Grading Toxicty

**Arthralgia**

**Definition:** A disorder characterised by a sensation of marked discomfort in a joint.

**Arthritis**

**Definition:** A disorder characterised by inflammation involving a joint.

**Management**

**Overall Strategy:**

- Assess for other etiologies, such as lytic or osseous metastasis.
- Early intervention to maintain or improve physical function and impact on QOL: symptom control through the treatment of inflammation and pain is often achieved with NSAIDs, corticosteroids, and other adjunct therapies.

**Grading 1 (Mild)**

**Arthralgia**

- Moderate pain, limiting instrumental ADL

**Arthritis**

- Moderate pain with inflammation, erythema, or joint swelling

**Management**

- Identify barriers to adherence
- Assess patient & family understanding of toxicity and rationale for treatment discontinuation
- Anticipate referral to rheumatology for collaborative management and treatment

**Grading 2 (Moderate)**

**Arthralgia**

- Mild pain with inflammation, erythema, or joint swelling; limiting instrumental ADL

**Arthritis**

- Moderate pain associated with signs of inflammation, erythema, or joint swelling; limiting instrumental ADL

**Management**

- Anticipate immunotherapy to continue
- Encourage physical activity
- 30 minutes of low-to-moderate–intensity physical activity 5 days per week can improve physical conditioning, sleep, and decreases pain perception
- For physically inactive patients, advise supervised exercise, resistance training
- Other: yoga, tai chi, Qigong, Pilates, aquatic exercise, focused dance program
- Anticipate use of analgesics
- Low-dose NSAIDs
  - Topical: diclofenac (gel or patch). Best for localized, limited, superficial joint inflammation or for use in patients who cannot tolerate oral NSAIDs
  - Oral: ibuprofen, naproxen, celecoxib
- Anticipate guidance on proper administration
- Assess patient & family understanding of recommendations and rationale
- Identify barriers to adherence

**If symptoms do not improve in 4–6 weeks, escalate to next level of therapy**

**Grading 3 (Severe)**

**Arthralgia**

- Severe pain; limiting self-care ADL

**Arthritis**

- Severe pain associated with signs of inflammation, erythema, or joint swelling; irreversible joint damage; disabling; limiting self-care ADL

**Management**

- Patients should consider patient’s current symptom profile
- Close follow-up in person or by phone, based on individual need & symptomatology
- Steroids cause indigestion; provide antiulcer therapy also gastric ulcer prevention while on steroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage is >10 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 recurrent symptoms as steroids taper down & report them (taper may need to be adjusted)

**Grading 4 (Potentially Life-Threatening)**

**Arthralgia**

- Potentially life-threatening:
  - Pembrolizumab or nivolumab to be withheld to first-occurrence Grade 3 event and permanently discontinued if:
    - Grade 3 event recurs
    - Prednisone >32 mg/day
  - Pembrolizumab or nivolumab to be discontinued for Grade 2 events persisting >12 weeks
  - Prednisone ≤12 weeks
  - Pembrolizumab or nivolumab to be discontinued for any Grade 3 event/4 event
  - High-dose steroids to be used (1 mg/kg) daily (rapid effect within days)
  - Onset of action is rapid, typically within days
  - Progression with corticosteroids in 2 weeks, consider infliximab or localizumab
  - Anticipate referral to rheumatology for collaborative management and treatment

**Arthritis**

- Potentially life-threatening:
  - Pembrolizumab or nivolumab to be withheld to first-occurrence Grade 3 event and permanently discontinued if:
    - Grade 3 event recurs
    - Prednisone >32 mg/day
  - Pembrolizumab or nivolumab to be discontinued for Grade 2 events persisting >12 weeks
  - Prednisone ≤12 weeks
  - Pembrolizumab or nivolumab to be discontinued for any Grade 3 event/4 event
  - High-dose steroids to be used (1 mg/kg) daily (rapid effect within days)
  - Onset of action is rapid, typically within days
  - Progression with corticosteroids in 2 weeks, consider infliximab or localizumab
  - Anticipate referral to rheumatology for collaborative management and treatment

**Grading 5 (Death)**

**Arthritis**

- Potentially life-threatening:
  - Pembrolizumab or nivolumab to be withheld to first-occurrence Grade 3 event and permanently discontinued if:
    - Grade 3 event recurs
    - Prednisone >32 mg/day
  - Pembrolizumab or nivolumab to be discontinued for Grade 2 events persisting >12 weeks
  - Prednisone ≤12 weeks
  - Pembrolizumab or nivolumab to be discontinued for any Grade 3 event/4 event
  - High-dose steroids to be used (1 mg/kg) daily (rapid effect within days)
  - Onset of action is rapid, typically within days
  - Progression with corticosteroids in 2 weeks, consider infliximab or localizumab
  - Anticipate referral to rheumatology for collaborative management and treatment

**Arthralgia**

- Potentially life-threatening:
  - Pembrolizumab or nivolumab to be withheld to first-occurrence Grade 3 event and permanently discontinued if:
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**Implementation:**

- Identify high-risk individuals and those with underlying autoimmune di...