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Oral cancer early symptom variations: pain as the first symptom in oral cancer patients

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ABSTRACT

Introduction: Although oral cancer is amenable for early detection, it often presents as advanced disease in many of patients. Long-lasting ulcer or mucosal discoloration has been described as the key to an early diagnosis; however other symptoms may also exist. The present study aims to describe the frequency of the early symptoms in oral cancer patients, with a special focus on pain.

Materials and Methods: Patients (n=100) with primary oral squamous cell carcinoma (SCC) treated in three university hospitals during 2004-2006, in Tehran, were included in this study. Oral cancers were defined as SCCs of the oral cavity (ICD-10 anatomical sites C01-C06). Questionnaire-interviews were made and all the patient records were reviewed for retrieving data. Data analysis was done by means of SPSS version 20, by Chi-squared test and multinomial regression.

Results: Majority of patients (73%) reported to have painless ulcer as the first symptom. Pain was reported to be the earliest symptom in 10% of oral cancer patients. Other symptoms were swelling, white patch, and paresthesia. Stage of tumor at the time of diagnosis and source of referral were related to initial symptom ($p< 0.05$). Patients who had pain as the first symptom was mostly referred to hospital by a medical professional rather than a dentist or any other dental professional. They were also at an advanced stage of tumor when being diagnosed.

Conclusion: This study supports the importance of initial symptoms in the detection of oral cancers in the earliest stage, in order to improve patients' prognosis and quality of life.

Key words: pain, Iran, oral cancer, early symptom.

Introduction

Oral cancer outcomes in Iran are poor and this is considered to be due, at least in part, to tumors being identified at a late stage as a consequence of delayed diagnosis [1, 2]. Improvement in early diagnosis is therefore a critical element of oral cancer prevention strategy. Tumors of oral cavity are in more than 90% squamous cell carcinomas (SCC) which are considered to be amenable to early diagnosis [2, 3]. However, they are often associated with prolonged time to help seeking, multiple consultations before referral to a qualified specialist, diverse referral pattern and an increased risk of being diagnosed at advanced stages [5, 6, 7]. Several studies in which oral cancer patients report their symptoms indicate that not accounting a symptom as possibly due to cancer (lack of knowledge) and / or symptom ignorance are essential determinants of patient delay in seeking care [8, 9, 10, 11]. Promoting evidence-based knowledge about factors influencing on the diagnostic delay of these cancers, and facilitating prompt diagnosis is therefore of particular importance. Malignant tumors of oral cavity are associated with easily detectable signs [3, 4], which should assist diagnostic process and early diagnosis. This, together with rapid referral, and improved patients' access to multidisciplinary specialist care are encouraged by the World Health Organization (WHO) to be set as priority topics in oral health care services [4]. Oral SSC normally presents as a persistent mass or indurate ulcer. Involvement of nearby tissues represents local tumor invasion [12]. Enlarged cervical lymph nodes may be detectable by palpation. Symptoms of oral cancer include pain, swelling, paresthesia and

and anesthesia in the absence of a history of trauma, bleeding, and difficulty in speaking, eating, swallowing, and opening the mouth [13]. Symptoms are infrequent in earlier tumor stages but become common with advanced local invasion [12]. In advanced stages, a large ulcerative mass, with extension to adjacent tissues may be evident [13]. Distant metastases occur throughout the regional lymphatic system and regularly spread to the lungs [12].

A dentist can diagnose oral cancer early or contribute to early oral cancer diagnosis through attentive and rational clinical examination and referral to more specialized services [4]. Study of oral cancer symptoms produces useful evidence for improvement of performance of clinical examinations, and referrals. Several reports showed that oral cancer patients had presented one or more symptoms months before cancer diagnosis [14, 15, 6, and 7]. Pain is a common symptom in cancer patients as in cancers of the head and neck area including oral cancers [16,17]. Tumor growth increases inflammatory factors in the body which can cause pain around the tumor site [16].

Although numerous studies have been done regarding oral cancer symptoms in different settings, less is reported about the pre-diagnostic, early symptoms, or pretreatment especially those which are of lower frequency. In this retrospective descriptive article the objective was to report findings about the frequency of early symptoms in oral cancer patients, with a special focus on pain.

Methods and Materials

The study population consisted of 100 consecutive patients with primary oral squamous cell carcinoma (ICD-10 sites C01–C06) who referred to three university hospitals in Tehran, between 2004 and 2006 for treatment. Questionnaire- interviews were used to obtain data before treatment; in addition the medical records of patients were reviewed. Acquired data included: gender, age, early symptoms, date of onset of symptoms, date of diagnosis, primary tumor site, source of referral, tumor histopathologic grade and TNM stage of the tumor at the time of diagnosis. Early symptom was defined as the symptom which was first noticed by the patient.

To reduce recall bias, if a patient was unable to remember the exact date of onset of symptoms, but remembered only the month or the season, then the median date was chosen. The relationship between symptoms and the other study variables were analyzed by means of SPSS version 20, by Chi-squared test. Associations were considered significant when $p < 0.05$. The Ethics Committee of the School of Dentistry, Shaheed Beheshti Medical University, approved the study protocol.

Results

Patient distribution by study variables is shown in Table 1. Of all the patients females were 47%, and the mean age of patients was 61.5 (SD 15.8, range 24- 100) at the time of diagnosis. Ulcer was the first symptom which was noticed by the majority of patients (73%). Pain was reported as an initial symptom in 10% of the oral cancer patients. Tumor site distribution was 60%, 11% and 29% for tumors of tongue (C01-C02), tumors of gingiva and floor of the mouth (C03-C04) and tumors of hard and soft palate, buccal and vestibular mucosa (C05-C06) respectively. Of all the tumors 61% were at advanced stages (stages III and IV) at the time of diagnosis. The time elapsed between symptom notice by the patient and final tumor diagnosis (diagnostic delay) was 3 months or more in majority of the patients.

Distribution of oral cancer patients' initial symptom, by gender, primary tumor site, stage, grade, source of referral and diagnostic delay is displayed in Table 2. Of those patients who had pain as the first symptom (n= 10), the majority were females (n= 7), had diagnostic delay of equal or more than 3 months (n= 9), and were diagnosed at advanced stages (n= 7). Medical professionals were the major source of referral in oral cancer patients who had pain as the first symptom. In contrast, dentists or other dental professionals mostly referred those oral cancer patients who reported ulcer as their initial symptom. Stage of tumor at the time of diagnosis and source of referral were significantly associated with initial symptom ($p< 0.05$). None of the other study variables were related to initial symptom. Further analysis i.e. multinomial regression, confirmed the above mentioned association (Table 3).

Discussion

Despite the advances in oral cancer treatment, the related morbidity and mortality have not been changed significantly. This may in part be due to the late diagnosis, which either is related to patient's late symptom notification i.e. patient delay, or professional delay which is the time from patients' first visit by a professional to final diagnosis. Predictably, 'common, classic' oral cancer symptoms such as 'persistent ulcer' or 'unexplained change in the appearance of oral mucosa'

were most likely to arouse patient and professional suspicion; however, even for those symptoms, the rate of cancer suspicion is modest [10].

The intention of the present study was to describe early oral cancer symptoms that contributed to the diagnosis of cancer. The most common symptom reported was ulceration. More than two thirds of patients reported ulcer (73%) and 10% experienced pain as the initial symptom. This is in line with the reports from different parts of the world [18, 19, 20].

These figures testify to the importance of well-known oral cancer symptoms and to the variety of other symptoms, such as pain, that also may signal cancer. Despite the fact that pain is usually considered as the most provoking factor for patients' dental visit –especially in developing countries [21], results of the present study show that the majority of oral cancer patients who reported pain as their initial symptom were diagnosed late when the tumors were at advanced stages. Although pain has been mentioned as a common symptom in oral cancer patients, it regularly occurs when the tumor have gained a notable size. Thus early stage tumors are often painless [17].

Pain caused by tumor growth can occur as a result of direct tissue damage or of the invasion to nerves. Reyes-Gibby and his colleagues show that pretreatment pain is an independent predictor of the survival rate in head and neck SCC patients, even after adjusting for important prognostic factors such as TNM stage, smoking and age [22]. Thus pain is the worst symptom for oral cancer patients, which enormously affects both the length and the quality of their life [23, 16].

Table 1. Distribution of oral cancer patients by initial symptom, gender, primary tumor site, stage, grade, source of referral and diagnostic delay (n=100).

Variable		*N*
Initial symptom		
	Ulcer	*73*
	White patch	*6*
	Swelling	*10*
	Pain	*10*
	paresthesia	*1*
Gender		
	Male	*53*
	Female	*47*
Tumor site		
	C01-C02	*60*
	C03-C04	*11*
	C05-C06	*29*
Tumor stage		
	I & II	*39*
	III & IV	*61*
Histologic grade		
	I	*68*
	II	*24*
	III	*4*
Source of referral		
	Dental professional	*45*
	Medical professional	*55*
Diagnostic delay		
	< 3 months	*30*
	≥ 3 months	*70*
Total		*100*

Table 2. Distribution of oral cancer patients' initial symptom by age, gender, diagnostic delay, primary tumor site, stage, grade and source of referral (n=100).

Variable	Initial symptom					p- value
	Ulcer	White patch	Swelling	Pain	Paresthesia	
	No (٪)	No (٪)	No (٪)	No (٪)	No (٪)	
Age						
≤ 44	14 (82)	0 (0)	2 (12)	1 (6)	0 (0)	
45-64	21 (64)	4 (12)	4 (12)	4 (12)	0 (0)	**0.66**
65+	38 (76)	2 (4)	4 (8)	5 (10)	1 (2)	
Gender						
Male	40 (75)	3 (6)	6 (11)	3 (6)	1 (2)	**0.50**
Female	33 (70)	3 (6)	4 (9)	7 (15)	0 (0)	
Diagnostic delay						
< 3	23 (77)	2 (7)	4 (13)	1 (3)	0 (0)	**0.57**
≥ 3	50 (71)	4 (6)	6 (9)	9 (12.5)	1 (1.5)	
Tumor site						
C01-C02	45 (75)	4 (6)	3 (5)	7 (12)	1 (2)	
C03-C04	8 (73)	0 (0)	2 (18)	1 (9)	0 (0)	**0.68**
C05-C06	20 (69)	2 (7)	5 (17)	2 (7)	0 (0)	
Stage						
I & II	26 (67)	6 (15)	4 (10)	3 (8)	0 (0)	**0.03***
III & IV	47 (77)	0 (0)	6 (10)	7 (11.5)	1 (1.5)	
Grade						
I	42 (74)	3 (5)	6 (10)	6 (11)	0 (0)	
II	21 (75)	2 (7)	2 (7)	2 (7)	1 (4)	**0.93**
III	3 (75)	0 (0)	0 (0)	1 (25)	0 (0)	
Source of referral						
Dental professional	38 (84)	3 (7)	1 (2)	2 (5)	1 (2)	**0.04***
Medical professional	35 (64)	3 (5)	9 (16)	8 (15)	0 (0)	
Total	73	6	10	10	1	

Table 3. Results of multinomial regression analysis

Effect	Model Fitting Criteria	Likelihood Ratio Tests		
	-2 Log Likelihood of Reduced Model	Chi-Square	df	Sig.
Intercept	109.707*	.000	0	.
Age group	115.333	5.626	8	.689
Gender	113.826	4.119	4	.390
Diagnostic delay	112.843	3.137	4	.535
Primary tumor site	113.419	3.712	4	.446
Stage	122.906	13.199	4	.010**
Grade	115.436	5.729	8	.678
Referral source	121.719	12.012	4	.017**

*. This reduced model is equivalent to the final model because omitting the effect does not increase the degrees of freedom.

**. P< 0.05

In the present study we found that, it was medical professional who referred the majority of those who reported pain, not the dental professional. This indicates that dental professionals especially dentists may need more knowledge about the oral cancer early symptoms including pain. The important point is that such symptoms offer diagnostic possibilities for the dentist and consequently will decrease the professional diagnostic delay. Numerous reports support the opinion that a dental professional is more likely to detect a suspicious lesion during a routine appointment than a medical professional [24, 25, 26].

Strengths and weaknesses of our study: The combination of questionnaire-base data with medical record-based symptom information allowed for a more complete picture of the diversity of symptoms preceding diagnosis of oral cancer, but potential of recall bias, still exists. Data in medical records may be deficient, but they offer an opportunity to review a complete clinical case.

Conclusion

Findings of the present study signify that dentists and other dental professionals, should be empowered by educational programs focused on oral cancer early symptom variations, to improve early diagnosis and gain better prognosis for oral cancer patients in Tehran, Iran.

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