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Head and Neck Squamous cell Carcinoma (HNSCC) masquerading as non-neoplastic lesions

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Abstract

Background: Head and neck squamous cell carcinoma (HNSCC) most often spreads to regional deep cervical lymph nodes. Usually, these metastases present as firm, solid masses in the lymph nodes. A distinct subset of metastatic nodes present as cystic masses, with a liquid center surrounded by a thin solid rim. It has been observed that primaries from certain squamous cell carcinoma (SCC) sites are more likely to produce metastases that are cystic. These sites predominantly include primary tumors of tonsillar tissue from Waldeyer's ring. Also, SCC rarely presents as discharging sinuses and mostly presents as raised, firm, keratotic papule or plaque arising in sun-exposed areas. However, discharging sinuses over the face should include cutaneous malignancy as a differential. We present two cases of SCC presenting as cystic metastases and discharging sinuses.

Aim: To study diagnostically challenging HNSCC cases that may mimic non neoplastic lesions

Settings and Design: This is a retrospective study.

Methods and Material: HNSCC was diagnosed on the basis of following clinical, cytological and histopathological setting. Two cases of unusual presentation of HNSCC were selected.

Results: We report two cases, first is a case of a 47 year old female with a cystic swelling in the right submandibular region. A full workup was performed but failed to provide any evidence of malignancy. Histological examination revealed a lymph node showing metastasis of squamous cell carcinoma from an unknown primary.

The second case is that of a 60-year-old male patient who presented with a 2-year history of multiple discharging sinuses on his chin, which on microscopy was found to be an SCC.

Conclusions: We conclude that SCC and its metastasis should not be directly ruled in unusual presentation such as discharging sinuses in primary cutaneous SCC or cystic metastases.

Keywords: Cytology; metastasis; squamous cell carcinoma, cystic metastasis, pitfalls

Introduction

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common noncutaneous cancer worldwide, it accounts for over 550,000 cases and 380,000 deaths annually (1).

Certain neoplastic and infectious processes of the head and neck may be difficult to clinically distinguish from each other clinically and should be included in the differential diagnosis (2). In such patients, obtaining adequate biopsies for histopathological examination is pertinent to reach the correct diagnosis and a multidisciplinary approach should be utilized ideally during the diagnostic process (2).

HNSCC is most commonly seen in older patients; however recent epidemiological studies have shown that the overall incidence amongst patients under the age of 45 has been showing an increasing trend worldwide in recent years (3)

Oral cavity irritation and inflammation are independently associated with early-onset HNSCC as per older studies (4). This is due to mucosal irritation which disrupts the barrier function of the oral epithelium and increases susceptibility to infections along with subsequent cellular repair mechanisms that can create localized genetic instability (5). This process is thought to be pathognomic in the development of leukoplakia and squamous intraepithelial neoplasia (SIN), a preneoplastic precursor to HNSCC (5).

Epidemiological especially geographical differences are seen in the incidence and primary site of head and neck cancers. These reflect the prevalence of risk factors like tobacco and alcohol consumption, as well as ethnic and genetic differences among populations (6).

Tobacco is the most important known risk factor for the development of head and neck cancer. There is some evidence of a genetic predisposition to the carcinogenic effects of tobacco. In addition, tobacco and alcohol consumption appear to have a synergistic effect as carcinogens. The repeated exposure of the mucosa of the upper aerodigestive tract to the carcinogenic effects of tobacco, alcohol, or both appears to cause multiple primary and secondary tumors in this region, this is described as "field cancerization" (6).

Fine needle aspiration (FNA) biopsy is routinely used to make an initial tissue diagnosis of patients who present with a neck mass such as metastatic cervical lymph node without an obvious primary tumour site. This technique has high sensitivity and specificity with a diagnostic accuracy that ranges from 89 to 98 percent (7) . Nondiagnostic aspirations can occur in 5 to 16 percent of cases, especially in cystic neck masses, which are seen in patients with HPV associated oropharyngeal cancers. If an initial FNA is negative from a suspicious neck node, repeat FNA may be considered before doing an excisional biopsy.

Head and neck squamous cell carcinoma (HNSCC) commonly spreads to regional deep cervical nodes. In most cases, these present as firm, solid masses in the corresponding lymph node chains. A distinct subset of metastatic nodes may present as cystic masses, with most of the volume made up of a liquid center surrounded by a thin solid rim. It has been observed that certain squamous cell carcinoma (SCC) subsites are more likely to produce cystic metastases. These sites predominantly include primary tumors of tonsillar tissue from Waldeyer's ring(8)

Squamous cell carcinoma (SCC) usually presents as a raised, firm, pink to skin-coloured keratotic papule, plaque or ulcer, arising on sun-exposed skin (9).

Cutaneous SCC is the most common cutaneous malignancy in African and South Asian populations, representing 30–65% of skin cancers in both races, and is the second most common cutaneous neoplasm in white populations, accounting for 15– 25% of skin cancers.(10)

We report two unusual cases of HNSCC. First that of a 47 year-old female with a 25 day history of a painless cystic right submandibular mass which was clinically diagnosed as a non-neoplastic lesion and was diagnosed later post operatively on Histopathology. Second a 60-year-old male patient who presented with a 2-year history of multiple discharging sinuses on his chin, which on investigation was found to be an SCC. Cutaneous malignancies presenting as discharging sinuses are very rare. We report this case as it illustrates an unusual presentation of SCC, which should be considered in the differential diagnosis of cases presenting with multiple discharging sinuses on the face.

Material and Methods

This is a retrospective study, we have selected two cases of unusual presentation of HNSCC for this study. Data were obtained regarding the clinical presentation from the indoor case sheets. HNSCC was diagnosed on the basis of following clinical, cytological and histopathological setting. The relevant slides were retrieved and reviewed. All histopathology sections were stained with hematoxylin and eosin. FNA slides were stained with Fields stain and rapid Papanicolaou (PAP) stain

Results

The clinicopathological details as well details of other ancillary tests were as follows:

Case One

A 47 year-old female was referred to our department with a 25 day history of a painless right submandibular mass. She denied any other symptoms. Clinical examination revealed a well-defined, painless neck lump. The lump was 4 x 3 centimeters in size, roughly oval, and mobile. There were no surrounding skin changes or other associated findings. Ultrasonography (Neck) showed enlarged heterogenous lymph node at right side Level IB, measuring 3.6 x 2.8 centimetres. It showed loss of fatty hilum, early cystic change along with necrotic changes in the centre. Also, a bulky thyroid with multiple colloid nodules was noted. The other neck structures were sonographically normal.

Computed tomography (CT) showed a cystic lesion with an irregular wall at right side Level IB, showing central area of necrosis (Figures 1 A, B)

Fine-needle aspiration cytology (FNAC) revealed cellular smears showing numerous nucleate and anucleate squames along with diffuse and dense neutrophilic infiltration. Occasional cells showed high nucleocytoplasmic ratio with nuclear pleomorphism. This was misdiagnosed as Infected epidermal inclusion cyst owing to the predominant population of mature squames , the occasional cells showing nuclear pleomorphism was mistaken for reactive atypia. (Figures 1 C, D) The cyst was sent for histopathological examination after excision using 10 % buffered formalin as the fixative.

Grossly, the specimen consisted of an already cut open lymph node measuring 3.6x 2.5 x1 cm. The wall was thickened, irregular and showed maximum thickness of 1.4 centimeters along with few whitish areas

On microscopic examination, sections studied from the lymph node showed partly effaced architecture replaced by tumour cells. Individual cells were large, with hyperchromatic nuclei , prominent nucleoli and moderate amount of eosinophilic cytoplasm.

Numerous keratin petals were seen. This was suggestive of metastasis of squamous cell carcinoma from an unknown primary. (Figures 1 E, F)

Case Two

A 60-year-old man presented with 2-year history of a facial swelling with multiple sinuses. There was no

history of cough, prolonged fever or loss of appetite, but the patient complained of difficulty in mastication over the last few months. He received treatment which included a combination of oral and topical antibiotics and steroids under an alternative medicine practitioner for almost a year but showed no improvement. The patient was a chronic smoker and tobacco chewer since over 10 years. The patient did not have any history of trauma, previous surgeries in that region, or dental extraction. There was no history of discharge of grains from the sinuses.

On physical examination, an ulcero-proliferative growth was seen over his left cheek, extending from lateral angle of his mouth to his jaw (Figures 2 A). It showed four sinuses each measuring about 0.5 to 1.0 centimeters in diameter that produced a thick yellowish discharge on applying pressure around it . There was scarring of the skin in the involved area. On palpation, the lesion was extremely tender, and the consistency was variable, ranging from firm to hard in different areas. The growth was seen involving the underlying buccal mucosa. No lymphadenopathy was noted the systemic examination was within normal limits. The provisional differential diagnosis included mycetoma, cutaneous tuberculosis, actinomycosis, and cutaneous malignancy.

Laboratory investigations, including full blood count, liver and renal function tests did not reveal any abnormality.

Fine-needle aspiration cytology (FNAC) from the growth was performed. The smears studied showed mature squamous `cells along with dense neutrophilic infiltrate. Some cells showed nuclear pleomorphism and occasional Tadpole like cells were noted. (Figures 2 B, C, D)

Impression was given as possibility of squamous cell carcinoma and biopsy was advised for confirmation by histopathology.

The biopsy sent showed hyperkeratotic acanthotic stratified squamous epithelium along with a tumour. Tumour cells were seen infiltrating as nest and cords. Individual cells were large to medium sized with hyperchromatic pleomorphic nuclei , prominent nucleoli and abundant eosinophilic cytoplasm. Few mitotic figures seen. At one place the basement membrane is breached. Dermis showed dense lymphoplasmacytic infiltrate. Few mitotic figures were seen. Impression was given as invasive moderately differentiated squamous cell carcinoma. (Figures 2 E, F, G)

Discussion

Our first case was that of 47 year old who presented with cystic metastasis over her submandibular region from an unknown primary. This presentation was in concordance with the study done by Vital et al (11) who concluded that in patients older than 40 years, especially with risk factors for malignant disease, it is prudent to consider all cystic lesions of the neck as malignant until proven otherwise. This is because predominantly cystic squamous cell carcinomas in the neck often present without a clinically apparent primary.

The study by Firat et al and Mallet et al (12,13) also suggested that in terms of malignant lesions, squamous cell carcinoma (SCC) of tonsillar tissue from the Waldeyer's ring (e.g., palatine and lingual tonsils) and papillary thyroid cancers have a predilection for cystic lymph node metastases. The expression of cytokeratin 7 has led some to hypothesize that a subset of SCC of Waldeyer's ring may originate from excretory ducts of minor salivary glands and thus show the tendency to form cystic lesions (14)

However, the exact mechanism for the development of cystic lymph node metastases is yet unclear. Some have suggested that Tumor necrosis forming a pseudocyst have been found along with true cystic cavities which are lined by neoplastic epithelium (11).

Sira et al suggested that these patients presenting with cystic masses should be advised ultrasonography of the neck , FNAC and 3-dimensional imaging either with computed tomography (CT) or Magnetic resonance imaging (MRI) after a careful history and thorough clinical examination(15). In view of the likely origin of such cystic metastases from a primary site in the Waldeyer's ring , the management protocol should be planned keeping in mind to include panendoscopy of the upper aerodigestive tract along with biopsies or intra operative frozen sections if any primary lesion can be identified.

Ultrasound-guided FNAC is often diagnostic but its sensitivity drops from >95% in solid tumors (12) to 50%–73% in cystic lesions [16, 13] as in our case where negative FNA findings we're misleading . Therefore, an excisional biopsy and examination under anesthesia with directed biopsies of Waldeyer's ring and bilateral tonsillectomy should be considered a part of the diagnostic workup in such cases.

Our second case was that of a 60 year old male with mass over his cheek with discharging sinuses which on histopathologic examination was proved to be SCC despite the presence of discharging sinuses which can be mistaken clinically for an infective or inflammatory lesion.

SCC most often arises on the sun-exposed skin of middle- aged and elderly people. Approximately 70% of all SCCs occur on the head and neck and 15% occur on the arms.

The characteristic SCC presents as a raised, firm, keratotic papule or plaque arising on sun-exposed skin. Surface changes may include scaling, ulceration or crusting, or the presence of a cutaneous horn (10)

SCC is capable of locally infiltrative growth as well as spread to regional lymph nodes, and distant metastasis, most commonly to the lungs. In our case, a malignancy was clinically suspected due to the patients history of chronic consumption of tobacco as well as due to the hard consistency of the lesion, it's fixation to underlying tissue and the infiltration to the buccal mucosa which was noted on examination.

Shinn et al suggested that any nonhealing lesion of the head or neck with infectious etiology should be promptly treated with broad- spectrum antimicrobials. If the lesion is refractory to medications, develops poor healing, or shows marked ulceration or granulation tissue, malignancy should be considered with a low threshold for biopsy or debridement (2).

Other neoplasms such as Non-Hodgkin lymphoma , (17) histiocytosis-X (18) and infective lesions such as mycetoma, actinomycosis and cutaneous tuberculosis can also present with discharging sinuses. Cases of malignancies on the skin presenting with discharging sinuses have been reported, these include sarcomatoid SCC, thyroid carcinoma and malignant melanoma (19). Thus, cutaneous malignancies should be included in the differentials of discharging sinuses over the face along with the more common infective etiologies.

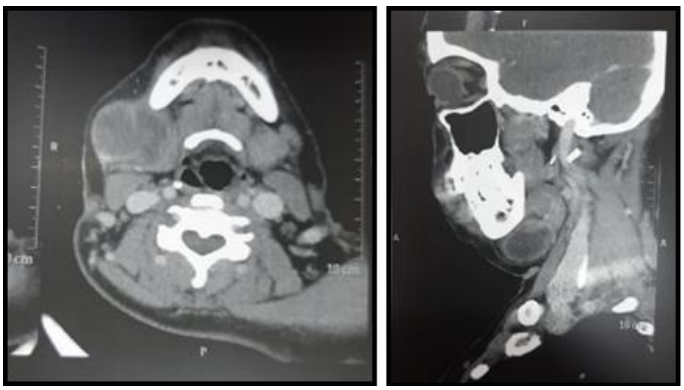

Figure 1 (A, B): CT scan (Axial and lateral view) showing cystic lesion with an irregular wall at right side Level IB, showing central area of necrosis

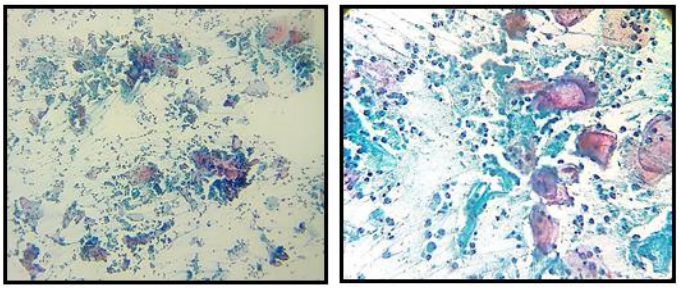

Figure 1 (C, D) (PAP, 100x , 400x): Cytology smears showing mature squamous cells with neutrophils in the background

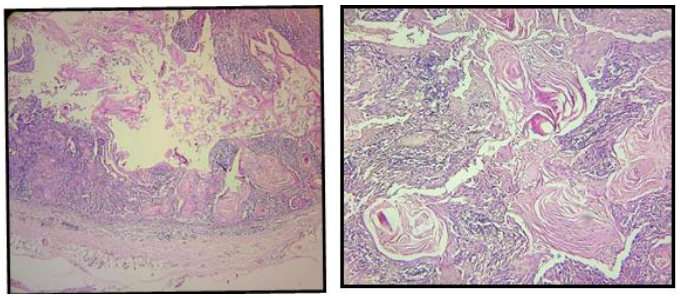

Figure 1(E,F) (H&E, 100x, 400x): Sections show lymph node showing metastatic squamous cell carcinoma along with many keratin pearls.

Figure 2 A: Ulcero-proliferative growth over left cheek, extending from lateral angle of mouth to jaw. It showed four sinuses each measuring about 0.5 to 1.0 centimetres in diameter.

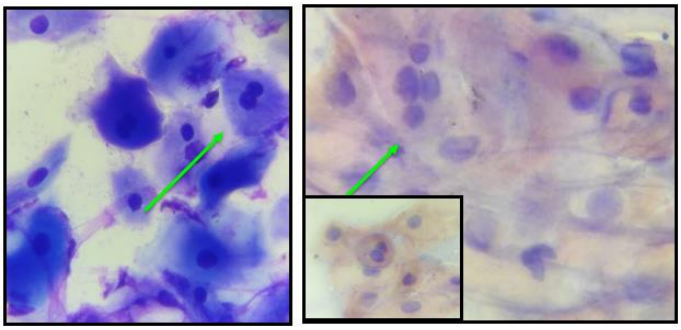

Figure 2 (B,C): Mature squames along with cells showing pleomorphic hyperchromatic nuclei (Fields Stain, 400x & Pap Stain 400x)

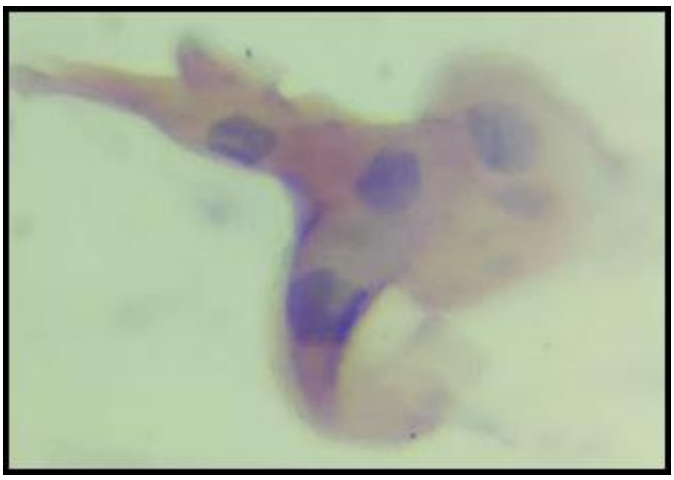

Figure 2D: Tadpole cells with abundant orangeophilic keratinisation. (Pap Stain 400x)

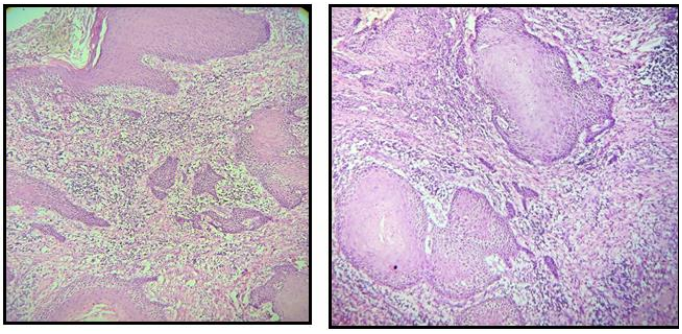

Figure 2(E, F): Tumours cells infiltrating as nest and cords. Individual cells are large to medium sized with abundant eosinophilic cytoplasm. Few mitotic figures seen. (H&E, 100X, H&E, 400X)

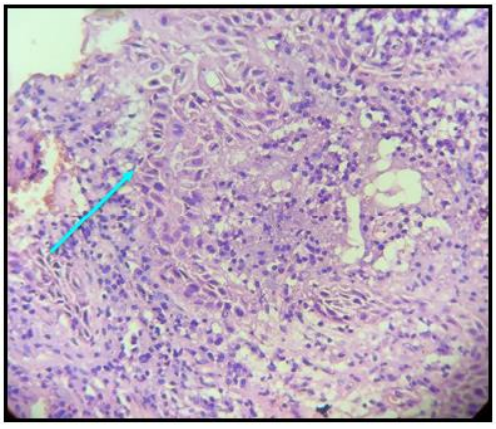

Figure 2 G: Tumour cells infiltrating as cords and single cells with hyperchromatic, pleomorphic nuclei, moderate to scant cytoplasm. Stroma shows necrosis and chronic inflammatory infiltrate (H&E, 1000x)

Conclusions:

We conclude that SCC and its metastasis should not be directly ruled out in unusual presentations such as discharging sinuses in primary cutaneous SCC or cystic metastases.

Adult patients above the age of 40 who are initially seen with a lateral cystic neck mass must be presumed to have a cancer until proven otherwise. Upon diagnosis of cystic metastasis of SCC, the management protocol should include a thorough panel of investigations to look for primaries from the Waldeyer's ring or thyroid.

Cutaneous malignancies developing as discharging sinus is a rare occurrence but possible and thus it should be included in the differential diagnosis for discharging sinus over the face.

Abbreviations

HNSCC: Head and Neck Squamous cell Carcinoma

SCC: Squamous cell carcinoma

FNA: Fine needle aspiration

PAP stain: Papanicolaou stain

Key Messages

Case One: Adult patients above the age of 40 who are initially seen with a lateral cystic neck mass must be presumed to have a cancer until proven otherwise.

Case Two: There are multiple possible diagnoses for sinuses on the face. Multiple sinuses are an uncommon presentation for a malignancy. Cutaneous SCC can present clinically as sinuses.

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