40 year old woman with malignant melanoma

June is a 40-year-old woman who was diagnosed in the autumn of 2020 with a BRAF+ malignant melanoma on her upper arm with local lymph node metastasis. She was treated successfully with surgery and received adjuvant immunotherapy.
Two months later she was admitted to your hospital with pain in her shoulder and thoracic column. A junior doctor started her on low-dose opioids with little effect and consults you for advice

1. What could be the probable cause of her pain? - Recurrent disease, metastatic growth, neuropathic pain, treatment side effect, Something Completely Different
2. How do you advise the junior doctor on pain treatment and diagnostics? Increase medication dose or do rescue i.v. or s.c. depending on the pain levels. Take care of anxiety! Take a CT to see if it's a recurrent disease or even an inflammation or an embolus / dissection, take basic vitals, labs, ECG etc.

The next day there is a CT scan of the patient's thorax and upper humerus and it shows bone metastases in Th2 and Th3

The patient who has started long-acting morphine tablets has also received fast-acting morphine 10 times in the last 24 hours. She has pinpoint pupils and seems a bit agitated.
The junior doctor has contacted the oncologist who is busy in the outpatient clinic and not able to see the patient until late in the afternoon

3. How do you advise the junior doctor today on:
    a. -pain treatment Start a pump. I.v. or s.c. with i.e. morphine + benzodiazepines + dexamethasone (plausibly, but depending on overall situation, for example can't start if we assume this is melanoma before we take a biopsy), start on laxatives. Consult for non-pharmacological measures (priest, psychologist, getting their relatives to visit, get a physiotherapist etc.)
    b. -clinical examination and diagnostic work-up Neurological status. This could be the disease in the brain. Or patient anxiety and total pain. Non-pharmacological measures too.
4. If examination makes you suspect a malignant medullary compression, what would you do?

- Contemplate if the dosage of dexamethasone I maybe started in 3a is sufficient, contemplate if you wish to get a brain MRI and contemplate radiotherapy's urgency based on the total disease burden and patient situation; i.e. will radiotherapy have a rapid effect on the pain and is medullary compression the only target. Consult an oncologist to tell me the aforementioned, and consult a neurosurgeon. Take an MRI of the spinal column.

5. Are you sure the patient's metastases are from malignant melanoma?

- No, I am not sure.

In the next couple of days, the patient has had an MRI of the column and further CT scans of the abdomen and pelvis. This shows that the patient also has metastases in the liver and in a lumbar vertebra in addition to what you already knew. A liver lesion has been biopsied. The patient does not have a medullary compression, but you do not have pain control with an opioid infusion and pregabalin.

6. The junior doctor suggests starting the patient on steroids and referring to radiotherapy. Do you support that decision? Would steroids provide pain relief?

- Steroids can help faster than radiotherapy. Radiotherapy is long-acting but will enable us to taper down the steroids later.
- We might want to ask an oncologist before starting the steroid. We might also want to consult the pathologist on how long the biopsy will take. Even a radiologist on what they think this could be (best estimate, does it look like melanoma). And an anaesthesiologist or pain specialist on ways to treat the pain.

The oncologist wants to start double immunotherapy (ipilimumab-nivolumab) and stresses “no steroids”

7. Why? Steroids before or during ipilimumab-nivolumab (an immune-oncology therapy) will have an adversal effect on treatment effectiveness.

The patient is treated with immunotherapy and also receives radiotherapy towards the thoracic column and the pain medication is tapered successfully over the next weeks. Then the patient is admitted again to hospital this time to the palliative ward. She has some upper abdominal pain, and she is agitated, restless and you suspect a delirium.

8. What could be the cause of the patients’ symptoms? Suggest diagnostic work-up

- Abdominal pain could be from the liver metastasis, or a complication from the biopsy (no timeframe given in here), could be an autoimmune colitis, hepatitis, diabetes, thyreoditis, you-name-it-itis. It could also be the brain metastasis we missed at the beginning and immune-oncology response is coming in late or doesn’t affect the brain. Or the patient has pain and has overdosed on medication. Or the bone metastasis + radiotherapy might cause hypercalcemia. Patient might have bleeding metastasis or gastrointestinal bleeding. Or just a plain meningitis or a severe infection. Lots of labs, CT and that brain MRI/CT we didn’t take earlier might be suggestive of the causes.

Bloodwork shows liver enzymes and bilirubin 5 times normal, otherwise an almost normal hemogram, electrolytes, and kidney function

A new CT scan shows disease progression – but only some progression in the liver.
Cerebral MRI seems normal.
You are waiting for her oncologist to come visit your ward.

9. Is there any other blood work you would consider at this point? What's included in the previous labs? Thyroid / pituitary gland function, hepatitis, colangitis?

10. What do you suspect and how would you treat the patient?
Ultrasound (gallstones, colangitis), surgeon consultation? Autoimmune (immune-oncology related) hepatitis would need steroids.

A month or so later the patient has increasing pain in her thoracic column, liver enzymes are approaching normal, but the patient has a lot of anxiety. She is sometimes agitated, has trouble sleeping. She constantly wants to get up and out of bed and is afraid to sleep. She begs the nurses and doctors to provide her with some hope of a longer life or a cure. She has small kids and repeatedly says she finds it impossible to comprehend her situation with a terminal disease.

The oncologist agrees to start treatment with a BRAF inhibitor. Her ECOG (or WHO performance status) is assessed to be 2-3

11. What does ECOG/WHO PS mean? Performance status and symptoms (ability to walk, do daily functions, general symptoms and how much they restrict the patient)
12. How can an ECOG status help the oncologist choose a treatment plan? It is predictive for how well the treatment is tolerated and if it can be assessed to be effective. Worse condition when starting treatment often means shorter lifespan and poorer response as well as more risks with treatment.
13. What does ECOG or WHO say about life expectancy? See above. Only exception is if the PS is low (so ECOG or WHO score is high) due to disease burden, in which case in for example colorectal cancers / lymphomas PS can rise from treatment and survival remains unaffected.
14. You have learned that ECOG 2+ probably is a contraindication for palliative chemotherapy. Does it apply to immunotherapy, BRAF inhibitors, and other targeted treatments? Not if you work in a certain unnamed private clinic :) But in all seriousness, see above. Poor performance status still means complications are potentially fatal and patient may not survive the time it takes for treatment to start having an effect.

The patient starts with BRAF and MEK inhibitor, but after a few weeks, she is in an agitated irreversible delirium and dies with palliative sedation in the palliative ward.

Harald is a 53 years old man who was diagnosed with cancer coli with liver, lung and bone metastases.

He now receives 2. line chemotherapy.

He is reffered to the «APCU*-integrated pathway» as an out-patient at the APCU at the Cancer Clinic

- Why should patients be referred to an «integrated pathway»? Having early palliative integration improves symptom control and survival.
- Which patients should be referred? Patients with symptoms or expected bad symptom or a combination of symptoms in the four dimensions.
- How should these patients be followed? Symptom assessment, oncological assessment.

After some weeks the patients is hospitalized at your APCU because of pain in the pelvic.

- What do you do? A good clinical status, analyze blood, contemplate a scan (consult the treating oncologist).

*APCU-acute palliative care unit

You are at duty some days after the patients is hospitalized.

The nurse calls you and tell that Harald has fever, temperature 39 degrees

- What is your considerations? Neutropenic fever, colitis.

You ask the nurse; when did Harald receive chemo? She says about 10 days ago.

- What will you do? Take lab count. Call the oncologist. Start antibiotics.
- Is this an emergency? This could be.

Haralds father see you after some days. He talks about his son but after a while he tells you that he has an heart failure and COPD. He has home care 4 times a day. You see that he is fragile. He ask you, «may I be referred to an integrated pathway as well?»

- How should we deal with integrated pathways for non-malignant diseases? A good discussion dependent also on hospital resources. But both heart failure and COPD are chronic and serious illnesses, so by principle, they would be welcome.