

Oral cancer pain: The most painful of all cancers

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Abstract:

Pain is the most early complaint seen in patients suffering from oral cancer. It should be taken seriously so that early diagnosis can be made as late diagnosis results in poor prognosis. The pain associated with oral cancer is the most severe of all the other types of cancers. It serves as the key for the diagnosis and the treatment initiation.

Introduction:

Pain is defined as- An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

One of the cancers included in the head and neck cancers category is mouth cancer. Treatment for head and neck malignancies, including mouth cancer, is frequently the same.¹⁷ Oral cancer constitutes the sixth most common malignancy in the world. Almost 40,000 new cases of oral cancer are diagnosed yearly, two-third of these cases are seen in Asian countries like Bangladesh, Sri Lanka, India, Pakistan and Indonesia.¹³ Each year, 25% of the new cancer cases is constituted by oral cancer in these high risk countries.¹³

According to ICMR, oral cancer is the most common cancer in Indian men (16.1% of all cancers) and fourth most common cancer in Indian women. The mean survival rate is 5 years in 40% of population and if diagnosed early, the survival rates can exceed 80%.¹⁴ The detection of oral cancer can be done early by screening. The early detection and treatment can improve the survival of the patient.

Mouth cancer symptoms and signs might include: an ulcer, a mouth or lip sore that doesn't go away, a spot inside of your mouth that is either white or red, missing teeth, interior of your mouth

has a growth or bump, mouth ache, an earache, difficulty in swallowing or discomfort.^{17, 25,27} Although, the initial symptom of the oral cancer is pain, both the patients awaiting treatment and the patients undergoing treatment, pain is a common complaint.⁸ Having mouth cancer can make chewing and swallowing food painful or burning. Or perhaps your meal feels like it is stuck in your throat.¹⁶

The cause of the cancer pain may be the progression of tumor, diagnostic or therapeutical procedures which are invasive, infection or muscle aches which are limiting the physical activity by the patients.⁹

Almost 50% of the oral cancers are diagnosed at an advanced stage as in the early stages the patients are asymptomatic so they do not go or any medical help until they suffer from symptoms like pain, bleeding or a mass or neck when the lymphatic also get invaded.¹⁵

At the site of the cancer, patients experience severe chronic and mechanically induced pain¹⁻³. The quality of life of these patients is degraded as the pain causes interference with eating, talking and drinking. After surgical removal of cancer, there is no pain experience.⁴ It explains that the initiation and maintenance of the oral cancer is maintained in the cancer microenvironment.

Pathogenesis:

The different mechanisms involved in the pathogenesis of the oral cancer are- the stimulation of the nerve endings present in the oral mucosa, the sensory nerves like trigeminal nerve getting compressed due to the tumor growth, ulceration and subsequent infection of the tissue leading to inflammation resulting pain.⁸

Mouth cancers originate when cells in the mouth or on the lips experience DNA changes (mutations). The instructions that inform a cell what to do are encoded in its DNA. When healthy cells would stop growing and dividing, mutations tell the cells to keep doing so. A tumor might develop when the abnormal mouth cancer cells accumulate. They may eventually expand from the inside of the mouth to other parts of the head, neck, or the entire body.¹⁷

The flat, thin cells (squamous cells) that line your lips and the inside of your mouth are where mouth cancers most frequently start. Squamous cell carcinomas make up the majority of oral malignancies. The alterations in squamous cells that result in mouth cancer are not known to have a specific origin.¹⁷

The main cause of the oral cancer pain is the sensitization or activation of the afferent neurons by the mediators released from cancer and microenvironment. According to the current researches, there are two receptors in the peripheral neurons, TRPY1 (transient receptor potential cation channel subfamily V member 1) and TRPA1 (transient receptor potential cation channel subfamily A member 1)⁵. There was increase in the expression of TRPY1 and TRPA1 in the trigeminal or dorsal root ganglion in the oral cancer models⁶. The mechanical allodynia and thermal hyperalgesia can be relieved through the process of antagonism or the genetic knockout of the receptors.⁷

Causes of oral cancer:

Approximately 75% of people with oral cancer practice the following behaviors: Use a pipe, a cigar, or both, use smokeless tobacco products like hookahs or shisha, pipes, dip, chewing tobacco or snuff. The people with oral cancer consume excessive amounts of alcohol on a regular basis. Others spend a great deal of time in the sun without

wearing lip sunscreen. Also they may possess the oral HPV (human papillomavirus 16) which is spread mostly by practicing oral sex with partners having persistent genital HPV infections suggesting cross transmission between the mouth and genitals.²⁵ Therefore there is a direct association between the number of sexual partners and the likelihood of contracting oral HPV. In the developed countries, the most common HPV related cancer is oral squamous cell carcinoma surpassing cervical cancer. It has been estimated that by 2030, most squamous cell carcinomas will be HPV associated.²⁵ It was found that the people suffering from oral cancer might have oral cancer running in their family as its also genetic. So the etiology might be tobacco alone or a combination of the above factors. Also practicing smoking and drinking increases the likelihood of development of HPV into oral cancer if the patient is already harbouring HPV virus. The main risk factor was initially tobacco and alcohol use but now HPV transmission has overtaken smoke use and heavy alcohol consumption as the main risk factor for oral cancer.²⁶ So the fact that 25% of people who get oral cancer don't smoke or have any other known risk factors should not be overlooked.¹⁹

Nature of pain:

The oral cavity is innervated by dense trigeminal nerve causing localization of pain in the primary site of the oral cancer whereas the cancers of the other primary sites like gastrointestinal tract or pelvis are more visceral in nature.¹⁵ A pain questionnaire can be used to measure pain. For measuring oral cancer pain, the University of California San Francisco Oral Cancer Pain Questionnaire (UCSFOCPQ) was created and validated. Eight questions on the questionnaire ask patients to rate the severity of their pain on a 0-100 point VAS.²⁰

According to a team of researchers at New York University (NYU) College of Dentistry who discovered genetic and cellular hints as to why metastatic oral cancers are so painful, oral cancer is more likely to spread in patients who are experiencing high levels of pain.²¹

Pain is experienced with or without treatment:

The primary treatments in the patients suffering from the advanced stage disease are radical dissection and radiotherapy¹⁰. Even after survival, the primary concern of the patient remains pain. The worst symptom by the patients of oral cancer remains pain.¹¹The reason for the late orofacial pain in the treatment course could be due to surgery, chemotherapy and radiation therapy.¹² Chemotherapy and radiation therapy may result in painful mucositis and neurotoxicity. Also surgery results in nerve and tissue damage leading long term complications like myofascial and neuropathic pain syndromes. All these treatment modalities cause severe pain which affect the prognosis of the patient along with their daily life.

Patients who suffer from either head and neck cancer rarely find relief despite pain management techniques that include high-dose opioid analgesics. Effective pain management necessitates therapies for both nociceptive and neuropathic processes since oral pain in cancer patients is probably brought on by both of these mechanisms.¹⁸

Almost always, pain can be treated with less potent medications like ibuprofen or acetaminophen, or if necessary, with stronger drugs like morphine or similar opioids. It is possible to reduce pain occasionally by undergoing procedures like surgery, a nerve block, or radiation.²³

Studies are being done to establish the use of cannabinoids to reduce pain associated with oral cancer.²⁴

How to lower the risk of oral cancer:

Although oral cancer can affect anyone, there are a number of things you can do to reduce your risk. Don't use any type of tobacco products. Lessen your exposure to the sun. Have only moderate alcohol consumption. Practice daily brushing and flossing. As oro-genital sex is the profound risk factor found in association with HPV related OSCC, its advised to not indulge in oral sex with multiple partners as it can lead to HPV associated oral cancer if the sexual partners have this virus in their cervix. Also HPV vaccination is

recommended to counteract the increasing cases of OSSC. Maintain twice yearly visits to the dentist.²²

Conclusion:

The oral cancer pain is rated as the most painful amongst all the other types of cancer. The pain is not present in pre-cancerous lesions and conditions and pain is experienced when the patient is suffering from oral cancer. Also presence of precancerous lesions and conditions should be taken as an alarm as if they are not treated at this time, they will convert into oral cancer if the habits causing it continues. Therefore it is very important to visit the dentist regularly and inform if there is pain or a lesion in the oral cavity so that other signs can also be found out. If the oral cancer is diagnosed at an early stage then the chances of survival are high and pain being the first symptom should not be overlooked.

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