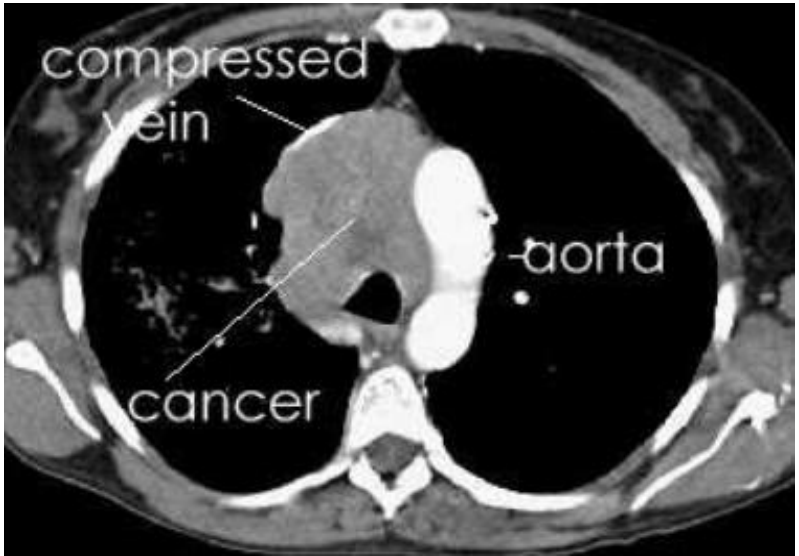
- **Management**
  - **Immediate management**
    - Corticosteroids (DXM 8mg p.o. 2-3 times a day) + Diuretics
    - Stent placement
      - The most rapid relief → in the presence of cerebral edema or disabling symptos or in the case of chemo/radio-resistant disease
    - Thrombolysis (if thrombus is documented)
    - Surgery (bypass or thrombectomy, primarily in pts with good prognosis or in benign causes of VCS)
  - **Treatment of the uderlying malignancy**
    - Chemotherapy (SCLC, lymphoma, germ cell tumours)
    - Radiotherapy (for non-chemosensitive disease)
  - **Prognosis dependent on the type of cancer and the patients general condition. VCS commonly relapses.**

Vena Cava Syndrome (VCS)

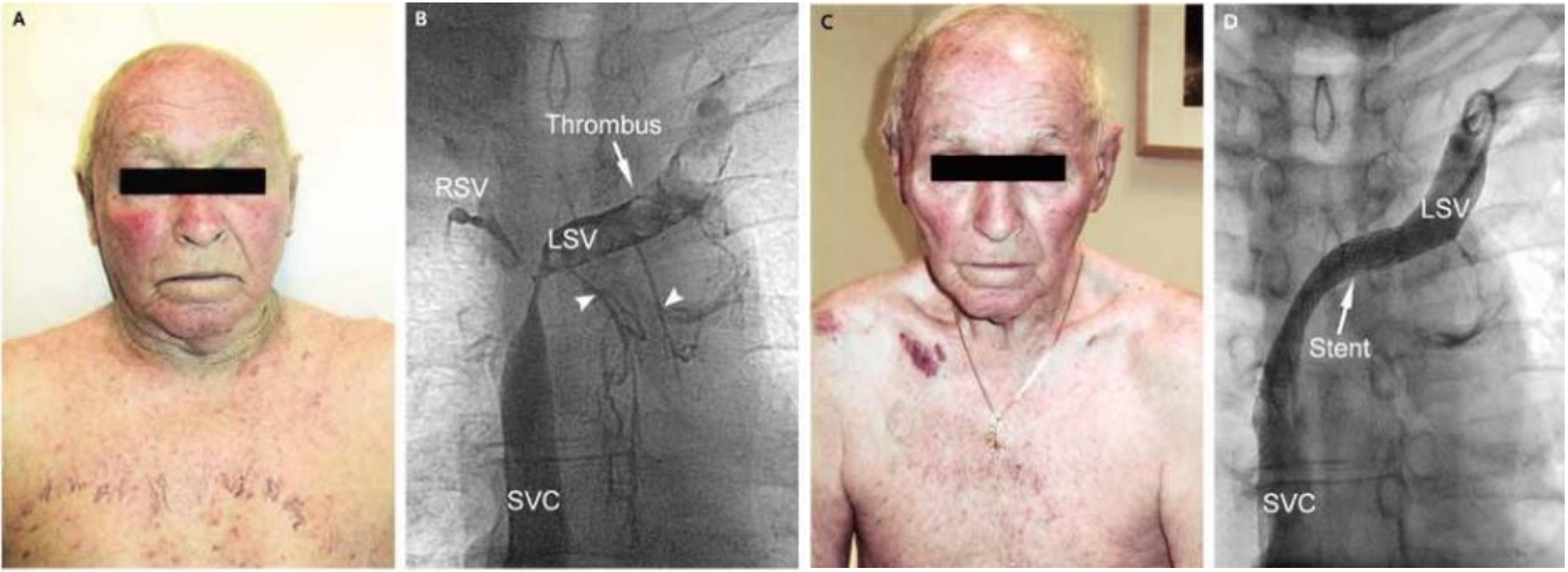


http://www.aboutcancer.com/svco.htm





Vena Cava Syndrome (VCS)



A men with VCS before and after stenting

http://www.aboutcancer.com/SVCO_image_NEJM.jpeg

Tumour Lysis Syndrom (TLS)

- **TLS is a group of metabolic complications arising from treatment of a rapid proliferating neoplasm. Occasionally TLS can occur prior to the initiation of the treatment.**
- **Cancer therapy (ischemia) → cell death / lysis → release of intracellular product into the circulation**
  - **Hyperuricaemia**
    - Purine nucleic acid breakdown → hypoxanthine →xanthine →→→ (xanthine oxidase) →→→ uric acid → kidney → precipitation in the tubules → URATE NEPHROPATHY → ARF
  - **Hyperphosphataemia**
    - Phosphate + calcium → precipitation → Acute Renal Failure (ARF)
  - **Hyperkalaemia** (↑↑↑ K^+ → fatal arrrhythmias)
  - **Hypocalcaemia** (precipitation with phosphate in kidney, skin…)
  - **Uraemia** (consequence by TLS)

Tumour Lysis Syndrom (TLS)

- **Clinical signs**
  - **Hyperuricaemia**
    - Haematuria, flank pain, acute obstructive nephrophaty (AON) (anuria / oligouria)
  - **Hyperphosphataemia**
    - Nausea, vomitin, diarrhoea, seizures, hypocalcaemia, AON
  - **Hyperkalaemia**
    - Nausea, vomiting, diarrhoea, cramps, weakness, paraesthesiae, arrhythmias, sudden death
  - **Hypocalcaemia**
    - Muscle cramps, spasms, tetany, arrhythmias, confusion, hallucinations, seizures
  - **Uraemia**
    - Lethargy, anorexia, nausea, vomiting, confusion, encephalopathy, perciarditis, acidosis, oedema, hypertension

Tumour Lysis Syndrom (TLS)

- **Clinical TLS**
  - Creatinin > 1,5x upper limit of normal
  - Cardiac arrhytmia / sudden death and/or seizure

- **Cairo-Bishop laboratory definition**
  - Uric acid > 476 umol/l or 25 % increase from baseline
  - K > 6,0 mmol/l or 25 % increase from baseline
  - Phosphate > 1,45 (2,1 children) mmol/l or 25 % increase from baseline
  - Ca < 1,75 or 25 % decrease from baseline

TLS – treatment:

- **Correction of the electrolyte imbalances and optimazing renal function**
  - Hyperuricaemia: Intravenous fluids and loop diuretics, rasburicase (urate oxidase)
  - Hyperkalaemia: Aovid IV or p.o. K supplements. Calcium gluconate (10 ml of 10 % iv over 2 min) as a cardioprotectant, if K+ > 6,0 → Actrapid insulin 10 units plus 50 ml of 50 % dextrose over 30 min iv infusion, Calcium resonium 15g p.o. 3-4x daily, correct acidosis (50-100 ml 8,4 % $NaHCO_3$ via central line)

- **Haemodialysis may be needed for:**
  - **K > 7 mmol/l**
  - **Symptomatic ureamia (tremor, seizures, confusion, pericarditis, coma)**
  - **Metabolic acidosis (arterial pH< 7,1, [HCO_3] < 12 mmol/l**
  - **Fluid overload unresponsive to diuretics**

TLS - identification of high risk patients:

- **Patient-releated factors**
  - decreased urine output,
  - pre-existing renal impairment or hyperuricaemia,
  - dehydratation
  - acid urine
- **Tumour-releated factors**
  - high proliferative rate
  - high tumour burden
  - high sensitivity to cytotoxic agents
  - ALL, High grade NHL, CLL, Myeloma,
  - testicular cancer, SCLC, breast cancer

TLS – prevention:

- Vigorous **hydratation** (app. 3l/m2/d) with a urine output of > 100 ml/m2/h
- **Allopurinol** 300 mg daily increasing 600-900 mg in 2-3 doses. Start allopurinol 24 h before the first chemotherapy treatment
- High risk patients: **Rasburicase** (200 ug/kg once daily for up to 7 days according to plasma uric acid concentration.
- **Urinary alcalization**

Hyperviscosity

- Viscosity pending on a number of blood cells, total amount of proteins, hydratation, temperature…

Symptoms

- impaired blood suplly (headache, fatigue, dizziness), dysopnea, cough, heart failure, AKI, bleeding…)
- Polyglobulia, leucostasis (AML, ALL, CML), monoclonal gamapathies (MM, Waldeström)

Management:

- fluids + aferesis (erythrocyto, leukocyto, plasma)

Hypercalcemia

- 10% pacients, 30-day mortality 50%
- PTHrP tumour related, osteolytic MTS, hyperproduktion of vit D, ectopic production of PTH

Symptoms

- nausea, vomiting, fatigue, depression, constipation, AKI, coma, heart arrest
- EKG: short QT, ST depression
- **Lab**: increased Ca i Ca^{2+}, highPTHrP a low/normal PTH

Management

- Fluids - saline +/- furosemide
- Steroids
- Bisfosfonates
- Hemodialysis
- Phosphate supl - later

Neurological

- **Malignant extradural spinal cord compression**
- **Raised intracranial pressure**
- **Leptomeningeal metastases**

Spinal cord compression

- **Important medical emergency, treatment must begin within hours, to maximize the chance of neurological recovery**
- **5-10 % of all patients with a known diagnosis of malignancy: breast, lung, prostate, uknown primary, myeloma, rencal, other**
- **May be the first presentation of malignancy (up to 20 %): prostate, breast, myeloma**
- **Site of compression: thoracic (60 %), lumbar (30 %), cervical (10 %) → 30 % multiple sites**

Spinal cord compression

- **Causes**
  - Expanding metastases to the vertebral body
  - Vertebral pathological fracture with posterior displacement of bony fragments
  - Paraspinal mass gains access to the epidural space via neural foramina
  - Epidural metastases

- **Two phases of compression**
  - Reversible: obstruction of venous plexus and vasogenic oedema → demyelinisation
  - Ireversible: ischemic damage and cord infarction

Spinal cord compression

Symptoms:

Pain - usually the first symptom, localized and radicular

Neurological:

- weakness of the legs → paralysis
- sensory loss
- bladder dysfunction (urinary retention → incontinence),
- bowel dysfunction (constipation → incontinence),
- impotence

Spinal cord compression

Investigations

- Plain X-rays may demonstrate destruction and/or collapse of a vertebra. Paravertebral masses may sometimes also be shown. In 15–20% of cases, plain films show no abnormality.
- MRI scanning is the investigation of choice. It is advisable to include full spine, as it is not uncommon to find >1 critical lesion. It is particularly useful in cases of cauda equina syndrome.
- Where MRI is not available or contraindicated, myelography will show the anatomical location of a spinal cord lesion and whether a block is complete or not, but CT scanning will frequently yield sufficient information without delay. Simultaneous myelography improves the sensitivity of the investigation.

Spinal cord compression

Management

- Speed is of the essence in the management of spinal cord compression.
- <10% of patients with established paraplegia from metastatic disease walk again.
- Dexamethasone 16–20mg should be given immediately. This can reduce peri-tumoural oedema.
- If immediate surgery is not contemplated, the neurological status should be assessed at least daily, so that deterioration may be detected early and surgical intervention considered.
- Best outcomes reported with surgical decompression/stabilization of the spine, followed by radiotherapy.

Raised intracranial pressure

- Result of brain oedema due to either primary brain tumour or metastases

Symptoms:

- Hypertension, bradykardia, headache, nausea or vomiting without nausea, meningeal symptoms, confusion…coma

Management

- Manitol 1,5g/kg/day 3 day, tapering aftewards
- Dexamethason 24mg/day

Thrombembolic disease (TED)

- frequent complication of cancer
- PE is often succesive leading to PH
- 20% of new PE is dg in CA pts.
- PE risk is 6-7x higher
- CTPA

TED - risk factors

- direct procoagulation effect: tissue f. expresion, releasing TF bearing microparticles, cancer procoagulant
- indirect effect: increased NETS production (neutrophil extracelullar traps), pro infamatory
- ‚normal' risk factors + surgery, sepsis, CVL, lymphedemas
- pancreatic cancer, gastric cancer, lung cancer, myeloma, lymphomas, gynaecologic cancers, prostate cancer
- chemotherapy, G-CSF, EPO, platelets infusions, tamoxifen, steroids

TED - prophylaxis and treatment

Prophylaxis

- LMWH in all cancer inpatients
- If LMWH not possible: intermitent pneumatic compression +/- stockings
- In pts after major surgery 28 days

Treatment

- LMWH (dalteparin, enoxaparin, fondaparinux)
- Chronic:
  - In catheters-related 3 months
  - Others: lifetime in pts with active disease/ on treatment

Coronary artery disease / ischaemic heart disease

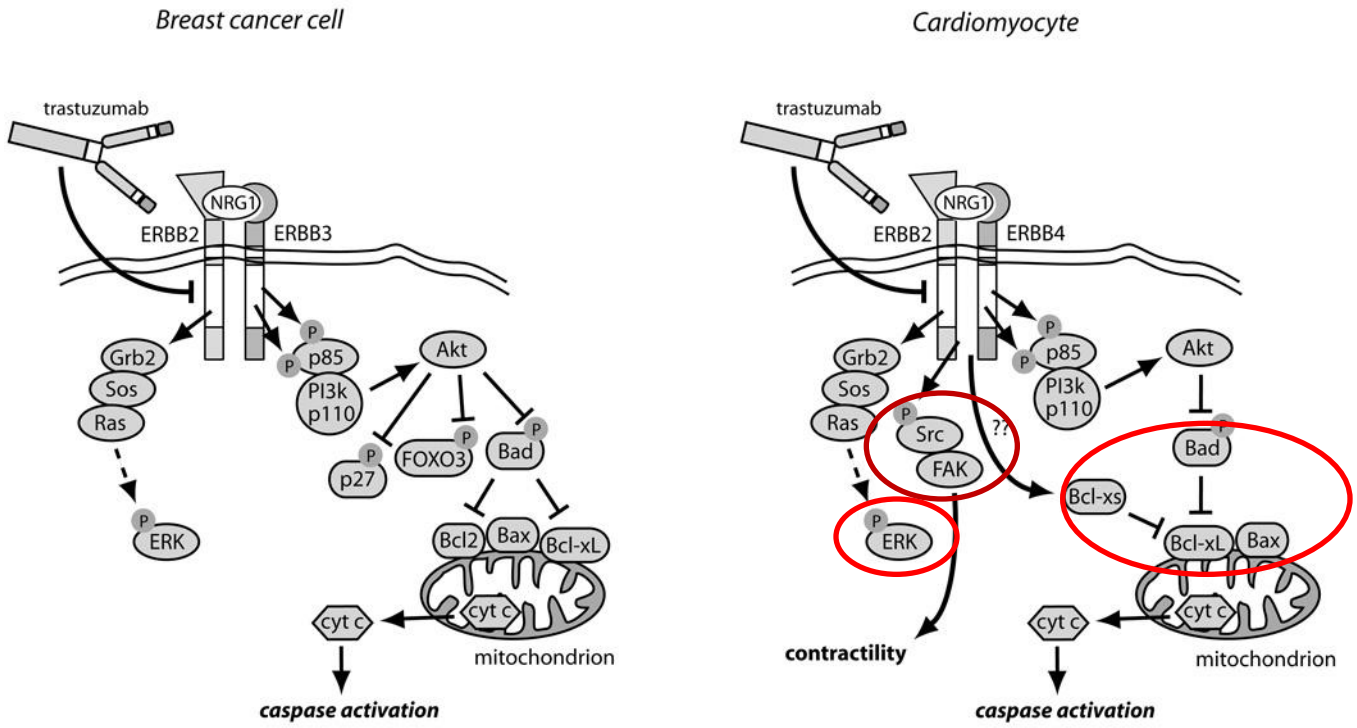
- **Chemotherapy**
  - 5-FU (vasospasm), capecitabin (vasospasm), cisplatine (both vasospasm + endoth. dysfuction), etoposide, taxanes (arhytmias), vinca alkaloids (spasm)
- **Thoracic irradiation**
- **Targeted treatment**
  - bevacizumab, TKI
- **Hormonal treatment**
  - Aromatise inhibitors (Ca prsu, prostaty)
- **Change of lifestyle**
  - Weight gain, lack of physical activity, thyroid gland impairment (TKI)

Heart failure I

- **Chemotherapy**
  - antracyclines, mitoxantron
  - CAD inducing drugs – cisplatine, 5-FU
  - Arrhytmogennic drugs – taxanes
  - Alkylating agents – cyclophosphamide, ifosphamide, busulfan, mitomycinC
- **Radiation therapy** (involving thorax)
  - O2 radicals- endothel. dysfunction – CAD – hypoperfusion – fibrotisation of myocardium

Heart failure II

- **Targeted treatment**
  - trastuzumab (breast Ca)
  - TKI (kidney, liver, CML, GIST…)



Heart failure III

- developement possibly during years post treatment
- subacute onset after anthracycines within a year
- **Acute** – within days - after anthracyclins
- **Weeks to months** – after targeted therapy
- **Prevention:**
  - Follow RF (age, diabetes, hypertension, CKD, prior RT, lipids)
  - Follow cumulative anthracycline doses
  - ECHO monitoring – anthracyclines, antiHER2 therapy, TKI

Heart failure IV

- **Late onset:**
  - Hematological malignancies
  - Childhood cancer
  - Breats cancer
  - Testicular cancer

- standard management of heart failure