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Daniel Tambunan, MD
- Consultant or Advisory Board: Boehringer Ingelheim (Atrial fibrillation)

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The content of my material/presentation in this CME activity will include discussion of unapproved or investigational uses of products or devices as indicated:
- Prothrombin complex concentrate (PCC)

Learning Objectives

1. Practice applying new knowledge and skills gained from Thromboembolic Disease sessions, through collaborative learning with peers and expert faculty.
2. Identify strategies that foster optimal management of thromboembolic diseases, within the context of professional practice.
3. Formulate an action plan to implement practice changes, aimed at improving patient care.

Associated Session

- Pulmonary Embolus & Deep Vein Thrombosis: The New Frontier

Daniel Tambunan, MD
Assistant Director, Florida Hospital Internal Medicine Residency; Assistant Professor of Medicine, Loma Linda University School of Medicine Clinical Assistant Professor, University of Central Florida. College of Medicine: Clinical Assistant Professor, Florida State University College of Medicine

Dr. Tambunan is a frequent and popular FMX presenter. He practices internal medicine and has been teaching for 20 years. He specializes in anticoagulation, venous thromboembolism, and viral hepatitis.
Audience Engagement System

Step 1

Step 2

Step 3

Chief Complaint

• Left leg pain

History of Present Illness

• SD, 65 year old woman comes in with acute shortness of breath for the last 2-3 days. She just returned from visiting her daughter in Indonesia last week. Pt also noticed that her left leg was more swollen than usual. Denies any cough, fever, or vomiting or coughing of blood.

PMH

• DM type 2 for 10 years
• Hypercholesterolemia

FH

• Mother: Diabetes, Hypertension, Breast CA
• Father: Hypertension
• Sibling: Sister has breast cancer

Medications

• Metformin 1000 mg BID
• Lisinopril 2.5 mg Qday
• Estrogen 0.625 mg ½ tab Qday
• Atorvastatin 40 mg Qday

• Allergy: NKDA
Immunizations
• MMR as a child
• Td – 7 years ago
• Pneumoniae vaccine up to date

Social History
• Tobacco – Denies
• EtOH - Denies
• IVDA – Denies
• Occupation – retired. Previously an accountant

Review of Systems
• Gen: More easily fatigued
• Resp: Shortness of breath
• GI: Intermittent nausea feeling
• MSK: Leg pain on the left

Physical Examination
• Vitals: B/P 122/74, HR – 115, O2 sat = 91% on RA
• Neck: JVD – normal
• Heart: Tachycardic but regular with no murmur or gallop or rub
• Lung: CTAB
• Abd: Soft, NT, NABS, no HSM
• Ext: good pulse, mild asymmetry in leg size L>R, no peripheral edema

Laboratory/Radiology
• Na = 136, K = 4.1, Cl = 104, HCO3 = 22, BUN = 24, Creat = 1.1, Gluc = 99, ALT/AST = 48/58, Alb 3.5, Bili = 0.8
• WBC 9.9, Hgb 12.9, Hct = 38, Plt = 333
• EKG shows sinus tachycardia, T wave inversion on V 1-4
• CXR: Normal

AES POLL QUESTION
• What is the patient’s Well Score?
  – A. 1
  – B. 2
  – C. 4
  – D. 5
  – E. 7.5
Pretest Probability of PE

- Clinical signs and symptoms of DVT
- An alternative diagnosis is less likely than PE
- Heart rate > 100
- Immobilization or surgery in previous 4 weeks
- Previous DVT/PE
- Hemoptysis
- Malignancy

3 points
3 points
1.5 points
1.5 points
1.5 points
1 point
1 point


Low – Less than 2 points → 3% probability
Moderate – 2 – 6 points → 28% probability
High – > 6 points → 78% probability

AES POLL QUESTION

- What test(s) would you order?
  - A. D-dimer ELISA
  - B. Doppler ultrasound
  - C. CT angiogram of the chest
  - D. Pulmonary angiogram
  - E. B and C

AES POLL QUESTION

- What would your next management step if the Doppler ultrasound of the left leg and the CTA are positive?
  - A. Send home and start patient on a NOAC
  - B. Admit and start unfractionated heparin & warfarin
  - C. Admit and start low molecular weight heparin
  - D. Admit and consult the vascular surgeon for thrombolytics

AES POLL QUESTION

- What is your oral anticoagulation choice?
  - A. Warfarin
  - B. Apixaban
  - C. Dabigatran
  - D. Edoxaban
  - E. Rivaroxaban

Dabigatran
Apixaban
Rivaroxaban
Edoxaban

Indications
Nonvalvular AF
DVT & PE treatment
DVT prophylaxis
Nonvaluable AF
DVT & PE treatment
DVT prophylaxis
Nonvaluable AF
DVT & PE treatment
Nonvaluable AF
DVT & PE treatment

Mechanism of action
Thrombin inhibitor
Factor Xa inhibitor
Factor Xa inhibitor

Administration route
Oral
Oral
Oral

Clearance
Renal
Renal & Hepatic
Renal & Hepatic
Renal & Hepatic

Dosage
150 mg BID
5 mg BID
20 mg QDay
60 mg QDay

Antidote
None
None
None

Pregnancy
C
B
C
C

Severe drug interactions
AZOLE, diltiazem
AZOLE, diltiazem
AZOLE, HIV protease inhi,
quinidine

Dose adjustments
load 15 mg kg

Switching anticoagulants

Agents
VKA to NOAC
NOAC to VKA
NOAC to parenteral
Parenteral to NOAC
UHF
LMWH

Recommendations
INR <2.0: immediate
INR 2.0-2.5: immediate or next day
INR >2.5: follow INR till <2.5
Administer concomitantly until INR is appropriate
Start once UFH is discontinued. Caution: Renal
Start when next dose would be given
Start when next dose of NOAC is due
Assessment

- Pt was admitted and was placed on UFH drip. CTA shows multiple clots at the secondary branches of the pulmonary artery and positive Doppler ultrasound on the left popliteal vein. After five days of hospitalization, pt was noted to have epistaxis and platelet count of 80,000 with stable Hgb.

AES POLL QUESTION

- What is the cause of the drop in platelets in the patient?
  - A. Lab error
  - B. Citrate induced thrombocytopenia
  - C. Heparin induced thrombocytopenia
  - D. Massive internal bleeding

Heparin Induced Thrombocytopenia (HIT)

- Definition: + heparin antibody with fall of platelets (> 50%) or skin lesions at injection site or systemic reactions post heparin infusion
- Bovine UFH > porcine UFH > LMWH
- Recommend to monitor platelets every-other-day between days 4 – 14 (especially in postoperative patients)
- DO NOT use warfarin solely in HIT-associated DVT – may cause venous limb gangrene

Direct Thrombin Inhibitor

- Identical to the natural hirudin found in leeches
- Cleared thru the kidney, adjust as needed
- Two agents: Argatroban and Lepirudin
- Lepirudin: Two prospective studies involving 380 pts, showing >90% platelet recovery and >75% effective anticoagulation. In addition, the difference in cumulative risk of death, limb amputation, or new thromboembolic complications are statistically significant in favor of lepirudine, p <0.004
  - Dosage: 0.4 mg/kg (max 110 kg) bolus, then 0.15 mg/kg (max 110 kg)
- Other agent is argatroban 2 mcg/kg/min IV to maintain aPTT 1.5-3 times baseline

Other management options

- Inferior Venal Caval Filter
  - contraindication or complication from anticoagulant therapy
  - recurrent thromboembolism despite adequate anticoagulation
  - chronic recurrent embolism with pulmonary hypertension
  - concurrent performance of surgical pulmonary embolectomy
- Thrombolytic Therapy
- Surgical Pulmonary Embolectomy
- Catheter Transvenous Extraction

Which anticoagulant?

- Cancer
- Poor compliance
- Pregnancy
- Reversal agent needed
- Liver disease
- Renal disease & CrCl < 30 mL/min
- LMWH
- VKA
- LMWH
- VKA, UFH, Dabigatran
- LMWH
- VKA

Patient Education and Follow up

• Take prescribed medications as directed
• Watch how much vitamin K intake (warfarin)
• Be on the look for excessive bleeding/bruising
• Wear compression stockings
• Avoid sitting still
• Make lifestyle changes
• Get regular exercises
• Check in with your doctor regularly