Managing Adverse Events Associated with Immuno-oncologic Agents

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Objectives

By the end of this e-course, participants will be able to:

– Understand adverse events and toxicities related to immunotherapy checkpoint inhibitors

– Understand how immune-related Adverse Events (irAEs) present in patients taking checkpoint inhibitors

– Understand ways of managing irAEs as it applies in real-world practice
Adverse Events differ between cytotoxic agents and immuno-oncologic agents

Differences in Mechanism of Action (MOA) between cytotoxic agents and immunotherapies result in different adverse event profiles

Cytotoxic Agents

• Directly kills or prevents cells from dividing (e.g. chemotherapy); lack of selectivity between normal cells and tumor cells causes unwanted toxicities

Immunotherapy

• Stimulates an innate immune response against the tumor resulting in irAEs

Novel immunotherapy agents are becoming the new standard of care in oncology; clinicians will need to understand and learn how to manage irAEs related to these agents
FDA approved immunotherapy checkpoint inhibitors include ipilimumab, nivolumab, and pembrolizumab

- **Ipilimumab**: human, monoclonal antibody that binds to the cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) on T cells.
  - Ipilimumab is indicated for the treatment of unresectable or metastatic melanoma

- **Nivolumab** or **pembrolizumab**: Human monoclonal antibodies directed against the programmed death-1 (PD-1) receptor of the T Cell
  - Nivolumab has indications for use in patients with unresectable or metastatic melanoma and in patients with metastatic squamous or non-squamous non-small cell lung cancer (NSCLC).
  - Pembrolizumab is indicated for the treatment of patients with unresectable or metastatic melanoma
**Immunotherapy checkpoint inhibitors**

*Checkpoint inhibitors*: tumors express “checkpoint” proteins on their cell surface to escape detection from the immune system; targeted inhibition towards these receptors enhances T cell response towards the tumor.
Ipilimumab Adverse Events (melanoma)

*Phase II, randomized, double-blind, dose-ranging study, patients with pretreated advanced melanoma, ipilimumab monotherapy every three weeks for four cycles, followed by maintenance therapy every 3 months*

### Toxicities are dose-related

<table>
<thead>
<tr>
<th>Dose</th>
<th>0.3 mg/kg (n=72)</th>
<th>3 mg/kg* (n=71)</th>
<th>10 mg/kg (n=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Adverse Events (Grade 3-4)</td>
<td>0%</td>
<td>7.0%</td>
<td>25.4%</td>
</tr>
</tbody>
</table>

### Most common Grade 3-4 adverse events:

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>0.3 mg/kg (n=72)</th>
<th>3 mg/kg (n=71)</th>
<th>10 mg/kg (n=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>0</td>
<td>2.8%</td>
<td>15.5%</td>
</tr>
<tr>
<td>Skin</td>
<td>0</td>
<td>1.4%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Endocrine</td>
<td>0</td>
<td>2.8%</td>
<td>1.4%</td>
</tr>
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</table>

### Adverse Events leading to discontinuation (drug-related, Any Grade)

<table>
<thead>
<tr>
<th>Dose</th>
<th>0.3 mg/kg (n=72)</th>
<th>3 mg/kg (n=71)</th>
<th>10 mg/kg (n=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Discontinuation</td>
<td>2.8%</td>
<td>7.0%</td>
<td>15.5%</td>
</tr>
</tbody>
</table>

### Reasons for drug-related discontinuation include:

- 0.3 mg/kg dose: Asthenia and bone pain
- 3 mg/kg dose: enteritis (Grade 2), hypopituitarism, hydrocephalus, confusion, respiratory tract infection, diarrhea (Grade 3)
- 10 mg/kg dose: most frequent was diarrhea (Grade 3)

*Ipilimumab’s indicated dose is 3 mg/kg

(sources: Wolchok et al., 2010; Weber et al., 2015)
Nivolumab Adverse Events (melanoma)

Patients with advanced melanoma who have received greater than 1 but not more than 5 prior systemic cancer therapies enrolled between 2008 and 2012 receiving nivolumab every 2 weeks for up to 96 weeks (n=107)

Toxicities do not appear dose-related

<table>
<thead>
<tr>
<th>% Adverse Events (Grade 3-4) by Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3 mg/kg (n=18)</td>
</tr>
<tr>
<td>3 mg/kg* (n=17)</td>
</tr>
<tr>
<td>10 mg/kg (n=20)</td>
</tr>
<tr>
<td>16.7%</td>
</tr>
<tr>
<td>35.3%</td>
</tr>
<tr>
<td>25.0%</td>
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</tbody>
</table>

* nivolumab’s indicated dose for melanoma is 3 mg/kg

Most common Grade 3-4 adverse events (n=107):

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>1.9%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1.9%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>1.9%</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

Discontinuation rate can vary - in a randomized, open-label trial with 268 patients with unresectable or metastatic melanoma receiving nivolumab 3 mg/kg every 2 weeks; discontinuation from adverse reactions was ~9%

(sources: Topalian et al., 2014; Weber et al., 2015; Opdivo (nivolumab FDA approved label))
Nivolumab Adverse Events (Non-Small Cell Lung Cancer)

Phase I dose-escalation cohort expansion trial for Patients with advanced Non-Small Cell Lung Cancer (NSCLC) (squamous and non-squamous) heavily pre-treated to receive nivolumab once every 2 weeks in 8-week cycles for up to 96 weeks

Toxicities do not appear dose-related

% Any Adverse Events* (Grade 3-4) by Dose

<table>
<thead>
<tr>
<th>Dose</th>
<th>% Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg/kg  (n=33)</td>
<td>15.2%</td>
</tr>
<tr>
<td>3 mg/kg**  (n=37)</td>
<td>13.5%</td>
</tr>
<tr>
<td>10 mg/kg (n=59)</td>
<td>13.6%</td>
</tr>
</tbody>
</table>

* Patients were counted only once for “any adverse event”; data for only those events that were reported in at least 3% of the treated population was presented

** nivolumab’s indicated dose for NSCLC is 3 mg/kg

Most common Grade 3-4 adverse events (n=129):

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>% Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>3.1%</td>
</tr>
<tr>
<td>Decreased CD4 Lymphocytes</td>
<td>2.3%</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

For those patients experiencing treatment-related adverse events of any grade, the most common were fatigue (24%), decreased appetite (12%), and diarrhea (10%)

3 treatment-related deaths were associated with pneumonitis; authors did not observe a relationship between the occurrence of pneumonitis and dose level or treatment duration.

Higher grade select adverse events with immune etiologies were manageable in most cases through drug discontinuation, immune suppressive agents, and/or hormone replacement.

(source: Gettinger et al., 2015)
Pembrolizumab Adverse Events (melanoma)

Phase I trial, patients with advanced melanoma who have progressed after prior ipilimumab therapy, treated with pembrolizumab every 3 weeks

Toxicities do not appear dose-related

% Adverse Events (Grade 3-4) by Dose

<table>
<thead>
<tr>
<th>Dose</th>
<th>2 mg/kg* (n=89)</th>
<th>10 mg/kg (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15%</td>
<td>8%</td>
</tr>
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</table>

* pembrolizumab’s indicated dose for melanoma is 2 mg/kg

Grade 3 fatigue reported in 5 patients in the 2 mg/kg pembrolizumab group, this was the only Grade 3-4 event reported in more than one patient

Adverse Events leading to discontinuation (drug-related, Any Grade)

<table>
<thead>
<tr>
<th>Dose</th>
<th>2 mg/kg (n=89)</th>
<th>10 mg/kg (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.0%</td>
<td>11%</td>
</tr>
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</table>

Most common drug-related adverse events include fatigue,

<table>
<thead>
<tr>
<th>Event</th>
<th>2 mg/kg (n=89)</th>
<th>10 mg/kg (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>32.6%</td>
<td>36.9%</td>
</tr>
<tr>
<td>Pruritis</td>
<td>25.8%</td>
<td>19.0%</td>
</tr>
<tr>
<td>Rash</td>
<td>18.0%</td>
<td>17.9%</td>
</tr>
</tbody>
</table>

(sources: Robert et al., 2014; Weber et al., 2015)
Most irAEs occur within the first 3 months of treatment with an immunotherapy; some occur after the final dose of therapy

- Toxicities may be dose-dependent depending upon the immunotherapy (e.g. ipilimumab)

- irAEs can differ depending upon tumor types

- The severity of the toxicity (Grade 1 – 4) dictates how to manage the irAE

- In general, treatment is either withheld or discontinued in patients experiencing moderate or severe irAEs (Grade 2-4)

- Thyroid function, blood counts, liver function, and metabolic panels are tested/taken during treatment of checkpoint inhibitors

*The following slides will focus on the presentation and management of irAEs as they apply to ipilimumab, nivolumab, and pembrolizumab*
Presentation and Management of Dermatologic irAEs

• Dermatologic irAEs are the most frequently reported Adverse Events; they are typically mild to moderate in severity (<3% are Grade 3 or higher); types of irAEs include:
  – Maculopapular rash and pruritis
  – Vitiligo, alopecia

Management:

**Grade 1 – 2**: symptomatic therapy such as moisturizers, ointments, low-dose topical corticosteroids, antihistamines

**Grade 3 – 4**: evaluate by a dermatologist, administration of systemic corticosteroids (prednisone or equivalent) and drug interruption

Presentation and Management of Enterocolitis / Gastrointestinal irAEs

- Disregulation of GI mucosal immunity can result in diarrhea, colitis, abdominal pain, or blood/mucus in the stool without fever
- Diarrhea is a more common complaint with use of a CTLA-4 inhibitor vs. an anti-PD1

**Management:**

**Grade 1 – 2:** treat symptomatically

**Grade 3 – 4:** discontinue treatment; rule out bowel perforation – if present do not administer corticosteroid; treat patient with high-dose intravenous methylprednisolone; other steroids can be used such as dexamethasone; with no improvement, consider single-dose infliximab

Presentation and Management of Endocrinopathies

• Endocrinopathy irAEs include inflammation of the pituitary, thyroid, or adrenal glands and occurs in <5% of patients, with <3% being Grade 3 or higher; endocrinopathies can present with non-specific symptoms including:
  o Headache and fatigue (most common)
  o Visual field defects
  o Decreased libido
  o Hypotension
  o Mental status change
  o Abdominal pain
  o Unusual bowel habits
  o Abnormal thyroid tests

Management:
Grade 1 – 2: without adrenal crisis, may resolve spontaneously; monitor closely with potential endocrinological consultation; short-term, high dose corticosteroids if needed with relevant hormone replacement

Hypophysitis: high dose corticosteroids; supplementation of affected hormones

Adrenal Crisis: treat as medical emergency, give IV glucocorticoids and IV saline with dextrose

Presentation and Management of Hepatotoxicities

• Inflammatory hepatitis has been reported in patients taking CTLA-4 inhibitors or PD-1 inhibitors. In patients taking ipilimumab, <2% present with hepatotoxicity, ~1% are Grade 3-4. Liver tests should be performed to determine AST (aspartate aminotransferase) or ALT (alanine aminotransferase) levels, most episodes are asymptomatic.

**Management:**

Monitor transaminases and bilirubin prior to each dose to exclude other causes of hepatitis

**Grade 2:** AST or ALT levels > 2.5 times but ≤ 5 times the upper limit of normal (ULN); total bilirubin > 1.5 times but ≤ 3 times the ULN; treatment should be withheld

**Grade 3 or greater:** AST or ALT >5 times the ULN, bilirubin >3 times the ULN; permanently discontinue treatment. Provide high-dose IV corticosteroid therapy; if refractory to corticosteroid treatment, mycophenolate mofetil is recommended

*(sources: Tarhini, 2013; Yervoy (ipilimumab) Immune-mediated Adverse Reaction Management Guide; Postow M., Callahan, M., and Wolchok, J., 2015)*
Presentation and Management of Pneumonitis

- Pneumonitis can present as cough, chest pain, and shortness of breath; imaging should be considered; occurs with both CTLA-4 inhibitor and PD-1 inhibitor use, higher rate of occurrence with anti-PD-1s (~3%)

**Management:**

**Grade 1:** May present without symptoms, but shown on scans

**For moderate to severe symptoms or radiographic findings:** Pulmonary consultation is suggested as well as a bronchoscopy to evaluate for infectious etiology; severe cases may warrant use of IV methylprednisone and the possible consideration of other immunosuppressant agents (e.g. infliximab, mycophenolate mofetil, cyclophosphamide)

Other irAEs

Ocular irAEs:
• Eye inflammation from episcleritis, conjunctivitis, uveitis, ophthalmopathy associated with Graves disease
  • Symptoms: photophobia, pain, dryness, blurred vision
  • Recommended to consult with an ophthalmologist if experiencing visual disturbances
  • Topical corticosteroids may be useful; for Grade 3-4 events, oral corticosteroids may be used

Neurologic irAEs:
• Guillain-Barre Syndrome, inflammatory myopathy, posterior reversible encephalopathy syndrome, aseptic meningitis, enteric neuropathy, transverse myelitis are a few neurologic irAEs associated with checkpoint inhibitors
  • Symptoms: muscle weakness, sensory neuropathies, or motor neuropathies confirmed by examination
  • Serious events are treated with corticosteroids; consultation with a neurologist recommended

Additional irAEs in patients taking immunotherapy checkpoint inhibitors can also include adverse events related to the Kidneys and Pancreas, and can be Hematologic

(sources: Tarhini, 2013; Postow M., Callahan, M., and Wolchok, J., 2015)
Key Takeaways

• Adverse Events differ in patients taking cytotoxic agents versus patients taking immunotherapy checkpoint inhibitors; this is a result of the Immunotherapy’s unique MOA
  – Clinicians need to understand how irAEs present as well as how to manage them to maintain effective use in patients

• Three checkpoint inhibitors are approved by the FDA. irAEs occur including, but not limited to, Dermatologic Toxicities, Enterocolitis / Gastrointestinal irAEs, Endocrinopathies, Hepatotoxicities, and Pneumonitis

• Severity of the toxicity (Grade 1-4) dictates how to manage the irAE; in general, treatment is either withheld or discontinued in patients experiencing moderate or severe irAEs (Grade 2-4)
  – Less severe irAEs can be treated symptomatically; with more severe irAEs often requiring steroid use (e.g. corticosteroids, glucocorticoids)
  – Consultation with a specialist is often recommended
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

• A 67 year old male with stage IV melanoma (lung, adrenal, liver) on a clinical trial utilizing sequential ipilimumab followed by PD1 AB-randomized to receive ipilimumab first.

• Week 7
  – Previously tolerating treatment well
  – Presents for dose 3 ipi
  – Continues to feel well: active, walking, playing golf 2-3 times a week
  – No complaints of diarrhea, cramping abdominal pain or blood per rectum
  – Reminded to call for adverse effects- fatigue, rash, itching, diarrhea, shortness of breath or cough
  – RTC 3 weeks or call for issues
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

• Week 8 (phone call)
  – (5 days post treatment)
  – Patient calls stating he has had diarrhea x 4 days. He is unsure how many episodes per day and he has been taking Imodium sporadically

• Contact MD-
  – Instructions:
    • Imodium- 2 tabs po with first diarrhea of the day, 1 tab with each additional diarrhea, up to 8 tabs a day
    • Lomotil- 1 tab po QID on days with diarrhea
    • Budesonide – three 3 mg tabs po q am x 10 days (take all 10 days- even if diarrhea stops)
    • Call MD if no improvement
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

• Week 8 ½ (phone call)
  – Patient continues with diarrhea
  – Stools are firmer, not as watery as last week
  – Had 3 stools yesterday (continues with Imodium, Lomotil and budesonide) but probably up to 7 stools the day before.
  – Lab report received from PCP-stool positive for occult blood

• Contact MD
  – Instructions- continue Imodium, Lomotil and budesonide
  – Add prednisone taper starting at 80 mg a day, decrease by 10 mg every 3 days. (24 days)
  – Patient to call if no improvement
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

• Week 10 clinic visit on schedule (for dose 4 Ipilimumab)
  – 15 days into steroid taper
  – Diarrhea completely resolved within days after starting steroids
  – Patient feeling well, energy 80-90%, played golf twice last week

• Plan
  – Continue steroid taper
  – Will skip dose 4 ipilimumab
  – Get rescanned as planned and RTC in 3 weeks
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

• **Week 13 clinic visit (post scans, pre PD1 AB)**
  – Off steroids for 10 days
  – 1 episode of diarrhea last week controlled with Imodium
  – Scans show stable disease

• **Plan**
  – Proceed on trial with PD1 AB
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

- Week 26 clinic visit-
  - Has been tolerating PD1 AB without toxicities so far
  - CT scans show a partial response
  - Grade 1 diarrhea – controlled with Imodium
  - Grade 1 elevated Lipase

- Plan
  - Proceed with PD1 AB
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

- Over next 5 months patient had occasional grade 1-2 elevated amylase and/or lipase (asymptomatic)
- Patient was treated on schedule

- Week 47 Clinic visit
  - Patient presents to clinic for PD1 AB on schedule
  - Grade 3 amylase (2-5 x ULN)
  - Grade 4 lipase (> 5 x ULN) – asymptomatic

- Plan-
  - hold PD1 AB
  - Medrol dosepak
  - RTC 2 weeks on schedule (after CT scans)
  - Call asap for indigestion, abdominal pain or discomfort, nausea and/or vomiting or proceed to ER
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

- Week 49 clinic visit
  - Scans show confirmed PR
  - Grade 2 lipase (1.5-2 x ULN) asymptomatic

- Plan
  - proceed with PD1 AB

- Week 51 clinic visit
  - Grade 3 lipase – asymptomatic

- Plan
  - proceed with PD1 AB
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

- Week 64- (ER visit)
  - Presents to ER with abdominal pain, bloating and nausea (no vomiting)
  - Patient had called MD and was instructed to proceed to ER if it did not clear up soon

- Findings in ER
  - Lipase was 1348
  - CT ABD shows inflammation surrounding pancreatic head consistent with pancreatitis

- Treatment:
  - IV solumedrol in house x 2 days
  - D/C home 2 days after admit on a medrol dosepak
  - Amylase at discharge 69, lipase at discharge 300
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

- Week 65 clinic visit
  - Patient feels much better
  - Grade 1 lipase

- Plan
  - Due to admit for acute pancreatitis decision was made to discontinue therapy and continue to monitor patient on trial but off active treatment
  - Complete medrol dosepak
  - Avoid fatty foods and ETOH intake
  - RTC 2 weeks
  - Call clinic for any issues
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

• Week 67 clinic visit
  – Following bland low fat diet with decreased ETOH
  – Back to usual activity (golf 4 times a week)
  – Lipase 197 (grade 3)
  – Amylase 98 (grade 3)

• Plan
  – Check labs at PCP in 2-3 weeks
  – Call asap for any abdominal symptoms

• Week 69
  – Labs at PCP-Lipase 54, amylase 45 (WNL)
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

• Week 84
  – Scans stable
  – Symptoms- new chronic dry cough; no SOB, hemoptysis, increased sputum or DOE

• Findings
  – O2 saturation 99% at rest and after activity
  – CT scan shows possible pneumonitis

• Plan
  – RTC in 6 weeks for an interim CT scan
  – Call asap for worsening pulmonary symptoms or any other issues
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

• Week 90
  – Patient feels good with 90% energy
  – Playing golf daily
  – Cough is the same without change in sputum production
  – Patient denies SOB at rest but does have some DOE

• Findings
  – O2 saturation 97% at rest and 90% after activity
  – CT scan shows progression in pneumonitis
  – PE exam reveals rhonchi bilaterally

• Plan
  – Prednisone 30 day course with a decline by 10 mg every 3 days until finished
  – Add Zantac to Protonix due to known reflux with steroid therapy
  – RTC 2 ½ week for PE and labs
Case Study 1
Colitis Followed by Pancreatitis and Pneumonitis

Week 93
- Feels much better
- Patient is currently at dose of 40 mg in prednisone taper
- Patient has minimal cough but denies SOB, increased sputum, hemoptysys or DOE

• Findings
  - O2 saturation 96% at rest and 95% after activity
  - PE exam reveals lungs clear to auscultation

• Plan-
  - Continue Prednisone 30 day course with a decline by 10 mg every 3 days until finished
  - Continue Zantac and Protonix due to known reflux with steroid therapy
  - RTC 4 weeks for restaging scans on protocol
Case Study 2: Enteritis Then Nephritis

- A 42 year old male with a history of stage IIIC resected melanoma from the right groin with 10/24 positive nodes received 6 doses of nivolumab on an adjuvant trial, then had a re-staging evaluation/scans showing no disease.

- 2 weeks later, just prior to the scheduled 7th dose, he came to clinic complaining of 2 days of anorexia, nausea, one episode of vomiting and one episode of diarrhea. The temp was 101.5 degrees F, creatinine was 1.2, and he mentioned that he had dark urine.
Case Study 2: Enteritis Then Nephritis

• He was admitted to the hospital, had blood cultures, was started on broad spectrum antibiotics and had another diarrheal stool just after admission.

• C Diff titres were taken, and he was hydrated. KUB/upright showed an ileus. CT scan showed no colitis, but some small bowel stranding. The C Diff was positive.
Case Study 2: Enteritis Then Nephritis

• The patient was treated for C diff with vancomycin, but the ileus did not improve, with requirement for narcotics for pain relief

• The patient had 7 diarrheal BMs the next day

• Steroids were instituted 48 hours after admission, with 125 mg Solumedrol given twice a day IVPB, then 125 mg once IVPB
Case Study 2: Enteritis Then Nephritis

- The patient improved rapidly, the diarrhea disappeared, and he was discharged on a 100 mg prednisone taper orally on the 5th day after admission, eating normally.

- He was better when seen a week later, and then 2 weeks later felt well.

- The steroids finished in 40 days, and he returned to work as a PE instructor and coach 2 weeks after discharge, on steroids.
Case Study 2: Enteritis Then Nephritis

- 2 weeks after finishing the steroids, he began to have nausea and anorexia

- 2 days later he developed a fever and contacted the on call physician; he was told to come to be seen at the hospital

- He had a fever to 102 degrees F, Cr of 1.3, dark urine and severe nausea

- The abdominal exam showed minimal diffuse tenderness without rebound noted

- CT scan showed no changes of enteritis or colitis, but stranding around both kidneys
Case Study 2: Enteritis Then Nephritis

• The patient was hydrated and treated with empiric antibiotics; there was no clear diagnosis

• The next morning he still felt poorly, with low grade fevers, and Cr 1.4, taking nothing by mouth. KUB/abdomen upright were unrevealing

• 48 hours after admission, Cr=2.0, with less than 1 liter of urine, feeling a bit improved, with low grade fevers

• The next day his creatinine was 2.8, BUN 12, with continued anorexia, nausea, and vomiting controlled with zofran
Case Study 2: Enteritis Then Nephritis

• He was started on IV solumedrol at 125 mg BID for 2 days; the next day the creatinine was 2.4, then 1.9 the day after.

• He started to take fluids by mouth and was afebrile. He was switched to 120 mg prednisone PO tapering over 48 days, and was discharged home 6 days after admission, tolerating a bland full diet.
Questions?
Register today!
accc-iclio.org
References


Kudchadkar, R. Winship Cancer Institute, Emory University Presentation

Opdivo (nivolumab) FDA Approved Label


