Care Step Pathway - Ocular Toxicity

Nursing Assessment

Look:
- Does the patient look unwell (or ill)?
- Does the patient look uncomfortable?
- Does the patient look jaundiced?
- Is there any eye redness? Drainage? Tearing?
- Is the patient sensitive to light?
- Is there lid or periocular edema?
- Are there skin lesions surrounding the eye(s)?
- Are pupils reactive?
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Listen:
- Patient and family descriptions of ocular health and any current or prior history of eye problems (e.g., glaucoma, retinal issues, eye inflammation)
- Reports of specific eye complaints: redness, watering, drainage, change in acuity, diplopia (double vision), floaters, photophobia?
- When did symptoms start?
- Any recent eye injury, new medications, or exposure to toxic chemicals?
- Does the patient wear contact lenses?
- Is the patient diabetic?
- Associated symptoms: headache, vomiting, nausea?

Recognize:
- Patients at risk for ocular issues (history of glaucoma, dry eyes, uveitis, retinal disease, macular degeneration, or diabetes)
- The specific ocular complaint (if possible) and determine grade
- Other treatment-related symptoms

Grading Toxicity (Overall, Eye Disorders)

Grade 1 (Mild)
Asymptomatic; clinical or diagnostic observations only

Grade 2 (Moderate)
Symptomatic (pain, irritation, photosensitivity, etc.); visual acuity falls to 20/40 or better in affected eye(s); limiting instrumental ADLs

Grade 3 (Severe)
Highly symptomatic (pain, irritation, photosensitivity, etc.), marked decrease in visual acuity (worse than 20/40) in affected eye(s); limiting self-care ADLs

Grade 4 (Potentially sight-threatening)
Blindness (20/200 or worse) in affected eye(s)

Management

Overall Strategy:

- Refer for baseline ophthalmic examination before beginning therapy (ophthalmologist should be made aware that patient is to start combination therapy)
- Follow-up exam if patient develops symptoms
- Advise patient to promptly report any changes in vision or any eye symptoms (and anticipate treatment hold pending further evaluation)
- Identify and closely monitor at-risk patients (including those with a history of glaucoma, dry eyes, uveitis, retinal disease, macular degeneration)
- Promote healthy lifestyle:
  - Diet (potentially including dietary supplements containing omega-3 and omega-6 fatty acids for dry eye syndrome)
  - Smoking cessation, control of comorbidities
  - Encourage use of sunglasses and reduction in sun exposure
  - Promote good hand hygiene
  - In patients with diabetes, promote good control of blood glucose since it reduces risk of retinal disease
- If contact lenses are worn, advise patients to be meticulous about eye hydration, lens hygiene, and not using lenses beyond their disposal time
- Whenever binimetinib is held, the dose of encorafenib should be reduced to less than 300 mg once daily until binimetinib is resumed

Specific Ocular Issues:

- When ocular issues are identified, anticipate management by the treating ophthalmologist (and provide anticipatory guidance/assistance, as appropriate):
  - Keratitis (inflammation of cornea): artificial tears, lubricants, or CS drops, antibiotics
  - Uveitis (inflammation of various portions of the eye): CS drops, beta blockers, alpha antagonists, mydriatic ophthalmic drops
  - Conjunctivitis (inflammation of the interior eyelids): antihistamines, CS, cool compresses, artificial tears, antibiotics if needed
  - Photophobia (oversensitivity to light): sunglasses, dim lights
  - Serous retinal detachment (fluid accumulation under layers of retina): drug hold/dose reduction/discontinuation
  - Retinal vein occlusion (vascular event leading to vision changes, macular edema, glaucoma): anti-VEGF and steroid injection in addition to drug discontinuation
  - Retinal pigment epithelial detachment (bilateral or multifocal separation of the retina from back of eye, leading to sudden vision changes): drug hold/dose reduction/discontinuation

Grade 1 (Mild)

- In general, anticipate referral to ophthalmology
- Specific targeted therapy dose modifications:
  - Uveitis: BRAFi may be continued with caution; MEKi can be continued; obtain prompt visit with ophthalmologist
  - If no response to ocular therapy, withhold encorafenib/binimetinib for up to 6 weeks; if improved, resume at same or lowered dose; if not, permanently discontinue
  - Other ocular adverse events: follow standard dose modifications/holds based on grade
- Support adherence to eye drops/topical therapy

Grade 2 (Moderate)

- Urgent referral to ophthalmology (within 24 hours)
- Specific targeted therapy dose modifications/holds/discontinuations:
  - Uveitis (persistent Grade 2 or >6 weeks duration): hold BRAFi and binimetinib therapy (resume if improved to Grade 0/1)
  - Serous retinopathy: withhold MEKi until visual symptoms improve. Use dose reduction scheme based on severity
  - Retinal vein occlusion: permanently discontinue trametinib and binimetinib
- Retinal pigment epithelial detachment: hold trametinib; reduce dose or discontinue if no improvement after 3 weeks. Withhold binimetinib for up to 10 days; follow dose reduction and discontinuation recommendations
- Assess adherence to eye drops/topical therapy
- Anticipate drug holds/dose modifications of targeted therapy for other moderate ocular toxicities, per prescribing information
- Obtain ophthalmology clearance prior to restarting therapy

Grades 3 or 4 (Severe)

- Urgent referral to ophthalmology (within 24 hours)
- Specific targeted therapy drug modifications/holds/discontinuations:
  - Uveitis (severe): withhold dabrafenib, encorafenib, or binimetinib, permanently discontinue if no improvement within 6 weeks; resume at same or lower dosage if improved
  - Uveitis (sight threatening): permanently discontinue targeted therapy medications
  - Serous retinopathy: withhold MEKi until visual symptoms improve. Use dose reduction scheme based on severity
  - Retinal vein occlusion: permanently discontinue trametinib and binimetinib
  - Retinal pigment epithelial detachment: withhold trametinib; reduce dose or discontinue if no improvement after 3 weeks. Hold binimetinib for up to 10 days; follow dose reduction and discontinuation recommendations
  - Anticipate permanent discontinuation of targeted therapy for other severe ocular toxicities, per prescribing information
  - Assess adherence to eye drops/topical therapy
  - Obtain ophthalmology clearance prior to restarting therapy

RED FLAGS:

- Sudden vision disturbances such as photosensitivity, eye pain, and redness
- Patient is unable to perform regular ADLs because of ocular issues
- Gradual or sudden visual loss
- Concern for permanent loss of vision

ADLs = activities of daily living; CS = corticosteroids; QOL = quality of life