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Research Article

ORAL CANCER IN YOUNG NON HABITUATE PATIENTS- A CASE SERIES

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ABSTRACT

Oral squamous cell carcinoma (OSCC) is the most common (>90%) among all head and neck carcinomas. It is the sixth most common malignant disease worldwide. Oral cancer remains primarily a disease of elderly males during the fifth to eighth decades which can be attributed to tobacco and alcohol abuse. According to recent reports 1 to 6% of SCC cases occurs in patients under the age of 40 and is a cause of great concern. Its occurrence in children and adolescents are extremely rare so that when cases present they are often misdiagnosed and inappropriately treated leading to delay in definitive treatment. Such cases warrant careful clinical examination along with an analysis of etiologic factors.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most common (>90%) among all head and neck malignancies[1]. It is the sixth most common malignant disease worldwide[2]. Oral cancer remains primarily a disease of elderly males during the fifth to eighth decades which can be attributed to tobacco and alcohol abuse[3]. It rarely occurs in young patients under 40 years (1–6%)[4]. This can be ascribed to the fact that when younger patients indulge in the risk factors like tobacco and alcohol; it is for considerably shorter periods compared with the older age group to induce malignant transformation[5]. OSCC is extremely rare in paediatric patients especially during the first decade of life. However, several recent reports suggest an increasing incidence of this disease among younger persons in many regions of the world-a trend which is particularly concerning[3]. While isolated cases of adolescent OSCC have been documented, most lesions have been on tongue and lip. In this case series we report 5 cases of OSCC in non habituate young patients out of which 2 are seen on mandibular alveolar ridge, 1 on the lateral border of tongue and 2 on buccal mucosa.

Case Report

CASE 1

A 10 year old female patient presented with a painless swelling of 2 weeks duration in the lower right back tooth region. The mobile deciduous first molar which was present in relation to the swelling was extracted 1 week before from a private clinic and the patient had a course of antibiotics. The child never had tooth ache. On examination the patient was apparently normal. There was an ulceroproliferative lesion of size 1.5 x 1.5cm on right alveolar ridge extending to the buccal vestibule in the premolar molar region. On palpation the lesion was firm with indurated base. The right submandibular lymph node was palpable and mobile. The radiographic examination did not reveal any signs of bone destruction. There was no relevant medical and family history. Patient denied any history of trauma or other harmful habits.

Fig 1: Ulceroproliferative lesion on the right alveolar ridge

Incision biopsy was done from the lesion and histopathological examination revealed a dysplastic parakeratotic hyperplastic stratified squamous epithelium. Basement membrane was indistinct at many areas and the malignant epithelial cells seem to infiltrate into the connective tissue in the form of cords and islands. Multiple keratin pearls were noted. There was dense diffuse collection of inflammatory cells chiefly eosinophils along with lymphocytes and plasma cells. These features were suggestive of well differentiated squamous cell carcinoma.

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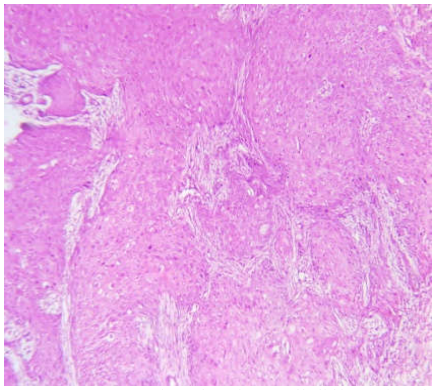

Fig 2: H & E section showing well differentiated squamous cell carcinoma (10x)

Case 2

A 19 year old male patient presented with a painful swelling of 1 month duration in relation to lower right back tooth. On examination multiple periodontal abscess in relation to 45, 46, 47 with grade III mobility of 46 and 47 were noted. Deep periodontal pocket was present in relation to 45, 46 and 47. Radiograph showed severe bone loss extending to the root tip of 46 and 47 giving a floating tooth appearance. The lesion did not respond to antibiotics. Culture and sensitivity showed heavy growth of Klebsiella species.46 and 47 were extracted due to poor prognosis. When patient was reviewed after 2 months, multiple indurated soft tissue mass were present on the right alveolar ridge extending from 43 to 48. Right submandibular lymph nodes were palpable and mobile.

Fig 3: a) Multiple indurated soft tissue mass on right alveolar ridge b): Radiograph showing severe bone loss

Incision biopsy was done and the histopathological examination revealed a parakeratotic hyperplastic stratified squamous epithelium exhibiting dysplastic features with infiltration of sheets of malignant epithelial cells into connective tissue stroma suggestive of well differentiated squamous cell carcinoma. There were large areas of keratin pools in the tissue. Epithelial microcysts with keratin were also observed.

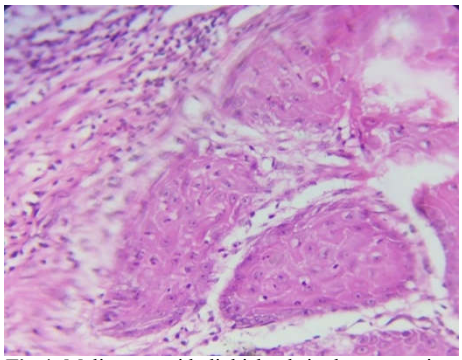

Fig 4: Malignant epithelial islands in the connective tissue (40 x)

Case 3

A 26 year old male patient reported with a complaint of burning sensation on left side of tongue since 1 month. On examination there was a non-healing ulcer of 2 x 2cm with induration on left lateral border of tongue. The sharp tooth (37) in relation to the swelling which caused irritation for a short duration was extracted. Incision biopsy was done and the histopathological examination revealed a connective tissue stroma infiltrated with malignant epithelial cells in the form of sheets, islands and cords suggestive of moderately differentiated squamous cell carcinoma. The invasive tumour front extended into submucosa amidst the muscle fibres.

Fig 5: Non healing ulcer on left lateral border of tongue

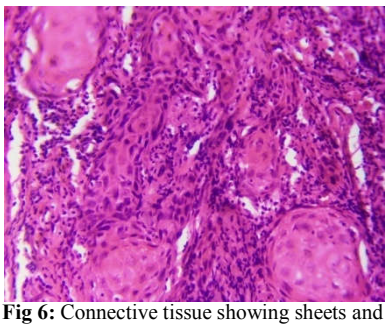

Fig 6: Connective tissue showing sheets and islands of malignant epithelial cells

Case 4

A 34 year old male patient presented with a non healing ulcer on the left buccal mucosa since 2 months. The ulcer of size 2 x 1.5cm had indurated margins. There were no sharp teeth. The left submandibular lymph nodes were palpable and tender. Histopathological examination of the incision biopsy specimen showed a moderately dysplastic epithelium with islands of malignant epithelial cells in the connective tissue stroma suggestive of moderately differentiated squamous cell carcinoma.

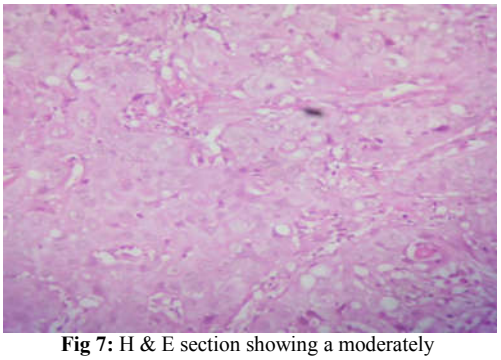

Fig 7: H & E section showing a moderately differentiated squamous cell carcinoma

Case 5

A 35 year old male patient presented with pain and burning sensation on the left buccal mucosa. On examination there was a well circumscribed ulceroproliferative lesion of size 2.5x 1.5 cm with indurated margins. The left submandibular lymph nodes were palpable and tender. Histopathological examination of the incision biopsy specimen showed a dysplastic epithelium with sheets and islands of malignant epithelial cells with multiple keratin pearl formation in the connective tissue stroma suggestive of well differentiated squamous cell carcinoma.

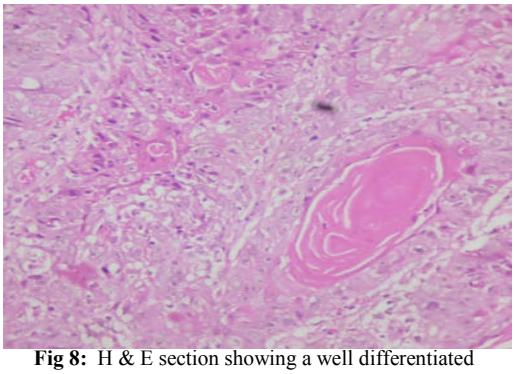

Fig 8: H & E section showing a well differentiated squamous cell carcinoma

DISCUSSION

Squamous cell carcinoma (SCC) in the head and neck region occurs primarily in the oral cavity and oropharynx and is generally regarded as a disease of the elderly (>45 years) [6]. A review of literature revealed that the incidence of SCC is not a frequent finding in young patients. Most authors consider young patients with SCC as those less than 40 years of age, even though others use reference ages under 20 or 30 years[4]. According to recent reports, 1 to 6% of SCC cases occurs in patients under the age of 40 and is a cause of great concern[3]. Its occurrence in children and adolescents are extremely rare so that when cases present they are often misdiagnosed and inappropriately treated leading to delay in definitive treatment. This may, in turn, lead to a poorer prognosis for these patients.

The average age of cases presented in the literature as young bearers of SCC ranges from 30.8 to 34.2 years, with a male predominance[7,8,9]. In this case series, 4 are male patients of age 19, 26, 34 and 35 years and one is a 10 year old female patient.

The tongue is the most common site for oral cancers in patients under 40, which is similar to that observed in older patients[10]. But in our case series, 2 patients had lesion on alveolar ridge which is a rare site.

There are no distinguishing features in clinical manifestation of SCC in young patients compared to that of older patients, but still many clinicians tend not to include SCC as a diagnosis in young patients, merely because such a disease is not compatible with their age range[11]. In these cases, differential diagnosis normally includes deep mycoses, primary syphilis, cancrum and tuberculosis[4].

Even though some studies have demonstrated that the same etiological factors are present for both age ranges, the possibility of the existence of a carcinogenic action of tobacco and alcohol in the young patient is low, since there is a relatively short exposure time for the establishment of a cause-effect relation in this group. Thus, other factors should be investigated in order to explain etiology of SCC in young patients, among which are included: genetic predisposition (Fanconi's anaemia, xeroderma pigmentosa, KID 'keratosis, ichthyosis and deafness' syndrome), previous viral infections, feeding habits, immunodeficiency states, occupational exposure to carcinogenic elements, socioeconomic condition, and oral hygiene and trauma[12]. Two theories have been proposed, but not proven, to explain the development of oral cancer in children: the passage of carcinogens from mother to foetus across the placenta and development from the epithelium derived from the first branchial arch. According to some authors, there can be three categories of etiological factors of SCC in children: (1) the immunosuppression induced by hemopathia (Fanconi's anaemia) or by chemotherapy allows viral infection with HPV; (2) the genodermatoses diseases such as xeroderma pigmentosum or KID syndrome (keratosis, ichthyosis, deafness) may predispose to SCC; and (3) a group characterized by no particular personal or family history[13].

Heterogeneity of oral cancer at cellular and molecular level and the large number of genes potentially involved in oral carcinogenesis emphasize the importance of studying gene expression changes in a global scale by proteomics. The modern high throughput genomic and proteomic approaches have been extensively used to study the altered expressions of genes and proteins in oral cancer. It may be helpful to facilitate the identification of potential biomarkers for oral cancer[14].

Lingen *et al*. found an overexpression of p53 without mutation in exon 5-9 in OSCC in young, non-smoking patients[15]. Schantz *et al*. reported greater chromosome fragility following bleomycin therapy in lymphocytes from young patients with head and neck cancer. Other authors have reported that cyclin D1 gene polymorphism (CCND1) was associated with the early onset of head and neck cancer particularly in young nonhabituates. The susceptibility of oral mucosa to herpes simplex virus (HSV) and human papilloma virus (HPV) has suggested that HSV and HPV play a role in the etiology of oral cancer[16]. Parkin *et al*. and zur Hausen reported that up to 25% of oral cancer is associated with HPV infection[17,18]. Hafkamp *et al* suggested that HPV is more commonly detected in young patients with head and neck cancer and it has been related to down-regulation of pRb, overexpression of $p16^{INK4A}$ and wild-type p53[19]. Kassim and Daley reported that HSV-1 has a direct relationship with OSCC, but its role in cellular transformation is not clear[20].

Regan *et al* evaluated p16 gene inactivation and p16 protein expression using methylation-specific polymerase chain reaction and immunohistochemistry. They observed that p16 methylation was a more common event in those younger than 40 years in contrast to p16 deletions, which were more common in those older than 40 years. This shows that specific modes of inactivation of p16 in HNSCC are related to specific patient risk profiles. Methylation of p16 was more often detected in females than males[21].

In the present report, the patients were young and did not report any smoking or drinking habits. Their medical histories were not significant either. There was no specific family history. Among our 5 cases one of them had trauma from sharp tooth which was of a very short duration of one month. Some studies have demonstrated an exaggerated response to inflammation due to polymorphisms of IL6 and TNF alpha in some OSCC patients. This could result in a carcinogenic effect at the site of inflammation. This warrants the need for the elimination of

factors causing chronic irritation to the oral mucosa at an early stage for the prevention of OSCC[22].

There is still controversy regarding the prognosis of SCC in young patients. Some authors consider the lesion to be particularly aggressive in the young, thus with a worse prognosis compared with that of older patients. Some studies have shown that young patients present a greater locoregional recurrence rate and a lower survival rate, whereas others have described a similar prognosis for both age ranges. Therefore, some authors have indicated a more aggressive treatment for SCC in young patients, while others recommend that the treatment should be instituted in a similar fashion to those with older age[4].

CONCLUSION

Oral cancer occurring in young adults is not common but nevertheless should always be considered in such patients when they present with persistent ulceration, leukoplakia, erythroplakia or swellings with no obvious local cause, particularly in the high-risk sites of the tongue and floor of the mouth. Such cases warrant careful clinical study along with an analysis of etiologic factors. The thrust on genetic and epigenetic factors in the development of OSCC is gaining momentum. Early diagnosis and treatment is important in the care of these patients.

References

1. Kaur J, Singh A, Chopra R. Unusual presentation of squamous cell carcinoma in young female patient: A case report and review of literature. *Journal of oral and maxillofacial pathology: JOMFP*. 2016 Jan;20(1):163.
2. Chiang WF, Yen CY, Liu SY. Squamous cell carcinoma of the oral cavity in young patients. Chin *J Oral Maxillofac Surg*. 2005;16:8-16.
3. Müller S, Pan Y, Li R, Chi AC. Changing trends in oral squamous cell carcinoma with particular reference to young patients: 1971-2006. The Emory University experience. *Head and neck pathology*. 2008 Jun 1;2(2):60.
4. Hirota SK, Migliari DA, Sugaya NN. Oral squamous cell carcinoma in a young patient–Case report and literature review. *An Bras Dermatol*. 2006;81(3):251-4.
5. Oliver RJ, Dearing J, Hindle I. oral cancer: Oral cancer in young adults: report of three cases and review of the literature. *British dental journal*. 2000 Apr 8;188(7):362-6.
6. Venturi BR, Pamplona AC, Cardoso AS. Squamous cell carcinoma of the oral cavity in young patients and its increasing incidence: literature review. *Revista Brasileira de Otorrinolaringologia.* 2004 Oct;70(5):679-86.
7. Burzynski NJ, Flynn MB, Faller NM, Ragsdale TL. Squamous cell carcinoma of the upper aerodigestive tract in patients 40 years of age and younger. *Oral Surg Oral Med Oral Pathol*. 1992;74:404-8.
8. Friedlander PL, Schantz SP, Shaha AR, Yu G, Shah JP. Squamous cell carcinoma of the tongue in young patients: A matched-pair analysis. *Head Nec*k. 1998;20:363-8.
9. Schantz SP, Byers RM, Goepfert H, Shallenberger RC, Beddingfield N. The implication of tobacco use in the young adult with head and neck cancer. *Cancer*. 1988; 62:1374-80.
10. Seyedmajidi M, Faizabadi M. Squamous cell carcinoma of the tongue in a 13-year-old boy. *Arch Iran Med*. 2008 May 1;11(3):341
11. França DC, Monti LM, De Castro AL, Soubhia AM, Volpato LE, de Aguiar SM, Goiato MC. Unusual presentation of oral squamous cell carcinoma in a young woman. *Sultan Qaboos University Medical Journal*. 2012 May;12(2):228.
12. Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for squamous cell carcinoma of the oral cavity in young people-a comprehensive literature review. *Oral oncology*. 2001 Jul 31;37(5):401-18.
13. Chaudhary N, Gupta DK, Verma RK, Choudhary SR. Squamous cell carcinoma of tongue in a 12-year-old child. *Acta Oto-Laryngologica Case Reports*. 2016 Jan 1;1(1):87-9.
14. Shah FD, Begum R, Vajaria BN, Patel KR, Patel JB, Shukla SN, Patel PS. A review on salivary genomics and proteomics biomarkers in oral cancer. *Indian Journal of Clinical Biochemistry*. 2011 Oct 1;26(4):326-34.
15. Lingen MW, Chang KW, McMurray SJ, Dlot DB, Kies MS, Mittal B, *et al*. Overexpression of p53 in squamous cell carcinoma of the tongue in young patients with no known risk factors is not associated with mutations in exons 5–9. *Head Neck*. 2000; 22:328–35.
16. Schantz SP, Hsu TC, Ainslie N, Moser RP. Young Adults With Head and Neck Cancer Express Increased Susceptibility to Mutagen-lnduced Chromosome Damage. *Jama*. 1989 Dec 15;262(23):3313-5.
17. Parkin DM, Bray F. The burden of HPV-related cancers. Vaccine. 2006 Aug 21;24:S11-25.
18. Zur Hausen H. Papillomaviruses and cancer: from basic studies to clinical application. *Nature Reviews Cancer*. 2002 May 1;2(5):342-50.
19. Klingenberg B, Hafkamp HC, Haesevoets A, Manni JJ, Slootweg PJ, Weissenborn SJ, Klussmann JP, Speel EJ. p16INK4A overexpression is frequently detected in tumour-free tonsil tissue without association with HPV. *Histopathology*. 2010 Jun 1;56(7):957-67.
20. Kassim KH, Daley TD. Herpes simplex virus type 1 proteins in human oral squamous cell carcinoma. Oral surgery, oral medicine, *oral pathology*. 1988 Apr 1;65(4):445-8.
21. O'Regan EM, Toner ME, Finn SP, Fan CY, Ring M, Hagmar B, Timon C, Smyth P, Cahill S, Flavin R, Sheils OM. p16 INK4A genetic and epigenetic profiles differ in relation to age and site in head and neck squamous cell carcinomas. *Human pathology*. 2008 Mar 31;39(3):452-8.
22. Serefoglou Z, Yapijakis C, Nkenke E, Vairaktaris E. Genetic association of cytokine DNA polymorphisms with head and neck cancer. *Oral oncology*. 2008 Dec 31;44(12):1093-9.

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