Care Step Pathway – Hepatic Toxicity (immunotherapy-induced inflammation of liver tissue)

Assessment

Look:
- Does the patient appear fatigued or listless?
- Does the patient appear jaundiced?
- Does the patient have yellowing of eyes?
- Does the patient appear icthyic?
- Does the patient appear diaphoretic?
- Does the patient have any ascites?

Listen:
- Change in energy level?
- Change in skin color? Yellowing?
- Change in stock color (paler)?
- Change in urine color (darken/tea colored)?
- Abdominal pain: specifically, right upper quadrant pain?
- Bruising or bleeding more easily?
- Fevers?
- Increased itching?
- Change in mental status?
- Increased sweating?

Recognize:
- Elevation in LFTs
  o AST/SGOT
  o ALT/SGPT
  o Bilirubin (total/direct)
- Alteration in GI function
- Symptoms such as abdominal pain, ascites, somnolence, and jaundice
- Other potential causes (viral, drug toxicity, disease progression)

Grading Toxicity: ULN

<table>
<thead>
<tr>
<th>Grade 1 (Mild)</th>
<th>Grade 2 (Moderate)</th>
<th>Grade 3 (Severe)</th>
<th>Grade 4 (Potentially Life-Threatening)</th>
<th>Grade 5 (Death)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST or ALT:</td>
<td>AST or ALT Abn. Baseline:</td>
<td>AST or ALT:</td>
<td>AST or ALT:</td>
<td>AST or ALT:</td>
</tr>
<tr>
<td>Binilirubin:</td>
<td>&gt;ULN – 3.0× ULN</td>
<td>&gt;3.0× – 5.0× ULN</td>
<td>&gt;5.0× – 20.0× ULN</td>
<td>&gt;20× ULN</td>
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<tr>
<td></td>
<td>&gt;1.5× – 3.0× ULN</td>
<td>&gt;1.5× – 3.0× ULN</td>
<td>&gt;3.0× – 10.0× ULN</td>
<td>&gt;10× ULN</td>
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</tbody>
</table>

Management of Transaminitis (without elevated bilirubin)
Management of Grade 2 or worse transaminitis with bilirubin >1.5x ULN: follow Grade 4 recommendations

Overall Strategy:
- LFTs should be checked and results reviewed prior to each dose of immunotherapy
- Rule out infectious, non-infectious, and malignant causes. Consider assessing for new onset or re-activation of viral hepatitis, medications (acetaminophen, statins, and other hepatotoxic meds, or supplements/herbals), recreational substances (alcohol); consider disease progression

Infliximab infusions are not recommended due to potential hepatotoxic effects

Implementation:
- Check hepatitis labs in any patient with a history of hepatitis
- Institute early identification and evaluation of patient symptoms
- Institute early intervention with lab work and office visit if hepatotoxicity is suspected
- Grade LFTs and any other accompanying symptoms
- As noted in overall strategy, do not use infliximab because of hepatotoxic effects
- Assess patient & family understanding of recommendations and rationale
- Identify barriers to adherence

*Administering Corticosteroids:
Steroid taper instructions/calender as a guide but not an absolute
- Taper should consider patient’s current symptom profile
- Close follow-up in person or by phone, based on individual need & symptomatology
- Steroids cause indigestion; provide antacid therapy daily as gastric ulcer prevention while on steroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage is >20 mg/day)
- Review steroid medication side effects: mood changes (angry, reactive, hyperaware, euphoric, manic), increased appetite, interrupted sleep, oral thrush, fluid retention
- Be alert to recurring symptoms as steroids taper down & report them (taper may need to be adjusted)

Long-term high-dose steroids:
- Consider antimicrobial prophylaxis (sulamethoxazole/trimethoprim double dose M/W/F; single dose if used daily) or alternative if sulf-a-allergic (e.g., atovaquone [Mepron®] 1500 mg po daily)
- Consider additional antiviral and antifungal coverage
- Avoid alcohol/acetaminophen or other hepatotoxins
- If extended steroid use, risk for osteoporosis; initiate calcium and vitamin D supplements

 implementations:  
- Severe abdominal pain, ascites, somnolence, jaundice, mental status changes

ALT = alanine aminotransferase; AST = aspartate aminotransferase; GI = gastrointestinal; LFT = liver function test; po = by mouth; SGOT = serum glutamic oxaloacetic transaminase; SGPT = serum glutamic pyruvic transaminase; ULN = upper limit of normal

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