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# Management of anal cancer

This type of cancer is usually linked with human papilloma virus. Here's what you need to know about staging, treatment, and caring for patients receiving chemotherapy, radiation, and immunotherapy.

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Anal cancer is predominately caused by human papilloma virus (HPV) that leads to squamous cell carcinoma (SCC). About 90% of anal cancers are SCC, whereas 10% are adenocarcinoma, basal cell carcinoma, melanoma, and lymphoma. 1,2 This article presents the pathogenesis, risk factors, staging, signs and symptoms, and treatment of anal cancer related to SCC. The adverse reactions and care of patients receiving chemotherapy, radiation, and immunotherapy are emphasized.

### **Epidemiology**

The American Cancer Society estimates that 6,078 women and 3,020 men had anal cancer in the US in 2021, leading to 1,430 deaths. Anal cancer occurs more often in adults older than age 50 and is more common in White women and Black men. The CDC reports that 45% of men and 39% of women in the US have HPV infection. Some HPV subtypes may lead to cancer of the anus, vagina, cervix, penis, and oropharynx.

Risk factors for anal cancer include a history of HPV infection, such as anal, perianal, or genital warts; receptive anal intercourse; multiple sex partners; vulvular, vaginal, or cervical cancer; Crohn disease; immunosuppression from diseases or medications; and smoking (see *Picturing anal cancer*).<sup>2,4</sup>

Multiple studies indicate that the incidence of anal cancer has increased by 2% in the last 10 years, which may be related to more people engaging in receptive anal intercourse. <sup>2,4</sup> The 5-year survival rate depends on the extent of the disease: localized disease, 82%; lymph node invasion, 66%; and metastasis to other body organs, 34%. <sup>5</sup>

## **Physiology**

The anal canal is the distal portion or termination of the large intestine that joins the rectum to the external anal opening.<sup>6</sup> The superior, middle, and inferior rectal arteries, sometimes referred to as hemorrhoidal arteries, perfuse the anal canal. In contrast, the hemorrhoidal plexus facilitates venous drainage through the superior and mesenteric rectal veins to the portal system.<sup>6</sup>

Lymphatic drainage in the anal canal is relative to the dentate line that separates the upper and lower anal canal and where glands empty mucus into the anal canal (see *Visualizing the dentate line*). Lymphatic drainage that occurs through the inferior mesenteric and preaortic lymph nodes superior to the dentate line involves the

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# **Picturing anal cancer**

Anal cancer arising in perianal Crohn disease



Source: Dimick JB. Mulholland & Greenfield's Surgery: Scientific Principles & Practice. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2021.

internal anal sphincter.<sup>6</sup> Lymphatic drainage that occurs through the inguinal lymph nodes inferior to the dentate line involves the external anal sphincter.<sup>6</sup>

Innervation to the internal sphincter is through the autonomic nervous system, whereas the pudendal nerve innervates the external sphincter, puborectalis muscles, and levator ani.<sup>6</sup> The anal sphincters and the puborectalis muscles preserve fecal continence and facilitate bowel movements.<sup>6</sup>

The anal canal is composed of squamous, glandular, and transitional epithelium.<sup>6</sup> The perianal region is surrounded by keratinized stratified squamous epithelium that's described as hair-bearing skin.<sup>6</sup>

## **Pathogenesis**

About 90% of anal malignancies are related to HPV infection, making it the most important risk factor for disease development.<sup>2,4,7</sup> HPV integrates into a person's genome of squamous epithelium.<sup>2,4,7</sup> A genome is a part of our DNA that allows an organism to develop.<sup>2,4,7</sup> There are 200 known HPV subtypes, with types 16 and 18 being the most carcinogenic.<sup>2,4,7</sup> Types 6 and 11 are the most common lesions associated with anal warts.<sup>2,4,7</sup> The treatment of HPV-related anal

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cancer and non-HPV-related anal cancer is similar, but there are some differences (see *Selected non-HPV anal cancers*).<sup>2</sup>

Patients may experience no symptoms initially or a feeling of fullness, pressure, pain, and itching in the anorectal area; bleeding and mucopurulent discharge; fewer bowel movements; straining at the stool; narrowing of stools; and lymph node enlargement in the anal and groin regions. <sup>2,4,7,8</sup> A bleeding lesion above the anal verge may be misdiagnosed as internal hemorrhoidal disease. <sup>2,4,7,8</sup> Prolapsed hemorrhoids, anal warts, and skin tags should be in the differential diagnosis. <sup>2,4,7,8</sup> Patients may present with a lesion in the anal verge or with a perianal lesion that appears as a persistent, nodular, red-scaly mass that bleeds. <sup>2,5-7</sup>

Dysplasia is a general term for abnormal tissues that are premalignant near the anus. <sup>4,9,10</sup> Anal epithelial neoplasia (AIN) or dysplasia is the most common premalignant lesion and is often associated with HPV infection that may progress to SCC. <sup>4,9,10</sup> A biopsy of a lesion may be performed using anoscopy, sigmoidoscopy, colonoscopy, and during examination for perianal lesions. <sup>4,9,10</sup>

A squamous cell lesion in AIN is an abnormal growth of squamous epithelial cells that may have similar histologic findings to cervical intraepithelial neoplasia. <sup>4,9,10</sup> AIN may be a finding at the anal verge when a lesion joins the perianal region to the lower half of the anal canal below the dentate line where flat-like squamous cells are located. <sup>4,9,10</sup> Cube-shaped cells called transitional cells are located above the dentate line where adenocarcinoma may be an underlying pathology. <sup>4,9,10</sup>

The pathologist may perform a stain for HPV-16 p16, a strong biomarker for SCC development. HPV-16 is the highest risk genotype that leads to carcinogenesis. HPV E7, which are proteins that regulate cell cycle, increases invasive SCC incidence. HPV vaccines are safe and effective to prevent most HPV infections, including HPV-16.

A low-grade squamous intraepithelial lesion (LSIL) is a proliferation of squamous cells in the lower half of the epithelium with abnormal epithelial cells known as koilocytes.<sup>9,10</sup> A high-grade squamous intraepithelial lesion (HSIL) consists of a proliferation of squamous cells from the basement membrane through the entire epithelium. 9,10 LSIL and HSIL lesions are described as grade 1, 2, or 3. Grade 1 is a low-grade dysplasia at the lower one-third of the epithelium. Grade 1 may spontaneously regress or progress to higher-grade lesions. Grade 2 is dysplasia reaching the middle one-third of the epithelium.<sup>9,10</sup> Grade 3, or high-grade AIN, is dysplasia reaching the upper onethird of the epithelium.<sup>9,10</sup>

Most researchers refer to grade 3 as the earliest form of SCC called "SCC in situ" or Bowen disease for perianal lesions. 9,10 Grades 2 and 3 are associated with a higher risk of invasive malignancy. 9,10 The overall progression of lesions to invasive malignancy of grades 2 and 3 ranges from 2% to 9% in the general population but may be as high as 50% in immunocompromised people. 2,4,9,10

## **Staging**

The spread of SCC is generally local and regional.<sup>2,14</sup> Anal musculature is involved because the mucosa is near the sphincters.<sup>2,14</sup> SCC encircles the sphincters, causing the sphincters to narrow.<sup>2,14</sup> Sphincter involvement causes the malignancy to spread from the lymphatic vessels to the lymph nodes surrounding the rectum through the superior rectal artery.<sup>2,14</sup> SCC invades the ischioanal fossa, bladder, prostate, and vagina.<sup>2,14</sup> Metastasis to the liver, lung, and bone is common.<sup>2,14</sup>

Computed tomography, MRI, positron emission tomography, and transanal ultrasound and a complete metabolic panel and complete blood cell count are commonly a part of the diagnostic evaluation in conjunction with the tumor staging system to determine the extent of anal cancer.<sup>2,14,15</sup>

The pathologic tumor stage is the most reliable prognostic indicator for anal cancer and provides a direction for treatment. <sup>2,14,15</sup> The American Joint Committee on Cancer (AJCC) created a TNM staging system for anal cancer that includes the primary tumor (T) size rather than the depth of cancer invasion using a I-to-IV scale. <sup>2,14,15</sup> Nodal (N) focuses on nodes involved rather than lymph node involvement. Assessment of metastasis (M) evaluates the distant spread of cancer to other body organs (see *Abbreviated AJCC TNM staging of anal cancer*). <sup>2,14,15</sup>

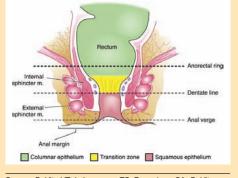
The size of a tumor is crucial to know, but whether the tumor is invasive will more significantly impact a person's morbidity and mortality.  $^{14,15}$  For example, a tumor that's  $\leq 2$  cm is classified as T1 and is stage I. However, if a T1 tumor invades other body organs, such as the liver or lungs, it becomes stage IV. $^{2,14,15}$ 

## **Treatment**

Stage 0 HSIL tumors and surrounding healthy margins are usually excised entirely without the need for radiation or

# **Visualizing the dentate line**

The anal canal begins at the anorectal ring and extends for 4 cm to the anal verge, outside of which lies the anal margin that's visible externally. The upper anal canal is lined by columnar epithelium that transitions to squamous epithelium at the dentate line.



Source: DeVita VT Jr, Lawrence TS, Rosenberg SA. DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology. 9th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

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chemotherapy.<sup>2,7,16</sup> Other surgical options include eradicating HSIL tumors through electrocautery ablation, infrared coagulation, and cryotherapy.<sup>2,7,16</sup> The US Food and Drug Administration hasn't approved topical medications for HSIL.<sup>2,7,16,17</sup> However, there are clinical studies conducted with topical 5-fluorouracil (5-FU) and imiquimod on HSIL tumors.<sup>2,7,16</sup> Surgical excision of stage I and II tumors may be an option when the procedure doesn't interfere with sphincter function.<sup>2,7,16-18</sup>

Chemotherapy with or without radiation therapy is considered the gold standard of treatment and is known as chemoradiation. <sup>2,7,16-18</sup> External beam radiation therapy (EBRT) is a standard approach to deliver high-energy beams to a tumor from outside the body. <sup>18,19</sup> Brachytherapy is high-dose radiation delivered in or near the tumor (internal radiation) and used less frequently than EBRT. <sup>18,19</sup> Patients

may experience decreased appetite, nausea, vomiting, fatigue, dermatitis, anal irritation, changes in bowel movements from anal scar tissue formation, infertility, and sexual dysfunction. <sup>18,19</sup> Patients with persistent or recurrent cancer may require an abdominal-peritoneal resection following chemo-radiation intervention. <sup>18</sup>

5-FU and mitomycin are the first-line systemic chemotherapy to treat stage I, II, and III tumors.<sup>2,18,20</sup> 5-FU is a metabolic inhibitor that interferes with the synthesis of DNA and RNA in rapidly growing cancer cells, causing cell death.<sup>2,18,20</sup> Adverse reactions include nausea, vomiting, diarrhea, stomatitis, alopecia, fatigue, leukopenia, cardiotoxicity, anemia, thrombocytopenia, cerebellar dysfunction, increased lacrimation, photosensitivity, dermatitis, and palmar-plantar erythrodysesthesia (redness, swelling, and blistering on the palms of the hands and soles of the feet,

Selected non-HPV anal cancers				
Adenocarcinoma	Adenocarcinoma is the second most frequent type of anal cancer that arises from the mucosa above the dentate line to the anal canal. It may also begin in the sweat-producing glands of the perianal region. Symptoms may include changes in bowel movements, blood in the stool, fatigue, weight loss, and abdominal pain. Patients are treated with a combination of surgery, chemotherapy, and radiation.			
Basal cell carcinoma	Basal cell carcinoma most often begins at the anal margin but may extend to the anal canal from changes in basaloid epithelial cells. Patients are likely to have a wartlike, nodular tumor in the anal area. Excision of the tumor is the first-line therapy, but cryotherapy, radiation, and chemotherapy are options when excision isn't possible.			
Melanoma	Anal melanoma is the third most frequent site of melanoma after the skin and iris, arising from changes in the melanocytes in the anal mucosa. Tumors near or above the dentate line correspond with advanced disease. Symptoms include pain; itching; a lump in the perianal region; and changes in bowel movements, including a feeling of not emptying the bowel after a bowel movement. Patients undergo surgery, radiation, immunotherapy, and targeted therapy. Melanoma doesn't generally respond therapeutically to traditional chemotherapy.			
Lymphoma	Anal and rectal lymphoma often occur at the same time and are usually non-Hodgkin lymphoma. Lymphoid tissue engulfing anal glands and sphincters can lead to abscess formation. Symptoms include abdominal pain, fatigue, fever, and changes in bowel movements. Treatment may include chemotherapy, radiation, immunotherapy, and targeted therapies.			

sometimes referred to as a hand-foot syndrome). <sup>2,18,20</sup>

Mitomycin is an antitumor antibiotic that inhibits DNA synthesis causing the death of cancer cells. <sup>2,18,20</sup> Adverse reactions include nausea, vomiting, stomatitis, desquamation (peeling of the skin), pulmonary toxicity, and leukopenia. <sup>2,18,20</sup> Hemolytic uremic syndrome may occur, which is progressive renal failure, anemia, and thrombocytopenia. <sup>2,18,20</sup>

Cisplatin, capecitabine, and leucovorin are additional chemotherapeutic agents that may be considered in combination with 5-FU.<sup>2,18</sup>

Immunotherapy may be an option in stage IV with or without radiation or systemic chemotherapy.<sup>2,18,21</sup> Immunotherapy strengthens a person's immune system to recognize, attack, and destroy cancer cells.<sup>21</sup> Immune checkpoint inhibitors

(ICIs) are a type of immunotherapy that's used in stage IV anal cancer.<sup>21</sup> ICIs block proteins that modulate the immune system to prevent T lymphocytes from recognizing and destroying cancer cells.<sup>21</sup> Two examples of ICI agents are nivolumab and pembrolizumab, which are also known as antiprogrammed cell death protein 1 or PD-1.<sup>21,22</sup> Adverse reactions include arthralgia, nausea, diarrhea, constipation, abdominal pain, pneumonitis, myocarditis, fatigue, mental status changes, itching, rashes, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis, anemia, bleeding, elevated liver enzymes, electrolyte imbalances, thyroid dysfunction, nephritis, inflammation of the pituitary gland (hypophysitis), and adrenal insufficiency. 21-23 ICIs stimulate autoimmune activity, resulting in a systemic inflammatory reaction.<sup>21</sup> Patients may receive

Stage	Tumor (T)	Node (N)	Metastasis (M)	Explanation
0	Tis	0	0	Tumor in situ; high-grade intraepithelial lesion
I	T1	N0	M0	Tumor ≤ 2 cm; no lymph node involvement or distant metastasis
IIA	T2	N0	MO	Tumor > 2 cm but ≤ 5 cm; no lymph node involvement or distant metastasis
IIB	Т3	N0	M0	Tumor > 5 cm; no lymph node involvement or distant metastasis
IIIA	T1-2	N1	M0	Tumor meets either T1 or T2 criteria (size) and involves invasion of lymph nodes, but there isn't distant metastasis
IIIB	Т4	N0	МО	Tumor is of any size and invading nearby organs, such as the urethra, bladder, prostate, and vagina, but not to nearby lymph nodes or distant sites
IIIC	T3-4	N1	МО	Tumor is > 5 cm and has spread to the lymph nodes around the rectum, but not distant sites or has spread to the urethra, bladder, prostate, vagina, and lymph nodes around the rectum, but not distant sites
IV	Any T	N1	M1	Tumor may or may not have invaded nearby organs or lymph nodes, but it has spread to distant organs, such as the liver and lungs

immunosuppression medications to offset the increase in autoimmune activity with ICIs.<sup>21</sup> For example, patients may receive corticosteroids or steroid-sparing immunosuppression medications such as mycophenolate.<sup>21</sup>

Ongoing studies indicate that targeted therapies may be beneficial in advanced SCC anal cancer and eventually included in the treatment algorithm. <sup>16</sup> For example, agents that target vascular endothelial growth factor receptors reduce blood supply to a tumor, which causes the tumor to

patient to use condoms during sex, particularly during anal intercourse, and limit sexual partners. <sup>25</sup> HPV vaccines are available to protect people who haven't been sexually active from infections. <sup>25</sup> However, people who are sexually active and have an HPV infection, particularly with HPV types 16 and 18, will also benefit from vaccination to prevent further infection, particularly with types 31, 33, 45, 52, and 58.<sup>2,5-7,10,25</sup>

A 5-FU and mitomycin chemotherapy regimen is administered I.V. in a vessel with well-established blood





Caring for a patient with anal cancer requires an interprofessional approach.

die. <sup>16</sup> A second example is agents that target epidermal growth factor receptors, which inhibit the growth of cancer cells. <sup>16</sup>

## **Priority management strategies**

Caring for a patient with anal cancer requires an interprofessional approach.<sup>24</sup> Perform a thorough health history interview and head-to-toe assessment focusing on the anus and perianal region for any lesions.<sup>27</sup> Also assess for comorbidities; a history of cancer; medication regimen; and social history, including smoking and sexual practices.<sup>2,7</sup> Asking the patient about sexual practices is very personal and should be conducted in a kind, gentle, respectful, and nonjudgmental manner.<sup>2,7</sup>

A digital rectal exam and anoscopy to visualize the anal mucosa and obtain a biopsy of suspicious lesions will be performed during the initial assessment.<sup>2,7</sup> Biopsy results that include HPV-driven lesions should be discussed with the patient.<sup>2,7</sup> For example, encourage the

return.<sup>20,24,26,27</sup> Extravasation of these vesicant agents must be avoided.<sup>20,24,26,27</sup> Expected adverse reactions are nausea, vomiting, and diarrhea.<sup>20,24,26,27</sup> Nausea and vomiting are treated with antiemetics and diarrhea with antidiarrhea medications, including mild opioids.<sup>20,24,26,27</sup>

Patients should report any sores on the lips and in the mouth.<sup>20,24,26,27</sup> Antibiotics or antifungals may be prescribed to decrease oral inflammation and pain.<sup>20,24,26,27</sup> Rinsing the mouth with a mixture of water and baking soda, eating soft foods, avoiding spicy and salty foods, using a soft toothbrush, practicing good oral hygiene, and staying hydrated will help manage symptoms.<sup>20,24,26,27</sup>

Patients should also report numbness and tingling of the hands and feet from peripheral neuropathy because 5-FU causes inflammation of nerves. <sup>20,24,26,27</sup> Antidepressant and antiseizure medications that target the nerves may be helpful to manage nerve pain. <sup>20,24,26,27</sup> Avoiding alcohol and

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smoking, wearing shoes with soft socks to protect the feet, removing loose rugs, and checking the temperature of bathwater with an elbow are important measures to ensure comfort and safety.<sup>20,24,26,27</sup>

Patients should protect the skin, including the conjunctiva and scalp secondary to alopecia, by limiting exposure to the sun or other light sources. <sup>20,24,26-28</sup> Using a sun protection factor of 30 and above is beneficial. <sup>20,24,26-28</sup> Pain and discomfort from rashes and lesions, including hand-foot skin reactions, are managed with emollient creams, anesthetic creams, and medicated baths. <sup>20,24,26-28</sup> Soaking the feet and hands in Epsom salts is soothing in hand-foot skin reactions. <sup>20,24,26-28</sup>

Severe adverse reactions and toxicity from the combination of 5-FU and mitomycin may occur.<sup>2,24,26,27</sup> Neutropenia may predispose the patient to infection. 20,24,26,27 Patients should report fever or sore throat and increasing fatigue that may indicate infection. 20,24,26,27 Patients should avoid sick people and crowds, use good body hygiene, and wear a mask.<sup>20,24,26,27</sup> Anemia results from a low red blood cell count, and easy bruising and bleeding result from a reduction in platelets.<sup>20,24,26,27</sup> Conversely, chemotherapy may also cause thrombosis. 20,24,26,27 Patients should report any redness, pain, and swelling in the legs immediately.<sup>20,24,26,27</sup>

Chest pain, cough, and shortness of breath may indicate a pulmonary embolus or myocarditis, interstitial pneumonia, or pulmonary fibrosis secondary to cardiovascular and pulmonary toxicity. <sup>20,24,26,27</sup> Assess breath sounds, respiratory rate and depth, oxygen saturation, and cardiac rate and rhythm that may indicate abnormalities associated with cardiopulmonary toxicity. <sup>20,24,26,27</sup>

Increased liver enzymes and bilirubin may indicate hepatotoxicity. <sup>20,24,26,27</sup> Increasing fatigue and onset of bleeding may indicate hemolytic uremic syndrome, especially in the presence of abnormal renal function studies. <sup>20,24,26,27</sup> Symptoms and conditions should improve with

reducing the dosage or discontinuing the 5-FU and mitomycin regimen.<sup>20,24,26,27</sup>

Patients receiving radiation therapy may experience fatigue from anemia and should spread activities out evenly throughout the day to conserve energy.<sup>24,29,30</sup> Low platelets may cause the patient to bruise and bleed easilv.24,29,30 Patients should avoid activities or situations that traumatize the skin.<sup>24,29,30</sup> Low white blood cell count predisposes the patient to infections. 24,29,30 Patients should avoid sick people and crowds, use good body hygiene, wear a mask, and report fever or other signs of infection.<sup>24,29,30</sup> Anorexia, nausea, vomiting, and diarrhea are common.<sup>24,29,30</sup> Patients should take antiemetics and antidiarrhea medications as prescribed, consume small meals throughout the day, and drink a sufficient amount of water. 24,29,30

Radiation therapy causes inflammation of the skin resembling a sunburn, including the anal region and sphincters. <sup>24</sup>,29,30 Inflammation causes the sphincters to become stenotic, affecting bowel continence. <sup>24</sup>,29,30 Emollients, anesthetic creams, and medicated baths may be ordered to decrease inflammation and pain. <sup>24</sup>,29,30 Staying hydrated and using daily fiber supplements with a balanced diet is helpful. <sup>24</sup>,29,30

Radiation may also cause inflammation of the bladder lining (cystitis). <sup>24,29,30</sup> Patients may have hematuria and painful urination. <sup>24,29,30</sup> Drinking plenty of fluids, particularly water and juices such as cranberry juice, is helpful. <sup>24,29,30</sup>

Drying and thinning of the vaginal mucosa is common. <sup>24,29,30</sup> Vaginal lubricants and dilators help increase vaginal tone and pliability so sexual intercourse is possible. <sup>24,29,30</sup> Radiation therapy causes erectile dysfunction because of inflammation of the nerves and blood vessels in the penis and a decrease in testosterone. <sup>24,29,30</sup> The skin of the penis may also be inflamed, causing pain with an erection and sexual intercourse. <sup>24,29,30</sup> Lubricants and emollients applied to the penis may be helpful. <sup>24,29,30</sup> Phosphodiesterase-5 inhibitors, such as sildenafil, may be helpful to achieve an

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erection.<sup>24,29,30</sup> Fatigue, pain, discomfort, and depression associated with chronic illness in anal cancer are also reasons why people experience sexual dysfunction. Infertility is possible in women and men.<sup>24,29,30</sup>

The most common adverse reactions of immunotherapy in anal cancer are dermatologic manifestations that affect the patient's quality of life. <sup>28,31</sup> A maculopapular or pruritic rash may appear for weeks to months after initiation of therapy. <sup>28,31</sup> To manage the dermatologic manifestations, patients should drink plenty of water; avoid alcohol and smoking; and use emollient creams, anesthetic creams, and medicated baths. <sup>28,31</sup> Patients should also use mild soap for sensitive skin and avoid perfumes, deodorants, and cosmetics. <sup>28,31</sup> Antidepressants, antihistamines, and mild sedatives may be prescribed to alleviate pruritus. <sup>28,31</sup>

SJS is a mucocutaneous hypersensitivity reaction that causes sloughing and blistering of the skin.<sup>22</sup> Toxic epidermal necrolysis is a severe and life-threatening form of SJS that causes widespread blistering, peeling, and sloughing of the skin and includes the eyes, mouth, and vagina. Infection of lesions and sepsis may ensue, leading to organ failure.<sup>22</sup> Corticosteroids, antibiotics, fluids and electrolytes, nutritional support, pain management, and consultation with wound management specialists are treatment strategies.<sup>22,24</sup>

Patients should be assessed for hypophysitis, including excessive thirst and urination, headache, weight changes, and mental status changes. Mental status changes may occur from hypophysitis and corticosteroids used to offset the increase in autoimmune activity from ICIs. 21,31

Renal involvement may be manifested by an increase in serum creatinine, a decrease in urinary output, edema, and hematuria. <sup>21,31</sup> Elevated liver enzymes and bilirubin may indicate immune-mediated hepatitis (not viral hepatitis). <sup>21,23,31</sup> Patients should also be assessed for immune-mediated colitis with abdominal pain, diarrhea, and blood or mucus in the stool. Thyroid function

tests should be assessed, indicating an immune-mediated reaction.<sup>21,31</sup> Monitoring electrolytes, cholesterol, triglycerides, and an elevation in blood glucose and BP are also interventions.<sup>21,31</sup>

## **Achieving the best outcome**

The main pathology of anal cancer is HPV infection leading to SCC. Risk reduction of HPV infection through patient education and early recognition and intervention will promote the best outcomes in anal cancer. Treatment strategies for HSIL stage 0 tumors usually present few challenges for the patient. However, stage I, II, III, and IV treatment strategies involving chemotherapy, radiation, and immunotherapy require an interprofessional team to help the patient navigate through the adverse reactions to these treatments to achieve the best possible quality of life.

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