Dermatologic Infections in Cancer Patients

Mona Gandhi, Joaquin C. Brieva and Mario E. Lacouture

Abstract

Dermatologic infections are among the most commonly experienced complications of cancer and anti-cancer therapy. Alterations in host immune function secondary to the underlying malignant process and/or its treatment have been linked to an increase in the risk of infections. The skin and its appendages (i.e., hair and nails) represent the first line of defense against infectious microorganism; its dysfunction as a physical barrier and an immunologic organ in cancer patients leads to an increased susceptibility to infectious organisms. Moreover, a cancer patients' vulnerable state facilitates dissemination of infections to other sites, secondarily involving the skin. This chapter delineates dermatologic infections that are unique to cancer patients as a result of their underlying malignancies and associated comorbidities as well as those resulting from antineoplastic therapies.

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M. Gandhi
Division of Dermatology, John H. Stroger, Jr. Hospital of Cook County, 1900 W. Polk Street, Administration Building, Room 519, Chicago, IL 60612, USA
e-mail: mona.gandhi1@gmail.com

J. C. Brieva
Department Matology, NMH, 676 N. St. clair #16, Chicago, IL 60611, USA
e-mail: JBrieva@nmff.org

M. E. Lacouture (✉)
Department of Dermatology, Memorial Sloan Kettering Cancer Center, 160 E. 53rd St, Suite 228, New York, NY 10022, USA
e-mail: lacoutum@mskcc.org

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1 Introduction

Dermatologic infections are among the most commonly experienced complications of cancer and anti-cancer therapy. Alterations in host immune function secondary to the underlying malignant process and/or its treatment have been linked to an increase in the risk of infections [1]. The skin and its appendages (i.e., hair and nails) represent the first line of defense against infectious microorganism; its dysfunction as a physical barrier and an immunologic organ in cancer patients leads to an increased susceptibility to infectious organisms. Moreover, a cancer patient's vulnerable state facilitates dissemination of infections to other sites, secondarily involving the skin. This chapter delineates dermatologic infections that are unique to cancer patients as a result of their underlying malignancies and associated comorbidities as well as those resulting from antineoplastic therapies (Table 1, Fig. 1).

Table 1 Dermatologic infections by cancer type

Cancer type	Clinical presentation or diagnosis	Pathogen(s)
Adult hematologic malignancies	Paronychia, subcutaneous nodules, abscesses, folliculitis, ulcers, and eschars	*Aspergillus, Mucor, Rhizopus, Fusarium,* and Phaeohyphomycosis
	Vesicles in a dermatomal distribution	Varicella zoster virus
	Clusters of vesicles	Herpes simplex types 1 and 2
	Erythematous, tender plaques, papules, or subcutaneous nodule (skin and soft tissue infections)	*Staphylococcus aureus*
		Cryptococcus neoformans
		Toxoplasma gondii
		Acanthamoeba
		Cytomegalovirus
	Intertrigo, rash, vaginitis, balanitis, and paronychia	*Candida albicans, Candida tropicalis, Candida glabrata, Candida krusei, Candida parapsilosis, and Candida lusitaniae*
Cutaneous T-cell lymphoma/Sezary syndrome	Erythematous, tender plaques, papules, or subcutaneous nodule (skin and soft tissue infections)	*Staphylococcus aureus*
Pediatric hematologic malignancies	Erythematous, tender plaques, papules, or subcutaneous nodule (skin and soft tissue infections)	*Corynebacterium bovis and Corynebacterium jeikeium*
	Metastatic cellulitis and mucocutaneous ulcers	*Stenotrophomonas maltophilia*
Pediatric solid tumors	Skin and soft tissue infection	*Mycobacterium* spp. *and Corynebacterium* spp.
Pediatric brain tumors	Skin and soft tissue infection	*Corynebacterium aquaticum*
Adult solid tumor	Erythematous, tender plaques, papules, or subcutaneous nodule (skin and soft tissue infections)	*Klebsiella pneumoniae, Escherichia coli, and Pseudomonas aeruginosa*
	Erythematous, tender plaques, papules, or subcutaneous nodule (skin and soft tissue infections)	*Staphylococcus aureus*
	Neutrophilic eccrine hidradenitis	*Serratia marcescens, Staphylococcus aureus, and Enterobacter cloacae*
	Intertrigo, rash, vaginitis, balanitis, and paronychia	*Candida albicans, Candida tropicalis,Candida glabrata, Candida krusei, Candida parapsilosis, and Candida lusitaniae*

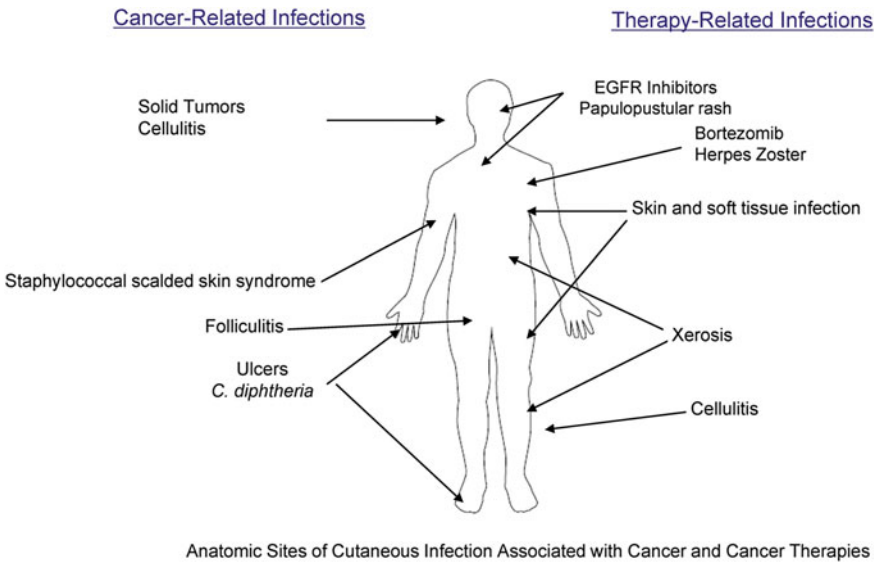

Fig. 1 Anatomical classification of cutaneous infection associated with cancer and cancer therapies

2 Bacterial Dermatologic Infections

2.1 Gram-Positive Infections

2.1.1 *Staphylococcus aureus* Skin and Soft Tissue Infections

Skin and soft tissue infections (SSTI) comprise 85–95 % of all infections caused by *Staphylococcus aureus* in the community [2, 3]. Notably, presence of an underlying malignancy is an independent risk factor for skin and soft tissue staphylococcal infection [2]. It has been demonstrated that 23 % of all bacteremic episodes seen in cancer patients are caused by *S. aureus*, and SSTI are the source in 60 % of cases, with only 6 % associated with granuloctyopenia [2, 4]. Conversely, staphylococcal scalded skin syndrome (SSSS), which is characterized by an acute, generalized exfoliation of the skin following erythematous plaques, has rarely been reported in the oncology setting, with only one case of a patient with T-lymphoblastic non-Hodgkin's lymphoma. The two epidermolytic exotoxins, exfoliatins A and B, which are synthesized by *S. aureus*, are proteases that cleave desmoglein 1, resulting in epidermal detachment between the stratum granulosum and the stratum spinosum. Whereas SSSS is rare in adults with cancer, it can occur in immunocompromised patients and those with renal disease [5].

Of 709 adult and pediatric patients having undergone allogenic stem cell transplantation (SCT), the incidence of late (occurring greater than 50 days post-

transplant) *S. aureus* bacteremia was found to be 6/100,000 patient-days [6]. Of the patients who developed bacteremia, 84 % were community acquired and 40 % were secondary to a focal infection. Risk factors for late *S. aureus* bacteremia included acute or chronic skin graft vs. host disease, corticosteroid use, liver dysfunction, and prolonged hospital stay. Based on this analysis, prophylactic anti-staphylococcal antibiotics can be advocated in the high-risk allogeneic stem cell transplant patients set forth previously [6].

S. aureus is a known colonizer of the nares, axilla, and intertriginous, inguinal, and perineal areas. In healthy adults, carrier rates are approximately 11–32 % [7]. Of 106 patients with mycosis fungoides (MF) and Sezary syndrome (SS), 42 % had cultures positive for *S. aureus* with 5 % of the cultures being positive for methicillin-resistant *S. aureus* (MRSA). The *S. aureus* skin colonization rate in MF/SS patients (42 %) was found to be higher than the 28 % reported in the general population and lower than that found in patients with psoriasis (48 %) [7]. Antibiotic therapy and sodium hyperchlorite baths [8] results in partial clearance of *S. aureus* colonization, both of which are noteworthy observations, as bacteremia and bacterial pneumonia are the most common causes of death in patients with MF and SS [7, 9]. In addition, *S. aureus* colonization in patients with cutaneous T-cell lymphoma (CTCL) was found to be directly related to a small increase in body surface area of CTCL involvement ($P = 0.05$) [8]. Increased rates of infection in these patients are hypothesized to occur as a result of an impaired skin barrier as well as a decrease in the function of normal circulating T cells, resulting in immunosuppression [8]. Infrequently, other organisms found in the skin and nares of such patients can include group B B-hemolytic *Streptococcus, Propionibacterium acnes, Bordetella, Haemophilus, Enterococcus, Escherichia coli, Pseudomonas, Serratia marcescens,* and *Pantoea agglomerans* [7].

2.1.2 Corynebacteria Infections: Non-healing Ulcers

Corynebacterium species are normal skin flora, but in the immunocompromised host, these gram-positive bacteria can be pathogenic due to higher colonization rates and increased antibiotic resistance [10]. *Corynebacterium diphtheriae* can cause painful, non-healing skin ulcers. Initially, lesions are vesicular, but with time, they become punched out and may become covered by an eschar [10].

In a case series of 16 pediatric oncology patients, five had skin and soft tissue infections caused by *C. diphtheriae*, three were central venous catheter associated, and two involved post-surgical wound sites. Of those with infections, three of the children had solid tumors and the remaining two had a hematologic malignancy, and all presented with soft tissue inflammation and fever. After initiation of antibiotic therapy, symptoms resolved within a median time of 48 h [11]. Notably, infection with *Corynebacterium* occurs late in the course of anti-cancer therapy and patients may develop symptoms as outpatients.

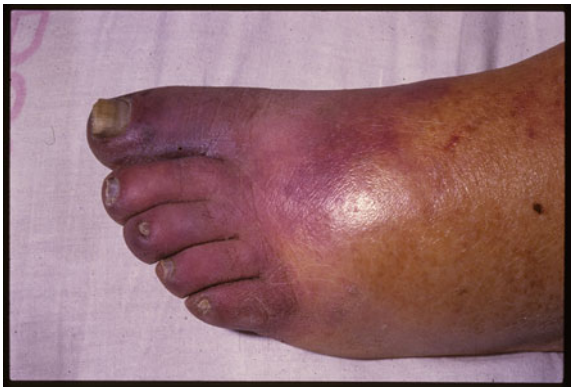

Fig. 2 Gram-negative cellulitis infection

2.2 Gram-Negative Skin and Soft Tissue Infections

2.2.1 Cellulitis and Wound Infections

In 772 hospitalized patients with both leukemic and solid tumors, 185 gram-negative bacterial isolates were found at sites of skin infection. Over half (64.5 %) of the gram-negative nosocomial infections in solid tumor patients affected their skin and included pathogens including *Klebsiella pneumonia* (25.4 %), *E. coli* (22.2 %), *and Pseudomonas aeruginosa* (18.9 %) (Fig. 2) [12]. In contrast, no gram-negative isolates were found in leukemic patients. Treatment of nosocomial gram-negative skin and soft tissue infections are based on cultures and antimicrobial sensitivities [12].

2.2.2 Neutrophilic Eccrine Hidradenitis

Neutrophilic eccrine hidradenitis (NEH), or inflammation of the excretory ducts of eccrine (sweat) glands, may occur as a result of therapy with cytosine arabosinide and granulocyte colony-stimulating factor [13] or secondary to bacterial infection (e.g., *S. aureus, Enterobacter cloacae, S. marcescens).* Clinically, NEH presents as crops of small, indolent, erythematous papules located on legs, thighs, and abdomen. Skin histology reveals focal necrosis of eccrine secretory coils extending to the excretory ducts with a neutrophilic infiltrate [13]. In cases where infection is the culprit, pathogenic microorganisms are also identified through gram stain and/or culture. When an infectious origin is identified, treatment with antibiotics is indicated, and topical corticosteroids are indicated when caused by cytotoxic chemotherapy.

2.2.3 *Stenotrophomonas maltophilia* Skin Infection

Stenotrophomonas maltophilia is an aerobic, gram-negative bacterium which is ubiquitous in aqueous environments, including water, urine, or respiratory secretions. It has been implicated in the cause of multiple SSTI in cancer patients including primary cellulitis, nodular skin lesions, gangrenous cellulitis, soft tissue necrosis, ecthyma gangrenosum, and mucocutaneous ulcers [14]. *S. maltophilia*

frequently colonizes breathing devices such as endotracheal or tracheostomy tubes, the respiratory tract, and indwelling urinary or intravenous catheters. Metastatic cellulitis is a form of cellulitis with tender, nodular, erythematous, and warm subcutaneous infiltrates surrounded by areas of skin inflammation usually located on limbs and chest [14]. Primary cellulitis is characterized by widespread tender erythema without distinct borders. Mucocutaneous infections with *S. maltophilia* have been reported in association with neutropenia, immunosuppression, prolonged hospital stay, intravenous catheter use, broad-spectrum antibiotics, and hematologic malignancies [14]. Clinical findings include ulceration of gingiva, lips, and buccal mucosa. Recommended treatment is trimethoprim–sulfamethoxazole, ticarcillin–clavulanate, or fluoroquinolones based on the results of antimicrobial susceptibility testing, but prognosis can be poor due to severe underlying immunosuppresion [14, 15].

3 Fungal Dermatologic Infections

There are two types of cutaneous fungal infections: primary, which develop *de novo* at a cutaneous site, and secondary which are caused by hematogenous spread of a fungal pathogen [16–18]. Neutropenic patients, especially those with leukemia and lymphoma who have undergone a SCT, are at highest risk to develop cutaneous fungal infections [16].

3.1 Cutaneous Candidiasis

In the majority of cancer patients, cutaneous candidiasis does not differ in presentation between the immunocompromised and immunocompetent host. Common manifestations include intertrigo, rash, vaginitis, balanitis, and paronychia [16]. For identification by light microscopy, a scraping or swab of the affected area is placed on a slide with 10 % potassium hydroxide (KOH) solution and specimens will show a deep dermal and subcutaneous necrosis accompanied by acute neutrophilic inflammation. Infectious organisms can be seen on routine hematoxylin–eosin (H and E); but cultures are recommended to confirm presence of pathogen.

Cutaneous candidiasis is caused by 13 different candidal species, including *Candida albicans, Candida tropicalis, Candida glabrata, Candida krusei, Candida parapsilosis,* and *Candida lusitaniae*, with *C. albicans* accounting for over half of the isolates recovered from infected patients. However, recent epidemiological data reveal a shift from *C. albicans* to the non-*albicans Candida* species, specifically *C. glabrata* and *C. krusei* [19]. Clinically, superficial pustules and vesicles are evidenced, and histology shows pseudohyphae and hyphae in the stratum corneum [19]. Patients with solid tumors, acute leukemia, and hematological cancer patients on antifungal prophylaxis are at significant risk for non-*albicans* candidemia and subsequent cutaneous infection [19].

3.2 Cutaneous Cryptococcal Infection

There are two forms of cutaneous cryptococcal infection: primary cutaneous cryptococcosis and cutaneous manifestation due to hematogenous dissemination, also known as secondary cutaneous cryptococcosis [20]. Clinically, a tender patch or plaque with ulceration, typically on an extremity, is observed, with regional lymphadenopathy. Risk factors include hematologic malignancies, especially when corticosteroids and polychemotherapy is being administered; however, granulocytopenia is the greatest risk factor for fungal infection [20]. Secondary cutaneous cryptococcosis is seen in 10–20 % of cases of systemic disease, which is most often caused by hematogenous spread of *Cryptococcus neoformans* after pulmonary inoculation. The skin is involved in 10–20 % of cases [20]. Diagnosis is achieved after identifying *C. neoformans* on biopsy, culture, or histological examination showing the spherical budding yeast within edema and a polymorphous inflammatory infiltrate [21]. Treatment consists of a course lipid-based amphotericin therapy or oral fluconazole, but in severe cases, life-long maintenance therapy is required. Risk factors are multiple and include the following: coexisting HIV infection, corticosteroid therapy, malignancy, autoimmune disease, and immune system disorder with CD4+ lymphopenia [21].

3.3 Opportunistic Cutaneous Fungal Infections

Aspergillus, Mucor, Rhizopus, and *Fusarium* are opportunistic fungi that are responsible for primary cutaneous infections in hospitalized neutropenic patients. Intravenous catheters, prolonged use of corticosteroids, and occlusive dressings contribute to these uncommon infections (Fig. 3) [16]. The opportunistic fungal pathogens can cause a variety of cutaneous lesions, including paronychia, subcutaneous nodules, abscesses, and folliculitis. Fungal paronychia presents with inflammation surrounding the nail plate accompanied by pain. *Fusarium* and *Aspergillus* can cause digital eschars after minor trauma to the digit [16, 22]. Eschars and ulcers can also occur on lower extremities and sites of venous stasis. Diagnosis is confirmed with skin biopsy; positive culture alone does not confirm the presence of an infection. Primary skin infection leading to hematogenous dissemination is rare but is associated with mortality. In a case series of 35 adult cancer patients who developed *Fusarium* skin lesions, the following hazards and physical findings were identified: hematologic malignancy, severe neutropenia, digital paronychia, presence of digital eschar, and disseminated skin lesions [23, 24]. Treatment for cutaneous lesions is with prolonged, systemic antifungal therapy. For the majority, disseminated mold infections are fatal unless neutropenia improves. In these instances, granulocyte colony-stimulating factor, granulocyte–macrophage colony-stimulating factor, white blood cell transfusions, and interferon-γ may provide some benefit [16].

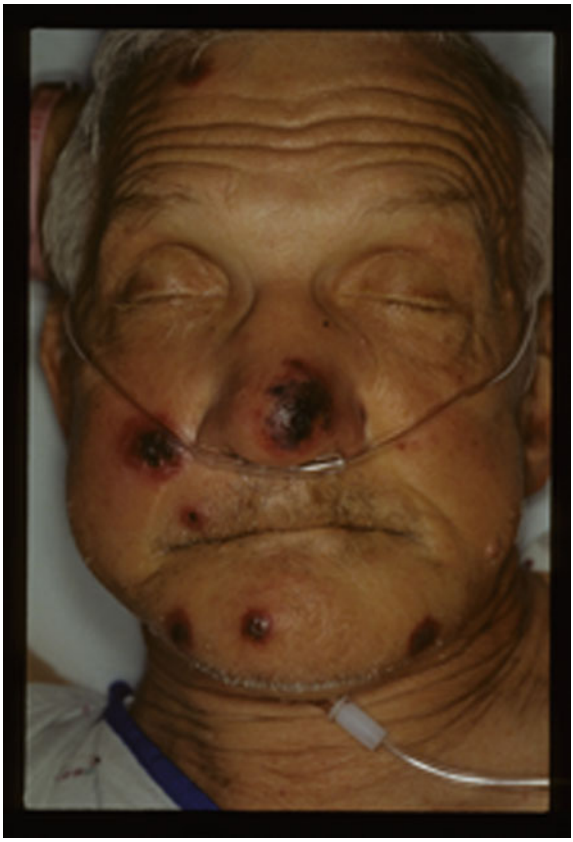

Fig. 3 Cutaneous *Mucor* infection

Phaeohyphomycosis is a rare opportunistic infection that is responsible for affecting various organs including skin, as well as causing invasive disease. From January 1989 through March 2008 at MD Anderson Cancer Center, 348 isolates of dematiaceous fungi were recovered in a retrospective analysis, and in 39 isolates (11 %) identified in 39 patients, an association with proven or probable invasive fungal disease (33 proven and six probable) was determined, and interestingly, the burden of disease increased from 1.0 to 3.0 cases per 100,000 patient-days during this 10-year period. Fifteen cases (38 %) were localized to the skin. Notably, many of these fungal isolates were not susceptible to either voriconazole or caspofungin [25]. Major risk factors for infection included the following: hematologic malignancy, anti-cancer treatment with induction chemotherapy, and subsequent neutropenia and lymphopenia [25]. Clinically, subcutaneous nodules, eschar, ulcers, and cellulitic lesions are present and gomori metheamine silver stain can aid in identification of fungal pathogen on skin histology [25]. Recommended management is with amphotericin B-based therapy combined with a triazole [25].

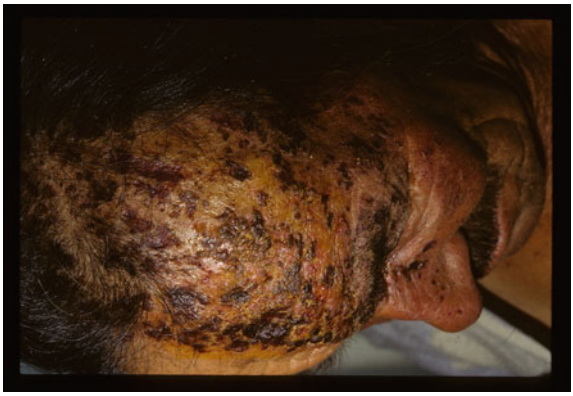

Fig. 4 Disseminated herpes zoster infection

4 Viral Dermatologic Infections

4.1 Varicella Zoster Virus

Varicella zoster virus infection in skin (VZV) occurs in approximately 30 % of allogeneic hematopoietic SCT [26] between 2 and 6 months after transplant (Fig. 4) [27]. Clinical significance of VZV infection lies in significant pain, post-herpetic neuralgia, scarring, and secondary infection [26]. Without appropriate treatment, disseminated VZV infection results in mortality in 10 % of patients with leukemia and/or allogenic SCT recipients [27].

In a retrospective analysis of 760 adult cancer patients with 766 episodes of a VZV, the highest risk for zoster was seen in patients with leukemia and lymphoma [28]. The presence of active tumor during the period of infection was associated with increased risk of VZV dissemination [28]. The median time to infection after therapy was 7 months post-radiation and less than 1 month post-chemotherapy [28]. In a cohort of 1,186 patients undergoing bone marrow transplantation (BMT), the following risk factors were identified: age >10 years, radiation pre-BMT, and VZV seropositivity. These variables were associated with a 44 % incidence by 3 years [29].

The use of prophylactic acyclovir, 800 mg twice daily given for 1 year post-transplantation has been found to be safe and highly effective in preventing VZV infection. Of the 38 subjects on acyclovir, only 2 (5 %) developed VZV disease compared to ten out of 39 in the placebo group (26 %). Graft versus host disease (GVHD) was also present in 82 % of those who developed VZV. However, GVHD is not an independent risk factor for development of VZV infection, as it can also occur in allogenic hematopoietic SCT recipients without GVHD as well as in autologous transplant recipients [26].

Regarding treatment, varicella-zoster immunoglobulin (VZIG) should be considered post-exposure in seronegative patients, at a dose of 12.5 units/kg or up to 625 units one time. If VZIG is unavailable within 96 h of exposure, then 400 mg/kg of standard intravenous immunoglobulin (IVIG) should be administered [27]. For treatment of acute zoster pain and post-herpetic neuralgia, tricyclic and anticonvulsant medications are recommended. The role of opiates in this setting has shown variable efficacy and is associated with more side effects [30].

4.2 Herpes Simplex Virus 1 and 2

Reactivation of herpes simplex virus (HSV-1 and HSV-2) after hematopoietic SCT occurs frequently and is most often associated with the underlying malignancy, mucosal damage, neutropenia, and lymphopenia. Reactivation occurs within the first few weeks after transplant with lesions most often presenting on mucocutaneous sites. In patients undergoing chemotherapy for leukemia, rates of reactivation are between 3 and 33 % [27]. Treatment with purine analogs or alemtuzumab and CD4 cell count less than 50 cells/mL increases the risk for infection [27].

Prophylaxis with anti-viral medication (i.e., acyclovir, valacyclovir) is strongly recommended for all seropositive SCT recipients from conditioning to 4 weeks post-transplant [27]. In high-risk leukemic patients receiving purine analogs or alemtuzumab and those with prolonged neutropenia prophylaxis is also recommended.

4.3 Cutaneous Cytomegalovirus Infection

Cutaneous cytomegalovirus (CMV) infection is rare even in the immunocompromised host. Typical CMV infection affects the eyes, central nervous system, gastrointestinal tract, and lung [31]. Cutaneous CMV can present non-specifically and must be considered in the immunocompromised cancer patient. A rare case reported in the literature describes an immunocompromised female with multiple red-brown papules located on upper and lower extremities and trunk accompanied by perianal ulceration, fevers, and weakness. Initial differential diagnosis included folliculitis, bacillary angiomatosis, and eosinophilic folliculitis. Biopsy with immunohistochemistry stains showing intranuclear inclusions confirmed cutaneous CMV; serologic studies showed high anti-CMV IgG titers with normal IgM [31].

Clinical appearance of lesions can be extremely variable including generalized macules and papules, vesicles, plaques, and/or nodules. It is hypothesized that cutaneous CMV may be a form of CMV microvasculitis. Recommended treatment is intravenous ganciclovir 5 mg/kg twice daily, valganciclovir 900 mg twice daily, or foscarnet 90 mg/kg every 12 h.

5 Cutaneous Parasitic Infection

5.1 Cutaneous Toxoplasmosis

Toxoplasmosis is a rare but fatal infection that can occur after SCT [32]. Skin histology reveals dermal edema, extravasated erythrocytes, necrotic collagen, and small cysts containing parasites within the epidermis, skin appendages, and endothelial cells in the dermis [32]; *Toxoplasma gondii* presence in skin can be confirmed by PCR.

Cutaneous toxoplasmosis has been reported in two cases following SCT. This presentation is rare, but there is an increased risk with development of GVHD and use of corticosteroids. If small parasite-containing cysts are seen in histology, then special staining and PCR should be performed to confirm diagnosis.

5.2 Cutaneous Acanthamoeba Infection

Acanthamoeba are free-living ameba that lives in the water and soil. In immunocompromised hosts, the most common manifestation of disease is subacute meningoencephalitis [33]. Skin lesions have rarely been reported, as in a patient with acute lymphocytic leukemia who developed extensive GVHD and became septic, with papular, ulcerative lesions on his face and extremities; histology of these sites confirmed presence of *Acanthamoeba*, despite being on prophylactic therapy with voriconazole. The patient was started on liposomal amphotericin B (5 mg/kg) daily in combination with trimethoprim–sulfamethoxazole (5 mg/kg of the trimethoprim component) every 8 h, but patient expired 5 weeks after diagnosis. Risk factors for development of this infection include: solid organ transplantation, connective tissue disease, diabetes, cirrhosis, renal failure, malignancy, and tuberculosis [33].

6 Dermatologic Infections from Anti-cancer Therapies

The effect of anti-cancer therapies on the systemic and cutaneous immune system, as well as on the structural and functional integrity of skin and nails, results in increased susceptibility of infections.

7 Cyototoxic or Targeted Therapy-Related Infections

Nowhere is the structural integrity of skin consistently in greater disarray and then with the use of epidermal growth factor receptor inhibitors (EGFRI), agents used to treat solid organ malignancies including those of the breast, lung, head and neck, and colon and rectum. The use of these drugs leads to a papulopustular rash,

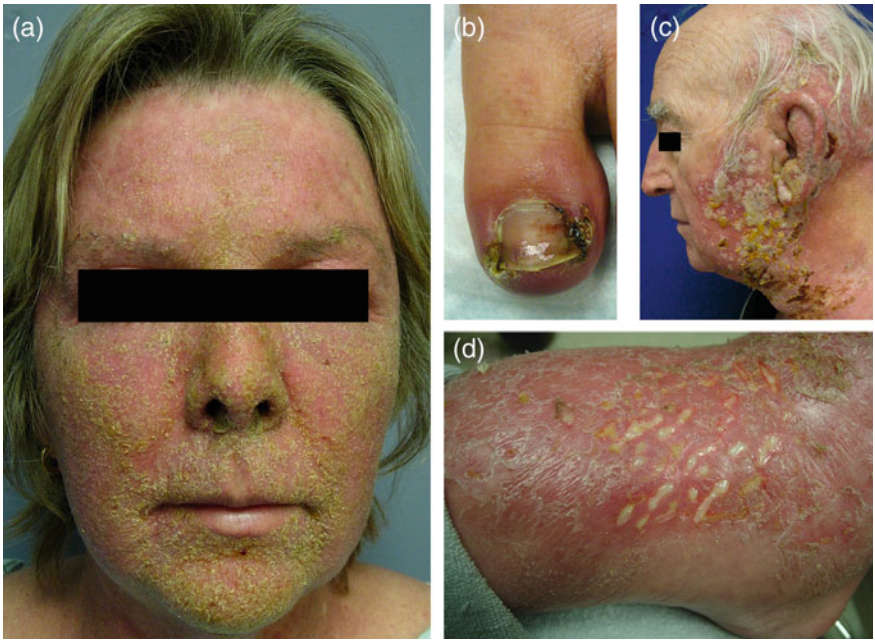

Fig. 5 **a** Papulopustular rash with secondary infection. **b** Paronychia. **c** Herpes zoster. **d** Xerosis with secondary infection

xerosis, paronychia, and hair abnormalities (Fig. 5). Cutaneous toxicities can be severe and lead to dose modification by 72–76 % of oncologists [34].

In a case series of 221 patients being treated with EGFRI, 29 % were secondarily infected at sites of dermatoxicity. Sixty-four patients had bacterial infections, and of those, 50 patients (78 %) were positive for *S. aureus,* four patients (6.3 %) cultured positive for *MRSA*, and 14 (21.9 %) cultured positive for other bacteria including *P. aeruginosa, S. marcescens, Enterococcus faecalis, and Klebsiella pneumoniae*. Of the 84 patients with dermatologic infection during EGFRI therapy, twenty-three had fungal infections [35]. The incidence of secondary herpetic infection was found to be 13 %. Seven of these patients developed herpes simplex infections, and four had herpes zoster while on EGFRI treatment. The data suggest that those with neutropenia and preexisting dermatoxicity are at a higher risk for developing secondary infection [35].

In multiple clinical trials [36], bortezomib has been shown to be associated with an increased risk of VZV infection in myeloma patients [37]. Rituximab, a monoclonal antibody used to treat B-cell non-Hodgkin's lymphoma, and temozolomide, an alkylating agent for solid tumors, have also been linked to VZV [38, 39]. The etiology for zoster development may be due to B-cell suppression and lymphopenia, but, notably, 400 mg acyclovir daily prophylactically has been shown to decrease incidence of disease [37].

Arsenic trioxide, used for the treatment of acute promyelocytic leukemia, lymphoma, myeloma, and other myeloproliferative disorders, has been linked to many dermatologic conditions including the following: pigmentation, keratosis, squamous cell carcinoma, and reactivation of herpes zoster [40]. In a study of 44 patients taking arsenic for hematologic malignancy, 11 developed VZV reactivation. At 1 year, actuarial risk was 26 % [40].

8 Radiation Therapy

Radiation therapy (RT) has been shown to decrease systemic host defense and compromise skin barrier function, leading to local invasion by colonizing pathogens [41–43]. In the oral cavity, RT results in proliferation of basal epithelial cells, causing atrophy and tissue edema largely contributing to development of systemic infection which can complicate therapy [41]. In skin, most of the post-radiation wounds are colonized with bacteria, including staphylococci and streptococci, which produce exogenous erythrotoxins or plasmid containing superantigens that cause severe skin inflammation leading to toxicity [44–46]. Superinfected radiation dermatitis presents with increased erythema and often times micropustules (Fig. 6) [46]. Current management includes culturing the pustule and initiation of appropriate oral antibiotic and topical mupirocin to lesions and nares [46].

It is interesting to note a case of Kaposi's varicelliform eruption in a patient being treated with electron beam radiation for MF. After receiving 500 cGy, the patient developed numerous 2–3-mm vesicles, pustules, yellow-crusted erosions, and hemorrhagic erosions on preexisting MF plaques. The patient was treated successfully with intravenous acyclovir, and RT was stopped indefinitely [47].

Radiation therapy also has been associated with the development of scabies infection in an 86-year-old patient with history of SS. It is hypothesized that RT significantly diminishes the number of Langerhans cells in the chest skin, allowing for increased susceptibility to scabies infection [48].

9 Lymphedema

Lymphedema is among the most frequent and clinically significant complications of breast cancer therapy; the reported incidence varies between 4 and 56 % [49]. Repeated episodes of lymphedema-associated infection require treatment with antibiotics and in severe cases necessitate hospitalization for parenteral antibiotic therapy.

A major contributing factor to lymphedema-associated infections is the alteration of lymphatic circulation (i.e., lymphatic stasis) secondary to radiotherapy and/or lymphadenectomy. Erysipelas is a soft tissue infection due to streptococci that affects the dermis and dermal lymphatic system [50, 51]. On clinical examination,

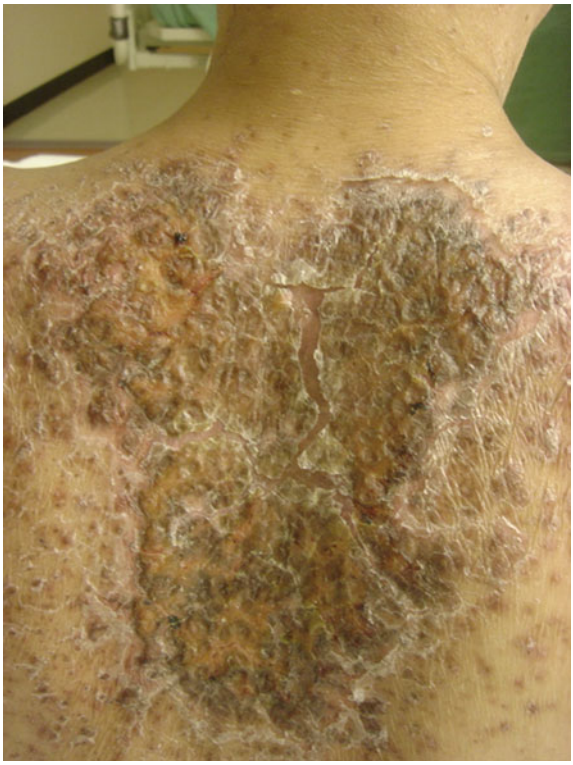

Fig. 6 Radiation dermatitis with secondary superinfection

warm indurated plaques with painful erythema are observed, which can mimic cutaneous metastasis [50], especially in immunosuppressed patients [51]. Portals of infection in 26 patients with lymphedema-associated erysipelas included post-traumatic wounds (16 patients), post-radiotherapy burns (3 patients), interdigital tinea (2 patients), infected eczema (1 patient), paronychia (1 patient), and herpetic whitlow (1 patient). Prophylactic intramuscular penicillin has been shown to decrease the rate of recurrent lymphedema-associated erysipelas in 48 patients, 66 % of whom did not experience recurrence during the first 2 years of prophylactic therapy [50]. Currently, there are no set guidelines for when prophylactic therapy should be initiated. However, if there is a known high risk of erysipelas, then therapy should be initiated prior to the first or second reoccurrence [50].

10 Subcutaneous Ports

Subcutaneous ports are frequently applied in oncology patients for the administration of chemotherapy and acquisition of blood samples. As foreign bodies and in the setting of a relative immunosuppresion, they can become a culprit for infections. Cutaneous flora can colonize the external catheter insertion site and

travel along the exterior of the catheter (extraluminal) or directly along inside of the lumen (endoluminal), reaching the blood stream [52, 53]. Extraluminal catheter-related bloodstream infection (CRBI) occurs primarily during this first week of insertion, whereas endoluminal CRBI tends to occur later and is attributable to catheter manipulation and use [52].

In a case series of 41 subjects with totally implanted venous access device, the incidence of positive skin and blood cultures was examined and related to development of CRBI [52]. Blood and cutaneous ($n = 163$) cultures were obtained. Four (2.5 %) positive blood cultures which yielded *Staphylococcus simulans, Staphylococcus capitis, and S. aureus* were obtained ($n = 3$ subjects) [52]. In contrast, those with negative blood cultures did not develop CRBI. In 11 subjects, there was bacterial colonization surrounding the device's surgical wound without sign of cutaneous infection. The greatest risk of infection is during the period shortly after insertion, but there is no correlation between risk of infection and perioperative use of antibiotics or frequency of port use [54, 55]. The most common infective pathogens include *S. aureus, Staphylococcus epidermidis, Klebsiella, E. coli, C. albicans,* and *Aspergillus* [54]. In regard to management, it is recommended to treat with appropriate antibiotics per culture and sensitivities [54].

11 Summary

Dermatologic infections generally occur more frequently in the setting of neutropenia, but can occur at any time point in oncology patients. Bacterial, fungal, viral, and parasitic skin infections are highly prevalent and necessitate early recognition and management, as they can lead to severe and sometimes fatal complications. Best clinical practice dictates culture and sensitivity when infection is suspected and prior to initiation of antimicrobial therapy. Anti-cancer therapy should also be recognized as a potential hazard for increasing the risk of skin infection.

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