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, progression -lung infection
Clinical exam

2. How do you advise the junior doctor on pain treatment and diagnostics?

CT scan
Short acting opioids

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

    Overdosed? Assess the pain! Steroids(but can accelerate agitation)? Longacting NSAID (GI bleeding, heart, kindey, ulcus)?
    Benso against agitation and to potense the effect of the opiods. Talk to her!

    b. -clinical examination and diagnostic work-up

    Neurological exam. If risk for the medulla - MRI scan

4. If examination makes you suspect a malignant medullary compression, what would you do?
    MRI scan! High dose steroids Betametason 8mgx2, Prednisolon 100-150mgx1. Dexametasone . If MRI shows threat to medulla - contact surgery! Kontact oncologist for irradiation acute og semi acute depending of surgery?

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

You never know… Divided opinions on whether to do a new biopsy.

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?

Yes! Yes! (NB; agitation)

Discuss with oncologist if lymfomea not steroids

Washout period from steroids to immunotherapy: a few days

Time from immunotherapy treatment to steroids: as soon as the dose is finished it may be ok (Swedish opinion) - Danish and Norwegian opinion more careful

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

7. Why?

Becasue steroids inhibit the clinical response to immunotherapy

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

Risk for liver metastases and brain metastasis - CT scan of thorax/abdomen and head
Could be side effects of immunotherapy (thyroiditis for instance) !
Ordinary blood samples. Check medication list
Immuntherapy blood test (includes -itis!)
Encephalitis?

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?

Immunology blood samples!

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

Thyroiditis - hepatitis?

Ultrasound of liver

High dose 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.

General prevention and treatment of delirium!

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?

The general function of the patient

12. How can an ECOG status help the oncologist choose a treatment plan?

Helps to know the balance between benefit and harm - plus the fact that studies are made on patients ECOG 1-2.

13. What does ECOG or WHO say about life expectancy?

Predictor of life expectancy (unless in certain cases hematological diseases where patients can improve!)

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?

ECOG 3 patients can sometimes have immunotherapy - but almost never ECOG 4

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»?

Early integation of palliative care is proven to increase QoL and longevity - and decreased chemo in the last weeks of life

- Which patients should be referred?

Patients with needs for speciliased palliative care - that it: heavy symtom burdens

- How should these patients be followed?

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

- What do you do?

Examination; look at old scans - if unclear make new DT scan / x-ray
Pain treatment!
Symtom scoring!

*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?

Chemoinduced neutropenia - bloodsamples!

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

- What will you do?

Blood tests! Take culture but start AB immediately

- Is this an emergency?

Yes (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?

Resource question!