FACULTY: Sarah B. Dubbs, MD, FAAEM, FACEP

PRESENTATION
Hidden Dangers: Cardiotoxicities of Cancer Drugs

DESCRIPTION
Cancer therapy may be life-prolonging and lifesaving but comes with many adverse effects and toxicities. Cardiotoxicities are a particularly important subset of these toxicities, which often come into play when cancer patients present to the emergency department. This talk highlight considerations in emergency department management for patients who have undergone various cancer therapies.

OBJECTIVES
• Patients with history of being treated with antineoplastic chemotherapy and/or chest radiation are at increased risk of cardiovascular events.

• Immune Checkpoint Inhibitor myocarditis is an increasingly recognized and potentially life-threatening complication of immunotherapy drugs.

DISCLOSURE
No significant financial relationships to disclose.
Hidden Dangers: Cardiotoxicities of Cancer Drugs

Sarah B. Dubbs, MD, FAAEM, FACEP
Assistant Professor
University of Maryland School of Medicine
No financial disclosures
Green, Belinda
MRN: 1234567
45 yo F

CC: “Chest pain and SOB”

Temp: 37.2
HR: 101
RR: 18
BP: 154/78
pO2: 98% RA
“Classic” cardiac risk factors

- Hypertension
- Hyperlipidemia
- Diabetes
- Obesity
- Smoking
- Family history
Time to add more?

- ESRD
- SLE
- HIV
- Marijuana
- …CANCER
A perfect storm

◊ Antineoplastic agents
◊ Chest radiation

→ Vasospasm
→ Accelerated atherosclerosis
→ Endothelial destruction
→ Hypercoagulibility/thrombosis
Special population: Breast Cancer

- Systematic review of breast cancer survivors showed almost 2x risk of CV death c/w age-matched population (Gernaat et al, 2017)
Table 1. Cancer Treatment and Cardiovascular Adverse Effects

<table>
<thead>
<tr>
<th>Cancer Treatment</th>
<th>Cardiovascular Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthracyclines (eg, doxorubicin, epirubicin)</td>
<td>Left ventricular dysfunction, heart failure, myocarditis, pericarditis, atrial fibrillation, ventricular tachycardia, ventricular fibrillation</td>
</tr>
<tr>
<td>Alkylating agents (eg, cisplatin, cyclophosphamide)</td>
<td>Left ventricular dysfunction, heart failure, myocarditis, pericarditis, arterial thrombosis, bradycardia, atrial fibrillation, supraventricular tachycardia</td>
</tr>
<tr>
<td>Taxanes (eg, paclitaxel)</td>
<td>Bradycardia, heart block, ventricular ectopy</td>
</tr>
<tr>
<td>Antimetabolites (eg, 5-fluorouracil, capecitabine)</td>
<td>Coronary thrombosis, coronary artery spasm, atrial fibrillation, ventricular tachycardia, ventricular fibrillation</td>
</tr>
<tr>
<td>Endocrine therapy (eg, tamoxifen, anastrozole, letrozole)</td>
<td>Venous thrombosis, thromboembolism, peripheral atherosclerosis, dysrhythmia, valvular dysfunction, pericarditis, heart failure</td>
</tr>
<tr>
<td>HER-2–directed therapies (eg, trastuzumab, pertuzumab)</td>
<td>Left ventricular dysfunction, heart failure</td>
</tr>
<tr>
<td>Cyclin-dependent kinase 4/6 inhibitor* (eg, ribociclib)</td>
<td>QTc prolongation</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>Coronary artery disease, cardiomyopathy, valvular disease, pericardial disease, arrhythmias</td>
</tr>
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</table>

Special populations: Pediatric Cancer Survivors

- Childhood Cancer Survivor Study found survivors of childhood cancer had a 15-fold increase in congestive heart failure (CHF), 10-fold increase in CAD, and 9-fold increase in stroke (Armstrong, 2014)

- Subclinical vascular injury may be present decades after completion of cancer-directed therapy (Brouwer, 2013)
Green, Belinda  
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**Patient #2**

**Name:** 12-Lead 1
**ID:** PR 0.180s
**Patient ID:** QT/QTc: 0.444s/0.451s
**Incident ID:** Age: 58
**Sex:** M
**P-QRS-T Axes:** QRS 0.070s
**aVR**

**HR:** 64bpm
**Sinus rhythm with 2nd degree A-V block, Mobitz I (Wenckebach)**

**Axis deviation:** Inferior infarct - age undetermined

**Possible lateral infarct - age undetermined**

**Tall R in V1/V2 probably reflect the infarct in V4**

**Possible LVH with secondary repolarization abnormality**

**Septal ST-T abnormality may be due to hypertrophy and/or ischemia**

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ST measurements are measured at the J point and are expressed in mm.

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>aVR</th>
<th>aVL</th>
<th>aVF</th>
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<th>V2</th>
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<th>V4</th>
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<td></td>
<td>-1.34</td>
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<td>-0.05</td>
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To ensure printer accuracy, confirm that the calibration markers are 10mm high and the grid squares are 5mm wide.
Why the hesitation with PCI?

- Overall prognosis
- Dual-antiplatelet therapy vs bleeding risk
- Malignancy is a key risk factor for early AND late stent thrombosis (Gori, 2019)
Changing tides with PCI in Cancer Pts with STEMI?

- Patients with cancer showed greater mortality after STEMI. A cancer diagnosis in the 6 months before primary PCI was strongly associated with early cardiac mortality (Velders, 2013)

- Cancer history portends worse acute and long-term noncardiac (but not cardiac) mortality (Wang, 2016)

- Patients with cancer have significantly worse in-hospital mortality compared to those without cancer, partly due to a relatively lower rate of PCI utilization in cancer patients with STEMI (Pothinini 2017)

- There was no significant difference for in-hospital complications in patients with a history of cancer and those without a history of cancer undergoing primary PCI for STEMI (Jacobs, 2019)
In-hospital mortality based on PCI utilization

<table>
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<tr>
<th>Cancer Type</th>
<th>PCI</th>
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<tr>
<td>Breast cancer</td>
<td>7.5</td>
<td>27.8</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>15.4</td>
<td>41.7</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>10.3</td>
<td>32.7</td>
</tr>
<tr>
<td>Non cancer</td>
<td>3.9</td>
<td>21.8</td>
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Current vs history of Cancer?

**Take home figure** The prognostic impact (odds ratio and 95% confidence intervals) of a historical diagnosis of cancer, current cancer with no metastases and current cancer with metastases on in-hospital mortality for prostate, breast, colon, and lung cancer.

Name:  
ID:  
Patient ID:  
Incident ID:  
Age: 58  
Sex: M  
P-QRS-T Axes:  

HR 64bpm  
Abnormal ECG **Unconfirmed**  
Sinus rhythm with 2nd degree A-V block, Mobitz I (Wenckebach)  
Left axis deviation  
Inferior infarct - age undetermined  
Possible lateral infarct - age undetermined  
Tall R V1/V2 probably reflect the infarct V4  
Possible LVH with secondary repolarization abnormality  
Septal ST-T abnormality may be due to hypertrophy and/or ischemia

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Physio-Control, Inc.  
Comments:  
MEDIC 5 BCOFD
Immune Checkpoint Inhibitor (ICI) Therapy

- Activated T cell
- Anti-PD-1
- PD-L1
- TCR
- MHC
- B7
- CD28
- CTLA-4
- Anti-CTLA-4

Tumor cell death

Renal cancer cell

Antigen-presenting cell
ICI-related cardiotoxicity

- LV dysfunction, Takutsubo
- Pericarditis/Pericardial effusion
- Myocarditis
ICI Myocarditis

- Low incidence (0.04-2.4%) under-recognized/reported
- Mortality 25-50%
- Median onset: 34 days (81% within 3 months, longest reported 454 days out) (Mahmood, 2018; Escudier, 2017)
- Most only received 1-2 doses at onset
Beware: Dysrhythmias

Any new conduction abnormality can quickly evolve into full block!
Laboratory
- Troponin
  - Preferably Troponin I
  - Consider Troponin T, CK-MB, Total CK
- Natriuretic Peptides
  - NT-pro BNP
  - BNP

Imaging
- Electrocardiogram, 12-lead
- Echocardiogram
- Cardiac Magnetic Resonance
- Telemetry Monitoring

Procedures
- Endomyocardial Biopsy
- Coronary angiography
Key Points

- History of cancer/cancer therapy should ABSOLUTELY be considered a CV risk factor, and increased risk remains for years after treatment
- STEMI- decision for PCI is complicated
- ICI toxicities- save a life by picking up on dysrhythmias early
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