

Malignant Fungating Wounds of the Head and Neck: Management and Antibiotic Stewardship

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Abstract

Objective. Malignant fungating wounds (MFWs) are unfortunate and underreported manifestations of some advanced head and neck cancers. The management of MFWs is complex and challenging. MFWs are often mistaken for infectious processes/abscesses and treated indiscriminately with oral or intravenous antibiotics. Our aim is to promote awareness of MFWs and provide education on their management. We summarize their cost-effective and evidence-based therapies and highlight antibiotic stewardship with respect to their management.

Data Sources. A literature review was performed of PubMed, Cochrane Review, SCOPUS, Embase, and Google Scholar databases regarding topical and systemic treatments for MFWs.

Review Methods. Full-text articles were identified with the following terms: fungating, ulcerative, wound, tumor, malignancy, antibiotics, topical, dressings, radiotherapy, head, neck, scalp, face, lip, and ear. Treatment recommendations were extrapolated, categorically summarized, and retrospectively assigned with an evidence level based on the GRADE system (Grading of Recommendations, Assessment, Development, and Evaluation).

Conclusions. In the absence of systemic signs and symptoms of infections, MFWs should not be treated as conventional infections or abscesses, with prophylactic oral or intravenous antibiotics. Topical treatments such as ointments and wound dressings are the mainstay in terms of managing the unsightly appearance and fetid odor from these entities.

Implications for Practice. MFWs are most often not amenable to definitive/curative surgical or nonsurgical therapy, but consultation with a head and neck oncologic specialist will help to determine if the underlying malignancy requires surgery, radiation therapy, or palliative treatment.

Keywords

malignant fungating wounds, head and neck cancer, malignancy, antibiotic stewardship, wound care

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Malignant tumors of the head and neck (eg, squamous cell and basal cell carcinoma) with cutaneous and subcutaneous involvement are very often unsightly and associated with fetid odor, drainage, bleeding, and sloughing. It is not surprising that tumors that breach the skin and create a malignant fungating wound (MFW) would be confused for an infection or abscess. As a result, these malignant tumors are subject to a variety of cognitive biases associated with medical decision making, including premature closure, representativeness restraint, Sutton's slip, and anchoring.¹⁻⁵ This holds particularly true for tumors that demonstrate aggressive and advanced local involvement. These tumors can present with a fungating and ulcerative appearance and are oftentimes accompanied by excoriation of the surrounding skin, intense malodor, profuse fibrinous or purulent exudate, bleeding, and pain.⁶⁻⁹ These clinical findings may be misleading to first-line providers, who are accustomed to treating common infections such as abscesses or cellulitis, which can have a similar appearance to these particular tumors.

Despite several articles describing MFWs in breast and genital cancers, which are mostly in the wound care literature

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and journals, there is a paucity of information related to fungating tumors and wounds of the head and neck region. In fact, to our knowledge, this may be the first article in the head and neck literature to specifically address this entity and its management. This is surprising considering that the head and neck is a common location for these particular tumors.¹⁰ MFWs can occur in primary, recurrent, and metastatic cancer settings. Unfortunately, MFWs are difficult to conceal in the head and neck region; they draw ready attention; and they can cause significant psychosocial dysfunction for the patients and distress and anxiety for their family members or caregivers. MFWs in the head and neck region also pose unique management challenges because they can readily affect the form and function of important structures and organs within this relatively compact surface area of the body. Because of a lack of awareness and readily available resources for guiding therapy, first-line providers often adopt a “trial and error” approach to the management of MFWs.

At our institution, we have observed numerous patients with MFWs who are prophylactically treated with systemic antibiotics at initial presentation, without head and neck oncologic team consultation. This appears to be a consistent pattern of practice. We believe that there are significant knowledge gaps in the management of MFWs among health care providers and that the lack of literature devoted to these entities contributes to the frequent misdiagnosis of a conventional infection and frequent misuse of antibiotics. In an effort to abide the core elements of antimicrobial stewardship, we have endeavored to research what the effective alternative strategies are for management of MFWs. The Centers for Disease Control and Prevention has defined antibiotic stewardship as “an effort to measure and improve how antibiotics are prescribed by clinicians and used by patients. Improving antibiotic prescribing is critical to effectively treat infections, protect patients from harms caused by unnecessary antibiotic use, and combat antibiotic resistance.”¹¹ Finally, we provide a summary of evidence-based recommendations on various therapies for treating MFWs, such as systemic antibiotics, topical antibiotics, and alternative wound management, with the purpose of creating a useful and practical resource for health care professionals.

Characterization of MFWs

MFWs are the result of cancer cells infiltrating and invading the dermis and epidermis and manifesting as an exophytic and/or ulcerative necrotic lesion. Regions of tissue hypoxia and necrosis ensue as a result of tumor proliferation, areas of variable vascularity, and tumor-related factors and by-products, as well as recruitment of inflammatory cells.¹²⁻¹⁴ This results in a tumor/wound with a common coexistent appearance: exophytic, fungating, necrotic, ulcerative, purulent, exudative, and bleeding. The most frequent sites for presentation are the breast (49%), neck (21%), chest (18%), and head (13%).^{10,15} These tumors/wounds frequently exhibit inflammation and discoloration beyond the wound borders, due to the presence of the underlying tumor and local tissue invasion. In more advanced tumors, large areas of necrosis may cause

significant anatomic disfigurement and patient distress.¹⁶ Debilitating pain, pruritus, exudate, and bleeding associated with these tumors may affect activities of daily living and diminish patient quality of life.¹⁷ MFWs are often malodorous, having been described as “rotting sulfide” or “cheese and vomit.”¹⁸ Anaerobic bacteria that reside in necrotic tissue generate volatile agents such as hydrogen sulfide. Despite bacterial colonization, there is no evidence that these odor-producing bacteria result in bacteremia or septicemia. One study analyzed 32 patients with breast cancer and fungating wounds and reported no systemic infections despite evidence of colonization in 78% of these tumors.¹⁶

Methods

A literature search of PubMed, Cochrane Review, SCOPUS, Embase, and Google Scholar databases was conducted independently by 2 authors (L.O., Z.N.). Full-text articles were identified with the following terms: fungating, ulcerative, wound, tumor, malignancy, antibiotics, topical, dressings, radiotherapy, head, neck, scalp, face, lip, and ear. Non-English studies and studies without a peer-review process were excluded. The search included randomized controlled trials, case reports, review articles, and expert opinions published in the last 40 years. Treatment recommendations were extrapolated, categorically summarized, and retrospectively assigned with an evidence level based on the GRADE system (Grading of Recommendations, Assessment, Development, and Evaluation).¹⁹ A “very low level” demonstrates extreme uncertainty in the recommendation; “low,” that additional research will likely change the confidence of the recommendation; “moderate,” that further research may change the recommendation; and “high,” when future research is unlikely to change the recommendation.

Discussion

Systemic Antibiotics

Recommendations.

- Systemic antibiotics should be avoided in patient with MFWs and given only when accompanied by signs and objective measures of infection. (Moderate)
- Side effects from systemic antibiotics can be significant and may exacerbate chemoradiation therapy–related adverse effects. (Moderate)

The benefits of prophylactic antibiotic therapy for preventing systemic infection have never been proven in the setting of bacterial colonization.¹⁶ Although MFWs are associated with extensive tumor necrosis and bacterial colonization, there have been no investigations, to our knowledge, that have shown an association with these and systemic infection. We believe that the decision to prescribe systemic antibiotics is not based on evidence-based recommendation but rather by poor understanding of the differences between a local infection/abscess and a fungating tumor. Because these tumors have a disfiguring and unsightly appearance and since they are frequently associated with drainage and a fetid odor, it is

common reflexive practice for first-line health care providers to prescribe prophylactic systemic antibiotics.

Systemic antibiotics are likely employed with the intent of improving the odor of MFWs via their bactericidal properties. However, several studies have demonstrated a lack of odor improvement or wound appearance with the use of systemic antibiotics. In a prospective double-blind crossover trial, Ramasubbu et al reported nonsuperiority with systemic metronidazole as compared with placebo in the reduction of malodor.¹³ Similarly, Ashford et al found no change in size or appearance of ulcerating breast tumors with the use of oral metronidazole vs placebo.²⁰ Another study hypothesized that areas of necrosis would prevent an effective concentration of antibiotics in tumors due to their interrupted blood supply.¹² Furthermore, a lack of validated tools to measure malodor results in heterogeneity and subjective bias in most reports to date.¹⁸

Topical Antibiotic Ointments

Recommendations.

- The use of topical antibiotics can be used to decrease tumor-associated odor. Application of 0.75%-0.8% metronidazole topical cream, twice a day, should be considered as the first-line treatment. (Moderate)
- Topical antibiotic treatment may have no significant effect on the production of wound exudate and tumor-associated pain. (Low)
- Topical antibiotics do not typically cause systemic effects (ie, vomiting, nausea, peripheral neuropathy, elevated creatinine) and should be considered safe for use in head and neck cancer cases without documented antibiotic-specific allergies. (Moderate)

Despite off-label use, metronidazole is the most widely accepted topical antibacterial for malodor management.^{14,21} It has been shown to be effective in odor reduction by killing anaerobic bacteria in up to 95% of cases.²² In a randomized controlled trial, Bower et al terminated the study early after observing the immense benefit of topical metronidazole on patient well-being as compared with the control group.²³ Other studies have supported the use of topical metronidazole by demonstrating decreases in patient perception of smell.²²⁻²⁴ Several studies have substantiated claims of odor reduction with bacteriology profiling.^{24,25}

While topical antibiotics are largely effective in odor reduction, there are practical challenges of applying ointments to tumors in the head and neck. Topical antibiotics are unsuitable for treating mucosal-based tumors such as cancers of the oral cavity.¹⁸ Topical antibiotics are typically more expensive than oral formulations, which poses a barrier to access for economically disadvantaged and uninsured patients.¹⁸ Finally, there is wide heterogeneity in reporting standards for topical antibiotics, as well as only a few studies with small sample sizes, warranting caution in interpreting conclusions.

Topical Dressings

Recommendations.

- Charcoal and silver dressings offer high conformability, ideal for wounds with irregular contours that can preclude traditional dressing applications. The net-like structure of these dressings also allows for exudative drainage and reduced moisture. (Low)
- Silver-based foam dressings may decrease tumor-associated biofilms and inflammation through bactericidal properties. (Low)
- Honey-coated dressings may be associated with patient discomfort and pain during application and removal. (Low)
- Charcoal and silver dressings may decrease caregiver burden due to ease of application and decreased frequency of dressing changes. (Low)
- The use of topical dressings has not been associated with significant adverse outcomes and should be utilized when clinically appropriate. (Moderate)

Unlike traditional wound management in which dressing application and dressing changes serve to facilitate wound healing, the use of these adjuncts in the treatment of MFWs has a different intent.²⁶ The benefits of dressings and dressing changes should be considered a palliative adjunct to help improve quality of life and patient comfort. By decreasing bacterial counts in necrotic tissue through absorptive or antimicrobial processes, topical dressings can help to control odor and exudate.²⁶ This has the additional benefit of positively affecting the well-being and comfort of patients, by concealing the ravages of tumor disfigurement.

Charcoal. Charcoal dressings are suitable choices for treating head and neck MFWs due to their unique properties. The highly porous nature of charcoal dressings allows for rapid absorption and evaporation of tumor exudate, effectively preventing maceration of surrounding tissue.^{9,27-30} Additionally, charcoal dressings tend to be thinner and less adherent, which allows tailoring to the concave and convex anatomy of the head and neck. Unlike conventional dressings, charcoal dressings have value in the management of certain fungating tumors with extensive necrosis.

Silver. Similar to charcoal, silver dressings have been shown to effectively absorb sloughed tumor material. However, these dressings are unique in regard to their substantial bactericidal properties.^{31,32} Kalemikerakis et al demonstrated that foam dressings impregnated with silver (1 mg/cm²) can subjectively reduce odor in nearly two-thirds of patients with malodorous fungating wounds after 4 weeks.³³

Silver may indirectly alleviate pain associated with these wounds via anti-inflammatory properties. Believed to downregulate matrix metalloproteinases, which delay wound healing, silver may blunt the hyperactive physiologic response seen in MFWs. Anecdotal evidence for silver's efficacy exists

over a wide spectrum of clinical situations, ranging from dental pain to thermal burns.⁶ However, these effects have not been corroborated in well-designed studies.^{26,34} Moreover, there is scant evidence supporting microbial resistance to silver.^{31,35,36}

Honey Coated. Historically, honey-based dressings have been used for acute and chronic wounds. Honey is postulated to create unfavorable environments for microbes and to facilitate exudate drainage and outflow from wound beds.³⁷ The high acidity in honey (pH 3.2-4.5) may also prevent the function of destructive proteases.³⁸ In a randomized controlled trial, Lund-Nielsen et al compared honey-coated dressings with silver-coated dressings for MFWs. While the authors did not show significant differences in subjective wound malodor, exudation, and pain, there was a trend to improved cleanliness at wound sites seen with honey dressings.³⁴ Of note, Obilor et al reported that the strong adherence of honey-based dressings to wounds was associated with a high degree of pain during dressing changes.³⁹ If utilized, caregivers may need to spend additional time applying and removing honey-coated dressings in comparison with the aforementioned dressings. As a cheaper alternative than silver- or charcoal-based dressings, honey may be considered in resource-deprived settings due to its wide availability and accessibility.

Implications for Practice

Highlights

- Systemic antibiotics have little effect in controlling the appearance or symptoms associated with malignant wounds. Our investigation recommends avoidance unless there is the presence of systemic signs and symptoms of infection.
- Topical metronidazole is an appropriate treatment modality for local superinfection in the setting of MFWs.
- Topical dressings (eg, silver, honey, charcoal) are low-risk and practical treatments that can reduce the odor and pain associated with MFWs and promote psychosocial well-being.

Our aim is to raise awareness of MFWs in the head and neck, distinguish MFWs from conventional infections and abscesses, and promote safe and practical wound management. The oncologic management of these tumors is outside the scope of this article. Since there are no population-based studies that provide data on the incidence and prevalence of MFWs, it is difficult to ascertain the magnitude of the issues that we have raised herein. However, with an increase in cancers in the aging population and an increase in the number of curative-intent and palliative treatment modalities for advanced-stage cancers, it is believed that there will be more patients who present with MFWs in the future. Therefore, there must be greater awareness of this entity, as well as practical wound management recommendations that are based on

evidence and avoid unnecessary and costly interventions, such as the use of antibiotics. The use of oral or intravenous antibiotics for MFWs is not based on evidence, nor does it adhere to the principles of antibiotic stewardship. A full assessment by a head and neck oncologic team should be considered prior to empirically prescribing systemic antibiotics. We believe that this report will serve as a guide for health care professionals in future management of MFWs.

Limitations

Gathering evidence for the role of antibiotic stewardship in the context of MFWs was limited by the low level of literature investigating this topic. The variability in MFW presentation and the absence of an objective set of unified assessment criteria created challenges in acquiring actual data on these entities. Our recommendations would be strengthened by presenting quantitative data that show the incidence and prevalence of MFWs and by determining the percentage of patients who were initially treated with antibiotics at our institution. These data would be augmented by assessing prescribers' perception of any benefit following administration of antibiotic therapy, as well as data on adverse outcomes associated with prescribing antibiotics, such as *Clostridioides difficile* infection. Future directions of study include assessing the rates of empiric antibiotic administration with subsequent discontinuation following consultation with a head and neck cancer specialist. Biomarkers, such as procalcitonin, and their role in prescribing patterns for MFWs should be investigated, particularly in the absence of signs of systemic infection. As this is an observational study based on pragmatic recommendations and extrapolation of data on MFW management from the wound care literature, there are significant biases, as well as limitations in providing high-level evidence for our assertions.

Authors' Note

The data presented in this report were selected for poster presentation at the AHNS 10th International Conference on Head and Neck Cancer scheduled on July 18, 2020 (meeting cancelled due to the COVID-19 pandemic).

Author Contributions

Liam O'Neill, conception and design, analysis and interpretation of data, drafting of manuscript, revising it for important intellectual content, final approval of the version to be published; **Zach Nelson**, conception and design, analysis and interpretation of data, drafting of manuscript, revising it for important intellectual content, final approval of the version to be published; **Nadir Ahmad**, conception and design, analysis and interpretation of data, drafting of manuscript, revising it for important intellectual content, final approval of the version to be published; **Alec H. Fisher**, drafting of manuscript, revising it for important intellectual content, final approval of the version to be published; **Ana Denton**, conception and design, analysis and interpretation of data, revising it for important intellectual content, final approval of the version to be published; **Michael Renzi Jr**, revising it for important intellectual content, final approval of the version to be published; **Henry S. Framow**, conception and design, analysis and interpretation of

data, drafting of manuscript, revising it for important intellectual content, final approval of the version to be published; **Luke Stanisce**, conception and design, analysis and interpretation of data, drafting of manuscript, revising it for important intellectual content, final approval of the version to be published.

Disclosures

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