Module 4 – Acute oncology and approach to the unwell cancer patient

Learning objectives

- Recognise the oncological emergencies and understand the principles of management
- Understand the mechanisms by which cancer patients may present acutely
- Think briefly about end-of-life care for cancer patients

Introduction

We are using increasingly aggressive approaches for cancer treatments, and we also treat patients with more advanced stages of malignancy than in the past. As a result it is inevitable that patients will develop complications of either their disease or treatment which lead them to present acutely.

However, there is no need to panic, because apart from one exception, oncological emergencies are the same as medical emergencies and managed in the same way. Want to know what the exception is? Well you'll have to keep reading…

When we get called down to A&E because an oncology patient has come in unwell, the one thing we want to establish from their records before we leave is their treatment intent, because this sets the tone for what we should do when we get there.

- Patients receiving treatment with curative intent may be having the proverbial book thrown at them. Bone marrow transplant, Nivolumab therapy in combination with another biological. These people might get really sick as a result of their tumour and we therefore pull out all the stops, including ITU admission and ventilation, to rescue them from the effect of treatment. We do this because the patient may be cured at the end of treatment. That's usually the first thing the ITU doctor wants to know when they arrive too.
- Patients receiving treatment with palliative intent require a bit more thought. They could be unwell because of their treatment, or because of their disease. Treatment is offered to improve quality of life, and you have to make a judgement call on what their predicted quality of life is likely to be, and thus establish an appropriate ceiling of care. It's often tough to do this, with anxious family on the one hand and ITU outreach team on the other!

The numbers game – high probability complications in cancer patients

Cancer patients are prone to the following conditions, and the most important thing that your can do is to consider them in your differential if they come in unwell

- Neutropaenic sepsis (if the patient is on chemotherapy)
- Dehydration and/or electrolyte imbalance, typically hypercalcaemia, hyponatraemia and hypomagnesaemia.
- Thromboembolic events
- Seizures (primary or secondary brain tumours)
- Bowel obstruction (particularly ovarian cancer patients)
- Cord compression

We'll step through the management of some of these in a bit more detail

Neutropaenic sepsis

More patients are being treated with aggressive chemotherapy, and some will developed neutropaenia due to the effect of treatment on their bone marrow. For most patients, this will not cause symptoms, but some may go on to develop neutropaenic sepsis. Typically neutropaenia occurs 10-15 days after chemotherapy, but can come on later than that (one drug called Gemcitabine can sometimes cause early neutropaenia, whilst another called Procarbazine can cause neutropaenia 5-6 weeks after therapy). The organism is usually from the patients own urinary or GI tract, and that is why we don't generally reverse barrier nurse patients with neutropaenic fever. Patients become at risk when their neutrophil count drops below 1.0 and the infections they get depends on the clinical context:

- Most patients with solid tumours get intermittent chemotherapy. This means that their white cell count is normal most of the time, and then dips. The bugs they get are gram negative ones.
- Patients with PICC lines or portacaths are prone to line related sepsis, which will usually be a staphylococcal infection.
- Haematology patients are a bit different as they may have abnormal white cell function to start with, and they can have prolonged neutropaenia, particularly in the course of a bone marrow transplant. They get all sorts of weird infections, especially fungal infections and pneumocystis pneumonia.

It's also mentioning a condition called typhlitis or neutropaenic enteritis. It's caused by translocation of bacteria across the bowel wall, and can present like appendicitis. Useful to know when you are on surgical take!

Another thing to consider, particularly for the teenage and young adult cancer patients, is that young patients may tolerate sepsis and hypotension very well, without appearing unwell, so it is very important to think of neutropaenic sepsis.

Neutropaenic sepsis is defined as

- ANC <0.5 (or less than 1.0 and expected to go below 0.5) and
- Temp >38C on two occasions or >38.5 on one occasion or
- Hypotension, desaturation, organ failure

The most important thing to remember in the whole of your attachment is this:

If you suspect neutropaenic sepsis in an unwell patient on chemo, start treatment immediately – do not wait for blood counts

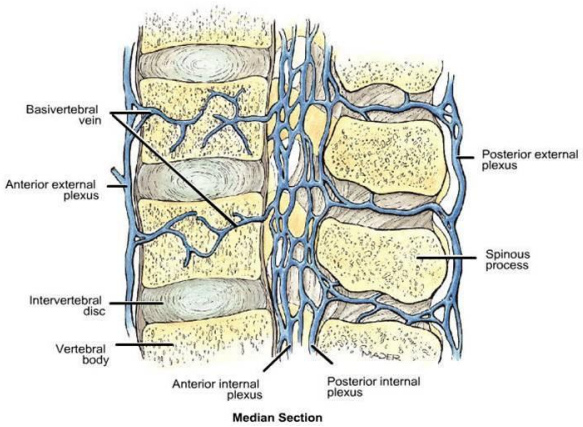
The reason for this is that sometimes it can take an hour or two for a full blood count result to come back, and the lab may not ring you with the result. In a patient with profound neutropaenia, the patient can go off very quickly indeed. Starting appropriate antibiotic therapy can prevent this deterioration. Check the current version of the neutropaenic sepsis protocol but the essence of treatment is as follows.

- Peripheral and central blood cultures
- IV antibiotics (piperacillin / tazobactam)
- Add Gentamicin is the patient is hypotensive

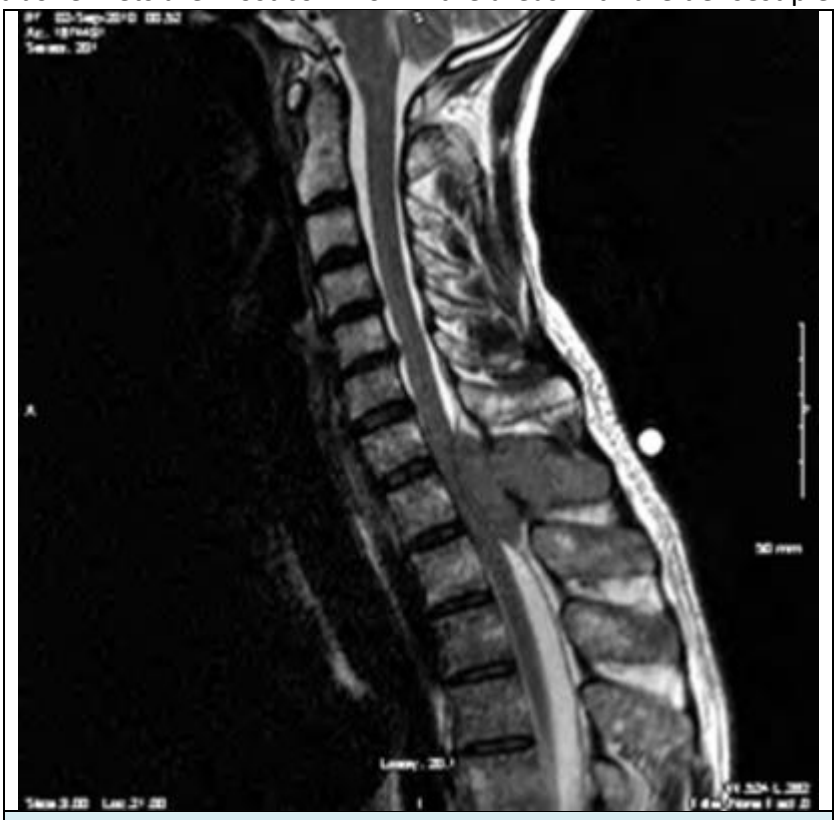
- Add Vancomycin if patient has a line
- 4 Hourly Obs and MEWS scores
- Add GCSF if patient in shock
- Regular review
- Don't perform a PR because of the risk of bacteraemia. If the patient has symptoms, inspect the perineum visually for perianal abscesses and ask for a surgical opinion.

Malignant spinal cord compression

This is becoming common as patients liver longer with bony metastatic disease. We even have a cord compression coordinator in the hospital. It is most commonly associated with bony metastases from breast, prostate and lung cancers.



The vertebro-venous plexus is a network of low flow vessels passing through vertebrae that join intrathoracic veins with external veins, and it is thought that negative intrathoracic pressure can stop and reverse flow in these vessels, acting as a nidus for metastases. I don't know if this is really true but it is certainly the case that bone mets are most common in the areas with the densest plexi.



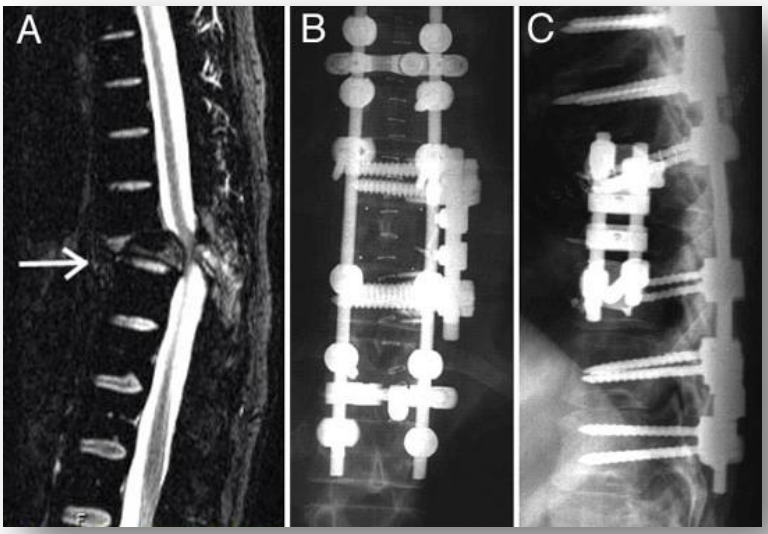
This coronal T2 weighted MRI scan shows the classic appearances for spinal cord compression at T1. A soft tissue mass arising from the posterior elements of the vertebra has grown into the spinal canal and is squashing the spinal cord.

You normally see two bright white areas of CSF either side of the spinal cord on a T2 image, and if you follow them down you'll see they both stop at the level of the tumour. Notice also that before scanning, they have placed a fish oil capsule at the level of the patient's pain symptoms. It looks like the patient got it right!

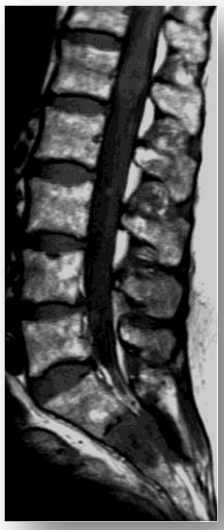
Patients can present with a range of symptoms, but the one that is most predictive is a **short history of radicular (band-like) pain with a sensory level**. Bone tenderness, distal weakness and hypre-reflexia, and bladder and bowel disturbance can all develop subsequently. These are the key steps in the management of MSCC:

- Analgesia
- Bed-rest
- Start Dexamethasone to reduce cord inflammation and oedema
- Urgent MRI spine with contrast (or CT myelogram if patient has pacemaker)
- (Catheter)
- Referral to MSCC coordinator (or oncology on-call out of hours)

Cord compression can be managed with surgery or radiotherapy. A large meta-analysis showed that in patients suitable for surgery, the best outcomes for radiation therapy were equivalent to the worst outcomes for surgery. Within our network we have a group of spinal neurosurgeons and orthopaedis surgeons that work together to provide a 'rota' for spinal cord compression surgery.



Surgery is best for fit patients with single level disease, particularly if they have vertebral collapse as surgery can restore vertebral geometry.



Radiotherapy is for more extensive multi-level disease, patients of poorer performance status or a high disease burden, and also for soft tissue masses.

Malignant hypercalcemia – bones, stones, groans and psychic moans

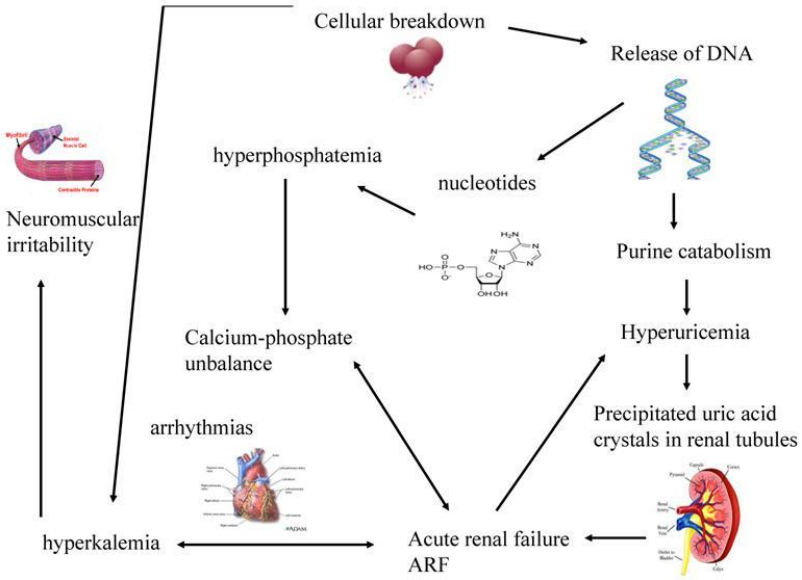
Malignancy hypercalcaemia can occur quite commonly in cancer patients, either in the context of diffuse bone disease, or as a paraneoplastic syndrome from ectopic PTHrP production by lung cancer and neuroendocrine tumours in particular. Patients may present with:

- Generalised malaise
- Bone pain (even if they don't have bone mets)
- Abdominal pain (groans)
- Hypercalciuria and renal stones
- Depression

These symptoms can be subtle so it is important to check calcium on any unwell cancer patient. Treatment is with fluid rehydration (commonly 4 litres or more are required to get the patient euvolaemic) followed by bisphosphonate therapy (bisphosphonates work by inhibiting osteoclast activity). Treatment of the underlying tumour will help with refractory hypercalcemia, and some patients have regular bisphosphonate infusions to prevent skeletal related events (SRE's) and hypercalcaemia.

Acute tumour lysis syndrome

It is one of those truths in oncology that rapidly proliferating tumours respond rapidly to therapy, and slow growing tumours respond slowly. This can sometimes be a problem for the really rapidly growing tumours such as Burkitt's lymphoma and germ cell tumours, which can have a doubling time of hours. Massive cell necrosis essentially exposes a whole load of intracellular contents (potassium, urate from purine, calcium and phosphate) into the vascular compartment and this causes major problems to the kidneys as wel as the risk of arrhythmia:



These days we look out for tumour lysis and give initial chemotherapy very slowly, with plenty of hydration, urinary alkalinisation (to increase urate solubility) and allopurinol, so this should become a thing of the past.

Rasburicase is a recombinant uric oxidase which converts urate to allantoin. Allantoin is about 10 times more soluble in water than urate. It is sometimes used in the treatment of tumour lysis syndrome. It costs around £30,000 for a five day course of treatment, so prevention is better than cure!

Hyponatraemia and malignant SIADH

Hyponatraemia is common in cancer patient, for the following reasons

- Many patients with advanced malignancy are on corticosteroids, which cause hyponatraemia
- Patients with oedema, diarrhea or vomiting get hyponatraemia
- Disease in the lung, liver and brain cause hyponatremia
- Some patients develop SIADH through ectopic ADH production

The problem is that most of these conditions are associated with hypovalaemia, and SIADH is a cause of euvolaemic hyponatraemia. It's a hard diagnosis to make if the patient comes in dehydrated, particularly as symptoms of lethargy, confusion, fatigue and muscle weakness are non-specific.

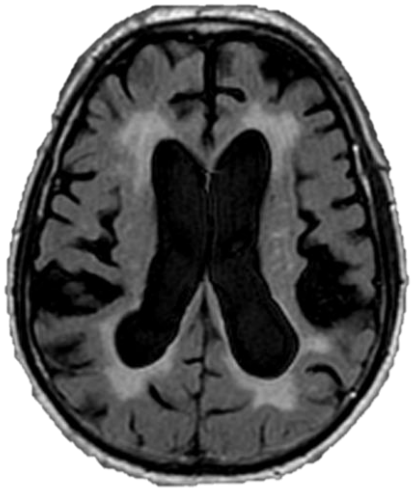
Diagnosis in a euvolaemic patient is made by paired urine and plasma osmolality. The patient is producing an inappropriately concentrated urine when their plasma sodium is low. The best treatment is to treat the underlying tumour, and liaise with the endocrine team regarding fluid restriction and the use of demeclocycline (a tubular poison).

Hydrocephalus

Wit improvements in cancer survival, cerebral metastases now affect about 25% of patients dying from cancer. Symptoms and signs of raised intracranial pressure include:

- Headache (present on waking in the morning)
- Nausea
- Seizures
- Focal neurological deficit (false localising 6th nerve palsy)
- Behavioural change
- Fluctuating level of consciousness

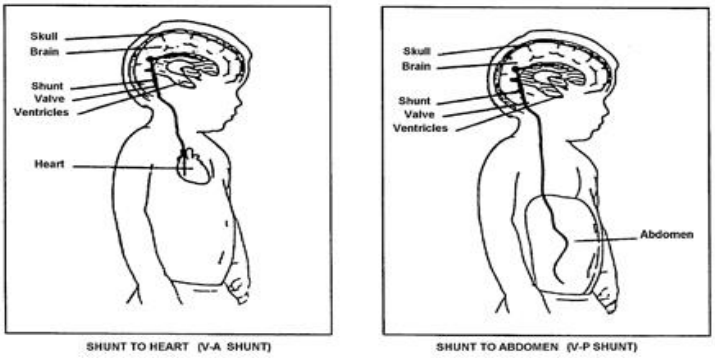
- Papilloedema

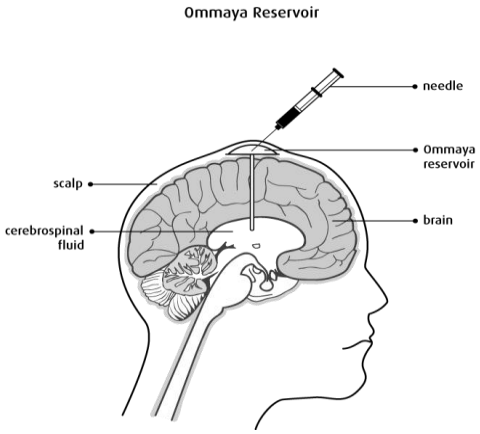


This MRI scan shows evidence of acute hydrocephalus. You can tell it is acute because the ventricles are dlated, the sulci around the grey matter have not yet become effaced (squashed) and there is perventicular fluid transudation visible as bright on the T2 weighted image (the so called 'capping sign').

A diagnosis of hydrocephalus can be confirmed with an urgent CT scan. Before talking to the neurosurgeons about shunting, it's worth thinking about an appropriate ceiling of care for your patient. As a mode of death, hydrocephalus is not a bad way to go, progressive drowsiness followed by respiratory arrest.

Surgeons can deal with hydrocephalus in a number of ways

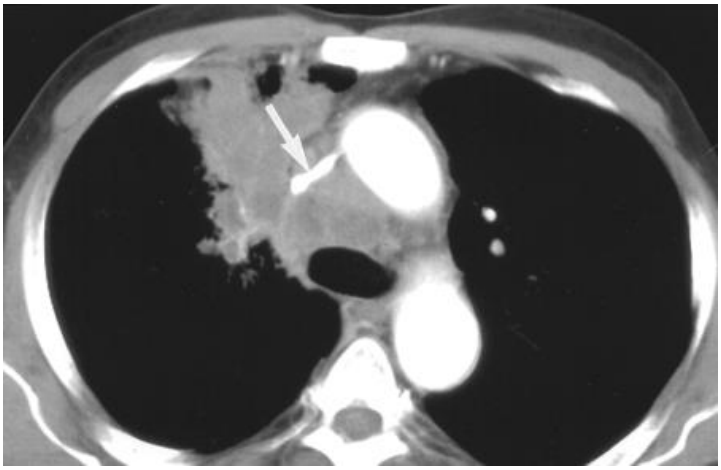




- An ommaya reservoir allows fluid to be drained off at the bedside, and also allows for intrathecal chemotherapy to be given
- Ventriculo-peritoneal shunts provide a more long term solution to chronic hydrocephalus. A programmable valve is usually inserted to prevent underdrainage or overdrainage through the shunt. Ventriculotrial shunts are no longer routinely used due to the risk of sepsis.
- For tumours blocking the ventricular outflow tract, and endoscopic third ventriculostomy can be performed to allow CSF to drain directly into the basal cisterns. Here is a short youtube clip showing how the procedure is performed.

Superior vena cava obstruction (not really an oncology emergency any more)

Superior vena cava obstruction was first described by William Harvey in the context of syphilitic aortitis. In these enlightened times, it is most commonly associated (85% of the time) with small cell lung cancer, because the disease commonly presents with bulky mediastinal lymph nodes.

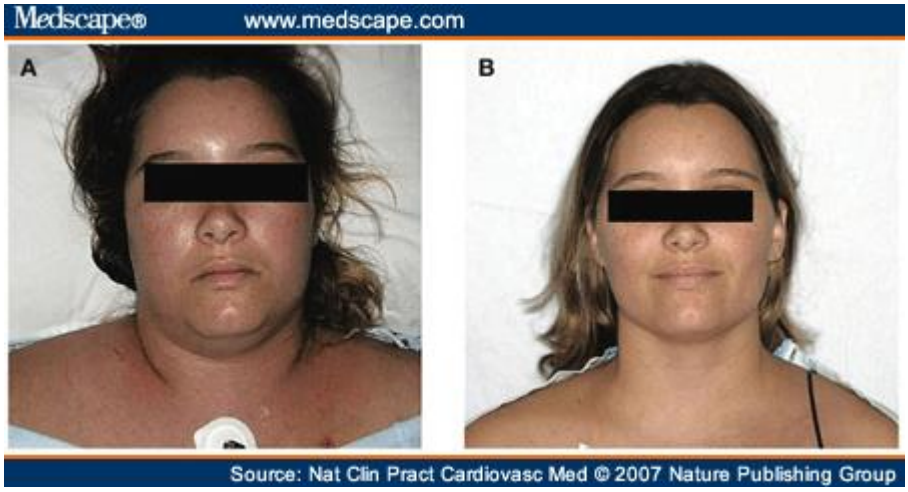


The is SVC surrounded by sternum, trachea, R bronchus, aorta, pulm artery, perihilar and paratracheal lymph nodes, and all of these structures are more rigid than SVC, which is easily compressed. The CT scan above shows contrast in the cava, which has been squashed down to a thin slit.

Clinically, patients present with marked dyspnea from high venous pressure, headache, dizziness, facial swelling and redness, and dilated veins over the chest wall (only if SVCO has occurred over a longer period of time allowing venous collaterals to develop).

Management is SVCO is as follows:

- Sit patient up
- Adminster high flow Oxygen
- Start high dose steroids
- Diagnosis is usually clinical (CXR/CT will confirm)
- Discuss with interventional radiologists about stenting of the SVC. Stenting leads to rapid resolution of symptoms as you can see in the picture below. However there are some situations where the radiologists will not advise stent insertion because of the presence of mural thrombus. Under such circumstances it is best to start definitive treatment (usually with chemotherapy if a small cell lung cancer diagnosis is established, or radiotherapy).



DNACPR and advanced directives

Sometimes it is not the right thing to prolong life if the patient has limited quality of life. It's always difficult to have this discussion with the patient in the thick of an emergency, and there never seems to be a good answer.

DNACPR orders are often used in hospital for patients with advanced malignancy and are appropriate in the following situations:

- The patient has terminal malignancy
- Resuscitation is likely to be futile
- No further treatment options exist to treat the underlying tumour

DNACPR order are made in hospital and last for the duration of the admission. Once the patient is discharged, a trust DNACPR form has no scope. We are now starting to see community DNACPR forms appearing, but again the scope of these forms is unclear.

An advanced directive or living will is a document made by a patient that is legally attested, outlining their wishes regarding treatment refusal and end-of-life care. What's confusing is that they often get conflated with issues of capacity and power of attorney. If the patient has one it is normally indicated in the medical notes. *Despite apocryphal tales I have yet to meet a patient with it tattooed on their chest!*

For me, the issue of DNA CPR documentation on admission is really tough, because in a patient's mind it gets wrapped up with withdrawal of patient care. Put yourself in a patient's shoes. You come in to hospital for symptom control and someone asks to if you want CPR if your circulation or breathing becomes compromised. If you are feeling well with an expectation of going home, the question seems vaguely ridiculous. If you are feeling really unwell, you would be worried that DNACPR equates to cessation of care. You might also feel that life is sweet, and even an extra day of it is worth the effort. What do you do? If you are on the ward, try to listen to discussion about CPR between patients, relatives and medical staff.

One thing that is very clear from recent rulings is that 'causing the patient distress' is no longer a good enough reason to not discuss DNACPR with the patient. You now have to consider that the discussion would cause "Physical or Psychological harm" if you discuss for this to be valid. Futility of CPR is also no longer a reason not to discuss the issue with the patient. One very good point is that DNACPR does not need to be discussed it cardiorespiratory arrest is not expected during a hospital admission.

The GMC has a really good resource on all of this, which I would urge you to take a look at. It goes through legal and ethical issues of DNA CPR.

Conclusion

What I hope is clear is that the most important thing in the management of oncological emergencies is to consider the diagnosis in your differential. If you do this you may save a life!

Proceeding with treatment is always easy, but it's not always the right thing to do. It is important to try and establish appropriateness of intervention, and consider advanced decisions made by the patient

Reflect on the situation regarding DNACPR in cancer patients, and the futility of resuscitation, but remember you must stay on the right side of the law.