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?
   Metastasis.Infection. Inflammation as a side effect of immunotherapy
2. How do you advise the junior doctor on pain treatment and diagnostics?
   Blood work. X-ray. CT scan, alternativ MR if available. If by low-dose meaning codeine, change to morphine/oxycodone.

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. Not clearly whether she has pain. steroids, overdosed on morphine
    b. -clinical examination and diagnostic work-up examination of nerve function. MRI
4. If examination makes you suspect a malignant medullary compression, what would you do? Steroids MRI
5. Are you sure the patient's metastases are from malignant melanoma? At this point in pain control doesn´t really mather, but matters later.

Discussion: Fast acting fentanyl is used in some areas (because of the price). Probably underused because of the price? Fast acting. Oxycodone as an alternative to morphine.

Discussion regarding the approach, should be treated in the line of "total pain" and managed accordingly.

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?

If edema/inflammatory component; can get effect of steroids. One can try, but there are exemptions where they should be used initially (lymphoma, melanoma - biopsy) Not for this patient eligible for immunotherapy?

Referral depends on judgment on prognosis and performance status - consult an oncologist.

Discussion: Consult an oncologist before starting steroids, if possible. There might be a conflict regarding effect if on steroids and starting immunotherapy

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

7. Why? To get the wanted initial effect of immunotherapy, later on the steroids can be added if needed

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

Ct scan of brain and abdomen. Blood work including liver, inflammation

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?
coagulationparameters, primary hepatitis,

10. What do you suspect and how would you treat the patient?

Inflammatory side effect of immunotherapy - hepatitis. Iv steroids, Immunotherapy on hold. Liverencephalopathy- treat with lactulosis

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? Daily functioning and symptom burden - tiredness and hours resting
12. How can an ECOG status help the oncologist choose a treatment plan? Performance does not necessarily correlate to disease burden in the body.
13. What does ECOG or WHO say about life expectancy?
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 in the same way, it can work well on prolonging survival

Discussion: Life expectancy and ECOG: Depends on cause of the cancer. Some cancer patients can have very good effect of treatment. But if everything else is “fixed”, the life expectancy of ECOG 4 = 14 days, ECOG 3 can be 7 weeks.

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»?

Adding palliative care earlier will likely be beneficial for the patient regarding symptoms and sometimes prolonging life.

- Which patients should be referred?

Should not only be dependent on the state/progress of the disease, could be relevant for patients with curable cancer depending on the symptom burden. But the practices differs regarding reimbursement, and it will also be a practical question of capacity in the palliative care unit.

- How should these patients be followed?

Discussion regarding different approaches depending on how the system is organized. As a ground rule the oncologists should be in charge of the cancer treatment.

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

- What do you do?

Work up and pain managment

*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? Dx neutropenic fever, or a primary infection

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

- What will you do? Blood work, clinical examination, etc.
- Is this an emergency? Yes. Probably ICU if relevant.

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?