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REVIEW ARTICLE

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Radiation-induced rhinosinusitis: Mechanism research and clinical progress review

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Abstract

Objectives: Radiation-induced rhinosinusitis is a vital dose-limiting reaction in patients with head and neck malignancy. Unlike oral mucositis during or after radiotherapy, radiation-induced sinusitis is easily overlooked in clinical practice and rarely included in experimental studies. Herein, we review the literature to date on radiation-induced rhinosinusitis.

Methods: Relevant studies published between 1995 and 2022 were determined through a detailed search using open keywords from PubMed, with manual search of the reference list of the identified articles. Keywords searched were "ionizing radiation," "radiotherapy," "intensity-modulated radiotherapy," "head and neck tumor," "nasopharyngeal carcinoma," "nasal epithelium," "radiation damage," and "radiation-induced rhinosinusitis." Full-text articles that clearly stated the pathogenesis, clinical manifestation, predictors, treatment, and prognosis of radiation-induced rhinosinusitis were included.

Results: Radiation-induced rhinosinusitis occurs during radiotherapy and can last for months or even years after radiotherapy. A mixture of cellular outcomes caused by ionizing radiation and persistent damage of the epithelial and submucosal tissues after the treatment result from the radiotherapy itself. Endoscopic sinus surgery improves symptoms but can be accompanied by intraoperative and postoperative complications. Nasal irrigation, steroids, and antibiotics appear to reduce inflammation and relieve symptoms to a certain extent. Studies on other potentially useful drugs are underway and in the exploration stage, without clinical application.

Conclusions: Despite its high incidence, radiation-induced rhinosinusitis is a type of dose-limiting toxicity that theoretically does not produce fatal effects at controlled doses and with adequate follow-up care. In moderate-to-severe cases, toxicity may be present. Currently, radiation-induced rhinosinusitis has potential prevention and treatment strategies. However, no unified management protocol has shown significant improvement in radiation-induced rhinosinusitis. Further research is necessary.

KEYWORDS

head and neck cancers, mucositis, nasopharynx cancer, radiation-induced rhinosinusitis, radiotherapy

Key points

- Radiation-induced rhinosinusitis is a common complication among patients with head and neck cancers during and after radiotherapy, which has not received enough attention.
- Multiple studies have proved that the mechanism of damage caused by radiation can be divided into acute stage and chronic stage.
- Evidence-based medical studies have shown that nasal irrigation and nasal steroids can relieve discomfort of patients.
- Current radiation therapy relies on the photon beam that has reached a plateau in terms of physical delivery, and proton therapy may be a new direction of causative therapy in the future.

INTRODUCTION

Head and neck cancers (HNCs) of the upper aerodigestive tract are broadly managed by surgical resection with wide margins.[1,2] Owing to the complex anatomical boundaries of the head and neck region and the aggressive behavior adjacency of HNCs to blood vessels and nerves, the desired therapeutic effect is difficult to achieve with surgical resection. Therefore, adjuvant radiotherapy (RT) is mainly used to cure macroscopic or occult microscopic foci of cancer postoperatively.[3] However, risks of acute and late RT toxicities enhance with the increase in total dose and duration of RT, leading to mucosal crusting, xerostomia, dysphagia, and hypothyroidism.[4,5] Mucositis, a frequent side effect of HNC during and after RT,[6,7] affects both oral and nasal cavities.[8] Patients with a tumor invading the nasal cavity and sinuses develop nasal obstruction, purulent nasal discharge, nasal hemorrhage, rhinalgia, nasal cavity dryness, and hyposmia after RT.[9,10] This symptom cluster is called "radiation-induced rhinosinusitis."[11] Although radiation-induced oral mucositis has been extensively researched, little is known about radiation-induced rhinosinusitis. Here, we researched the references whose keywords were "ionizing radiation," "radiotherapy," "intensity-modulated radiotherapy," "head and neck tumor," "nasopharyngeal carcinoma," "nasal epithelium," "radiation damage," and "radiation-induced rhinosinusitis" from PubMed between 1995 and 2022, with manual search of the reference list of the identified articles. Data were collected pertaining to pathogenesis, clinical manifestation, predictors, treatment, and prognosis of radiation-induced rhinosinusitis. We assessed the quality and extracted the data of these included references and summarized mechanism research and clinical progresses systematically.

EPIDEMIOLOGY

The epidemiology of radiation-induced rhinosinusitis has been associated with the history of RT technology. Conventionally, two-dimensional RT technology had been widely adopted. It provided effective disease control but carried a high risk of toxicity. Functional sinusotomy was often indicated in the follow-up.[12] Over the past 20 years, advancements in RT technology have included three-dimensional conformal RT, which relies on the guidance of computed tomography (CT) or magnetic resonance imaging and allows better localization of tumor boundaries.[13] Intensity-modulated RT (IMRT) is an advanced form of three-dimensional conformal RT that can provide a more accurate balance between target area coverage and protection of the adjacent organs.[14,15] The incidence of radiation-induced rhinosinusitis after the treatment of nasopharyngeal carcinoma (NPC) with IMRT ranges from 43.2% to 73.5%.[16]

The endpoint of RT is of acute and late types. Radiation energy directly results in acute endpoints, such as the onset of radiation-induced rhinosinusitis.[17] After RT, when destructive components of radiation accumulate to a certain extent, the protective repair mechanism of the body is initiated, leading to a competition between wound healing and ongoing injuries. This process is referred to as "chronic radiation-induced rhinosinusitis."[16,18] Among patients with NPC, the most common site of inflammation is the maxillary sinus, accounting for 84.85% of patients with sinusitis after RT, followed by the ethmoid (71.21%) and sphenoid (34.85%) sinuses.[19] The risk of radiation-induced rhinosinusitis increases rapidly within the first 3 months after RT.[16,20] The incidence peaks at 6–12 months and then stabilizes at 1 year or later.[9,21]

MECHANISM

The mechanism of damage caused by radiation is not exactly the same as that of chronic rhinosinusitis (CRS). According to the endotype dominance, primary CRS can be divided into type 2 and nontype 2, while the mechanism of secondary CRS can be summarized as mechanical, inflammatory, and immune.[22] Radiation-induced rhinosinusitis presents in a state of aseptic inflammation in the early stage and gradually presents as a tissue remodeling process similar to CRS in the later stage.[23]

This part focused on the mechanism of radiation-induced rhinosinusitis, divided into acute stage and chronic stage (Figure 1). In the acute stage, the pathological effects of radiation can be direct or indirect.[24] When X-ray energy is absorbed by biological ingredients, the target is ionized or excited, leading to direct biological damage. In quick succession, X-rays may react with cell components to produce damage-associated molecular patterns (DAMPs).[25] Toll-like receptors exhibit the most diverse variety of DAMP ligands among all innate immune receptors and control the release of downstream potent inflammatory mediators.[26] Radiation exposure tends to induce T-helper (Th) cell differentiation, which is mediated by tumor and multiple immune cells, ultimately causing the Th1/Th2 balance to shift toward Th2.[27,28] Th1 can enhance the inflammatory response and inhibit radiation-induced fibrosis, while Th2 cytokines act as both proinflammatory and profibrotic factors during irradiation.[29] With time, these pathologic signaling pathways can influence host susceptibility to infection and increase vascular permeability and transendothelial migration of leukocyte, leading to chronic radiation-induced rhinosinusitis dominated by nasal congestion, rhinalgia, and nasal dryness.[27,30]

Ionizing radiation can elicit immunogenic apoptosis, necroptosis, mitotic catastrophe, and senescence.[31] It induces direct damage to the DNA, causing single- or double-strand breaks.[32] While single-strand breaks are readily repaired, approximately 5% of double-strand breaks fail to be repaired and ultimately lead to cell death.[33] The outcome of irradiated cells depends on the cell type and radiation dose, and mucosal cells are more susceptible to ionizing radiation than other normal cell types because of their high replication rate.[31,34]

After the primary event, secondary reactions mainly produce reactive oxygen species (ROS) and induce overexpression of proinflammatory and profibrotic cytokines.[35–37] Under normal conditions, cells can maintain a constant redox level through internal homeostasis. However, ROS serves as a secondary messenger via ligand-/receptor-initiated pathways and induces cascade reactions, disturbing the original equilibrium and causing oxidative damage.[38,39] In addition to oxidative stress, another indirect mechanism of injury is the inflammatory process.[40] For example, Riva et al.[5] found that 13% of healthy people had neutrophilic inflammation, but 40% of patients undergoing RT show neutrophilic infiltration, which is difficult to explain without RT. Inflammatory cytokines, such as tumor necrosis factor-α, participate in the acute response and are expressed rapidly and continuously in irradiated and adjacent tissues.[30] In an animal model of radiation mucositis, messenger RNA levels of interleukin-1β correlated with mucositis severity.[41] Interleukin-1β induces cyclooxygenase-2, a key enzyme in the inflammatory process, which increases proinflammatory prostaglandin production and mediates tissue damage.[21] Overall, the threat of the indirect pathway is more than that of the direct one.[39] The initiation of oxidative stress and proinflammatory factors induce production of abundant ROS, chemokines, and proinflammatory cytokines shortly after irradiation, finally leading to acute radiation-induced rhinosinusitis.[40]

Radiation damage persists after discontinuation of RT.[9] In almost all patients with NPC, after 2–7 years of RT, dryness of the nasal mucosa persists, and the cilia architecture is frequently untidy, sparse, absent, or diverging, indicating another chronic mechanism of sustained damage mediating long-term deficits in nasal mucosal

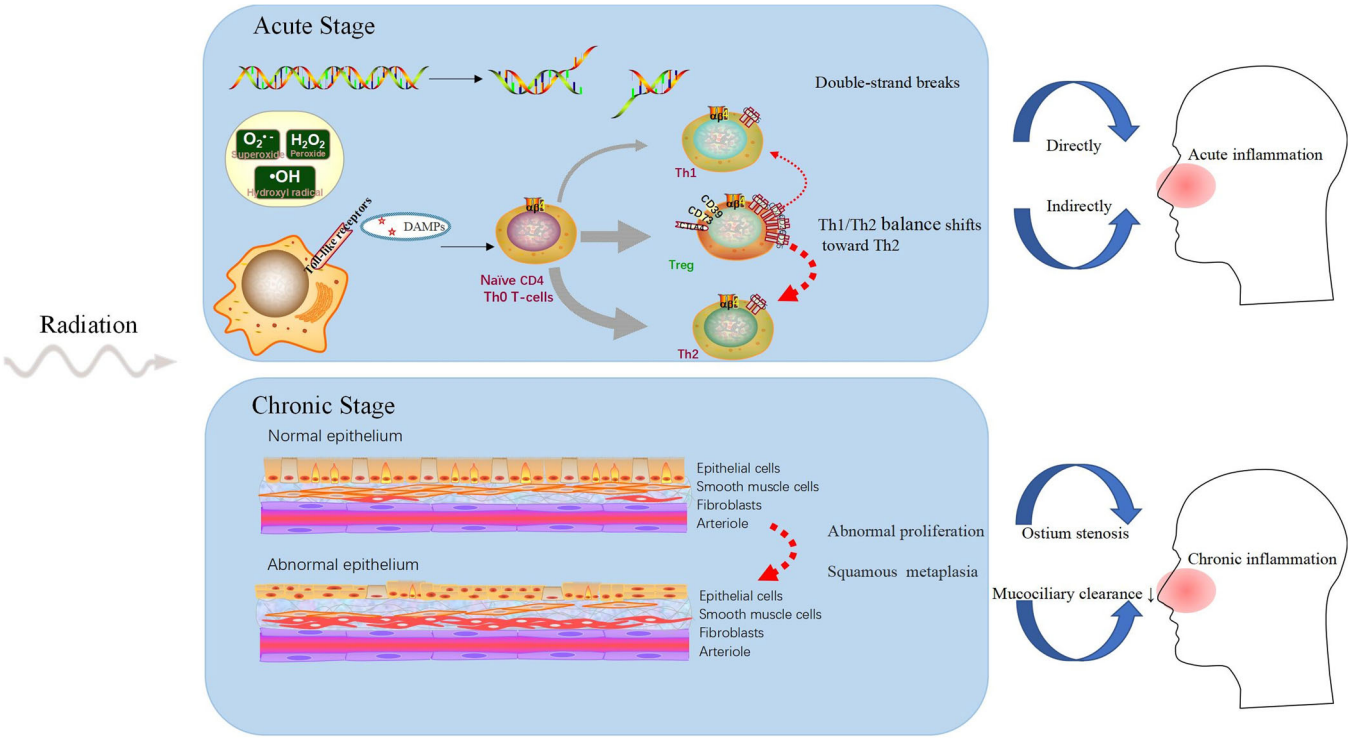

FIGURE 1 Radiation induces the development of radiation-induced rhinosinusitis through acute and chronic mechanisms.

function and structure after RT.[19] We outline the following mechanisms.

Inadequate drainage, which causes ostium stenosis or obstruction and mucociliary clearance (MCC), is responsible for the incidence of chronic radiation-induced rhinosinusitis.[21,42] Yin et al.[9] measured the thicknesses of the middle and inferior nasal concha and found a positive correlation between the thickness of the turbinate and the radiation dose. This implies that radiation can cause chronic mucosal hyperplasia, which obstructs drainage in anterior nasal sinusitis. At a radiation dose of approximately 65 Gy, nasal mucosa undergoes ischemic necrosis, shedding, and fibrosis, followed by abnormal tissue hyperplasia.[16] Inhaled particles are pushed toward the nasopharynx by movements of the nasal mucosal cilia, or MCC, which primarily depends on proper functioning of the mucosal cilia and physical properties of mucus.[43] Kamel et al.[44] found that MCC deteriorates up to 6 months after RT of patients with NPC. The cilia of respiratory mucosa are sensitive to radiation in animals and humans.[45] Irreversible ciliary dysfunction leads to chronic nasal sinusitis, and chronic inflammation can affect the ciliary structures, leading to a vicious cycle in the pathogenesis of radiation-induced rhinosinusitis.[46]

Regarding the histological perspective of the aforementioned mechanisms, RT is toxic to proliferative cells in epithelial and submucosal tissues.[47] Histological examination of nasal mucosa after RT shows lamina propria fibrosis, cilia malformation or loss, and intercellular and intracellular vacuolations.[48] These pathological changes can be explained by secondary squamous metaplasia (SM) in the nasal epithelium, a common pathological feature of radiation-induced rhinosinusitis.[5,18] In chronic upper respiratory disease, SM is an irreversible and severe form of epithelial remodeling, and the non-keratinized squamous epithelium replaces the normal columnar ciliated pseudolayered epithelium of respiratory mucosa.[49] The SM region lacks normal ciliary and goblet cell structures, thus limiting ciliary clearance and secretion.[50] Basal cells are considered to be airway epithelial stem cells because of their high proliferation and differentiation capacities.[18,51] When the airway epithelium is damaged, airway epithelial stem cells can proliferate and migrate to the corresponding site and subsequently differentiate into normal epithelial cell structures, such as goblet, ciliated, and non-ciliated columnar cells.[52] However, Huang et al.[18] discovered that most nasal epithelial stem cells lose the ability to regenerate after RT, and the remaining proliferating basal cells tend to differentiate into abnormal SM cells instead of normal nasal epithelial cells. Although these phenomena can occur in patients with chronic rhinosinusitis without nasal polyps, the frequency of SM and expression of basal cells, along with the loss of cilia and goblet cells in the nasal epithelium, are more serious in radiation-induced rhinosinusitis. Therefore, when the radiation-induced loss of the normal epithelium cannot be repaired, the repair signal is continuously activated, further exacerbating abnormal proliferation of basal cells.

At the molecular level, radiation-induced rhinosinusitis involves markers of inflammation and cell proliferation and differentiation. The effect of inflammatory processes can be acute or late.[53] Subsets of T lymphocytes differ in sensitivity to radiation, leading to differing degrees of recovery after radiation injury,[30,54,55] which may lead to an altered balance of T-cell subsets. This imbalance drives chronic inflammatory states through effector mechanisms.[56] Ordovas-Montanes et al.[57] demonstrated that human nasal epithelial stem cells may form memories of chronic exposure to inflammation, leading to a shift in cellular ecosystems from productive differentiation to transmissible disease. In NPC, messenger RNA and protein levels are significantly reduced for Ki67 (cell proliferation); p63+/KRT5+ basal cells; MUC5AC and MUC5B (secretary proteins from goblet cells); tubulin and TAp73 (ciliated cells); DNAH5, DNAI1, and RSPH4A (microtubule assemblies of motile cilia); and FOXJ1 and CP110 (ciliogenesis-associated markers).[18,19] As for the mechanism of action, radiation may produce ROS, causing signal transduction pathways to be unconventionally activated. The epidermal growth factor (EGF)/EGF receptor pathway can shift human airway basal cell potency toward SM, activated by oxidative stress.[58] Activated nuclear factor kappa B can cause mucosal damage by upregulating proinflammatory cytokines and inflammatory mediators.[59] Unlike the acute phase, the chronic phase shows stem cell genome mutations or epigenetic modifications that may affect the patient's long-term susceptibility to respiratory disease.[60]

Stable and diverse microbiota are essential for a host's physiological processes and mucosal immune functions.[61] The increased proportion of Gram-negative bacteria may facilitate the aggravation of mucosal inflammation by activating host pattern recognition receptors through bacterial components and formation of proinflammatory cytokines.[62] Most studies focused on the effect of the oral microbiome on the occurrence and development of radioactive oral mucositis. Based on changes in the relative abundance of oral bacteria during radiotherapy, a high-precision random-forest model can be generated to predict the exacerbation of mucositis, which would yield a novel pathogenesis and prognosis model of radiation-induced rhinosinusitis.[63]

Briefly, molecular events involved in this mechanism occur in parallel, sequential, and interlacing ways in time. Injuries caused by nondouble-strand breaks account for approximately 70% of the mechanism and cause sustained and irreversible damage to normal mucosa.[64]

IMPACT AND SIDE EFFECTS

Based on the mechanism, adverse effects of radiation-induced rhinosinusitis can be early or late. Early adverse effects occur during or shortly after RT, whereas late ones persist for several years.[65] Early adverse effects include swollen mucosa, increased excretions, and retention of excretions,[16] manifesting as fatigue, severe pain, thick secretions, and dehydration.[66] Late adverse effects include pallor and thinning of the epithelium, occasional chronic ulceration and necrosis, and exposure of the underlying bone and/or soft tissues,[5] which cause nasal obstruction, purulent nasal discharge, foul smell, nasal hemorrhage, rhinalgia, nasal cavity dryness, and hyposmia.[43]

Whether olfactory dysfunction depends on radiation-induced rhinosinusitis or not is debated. It includes a decline in detection sensitivity and odor identification.[15,67–69] For some sinonasal malignancies, the upper nasal vault, in which the olfactory epithelium is located, is included in the irradiated field. According to some studies, the volume of the olfactory bulbs diminishes following RT when they are included in the irradiated field[70,71]; therefore, the possibility of sensorineural olfactory dysfunction caused by RT cannot be excluded.[70,72] According to other studies, this might result from radiation-induced rhinosinusitis. In a study on olfactory function in patients with NPC, the change in the objective olfactory score after IMRT was directly proportional to the change in the sinus CT score with the Lund-Mackay staging method. The correlation was moderately negative, implying that objective olfactory obstacles might intensify with increased inflammation of the nasal cavity and sinuses caused by IMRT.[15] In studies holding the former view, most patients had received conventional RT. Bramerson et al.[73] found that high-dose radiation exerts a more powerful effect on olfactory performance compared to low-dose radiation, implying that olfactory dysfunction might result from limitations of conventional RT at that time rather than neurologic damage. However, the correlation between chronic rhinosinusitis and the CT score remains controversial.[74,75] Rates of false-positive and false-negative CT findings are high.[76] Therefore, the latter view is not well-founded.

Ear inflammation has been found in radiation-induced rhinosinusitis. Chronic rhinosinusitis predisposes to otitis media because of the eustachian tube.[77] Moreover, the bacteriology of nasal sinusitis has a microbiological association with otitis media with exudation (OME) in patients with NPC undergoing RT.[52] Nevertheless, the occurrence of postirradiation OME and rhinosinusitis shows no correlation in patients with NPC treated by IMRT in the 5-year follow-up.[78]

PREDICTIVE FACTORS

Among the advantages of IMRT over conventional RT, the probability and severity of toxicity and dysfunction correlates with higher doses. Yin et al.[9] explored the correlation between the radiation dose and the degree of nasal mucosal injury after IMRT and found that the radiation dose independently predicted nasal signs and symptoms and that the tolerable dose threshold of nasal mucosa was approximately 37 Gy, which is the average radiation dose throughout the nasal cavity during IMRT. At doses within this threshold, mucosal damage can recover in a few months.

The T stage and invasiveness of neoplasms are factors influencing the occurrence of sinusitis after IMRT.[16] However, this can be attributed to the expanded radiation field, leading to irradiation of a larger area of normal tissues.

Hsin et al.[20] found that the rate or severity of changes in sphenoid sinus mucosa at any time after RT did not increase significantly even after full-dose irradiation compared to pretreatment levels. However, the ethmoid and maxillary sinuses are extremely sensitive to radiation toxicity.[20,79] Thus, different irradiation areas can influence radiation-induced rhinosinusitis. The maxillary sinus opening is lower in position, making it susceptible to tumor invasion, and sinus mucosa is edematous after RT, both of which can exacerbate the retention of secretions in the sinuses. The air chambers of the ethmoid sinus are smaller and denser compared to those of other sinuses whose mucosa is more likely to be swollen and obstructed after RT. In addition, they participate in the composition of the ostiomeatal complex, and the relatively narrow space is vulnerable to be obstructed.[78] However, the sphenoid sinus opening is not as complex or narrow as the ostiomeatal complex, thus being highly resistant to radiation damage.[80] This implies the existence of a balance between focal location, radiation dose, radiation damage, and efficacy. Nevertheless, further investigation is required to shift the standard of high-dose treatments to a relatively low-dose treatment.

Imaging examination before RT has no value in predicting whether the mucosal morphology would remain stable, deteriorate, or improve.[10] The pre-existing sinus disease might improve when RT results in tumor shrinkage and reopening of drainage, with consequent improvement in signs and symptoms.

Based on dosimetry, probability models have been developed for tissue complications, such as xerostomia,[81–84] nasogastric catheter dependence,[66] hypothyroidism,[85] laryngeal edema,[86] nausea,[87] and acute oral mucositis.[88] In theory, based on clinical and dosimetric characteristics of patients with HNC, this type of model could also be established to predict the risk and severity of radiation-induced rhinosinusitis after RT. This model can suggest clinicians to perform interventions for patients with high-risk factors and improve their quality of life.

TREATMENT

Unlike nasal sinusitis, radiation-induced rhinosinusitis is difficult to treat because of the lack of appropriate methods to restore the structural and functional damage caused by radiation. We would elaborate specific treatment measures from two aspects: etiological and symptomatic.

Endoscopic sinus surgery improves symptoms but causes intraoperative and postoperative complications, such as poor wound healing and bleeding,[89] with unclear long-term effects.[58] Although the curative effect has been achieved, nasal symptoms often persist postoperatively, and long-term nasal care cannot guarantee a good quality of life during the follow-up.[89,90]

Nasal irrigation is the most common treatment for sinusitis after RT. It cleans the nasal cavity, enhances cilia function, and removes local inflammatory mediators.[91,92] Liang et al.[93] discovered that patients with NPC who received irrigation after RT had improved nasal symptoms and signs from before lavage to 6 months after lavage compared to those who did not receive irrigation. However, patients developed nasal symptoms with or without nasal irrigation that persisted for the following 6 months. Further, nasal irrigation

occasionally causes effusion in the middle ear, possibly because of impaired eustachian tube closure by irradiation.[94] Therefore, nasal irrigation should be performed in select cases.

Another safe and effective treatment for radiation-induced rhinosinusitis is nasal steroids. A clinical study randomized patients with NPC receiving RT and subsequently developing rhinosinusitis to receive a steroid spray or a nasal rinse.[21] The steroid spray group showed lesser nasal discomfort and a better quality of life and endoscopic findings compared to the nasal rinse group.

Some patients develop bacterial infection in the acute phase, and the number of bacteria decreases rapidly after RT.[11] Therefore, antibiotics are administered during RT. The main pathogens of acute sinusitis significantly differed between the general population and the patients with radiation-induced rhinosinusitis.[95] The middle meatus bacteriology of acute radiation-induced rhinosinusitis showed that the most common pathogen was *Staphylococcus aureus*, followed by Gram-negative and anaerobic bacteria. Moreover, the rate of multiple infections was higher.[96] Over 90% of the aerobic isolates were inhibited by cotrimoxazole, amoxicillin-clavulanate, and ofloxacin, and over 90% of anaerobic isolates were sensitive to clindamycin, chloramphenicol, and amoxicillin-clavulanate.[96] Resistance to β-lactamase and antibiotics covering anaerobic bacteria should be considered when choosing antibiotics.

Other potentially useful drugs include rebamipide, an antiulcer drug. Jang et al.[97] proved that rebamipide accelerated the recovery of defective tight connections and increased the number of goblet cells, which appears to partially address the chronic SM of radiation-induced rhinosinusitis. Further, glutamine, an L-α-amino acid, is a nitrogen donor in cell metabolism and immune cell maintenance.[98] Adequate glutamine levels in mucosal cells may help improve healing after radiation injury, and their antioxidant effect is important for free radicals produced by ionizing radiation.[99] Amifostine protects normal tissues during RT, probably by eliminating ROS produced after radiation exposure.[100] Unlike rebamipide, the effects of glutamine and amifostine seem to be more targeted to the acute-phase mechanism. However, more studies are required to explore these drugs for use in patients with radiation-induced rhinosinusitis.

All aforementioned treatments are symptomatic, and elimination of etiology would involve radiation itself. External photons are the most common treatment.[66] As aforementioned, the use of IMRT has allowed considerable improvements in conformality and reduction in radiation doses to the adjacent normal structures. However, the dose of the external radiation beam decreases exponentially. The healthy normal tissue in front of the tumor receives a large dose of ionizing radiation relative to the tumor, while the healthy normal tissue behind the tumor also receives the exit dose when the ray passes through the tumor. The photon beam reaches a plateau in terms of physical delivery, and the occurrence of radiation-induced rhinosinusitis is the inevitable result such that its medical application cannot be further improved.[101] In this context, the development of proton therapy may be a new direction for RT technology, which can reduce tissue toxicity and improve tumor control, and the patients receiving proton therapy had higher 5-year overall and disease-free survival compared to those receiving photon therapy.[102] Ultra-high dose rate (FLASH) radiotherapy is a form of proton beam therapy, and its ultrahigh dose rate radiation can deplete local oxygen and induce a short-lived protective hypoxic environment within the normal healthy tissues, increasing radioresistance.[103] Several factors contribute to the FLASH effect, including the total dose, pulse rate, pulse duration, pulse width, and pulse number. Therefore, translation into the clinic is difficult at this early stage.[104] However, FLASH provides a new idea for the prevention and treatment of radiation sinusitis from the perspective of enhancing tissue resistance.

PROGNOSIS

IMRT-induced rhinosinusitis may be self-limiting.[93] However, most studies suggest that the effect of RT on the sinonasal epithelium is profound and lasts for decades.[105] Chronologically, Lund-Mackay magnetic resonance imaging scores of the sinuses showed that all sinuses other than the frontal sinus had the highest abnormal rate at 3 months after RT. In the long-term follow-up, the incidence of mucosal abnormalities of any sinus did not differ 5 years after RT compared to pretreatment.[20]

CONCLUSIONS

Despite its high incidence, radiation-induced rhinosinusitis is a type of dose-limiting toxicity that theoretically does not produce fatal effects at controlled doses and adequate follow-up care. However, in moderate-to-severe cases, toxicity may be present. As some patients with HNC receive concurrent chemotherapy, the effect of chemotherapy on radiation-induced rhinosinusitis should also be considered in future studies. Currently, radiation-induced rhinosinusitis has potential prevention and treatment strategies. However, no unified management protocol can significantly improve radiation-induced rhinosinusitis to clinically relevant and satisfactory standards. We aim to bridge these gaps in future studies.

AUTHOR CONTRIBUTIONS

Yan Jiang proposed the topic of "radiation-induced rhinosinusitis" and the concrete ideas for the writing. Chunge Zheng is responsible for the literature reading and the paper writing. Longgang Yu have revised the content of their paper.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The literature included in this review and its data that support the findings of this study are available at PubMed.

ETHICS STATEMENT

The authors have nothing to report.

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