Annals of Medicine and Surgery 69 (2021) 102820

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Case Report

Managing misdiagnosed gingival squamous cell carcinoma (GSCC) with occult symptoms: A report of two cases

Fatima Alzhra Hanifa [a], Aya Zazo [a], Mohammad Kamel Fares [b], Mohamad AlHashemi [a], Bashar Bazkke [a,*], Bakr Haddad [c], Ammar Niazi [d]

[a] Faculty of Medicine, University of Aleppo, Aleppo, Syria
[b] Aleppo University Hospital, Aleppo, Syria
[c] Oral and Maxillofacial Surgery Department, Aleppo University Hospital, Aleppo, Syria
[d] General Surgery Department, Faculty of Medicine, Aleppo University Hospital, Aleppo, Syria

ARTICLE INFO

Keywords:
Gingival squamous cell carcinoma (GSCC)
Oral cancer
Mandibular neoplasms
Head and neck surgery
Case report

ABSTRACT

Introduction: importance: Gingival squamous cell carcinoma (GSCC) is a rare neoplasm. GSCC has nonspecific features which commonly misdiagnosed with a simple toothache.

Case presentation: These are two cases; the first one describes a 62-year-old female who presented with pain in her right posterior mandibular teeth, and she was misdiagnosed with periodontal disease, but later histopathological tests confirmed gingival squamous cell carcinoma (GSCC). Consequently, the patient underwent surgery, and the gingival tumor was totally resected. Afterward, the patient was receiving chemotherapy, and the radiotherapy was postponed until the chemotherapy completion.

The second case is of a 58-year-old female who presented with pain in her mandibular incisors, and she developed a dermal fistula on her chin and therefore underwent several gingival curettages. The following histopathologic tests confirmed GSCC so she underwent surgery, after the surgery it was planned to give her chemotherapy.

Clinical discussion: GSCC is a rare neoplasm with a 6% incidence of all oral malignancies. GSCC is a very challenging cancer for a physician or a pathologist to diagnose because GSCC usually mimics the characteristics of a large variety of diseases and abnormalities. Unlike oral neoplasms, GSCC has the least association with smoking. This may lead to make mistakes in the treatment or misdiagnose it until the late-stage of GSCC.

Conclusion: Despite the rare incidence of Gingival squamous cell carcinoma (GSCC), clinicians should consider GSCC while investigating any localized lesion with nonspecific oral symptoms.

1. Introduction

Gingival squamous cell carcinoma (GSCC) is one of the rare, dangerous tumors. Despite having histological characteristic appearances, the initial unremarkable presentation, such as a pain in the teeth, makes it escape from early disclosure [1,2]. One of the most worrying features is that it metastasizes to the lymph nodes, which is the indication of surgical interventions [3]. This case report is talking about how a rare oral cancer case was successfully managed in spite of spreading to local lymph nodes in a short period. This case report has been reported in line with the SCARE Criteria [4].

1.1. First patient case presentation

A 62-year-old woman presented to a dental clinic complaining of toothache in the posterior right side of the mandible. The patient never smoked or drank alcohol. There was no significant personal or familial medical history, nor an allergic history. On oral examination, the dentist noticed increased mobility of teeth in the affected area, so he extracted those teeth, but the pain was not relieved. Later, the patient visited another dentist who observed the molars loss, and swelling, congestion and bleeding in the gingival affected area. The clinical appearance of the lesion was suspected malignancy.

An incisional biopsy of the lesion showed fragments composed mainly of solid nests of malignant squamous cells surrounded by fibrous stroma, which confirmed the conventional type of invasive squamous

* Corresponding author. Faculty of Medicine, University of Aleppo, Aleppo, Syria.
E-mail address: bashar.bazkke@gmail.com (B. Bazkke).

https://doi.org/10.1016/j.amsu.2021.102820
Received 22 July 2021; Received in revised form 27 August 2021; Accepted 3 September 2021
Available online 4 September 2021

List of abbreviations

GSCC	Gingival squamous cell carcinoma
CT	Computed tomography
MRI	Magnetic resonance imaging
PEH	Pseudoepitheliomatous hyperplasia
NCCN	National Comprehensive Cancer Network

cell carcinoma in the gingiva (grade 2). Computed tomography (CT) and magnetic resonance imaging (MRI) of the head and neck were requested; the CT scan revealed destruction of the upper margin of the mandibular body, which means a localized invasion of the carcinoma in the adjacent bone (Fig. 1), while the MRI showed some swollen cervical lymph nodes. Chest X-ray and abdominal echography did not show distant metastases.

Therefore, a partial mandibular resection, with gingival removal along with a reconstruction plate insertion was performed. The right-sided submandibular gland and cervical lymph nodes were radically removed and sent to the histopathological examination. The histological changes included ulcerated squamous cell carcinoma of the gingiva (grade 3), the grade of tumor developed from 2 to 3 within two weeks between the histopathologic diagnosis and the surgical resection., extended to the mandibular bone (Fig. 2). The resection margins were free of tumor, while the submandibular gland, which was removed due to its suspicious gross appearance, revealed metastases with cystic changes. Metastases also appeared in one cervical lymph node out of the four resected nodes. therefore, the gingival squamous cell carcinoma was staged IVa. After the surgery, the patient was given intravenous antibiotics, analgesics, corticosteroids, and fluids.

Two months after the surgery, the patient was free of pain and receiving postoperative chemotherapy. Radiotherapy was delayed till the completion of the chemotherapy.

1.2. Second patient case presentation

A 58-year-old woman visited a dental clinic complaining of toothache in her mandibular incisors. The patient was a heavy smoker with 80 packets per year, without a history of using alcohol. There was no significant personal or familial medical history, nor an allergic history. On oral examination, the dentist noticed an inflammation of the gingiva around the mandibular incisors and diagnosed the patient with an apical cyst, so he extracted the affected teeth and did a gingival curettage. Later, the patient had a dermal fistula on the chin and underwent another gingival curettage with the removal of the inflamed periodontal tissues but the inflammation did not improve. After that, the patient visited another dentist who observed an irregular swollen area of the chin, with ulcerated bleeding gingiva.

An incisional biopsy showed fragments composed mainly of solid nests of malignant squamous cells surrounded by fibrous stroma with massive necrosis, which confirmed the conventional type of invasive squamous cell carcinoma of the oral gingiva (grade 2). The CT scan of the head and neck revealed localized invasion of the carcinoma in the adjacent bone presented as a destruction of the front part of the mandibular body, while the MRI showed many swollen cervical lymph nodes. Chest X-ray and abdominal echography were irrelevant.

The clinical, radiographic, and histopathological findings indicated surgery, the patient underwent resection of: the cutaneous and subcutaneous tissues of the chin with the muscles beneath, and the front part of the mandibular body, with gingival removal. A reconstruction plate was inserted, and five bilateral cervical lymph nodes were radically removed. After the surgery, intravenous antibiotics, analgesics, corticosteroids, and fluids were administered. The histological changes were those of ulcerated squamous cell carcinoma of the gingiva (grade 3), the grade of tumor developed from 2 to 3 within three weeks between the histopathologic diagnosis and the surgical resection. extended to the underlying mandibular bone and the surrounding soft tissue of the skin (Fig. 3). The bone resection margins were free of tumor, while the soft fatty and muscular resection margins were not free. One out of the five resected lymph nodes revealed metastasis; therefore, the gingival squamous cell carcinoma was staged IVa.

It was decided to give the patient chemotherapy, and afterward she would undergo corrective surgery.

2. Discussion

The tumor of the oral cavity, gingival squamous cell carcinoma (GSCC) in particular, has been documented as an extremely rare neoplasm with around 6% of all the oral malignancies as the oral lesions commonly affect the tongue rather than the gingiva [5,6].

In spite of numerous medical articles that have confirmed a strong link between smoking and the risk of developing oral cancer, GSCC has a minor association with smoking which makes detecting GSCC is more challenging, such as the patient in this case [7]. many nonspecific and subtle features of the GSCC lesions were reported and mostly were incorrectly diagnosed with benign and inflammatory conditions [5]. These reasons make it really challenging to make the diagnostic decision. Based on a retrospective analysis study that was conducted in Brazil from January 1959 to December 2012 with a sample size of more than 20 thousand patients, 76% of the GSCC cases present with pain that could be misdiagnosed with a toothache, such as in our case [7,8]

Clinically, GSCC commonly metastasized to the local lymph nodes or nearby structures, which is accompanied by extensive morbidity or even mortality [5].

Microscopic diagnosis is challenging because it usually looks similar

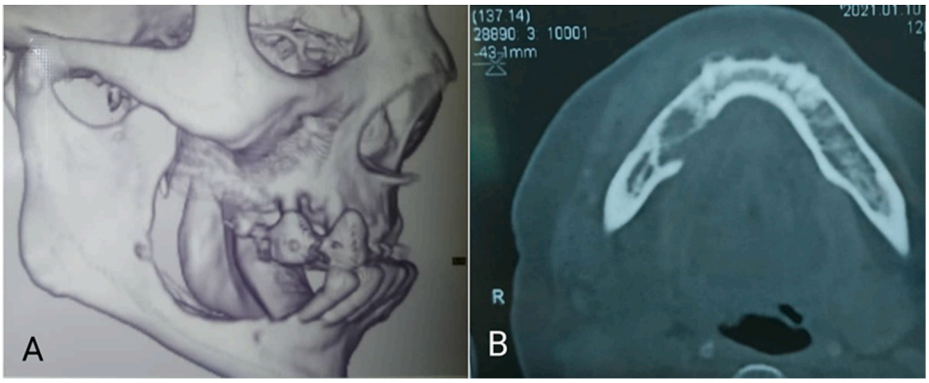

Fig. 1. 1A. Three-dimensional CT scan of the head and neck shows the erosion of the mandibular bone. 1B. Axial CT scan view presents the lesion extended to the mandibular bone and gived a lower density area.

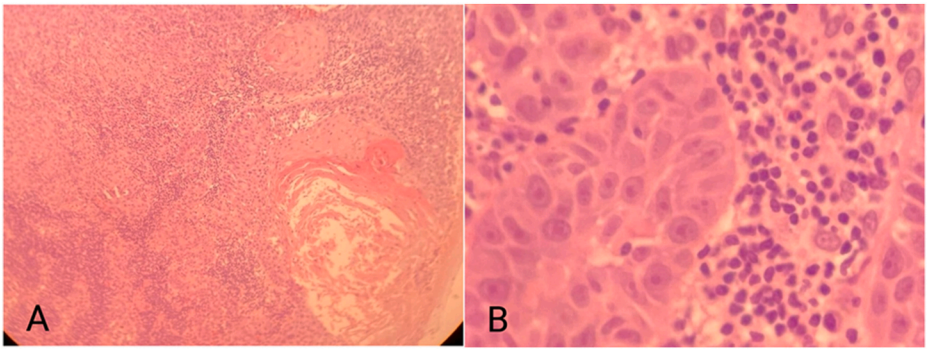

Fig. 2. 2A. Histopathological section shows gingival squamous cell carcinoma; which was stained with hematoxylin and eosin. The fibrous stroma surrounds the nests of dysplastic stratified squamous epithelium. There are also multiple areas of hyperkeratosis. 2B. Shows the dysplastic epithelial cells that contain large pleomorphic nuclei. The nucleoli are also prominent.

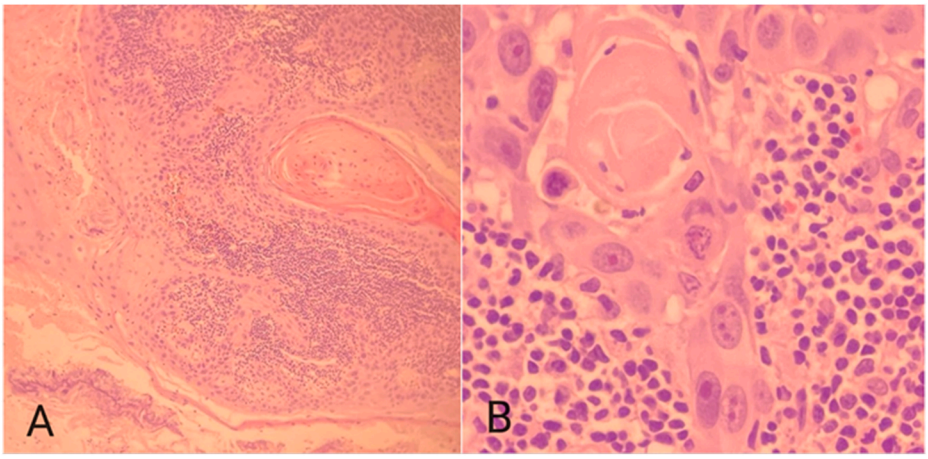

Fig. 3. 3A. Histopathological section stained with hematoxylin and eosin shows gingival squamous cell carcinoma. The solid nests of malignant squamous cells are surrounded by fibrous stroma with massive necrosis. 3B. Shows dysplastic epithelial cells with large pleomorphic nuclei. The nucleoli are prominent and many nuclei contain more than one nucleolus.

to pseudoepitheliomatous hyperplasia (PEH) and inflammatory lesions that can become highly proliferative and mimic the histological appearance of GSCC [9,10]. Microscopic examination in PEH shows irregular cords and nests of epithelial cells extending into the underlying connective tissue, whereas, in GSCC, it shows the irregular contour of nests and strands, hyperkeratosis, and papillomatosis, and the presence of occasional squamous pearls and mitotic activity and large hyper-chromatic nuclei [10].

Since early detection is critical, National Comprehensive Cancer Network (NCCN) guidelines strongly recommended that any lesions in the gingival area undergo an early evaluation by taking a biopsy, requesting radiological imaging, and checking the staging systems [5,11]. Despite that, oral cancer is still considered an epidemiological issue [5]. In most cases, a 15mm excision margin should be performed depending on the examination of frozen biopsies during the surgery. This mechanism is performed to assure that the margins are free of the tumor; in case it was not possible to use the frozen biopsies examination, an additional excision should be performed [12]. Neck dissections should be performed in case of any abnormalities showed by a physical examination of the lymph nodes or any suspected metastatic lesions [12].

In a retrospective consecutive case review on 519 cases of GSCC that was retrieved using the University of Florida College of Dentistry Biopsy service's database, 26% of the cases, the patient was presented with bone involvement that was either frank or suggestive features [13]. Therefore marginal or segmental mandibulectomies should also be taken into consideration depending on the bone invasion, which is followed by reconstruction to the lost bone tissue with flaps or fibula grafts [12,13].

Radiotherapy is used in many techniques, but in oral cancer management, external beam radiation is the most common way. Radiotherapy is significantly important if the margins of the removal were not enough [13]. In our case, the patient has undergone radiotherapy to ensure that there are not any malignant cells in the tumor area.

GSCC is not considered an aggressive tumor compared to SCC at other sites, and the survival outcomes are good in comparison with SCC at other sites [12]. The prognosis of GSCC has improved significantly in the last 40 years. The 3-year survival rate for the early-stage disease has increased from 78.0% to 92.2%, and late-stage from 51.9% to 70.3% [12].

3. Conclusion

Gingival squamous cell carcinoma (GSCC) is a rare neoplasm, which often presents with nonspecific features such as toothache, lymph nodes swelling, oral bleeding, and congestion that may lead to a misdiagnosing. physicians should have a high index of suspicion for untreatable localized lesions in the oral cavity with nonspecific symptoms and do not delay biopsy requesting. Oral SCC is managed mainly surgically, which could be minor or broad, and if SCC has a high stage, surgery may be followed by chemotherapy, radiotherapy, or both.

Funding

No funding was obtained for this case report.

Declaration of competing interest

Authors declare they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102820.

Annals of Medicine and Surgery.

Sources of funding

There are no sources of funding.

Ethical approval

Not required for case reports at our hospital. Single case reports are exempt from ethical approval in our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Authors' contributions

Fatima Alzhra Hanifa: data collection, revising critically, wrote the manuscript.

Aya Zazo: review and editing, wrote the manuscript, validation.

Mohammad Kamel Fares: design of the study, revision, wrote the manuscript.

Mohamad AlHashemi: patient care, data collection, wrote the manuscript.

Bashar Bazkke: patient care, revision, corresponding author.

Bakr Haddad: managed the patient and did the surgery, patient care, revising critically.

Ammar Niazi: managed the patient and did the surgery, the supervisor, patient care, revising critically.

All authors read and approved the final manuscript.

Registration of research studies

1. Name of the registry:
2. Unique Identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

Guarantor

Dr.Ammar Niazi.

References

[1] L. Yan, W. Deng, L. Guan, H. Xu, Nomogram forecasting 3-, 5-, and 8-year overall survival and cancer-specific survival of gingival squamous cell carcinoma, Cancer Medicine 9 (21) (2020 Nov) 8266–8274.

[2] M.M. Bornstein, C. Andreoni, T. Meier, Y.Y. Leung, Squamous cell carcinoma of the gingiva mimicking periodontal disease: a diagnostic challenge and therapeutic dilemma, Int. J. Periodontics Restor. Dent. 38 (2018 Mar 1) 253–259.

[3] S.W. Wang, C.H. Lee, M.S. Lin, C.W. Chi, Y.J. Chen, G.S. Wang, K.W. Liao, L. P. Chiu, S.H. Wu, D.M. Huang, L. Chen, ZnO nanoparticles induced caspase-dependent apoptosis in gingival squamous cell carcinoma through mitochondrial dysfunction and p70S6K signaling pathway, International journal of molecular sciences 21 (5) (2020 Jan) 1612.

[4] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the Scare Group, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.

[5] A. Keshava, S. Gugwad, R. Baad, R. Patel, Gingival squamous cell carcinoma mimicking as a desquamative lesion, J. Indian Soc. Periodontol. 20 (1) (2016 Jan) 75.

[6] R. Gupta, N. Debnath, P.A. Nayak, V. Khandelwal, Gingival squamous cell carcinoma presenting as periodontal lesion in the mandibular posterior region, Case Reports (2014 Aug 19) 2014, bcr2013202511.

[7] X. Jiang, J. Wu, J. Wang, R. Huang, Tobacco and oral squamous cell carcinoma: a review of carcinogenic pathways, Tob. Induc. Dis. 17 (2019).

[8] A.M. Alves, et al., Demographic and clinical profile of oral squamous cell carcinoma from a service-based population, Braz. Dent. J. 28 (2017) 301–306.

[9] Q. Sun, et al., Cervical metastasis of gingival carcinoma misdiagnosed as branchiogenic carcinoma, a rare entity - report of a case and review of literature, BMC Oral Health 17 (2017) 4–9.

[10] J.K. Brooks, et al., Gingival squamous cell carcinoma: an unexpected clincal presentation. Quintessence Int. (Berl). 50, 50–57, 2019. Brooks JK, Kleinman JW, Lubek JE, Price JB, Ghita I, Scurnick SA, Basile JR. Gingival squamous cell carcinoma: an unexpected clincal presentation. Quintessence Int. 2019 Jan 1;50 (1):50-57.

[11] National Comprehensive Cancer Network, NCCN clinical practice guidelines in oncology. https://www.nccn.org/professionals/physician_gls/pdf/head-andneck.pdf, 2021.

[12] L.X. Niu, Z.E. Feng, D.C. Wang, J.Y. Zhang, Z.P. Sun, C.B. Guo, Prognostic factors in mandibular gingival squamous cell carcinoma: a 10-year retrospective study, Int. J. Oral Maxillofac. Surg. 46 (2) (2017 Feb 1) 137–143.

[13] S.G. Fitzpatrick, A.N. Neuman, D.M. Cohen, I. Bhattacharyya, The clinical and histologic presentation of gingival squamous cell carcinoma: a study of 519 cases, Oral surgery, oral medicine, oral pathology and oral radiology 114 (4) (2012 Oct 1) 509–515.