ACC Case Challenges

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Case 1 - Atrial Fibrillation and Anticoagulation in the Cancer Patient with Thrombocytopenia

- 66 y/o female with mild HTN and a remote h/o of self terminating post-operative AF (< 24 hrs) s/p cholecystectomy
- Exercises regularly at least 30 minutes per day of aerobic activity
- Recently diagnosed with a large gastric leiomyosarcoma. Started on Adriamycin at 75 mg/m\(^2\) with Ifosfamide 10 gm/m\(^2\)
- After her 2\(^{nd}\) cycle she develops a neutropenic fever with Hgb 7.8, Platelets 38, and wbc 0.9 at nadir and an ECG consistent with atrial fibrillation with RVR. Hemodynamics stable.

How would you manage this patient’s atrial fibrillation? How does this change if it is paroxysmal or persistent?

What are the components of your diagnostic workup?
Diagnostic Workup

• $\text{CHA}_2\text{DS-VASC}_2$ score = 3

• Echocardiogram with an EF 60-65%, LA size: 50 mm, GLS -21% (no valvular disease)

• Nuclear Treadmill Stress Test shows normal myocardial perfusion with a calcium score of 347, primarily in the LAD territory and an EF of 75%

• Lipid panel reveals: TC 193, HDL 58, TG 65, LDL 121
Case 1 Continued...the story is never over

• Neutropenic fever treated with supportive care and antibiotics with resolution after 3 days
• AF is rate controlled with beta blockade which self terminates once acute febrile episode resolves
• Upon discharge, she continues to complain of palpitations.
• Event recorder shows paroxysmal atrial fibrillation of short duration occurring during her next neutropenic episode. She continues to become pancytopenic during these episodes with platelets decreasing as low as 10.

How would you manage her atrial fibrillation and anticoagulation?

Would you stop her chemotherapy?
Atrial Fibrillation in Cancer

Farmakis et al. JACC Vol 63, No 10, 2014: 945-53
Chemotherapy Agents Associated with Atrial Fibrillation

- Cisplatin
- 5-fluorouracil
- Doxorubicin
- Paclitaxel/Docetaxel
- Ifosfamide
- Gemcitabine
- Mitoxantrone
- Some TKIs – Ibrutinib
- Melphalan
Suggested Algorithm for Antithrombotic Therapy In Cancer Related Atrial Fibrillation

Farmakis et al. JACC Vol 63, No 10, 2014: 945-53
Useful References

• Farmakis, et al. Atrial Fibrillation In Cancer. JACC 2014; 63 (10): 945-53
• Lee, et al. Tinzaparin vs Warfarin For Treatment Of Acute Venous Thromboembolism In Patients With Active Cancer. JAMA 2015; 314 (7): 677-686
• Lee, et al. Low Molecular Weight Heparin Versus A Coumarin For The Prevention Of Recurrent Venous Thromboembolism In Patients with Cancer. NEJM 2003; 349: 146-53
Case 2

59 y/o male with Waldenstrom’s macroglobulinemia (2013), well controlled HTN treated with Coreg and Zestril.

Waldenstrom’s was initially treated with rituximab, but discontinued secondary to a severe allergic response. He proceeded to bortezomib and dexamethasone with mild progression of lymphadenopathy, and was placed on ibrutinib.

After 6 weeks of ibrutinib, he first noted palpitations and lightheadedness. He then developed syncope and was found to have recurrent VT with Torsades and VF requiring multiple episodes of defibrillation (29 shocks). VT is refractory to multiple medications requiring ECMO support for 3 days. His LVEF is mildly depressed at 35%.
Case 2

He is transferred on several agents including IV amiodarone and lidocaine drips. On arrival, his QT is prolonged approaching 600 milliseconds after correction for underlying rate. He has no family history of unexplained syncope of sudden cardiac death.

Would you have done anything differently prior to starting Ibrutinib?

What diagnostic tests should you obtain?
Case 2

- Cardiac Catheterization: No coronary artery disease.
- Echo after ECMO removal: EF 70-75%, otherwise unremarkable.

**What is long term management of this patient?**

**How should you monitor this patient?**
Chemo Agents Prolonging QT

- TKIs (nilotinib, sunitinib, vandetinib)
- HDAC Inhibitors (Histone Deacetylase)
- Vascular Disruption Agents
- Arsenic Trioxide
Useful References


• Fradley, Michael, et al. The QT Interval Conundrum in Cancer Patients – ACC.org Cardio-oncology Website (http://www.acc.org/cardio-oncology)

• Fradley, Michael, et al. Electrophysiologic Considerations in Cardio-Oncology. ACC.org Cardio-oncology Website (http://www.acc.org/cardio-oncology)
Case 3 – Cardiac Mass

- 32 year old female with left sided breast cancer. She is s/p doxorubicin (240 mg/m²), cytoxan and taxol and radiation therapy.

- Her echocardiogram reveals:

**How would you proceed?**

**Would you obtain additional imaging or other testing?**
# Common Primary Cardiac Masses of the Heart

<table>
<thead>
<tr>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myxomas</td>
<td>Sarcoma</td>
</tr>
<tr>
<td>Fibroma</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Lipoma/Lipomatous hypertrophy of septum</td>
<td>Thymoma</td>
</tr>
<tr>
<td>Thrombus</td>
<td>Paraganglioma</td>
</tr>
<tr>
<td>Pericardial Cyst</td>
<td></td>
</tr>
<tr>
<td>Papillary Fibroelastoma</td>
<td></td>
</tr>
<tr>
<td>Rhabdomyomas (Pediatric)</td>
<td></td>
</tr>
</tbody>
</table>
## Table 1. CMR characteristics of cardiac masses

<table>
<thead>
<tr>
<th>Cardiac Mass</th>
<th>T1 Weighted</th>
<th>T2 Weighted</th>
<th>Post Contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myxoma</td>
<td>Isointense, heterogeneous</td>
<td>Hyperintense, heterogeneous</td>
<td>Heterogeneous enhancement</td>
</tr>
<tr>
<td>Papillary fibroelastoma</td>
<td>Isointense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Rhabdomyoma</td>
<td>Iso- or hyperintense</td>
<td>Slightly hyperintense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Fibroma</td>
<td>Iso- or hyperintense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>Isointense</td>
<td>Hyperintense, heterogeneous</td>
<td>Hyperintense or heterogeneous</td>
</tr>
<tr>
<td>Paraganglioma</td>
<td>Iso- or hypointense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Intravenous leiomyomatosis</td>
<td>Isointense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Bronchogenic cyst</td>
<td>Hypointense</td>
<td>Hyperintense</td>
<td>None</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>Isointense, with hyperintense areas</td>
<td>Iso- or hyperintense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Undifferentiated sarcoma</td>
<td>Isointense</td>
<td>Hyperintense</td>
<td>Nonspecific</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>Isointense</td>
<td>Isointense, heterogeneous</td>
<td>Central nonenhancing areas</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
<td>Nonspecific</td>
</tr>
<tr>
<td>Malignant fibrous histiocytoma</td>
<td>Isointense</td>
<td>Hyperintense, heterogeneous</td>
<td>Nonspecific</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>Isointense</td>
<td>Hyperintense</td>
<td>Nonspecific</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>Isointense, heterogeneous</td>
<td>Hyperintense</td>
<td>Central nonenhancing areas</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Hypo- or isointense</td>
<td>Hyperintense</td>
<td>Variable</td>
</tr>
</tbody>
</table>

Neoadjuvant Chemotherapy for Tumor Reduction if no hemodynamic compromise

Cardiac Tumor Practice Guideline

Primary Cardiac Tumor Treatment

Malignant

- Metastasis
  - Not responsive to Chemotherapy
  - Responsive to Chemotherapy
    - Possible Surgical Resection
    - Investigational Therapy

- No Metastasis
  - Neoadjuvant Chemotherapy for Tumor Reduction if no hemodynamic compromise

Benign

- Establish Embolic Potential and assess for Surgery
  - Surgery
  - Chemotherapy
Case 3

How would you proceed with anticoagulation? Coumadin? NOAC? Lovenox?
And for how long?
Case 4 – Cardio-Oncology Patients in the Cardiac Cath Lab

• 55 y/o WM 1.5 ppd smoker for 30+ years with mild COPD on no treatment who presents with h/o AML and preoperative workup for allogenic hematopoietic stem cell transplant.

• Has received 7 + 3 induction of daunorubicin and cytarabine. He is complaining of mild chest pressure with stairs and while shoveling snow for several months preceding his diagnosis.

• Baseline ECG shows ischemic changes in V3-V6 with symmetrical T wave inversions.

How would you proceed?
Case 4

• He undergoes a nuclear perfusion stress test with reversible ischemia in the mid to distal anterior wall consistent with LAD territory, EF 60%. Current labs include Hgb 10 and platelet count of 60,000.

How would you proceed?
Case 4

• Left heart catheterization shows mid 90% LAD lesion

What next?

What is best antiplatelet regimen for this patient?
Cardio-Oncology Patients In the Cardiac Catheterization Lab

- Chemotherapy agents may injure LV myocardium, cause endothelial damage, abnormal vasoreactivity, vasospasm, platelet activation and aggregation, progressive peripheral arterial disease
- Radiation therapies are also associated with premature CAD, constriction, restriction
- Diagnostic catheterization can be performed at any platelet level.
- ASA can be given with platelets > 10,000; Clopidogrel if platelets > 30,000
  Prasugrel or ticagrelor should not be given if platelets <50,000.
Useful References

• Iliescu, CA et al. Cardio-oncology patients in the cath lab. ACC.org Cardio-oncology Website (http://www.acc.org/cardio-oncology)
• Garot, et al. 2 Year Outcomes of High Bleeding Risk Patients After Polymer-Free Drug-Coated Stents. JACC. 2017; 69 (2): 162-71
Case 5 – Chest Pain Management with 5-FU

- 67 y/o WM with no significant PMH, nonsmoker with metastatic colorectal cancer is being treated with FOLFOX therapy (Oxaliplatin 100 mg/m² IV infusion, given as a 120 minutes IV infusion in 500 mL D5W, concurrent with leucovorin 400 mg/m² IV infusion, followed by 5-FU 400 mg/m² IV bolus, followed by 46-hour 5-FU infusion (2400 mg/m²).

- On his second cycle, after 1 hour of 5-FU infusion, the patient develops chest pain. Initial troponin I is 2.2 with CKMB 16.

What is your differential? How would you treat?
ECG

Case 5 – Chest Pain Management with 5-FU

- Echocardiogram shows hypokinetic anterior wall of the LV
- Left heart catheterization reveals nonobstructive coronary disease with all lesions noted to be less than 20%; this was performed within 24 hours of event
- Lipid panel: TC 240, LDL 135, HDL 38

Would you give 5-FU again?

What other pharmacologic strategies would you use?
5-FU

- Antimetabolite that acts during S phase of cell cycle inhibiting DNA synthesis and interferes with RNA processing/function
- T1/2 10 minutes
- Liver Metabolism
- Manifestations: coronary vasospasm, ischemia/infarction, LV systolic dysfunction, arrhythmias (SVT, VT), sudden death
- Cardiotoxicity incidence 1.27 to 18%
- More often associated with infusion rather than bolus
- Bolus increases diarrhea, myelosuppression but some reports of less cardiotoxicity
- Calcium channel blockers, nitrates are often used