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REVIEW ARTICLE

Myiasis in patients with oral squamous cell carcinoma—a systematic review and protocol for management

Anuj Jain[1]

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Abstract

Background Oral squamous cell carcinoma results in various morbidities like pain, bleeding on provocation, loss of function, facial disfigurement, extra oral fungation, and tissue necrosis. Other than these dreadful complications, sometimes in advanced and incurable stage, the wound gets infested with maggots. Oral myiasis in association with OSCC is rare, and a very few reports have been mentioned in the literature.

Material and methods A literature search was performed on PubMed, Medline, and Cochrane databases on 1st November 2018 for all the articles focusing on oral myiasis in patients with oral squamous cell carcinoma.

Results A total number of nine cases with oral myiasis in association with OSCC have been reported till date. Out of these nine cases, five cases have been reported from India and four from Brazil.

Conclusion Oral myiasis is a possible risk for the patient with Oral squamous cell carcinoma. Good hygiene and general cleanliness along with educating the patients must be a practice to avoid this dreadful condition.

Keywords Oral myiasis · Oral squamous cell carcinoma · Maggots · Mechanical removal

Introduction

Squamous cell carcinoma constitutes about 90% of oral cancers causing significant morbidity and mortality [1]. Oral squamous cell carcinoma (OSCC) results in various morbidities like pain, bleeding on provocation, loss of function, facial disfigurement, extra oral fungation, and tissue necrosis. Other than these dreadful complications, sometimes in advanced and incurable stage, the wound gets infested with maggots. This pathological condition is called myiasis, which is caused by the presence of larvae of houseflies in human and animal tissues that evolve to a parasite [2].

Myiasis was defined as "the infestation of live human and vertebrate animals with dipterous larvae, which at least for a period, feed on the host's dead or living tissue, liquid body substances, or ingested food" by Fritz Zumpt, a German Entomologist in 1965 [3]. Myiasis can be categorized as primary and secondary. Primary myiasis is caused by biophagous larvae that feed on living tissue and is extremely rare in humans. However, secondary myiasis which is common in humans is caused by necrobiophagous flies which feed on necrotic tissue [4]. Aldo et al. [5] classified myiasis as obligatory and facultative. When the larvae require living tissue to survive, they can be termed as obligatory, whereas facultative myiasis is when the larvae develop in necrotic tissue. Myiasis can be seen globally; however, it is common in subtropical regions [6].

In the head and neck region, the commonly affected sites are eyes, ears, oral cavity, lymph nodes, paranasal sinuses, mastoid region, and tracheostomy wound [7]. Low socioeconomic status, unhygienic living conditions, advanced age, medical comorbidities, fungating lesions, poor access to health-care facility, and lack of knowledge are some of the predisposing factors. This condition requires immediate management as failure to treat may lead to fatal sequelae like hearing loss, blindness, and even death [8]. Lack of standard protocol in the line of management of this dreadful condition led to adoption of different therapies. Preferred treatment is mechanical removal of larvae with local application of one of the many agents like turpentine oil, chloroform, ethyl chloride, phenol, and olive oil [9]. Surgical debridement of the site is also being practiced and advocated. Apart from local

✉ Anuj Jain
dranujsinghvi@gmail.com

[1] Department of Trauma and Emergency Medicine, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India

measures, some authors suggest systemic ivermectin, albendazole, and clindamycin along with antibiotics in cases of infection [10].

Myiasis in oral cavity was first described by Laurence in 1909 as a rare entity. Oral myiasis in association with OSCC is even rare, and a very few reports have been mentioned in the literature. Also, a proper treatment protocol is lacking for the same. The purpose of this study is to review the cases of oral myiasis in association with OSCC and to device a proper treatment protocol.

Material and methods

Search strategies

Systematic review was conducted using PRISMA guidelines. An exhaustive literature search was done using electronic databases like PubMed, Medline, and Cochrane on 1st November 2018 for all the articles focusing on myiasis in patients with OSCC. The search was conducted using the following keyword combinations: oral myiasis and malignancy; oral myiasis and oral squamous cell carcinoma; oral myiasis and oral cancer; myiasis and oral cancer; myiasis and oral malignancy; and myiasis and oral squamous cell carcinoma. The relevant manuscripts published only in English language were given full consideration. Additional manual search was performed by reviewing the references of the selected articles. Gray literature was also evaluated for unpublished manuscripts but no data was found. Titles and abstracts of the selected articles were studied and evaluated for inclusion in the systematic review.

Inclusion and exclusion criteria

The studies on oral myiasis in patients diagnosed with OSCC were included in the review. Studies on squamous cell carcinoma of sites other than oral cavity and other variants of malignancies were excluded from the study. The manuscripts in any language apart from English, those with doubtful diagnosis, and incomplete information were also excluded.

Data extraction and quality assessment

After evaluating the titles, keywords, abstracts, full articles, and their references and applying inclusion as well as exclusion criteria, a total of seven manuscripts were selected for inclusion in our systematic review.

Results

After conducting the search with the previously mentioned keywords, a total of 12 articles were identified, out of which 2 were excluded due to irrelevance to the topic of our study. Ten full-text articles were assessed for eligibility and 3 were excluded; after which 7 articles were included in this systematic review (Fig. 1). The characteristics of the included and excluded studies are highlighted in Tables 1 and 2.

A total number of nine cases with oral myiasis in association with OSCC have been reported till date. Out of these nine cases, majority ($n = 4$) involved buccal mucosa as the site of disease. Five cases have been reported from India and four from Brazil. In all the cases, mechanical removal was carried out. Some were supplemented with asphyxiating agents and some with antiseptics and antibiotics. However, in 2017, oral ivermectin has been successfully used in the course of management.

Discussion

Myiasis is derived from the Greek word "myia," meaning invasion of vital tissue of humans or other mammals by larvae of fly species within the order of diphtheria [12]. The prevalence of this disease is high in tropical and subtropical regions [6]. There are numerous local and systemic conditions that are associated with this dreadful disease. Local factors include poor oral hygiene, mouth breathing, suppurative lesions, periodontal diseases, anterior open bite, lip incompetence, and trauma [4–6, 13]. The systemic conditions that predispose to the development of myiasis are epilepsy, cerebral palsy, alcoholism, senility, intellectual disability, and the conditions that are related to the low socioeconomic patients [6, 7]. Other than these conditions, neglect is one of the biggest reasons for development of myiasis.

The flies prefer a warm and humid environment. Many authors advocate that myiasis occurs predominantly in countries with hot weather [4]. The countries affected by this disease are India and Brazil which are the countries on their respective continents with this climate characteristic. Furthermore, India and Brazil are developing countries, thus demonstrating the social nature of the disease.

The incidence of intra-oral myiasis is lower than that of extra-oral myiasis because the tissues of the oral cavity are not permanently exposed to the external environment. The flies sit on the exposed wound and lay over 500 eggs at a time which hatch to become maggots in less than a week. The life cycle completes within 2 weeks when the maggots turn into flies. As soon as they mature, they wiggle out and fall to the ground to pupate. This developmental transition requires an intermediate host on which they feed. In the oral cavity, these larvae burrow deeper into the soft tissue making tunnels. They

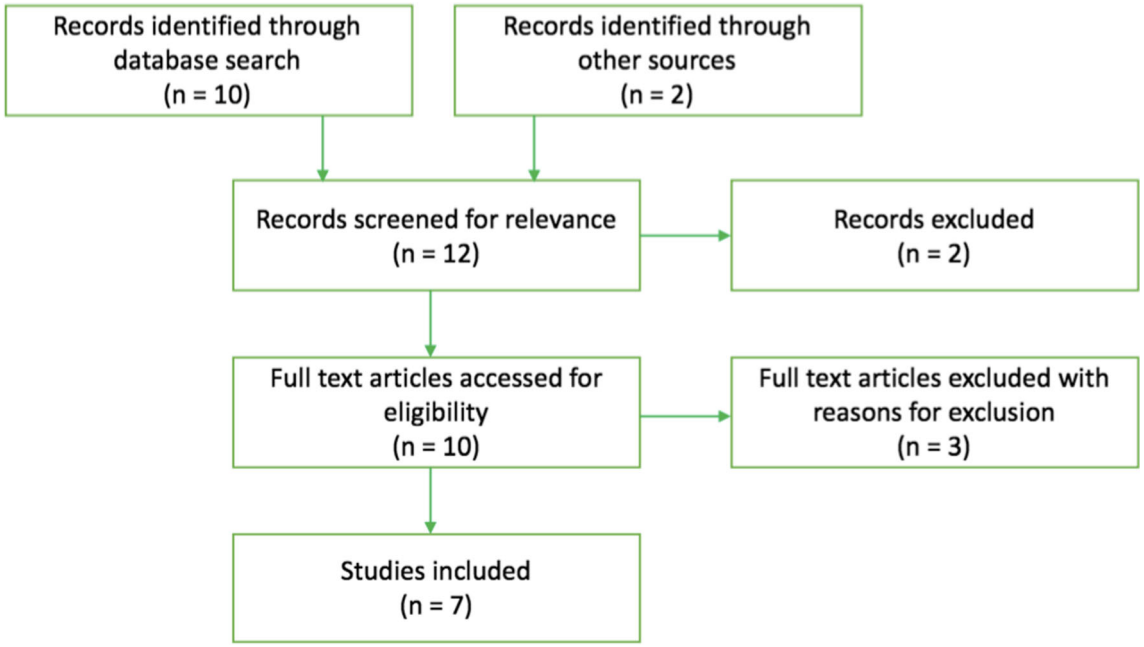

Fig. 1 Schematic representation depicting search strategy of the study

separate the gingiva and mucoperiosteum from the bone and obtain their nutrition from the surrounding tissues. They have a grayish white color with brown-black tip anteriorly, and a cork-screw appearance [14].

Patients with oral malignancy infested with maggots are generally negligent with advanced cases of OSCC [8, 15]. These patients generally belong to a low socioeconomic status with poor oral hygiene. They are malnourished and usually live alone in social isolation. Oral malignancy is characterized with ulcerative and necrotic lesions which are exposed to the environment. This provides an ideal condition for secondary myiasis as this kind of tissue is attractive to different species that may deposit their eggs which will eventually lead to the development of maggots. Furthermore, patients with OSCC cannot maintain proper oral hygiene and may suffer from alcoholism, diabetes mellitus, or other systemic conditions which may increase the risk of developing oral myiasis [15].

Myiasis associated with a malignant tumor can be related to the presence of ulcers and necrotic lesions exposed to the environment. However, cases of oral myiasis associated with malignancies are rare, and the maximum reports are from India. Extensive myiasis infestations in patients with OSCC have been reported in the literature but are very few. As per the literature search, a total of nine cases have been reported in 7 articles (Table 1). There can be a possibility that this condition is underreported, as OSCC is a common condition mainly in developing countries.

Four cases are from Brazil, reported by Carvalho et al. [16], Gabriel et al. [8], Pessoa and Galvão [17], and Girardi and Scrofernecker [18]. Carvalho et al. [16] reported a case of

Table 1 Characteristics of included articles

Sr. no.	Author	Country	Year	No. of cases	Site	Treatment
1	Carvalho et al.	Brazil	2008	1	Buccal mucosa	Mechanical removal with antiseptics and antibiotics
2	Gabriel et al.	Brazil	2008	1	Floor of mouth	Mechanical removal with application of ether embedded cotton
3	Gopalakrishnan et al.	India	2008	2	Lower lip; Buccal mucosa	Mechanical removal with application of turpentine oil; antibiotics and hematinic
4	Pessoa and Galvão	Brazil	2011	1	Mandible	Mechanical removal with antiseptics
5	Dharshiyani et al.	India	2012	1	Mandible	Mechanical removal with antiseptics, anthelmintic and antibiotics
6	Biradar et al.	India	2015	2	Buccal mucosa	Mechanical removal with surgical debridement, antibiotics
7	Girardi and Scrofernecker	Brazil	2017	1	Maxilla	Mechanical removal along with oral ivermectin

Table 2 Characteristics of excluded studies

Sr. no.	Records excluded	Year	Reason
1	Sadeq Ali Al-Maweri et al. [11]	2015	Review of previously published studies without any new cases reported
2	de Arruda JAA et al. [7]	2017	Review of previously published studies with new reports of oral myiasis but not in association with OSCC
3	Patel B et al. [10]	2018	Study performed on cases of Myiasis in patients with head and neck malignancy. However, nature of malignancy is not specified.

myiasis in a patient with OSCC with no physical or neurological deficit. Gabriel et al. [8] reported one case of a 72-year-old woman living in a rural area with extensive orofacial myiasis associated with SCC of the floor of the mouth. Pessoa and Galvão [17] reported one case of a 44-year-old male with habits of alcohol and tobacco consumption presenting with myiasis in advanced squamous cell carcinoma of the mandible. The patient was living in a rural area with low economic status and having poor living conditions. Girardi and Scrofernecker [18] reported a case of a 66-year-old male who presented with maggots in the maxillectomy wound.

Five cases were reported from India. Gopalakrishnan et al. [19] reported two cases of myiasis associated with OSCC of the buccal mucosa and lower lip. The authors also described two more cases of myiasis associated with malignancy on the neck. Dharshiyani et al. [14] reported a 75-year-old male who was a chronic alcoholic belonging to a very low socioeconomic status developed oral myiasis associated with OSSC of the mandible. Biradar et al. [15] reported two cases of oral myiasis associated with OSCC in adult males. In both the reported cases, the malignant ulcer started on the buccal mucosa, which progressed to involve the whole adjacent tissues, with marked extra-oral fungation. From all these cases, it is evident that the patients belonged to a low socioeconomic status and had poor living conditions and most of them were living in a rural area. This situation can be observed by the clinically advanced stage of the malignancy and its long term, indicating negligence and lack of knowledge.

There is no specific treatment modality for the management of myiasis. The preferred treatment modality is mechanical removal of maggots with the help of tweezers. The mechanical removal, however, is not a sufficient treatment modality as it does not warrant the complete removal of maggots because the larva uses its hook to grip the tissues and it buries deeper in the tissue. The use of various asphyxiating agents has been recommended in order to compel the maggots wiggle out of the host tissue. Whitehead varnish pack, which contains ether, can be applied to the raw wound for protection during the healing phase [14]. However, these agents have controversial results, whereas use of turpentine oil has promising results as it irritates the maggots causing larval asphyxia and forcing them out of their hiding place [9]. Surgical debridement of local site for management of myiasis has also been carried out by Biradar et al. [15]. Ivermectin, a semisynthetic macrolide antibiotic used in veterinary medicine, has been used in the management of oral myiasis. This medication activates the release of γ-aminobutyric acid which induces the death of the larvae and their spontaneous elimination [20].

Patel et al. [10] recommended a systemic treatment with ivermectin, albendazole, and clindamycin (triple therapy) along with turpentine oil dressing which enhances the removal of maggots, early recovery and relief from distress, and other associated symptoms. Albendazole is a broad- spectrum anthelminthic-antiparasitic agent which is being used as a management modality for intestinal myiasis [21] and cutaneous myiasis [22]. Malignant fungating wound is likely to have anaerobic environment which provides an ideal environment for the growth of house fly larvae. Development of this secondary infection necessitates the introduction of antibiotics in the treatment regimen. Clindamycin is used mainly to treat

Table 3 Jain Protocol for the management of oral myiasis associated with oral squamous cell carcinoma

Local treatment	Systemic treatment
• Flushing of wound with turpentine oil followed by mechanical removal once daily	• Tablet ivermectin < 15 mg/kg per day for 3 days
• Overnight dressing with turpentine oil	• Tablet clindamycin 300 mg thrice a day for 5 days
• Flushing of wound with normal saline and 5% povidone iodine solution twice daily	• Tablet albendazole 400 mg twice daily for 3 days
• Surgical debridement if possible	

anaerobic infections caused by susceptible anaerobic bacteria. It may be used to treat infections caused by susceptible aerobic bacteria as well [23].

Considering the various treatment modalities and their effectivity in the management of oral myiasis, specifically in cases of oral malignant tumors, the author has developed a protocol for the management of this disturbing condition. The following protocol (Jain Protocol) which is a combination of local and systemic treatment is recommended to treat cases of oral myiasis with OSCC (Table 3).

Conclusion

Oral myiasis is a possible risk for the patient with OSCC mainly with poor living conditions. The patients and caregivers must be really careful and prevent the flies form sitting on wound. Good hygiene and general cleanliness involving regular cleaning and dressing of wounds along with educating the patients must be a practice. Also, education of the susceptible population in developing countries about such diseases must be done through various awareness programs. Once affected, a proper treatment protocol must be followed.

Compliance with ethical standards

Conflict of interest The author declares that there is no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent This article does not contain any studies with human participants or animals performed by any of the authors.

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