Cancer Associated Thrombosis Training:

Answers to Case Studies

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Recommended Answers

Case 1, Question 1:

Patient's thrombocytopenia is likely secondary to chemotherapy with PCV – platelets likely to start to drop from day 7 with a peak at day 14. Normal life span for platelets = 8 – 10 days.

Unlikely to be secondary to treatment with dalteparin (i.e. heparin induced thrombocytopenia) as patient has been on this for 3 months and previous platelet counts = normal.

Thrombocytopenia is relevant as likely to increase the risk of bleeding with anticoagulation therapy. Note some bruising on her right arm which may be exacerbated by low platelet count and anticoagulation therapy.

Case 1, Question 2:

Ideally, the patient needs to continue anticoagulation as she has not completed 6 months of treatment and she has significant ongoing risk factors (i.e. chemotherapy, cancer). Also, significant previous PE. Note still a bit symptomatic.

Platelets may drop further and need to be repeated – nadir likely at day 14 post treatment. For this patient suggest repeating in 2 days' time (i.e. at day 14 post treatment). Platelets should then begin to recover. Need to inform oncologist if they are not already aware in case changes to next cycle of chemotherapy are needed.

Given platelets are less than 50 but greater than 20 x 10*9/L it would be reasonable to consider reducing the dose of dalteparin by 50% or to a prophylactic dose. For this patient this would be a dose of 5,000 units OD until platelets recover to above 50 x 10*9/L at which point full dose can be reinstituted.

As the patient has been given 3 months of anticoagulation it would be reasonable to avoid giving a platelet transfusion in order to give full therapeutic dose dalteparin.

If platelets drop further to below 20 then it would be reasonable to withhold anticoagulation entirely until platelets recover to above 20 Till (for reinstitution of prophylactic dose) and then above 50 (for reinstitution of full dose).

It is important to monitor for any signs of bleeding, especially the bruising on right arm in case it worsens.

Case 2, Question 1:

This patient has possible treatment failure with apixaban due to their cancer progression. Need to ensure that patient had been fully compliant with apixaban.

The medical team starting her on full dose therapeutic dalteparin was a reasonable option, as would have been continuing with a DOAC if this was the patient's preference. However, given this patient is now in the last days of her life and is not tolerating treatment well, it would be reasonable to consider discontinuing all anticoagulation. Of note her DVT was of mixed echogenicity. Study data has suggested that DVT diagnosis in this patient group does not affect overall survival [1].

Her chronic PE were relatively low burden.

She also has significant bruising from the injections, which is likely to be distressing for the patient and causing discomfort.

Focus of management is now purely on symptom control.

Bleeding risk factors also need to be considered such as reduced weight, renal and hepatic function, bed sores etc.

Reference

[1] White C, Noble SI, Watson M, Swan F, Allgar VL, Napier E, Nelson A, McAuley J, Doherty J, Lee B, Johnson MJ. Prevalence, symptom burden, and natural history of deep vein thrombosis in people with advanced cancer in specialist palliative care units (HIDDen): a prospective longitudinal observational study. The Lancet Haematology. 2019 Feb 1;6(2): e79-88.

Case 3, Question 1:

Answer is b)

Case 3, Question 2:

It is appropriate to try and salvage a functioning line as the patient will need it to complete 6 months of chemotherapy.

LMWH tends to be the conventional treatment used but there is evidence that DOACs may be equally effective so treatment of a lone DVT can mirror that of conventional VTE.

Treatment should last for as long as the line is in situ. In this case almost six months. Patient is likely to be cancer free at that time and completing chemotherapy, so provoking factors including the line will have been removed and treatment of the DVT can stop.

Case 4, Question 1:

Answer is d)

Case 4, Question 2:

Drop of GFR in a previously stable patient with no symptoms of diarrhoea or vomiting that could suggest dehydration, therefore points to a bladder retention from clots (a catheter and a washout is indicated).

Anticoagulants do not cause bleeding; they facilitate lesions to bleed so investigations are needed to find and treat the lesion (e.g. a bladder cancer or a stone or severe cystitis).

The bleed is non-major while the DVT was recent and there is still some residual swelling in the left leg so stopping anticoagulants altogether is not merited particularly since she is likely to be in hospital for a few days and immobilised.

Switching to LMWH gives greater flexibility for procedures and may be preferable under the circumstances due to the drop in eGFR.

Case 5, Question 1:

This appears to be a clear thrombotic recurrence on anticoagulant therapy. Therefore, an escalation in anticoagulant therapy is indicated. The most recent American Society of Hematology (ASH) guidelines recommend escalation of the patient's LMWH dosing to a supratherapeutic dose, which practically can be achieved by increasing the tinzaparin dose by 25% or switching to a BD LMWH such as enoxaparin.

For patients on dalteparin where the dose has decreased, an increase to full treatment dose may also be considered. Inferior vena cava (IVC) filters are controversial and not recommended in the most recent ASH guidelines.

Relevant Reading

Gary H. Lyman, Marc Carrier, Cihan Ay, Marcello Di Nisio, Lisa K. Hicks, Alok A. Khorana, Andrew D. Leavitt, Agnes Y. Y. Lee, Fergus Macbeth, Rebecca L. Morgan, Simon Noble, Elizabeth A. Sexton, David Stenehjem, Wojtek Wiercioch, Lara A. Kahale, Pablo Alonso-Coello; American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer. Blood Adv 2021; 5 (4): 927–974. doi: https://doi.org/10.1182/bloodadvances.2020003442

Watson, H. G., Keeling, D. M., Laffan, M. , Tait, R. C., Makris, M. and , (2015), Guideline on aspects of cancer-related venous thrombosis. Br J Haematol, 170: 640-648. doi:10.1111/bjh.13556

Carrier, M, Khorana, AA, Zwicker, JI, Noble, S, Lee, AYY, on behalf of the subcommittee on Haemostasis and Malignancy for the SSC of the ISTH. Management of challenging cases of patients with cancer-associated thrombosis including recurrent thrombosis and bleeding: guidance from the SSC of the ISTH. J Thromb Haemost 2013; 11: 1760– 5. DOI:10.1111/jth.12338

Case 5, Question 2:

On discharge this patient requires to be closely followed, including:

- Regular early ambulatory reviews to evaluate symptomatic improvement
- ECHO (if not already undertaken)
- Monitoring of bleeding risks given escalation in anticoagulant intensity, including pathology
- Consideration of anti-Xa in patients with ongoing concerns around further VTE recurrence or bleeding, suggested from ISTH as being a target of 1.6-2.0 iu/ml for once-a-day regimes and 0.8-1.0 iu/ml for twice-a-day regime.

Case 6, Question 1:

Advantages v disadvantages of each:

1. Rivaroxaban

Advantages: Oral option. Limited monitoring. Convenient for patient. Data for use in cancer. Absorption likely not affected by patient surgery.

Disadvantages: Possible increased bleeding risk, but here disease is resected. Needs to be taken with food. Response can't practically be monitored. May interact with chemotherapy, unsure at this stage.

2. Apixaban
Advantages: Oral option. Limited monitoring. Convenient for patient. Data for use in cancer. Large number of patients with colorectal cancer included in study.
Disadvantages: Theoretical concern regarding absorption due to surgery. Response can't practically be monitored. May interact with chemotherapy, unsure at this stage.

3. Warfarin
Advantages: Oral option. Can be monitored for response
Disadvantages: Inferior evidence to other treatments. Possible interactions with chemotherapy if starting. Will need regular monitoring which may be difficult for patient whilst having chemo. Absorption issues a concern due to surgery.

4. LMWH
Advantages: No concerns around oral absorption. Established treatment, extensive evidence and experience. No food requirements. Less drug-drug interactions if starting chemotherapy.
Disadvantages: Injectable, practically more difficult for patient. Surgery may affect areas which are suitable for injection.

Case 6, Question 2:

Realistically any option of rivaroxaban, LMWH or apixaban are reasonable options, but each has considerations that should be discussed with the patient.

LMWH is likely the most clinically appropriate option, at least until ongoing chemotherapy is established that will allow evaluation of possible drug-drug interactions or absorption concerns that develop. As this patient is in the acute phase of their thrombotic event, tight anticoagulant control is essential. Switching later to a DOAC is an option as shown in the COSIMO Study.

Warfarin is impractical and clinically inferior hence should not be considered for this patient

Other considerations include the patient taking clopidogrel which may increase bleeding risk. This should be considered for stopping whilst on anticoagulant therapy, especially as the indication was a previous TIA.

Relevant Reading

Picker N, Lee AY, Cohen AT, Maraveyas A, Beyer-Westendorf J, Mantovani LG, et al. Anticoagulation treatment in cancer-associated venous thromboembolism: Assessment of patient preferences using a discrete choice experiment (cosimo study). Thrombosis and haemostasis. 2021;121(2):206-15.