



SITC 2016

NATIONAL HARBOR, MD
NOVEMBER 9-13, 2016

Management of Complex Adverse Events: Case Studies

Brianna Hoffner, MSN, ANP-BC, AOCNP



Society for Immunotherapy of Cancer

#SITC2016



SITC 2016

NATIONAL HARBOR, MD
NOVEMBER 9-13, 2016

Disclosures

None



Society for Immunotherapy of Cancer

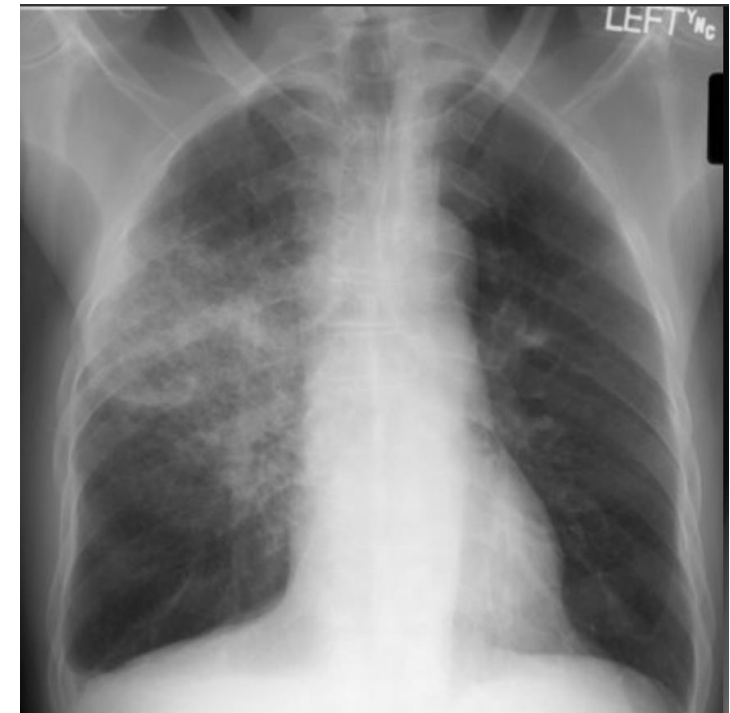
#SITC2016

Case #1

- 58 year old female with IV melanoma with metastases to the liver and bone
- PMH: Hypertension, Hypercholesterolemia, Asthma
- PSH: Cholecystectomy
- Initiated on Ipilimumab (3mg/kg) + Nivolumab (1mg/kg)
 - C1D1 7/1/16
 - C2D1 7/22/16
 - C3D1 8/19/16

Case #1

- 8/27/16 patient presents to outside hospital complaining of fever, cough and shortness of breath
- VS: BP 125/86, HR 90, RR 22, O2 90%, Temp 100.1
- CXR: Read as RML pneumonia
- Patient initiated on amoxicillin 875mg/125mg Q12



Case #1

- 8/30/16 patient presents to clinic with continued low grade fever, cough and diarrhea since 8/29/16
- Denies sick contacts, dietary changes
- Approximately 8 loose bowel movements per day (baseline 1 BM daily)
- No relief with loperamide
- Cough making it difficult to sleep at night

Case #1

GASTROINTESTINAL							Page 2 of 10
		Grade					
Adverse Event	Short Name	1	2	3	4	5	
Diarrhea	Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 – 6 stools per day over baseline; IV fluids indicated <24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL	Increase of ≥7 stools per day over baseline; incontinence; IV fluids ≥24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL	Life-threatening consequences (e.g., hemodynamic collapse)	Death	
REMARK: Diarrhea includes diarrhea of small bowel or colonic origin, and/or ostomy diarrhea.							
ALSO CONSIDER: Dehydration; Hypotension.							

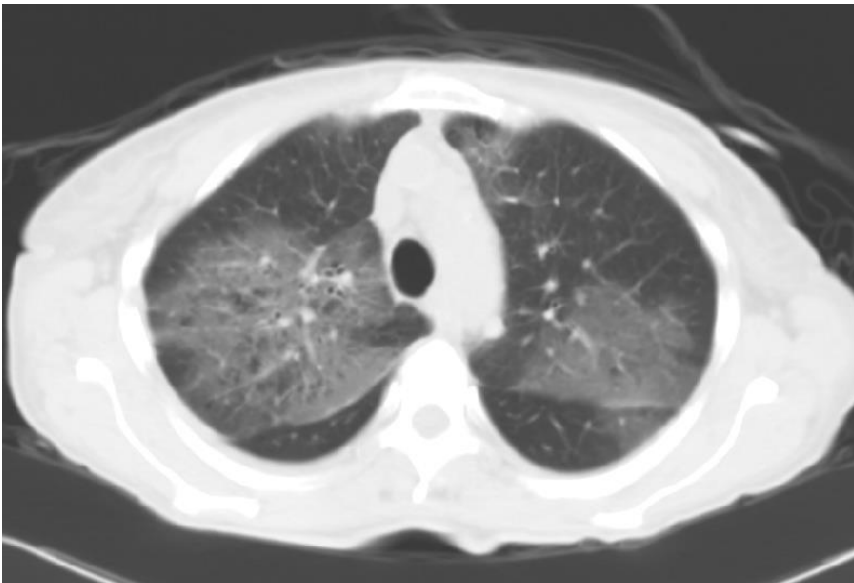
PULMONARY/UPPER RESPIRATORY							Page 1 of 4
		Grade					
Adverse Event	Short Name	1	2	3	4	5	
Cough	Cough	Symptomatic, non-narcotic medication only indicated	Symptomatic and narcotic medication indicated	Symptomatic and significantly interfering with sleep or ADL	—	—	
Pneumonitis/pulmonary infiltrates	Pneumonitis	Asymptomatic, radiographic findings only	Symptomatic, not interfering with ADL	Symptomatic, interfering with ADL; O ₂ indicated	Life-threatening; ventilatory support indicated	Death	
ALSO CONSIDER: Adult Respiratory Distress Syndrome (ARDS); Cough; Dyspnea (shortness of breath); Hypoxia; Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 ⁹ /L) – <i>Select</i> ; Infection with normal ANC or Grade 1 or 2 neutrophils – <i>Select</i> ; Infection with unknown ANC – <i>Select</i> ; Pneumonitis/pulmonary infiltrates; Pulmonary fibrosis (radiographic changes).							

Case #1

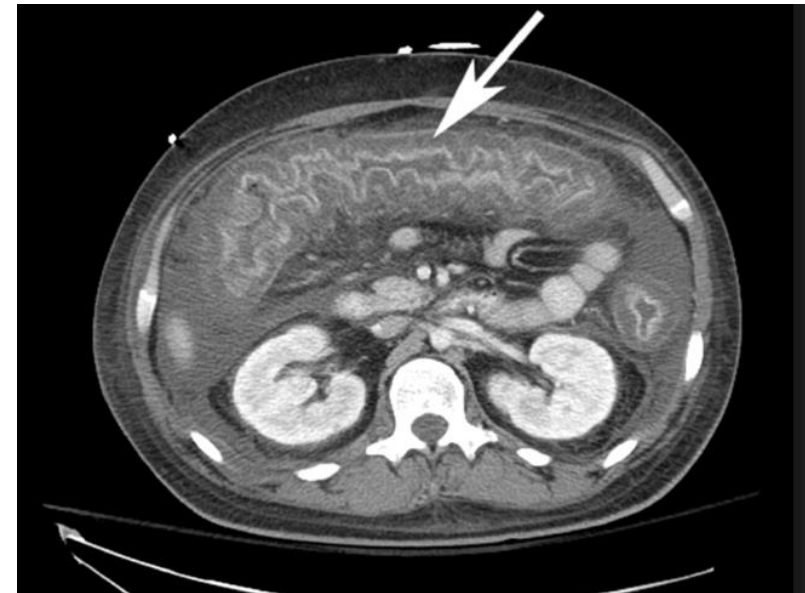
- Grade 3 Diarrhea Differential Diagnoses:
 - Infectious diarrhea (including c-diff)
 - Antibiotic associated diarrhea
 - Colitis secondary to immunotherapy
- Grade 3 Cough v Pneumonitis Differential Diagnoses:
 - Infectious
 - Inflammatory
 - Irritation

Case #1

Chest CT scan:



Abdominal CT scan:



Case #1

- Grade 3 Colitis and Grade 3 Pneumonitis
 - Initiate steroid at 1mg/kg of solumedrol or equivalent
 - Recommend IV steroid initially with colitis symptoms due to gut absorption issues
 - Taper slowly
 - Consider antibiotic prophylaxis during high dose steroid
 - Discontinue immunotherapy

Case #2

- 35 year old man with classic Hodgkin's lymphoma
 - Autologous stem cell transplant 1/25/16
 - Brentuximab Vedotin (Adcetris) 5/1/16-8/1/16
 - Relapsed disease noted on 8/1/16 scans
 - 8/8/16 initiated on Nivolumab 3mg/kg Q2 weeks

Case #2

- 10/3/16 patient presents for C5D1 complaining of fatigue and decreased appetite
 - Denies nausea, vomiting or diarrhea
 - Denies abdominal pain
 - Denies fevers or chills but states “I get cold easily”
 - States that his fatigue does not improve with rest

Case #2

CONSTITUTIONAL SYMPTOMS							Page 1 of 2
		Grade					
Adverse Event	Short Name	1	2	3	4	5	
Fatigue (asthenia, lethargy, malaise)	Fatigue	Mild fatigue over baseline	Moderate or causing difficulty performing some ADL	Severe fatigue interfering with ADL	Disabling	—	

- Grade 2 Fatigue Differential Diagnosis:

- Anemia
- Hepatitis
- Hypothyroidism
- Hypophysitis
- Disease progression
- Poor sleep quality
- Infection

Case #2

- Labs 10/3/16:
 - **Hgb:** 10.5 (12.1-16.3 g/dL) (baseline Hgb 10.9)
 - **LDH:** 261 (124-271 U/L)
 - **TSH:** 8.4 (0.34-5.6 mIU/L)
 - **T3:** 1.7 (2.3-4.2 pg/ml)
 - **T4:** 0.53 (0.89-1.76 ng/dL)
 - **AST:** 38 (12-39 U/L)
 - **ALT:** 50 (7-52 U/L)
 - **Tbili:** 0.5 (0.1-1.3 mg/dL)
 - **Alk Phos:** 105 (39-117 U/L)

Case #2

Investigations					
Adverse Event	Grade				
	1	2	3	4	5
Alanine aminotransferase increased	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN	-
Definition: A finding based on laboratory test results that indicate an increase in the level of alanine aminotransferase (ALT or SGPT) in the blood specimen.					
Alkaline phosphatase increased	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN	-
Definition: A finding based on laboratory test results that indicate an increase in the level of alkaline phosphatase in a blood specimen.					
Aspartate aminotransferase increased	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN	-
Definition: A finding based on laboratory test results that indicate an increase in the level of aspartate aminotransferase (AST or SGOT) in a blood specimen.					
Blood bilirubin increased	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN	>10.0 x ULN	-
Definition: A finding based on laboratory test results that indicate an abnormally high level of bilirubin in the blood. Excess bilirubin is associated with jaundice.					

Case #2

ENDOCRINE							Page 2 of 2
		Grade					
Adverse Event	Short Name	1	2	3	4	5	
Thyroid function, low (hypothyroidism)	Hypothyroidism	Asymptomatic, intervention not indicated	Symptomatic, not interfering with ADL; thyroid replacement indicated	Symptoms interfering with ADL; hospitalization indicated	Life-threatening myxedema coma	Death	

- Grade 2 Hypothyroidism
 - Initiate Levothyroxine at 1.7 mcg/kg PO daily
 - Consider referral to endocrinology
 - Counsel patient that this may not be reversible
 - OK to continue treatment with Nivolumab