CASE REPORT

Basaloid squamous cell carcinoma of oral cavity with incongruent clinical course

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SUMMARY

Basaloid squamous cell carcinoma (BSCC) is a rare variant of SCC having a marked predilection for the upper aerodigestive tract. It is regarded as a high-grade tumour with increased propensity for metastasis to distant sites. The histological hallmark of BSCC is its dimorphic pattern of presentation with a characteristic basal cell component associated with squamous component. We report two cases of BSCC on the buccal mucosa and gingiva, respectively, with the former presenting as a primary lesion in a patient without a positive history of tobacco and alcohol use and the latter present as a seemingly metachronous development from carcinoma lung. The proliferative index of the two diverse yet similar entities was assessed by Ki-67 labelling index (LI) and the association of human papillomavirus (HPV) was detected with p16 monoclonal antibody. The intrinsically aggressive behaviour of BSCC and its association with HPV is highlighted.

BACKGROUND

Basaloid squamous cell carcinoma (BSCC) is an aggressive variant of SCC, having a distinctive predilection for the upper aerodigestive tract.¹ It was first described by Wain *et al*² as a distinct entity exhibiting diverse histological arrangement of tumour cells. The WHO defines BSCC as an aggressive and a high-grade variant of SCC composed of the basaloid as well as squamous components.³ It is often reported among elderly men who indulge in excessive tobacco and alcohol use.¹ An exposure to benzene and the role of human papillomavirus (HPV) in the development of BSCC have been emphasised recently.⁴

BSCC carries the risk of distant metastases, which is sixfold more than oral SCC (OSCC) with an estimated rate of up to 64%. It is thus prudent to subject the patients with BSCC for a chest CT and a positron emission tomography scan to rule out distant metastases. Many views have been put forward to explain the histogenesis of BSCC. It has been perceived to originate from the totipotent primitive cells of surface epithelium, the proximal ducts of the minor salivary glands or the tissues of the primitive aerodigestive tract.³ Interestingly, Wain *et al*² have proposed this to be a carcinoma with adenoid cystic differentiation or even a collision tumour with an independent existence of two morphological components.

This paper describes two cases of BSCC with diverse clinical presentation. The role of Ki-67 and p16 to correlate its aggressive behaviour is

attempted. The pathogenesis and a review of this aggressive variant of SCC are presented herewith.

CASE PRESENTATION

Case 1 was a 46-year-old woman beedi worker who reported to the dental outpatient department with a chief symptom of swelling on the left side of the face of 1 year duration. Her medical history was unremarkable except for a history of weight loss and loss of taste sensation. Extraoral examination revealed a swelling on the left side of the face extending superoinferiorly from the infraorbital margin to the angle of the mandible and anteroposteriorly 1.5 cm away from the corner of the mouth extending posteriorly up to 2 cm anterior to the posterior border of the ramus. The swelling was firm in consistency. The mouth opening was restricted and intraorally, a large ulceroproliferative growth of 4×1.5 cm was present on the left buccal mucosa corresponding to the level of premolar and molar extending posteriorly to the retromolar trigone region. The tongue was depapillated on central region and its movements were not restricted.

Case 2 was a 59-year-old male patient referred to the university medical hospital with symptoms of cough of 6 months duration and breathlessness for 10 days. The patient completed an entire course of antituberculosis regime at the regional centre before 6 months. A chest X-ray revealed a radio-lucent mass in the right middle lobe and bronchoscopy revealed deviation of trachea to the right side. Ultrasonography showed hepatomegaly with multiple well-defined hypodense nodes suggestive of metastasis. The cytological smear was positive for malignancy and diagnosis of bronchogenic carcinoma with liver metastasis was made.

An oral examination revealed severe periodontitis for which the patient was referred to the oral and maxillofacial surgery unit. No abnormality was detected on an extraoral examination but the intraoral examination revealed 1×1.5 cm exophytic growth in relation to permanent left maxillary lateral incisor. The growth was erythematous, soft in consistency, tender on palpation and attached to the gingival margin with the associated tooth showing grade III mobility. Following tooth extraction, the curettage material from the extraction socket was submitted for histopathological examination.

INVESTIGATIONS

In case 1, an incisional biopsy was performed under local anaesthesia after obtaining a written

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Figure 1 Tumour islands with basaloid appearance with central areas of comedo necrosis (H&E stain, original magnification, $\times 10$).

consent from the patient. The section revealed an atrophic stratified squamous epithelium, which was ulcerated for most part and exhibited features of dysplasia. The underlying connective tissue showed infiltrated basaloid cells arranged in cords, glands and interlacing pattern with central comedo-like necrosis (figure 1). The predominant cell population was small cells having large central hyperchromatic nuclei and scanty cytoplasm and abundant mitotic figures. At places there was an abrupt association of these basaloid cells with few polygonal squamous cells having abundant cytoplasm (figure 2). The stroma surrounding the tumour was dense with chronic inflammatory cell infiltration. The basaloid cells were separated by few microcystic spaces containing mucin-like material, which was Periodic-acid Schiff stain positive. Based on these features a diagnosis of BSCC was made as it satisfied Wain's criterion for BSCC. The immunohistochemical work-up of the same has been shown in figures 3 and 4.

Microscopical examination of the tissue submitted from case 2 revealed a stromal tissue consisting of numerous tumour cells in the form of islands or follicles (figure 5). Tumour cells showed dysplastic features like increased nuclear cytoplasmic ratio, nuclear hyperchromatism, nuclear and cellular pleomorphism and numerous atypical mitotic figures. Few tumour islands showed peripheral palisading of cells, comedo-like

Figure 2 Tumour cells having large central hyperchromatic nuclei, scant cytoplasm and abundant mitotic figures (H&E stain, original magnification, $\times 20$).

Figure 3 p16 expression was only focally positive (original magnification, $\times 10$).

necrosis giving a basaloid appearance (figure 6). Connective tissue stroma showed numerous giant cells, blood vessels and chronic inflammatory cell infiltrate with haemorrhagic areas. The overlying epithelium was parakeratotic stratified squamous epithelium. In correlation with the clinical findings, the bronchoscopic findings and the cytological smear report, above features were suggestive of metastatic carcinoma of the lung. The cytological finding of the lung tumour was completely compatible with that of the maxillary lesion. A final diagnosis of BSCC of the lung metastasised to maxilla/second primary in maxilla was made pending investigation.

DIFFERENTIAL DIAGNOSIS

Bearing the clinical presentation in mind, benign neoplastic conditions were anticipated as differential diagnosis for case 1. Taking the history and the clinical presentation into account, the differential diagnosis contemplated for case 2 were periodontal abscess, periapical pathology and pyogenic granuloma associated with maxillary left lateral incisor.

TREATMENT

The treatment for case 1 consisted of hemi-mandibulectomy and neck dissection followed by radiotherapy and chemotherapy. Case 2 was treated with wide excision along with safety margin.

Figure 4 Ki-67 labelling index was low (original magnification, $\times 10$).

Figure 5 Connective tissue stroma consisting of numerous tumour cells in the form of islands (H&E stain, original magnification, ×4).

OUTCOME AND FOLLOW-UP

Immunohistochemical work-up of case 1 showed weak focal positivity of p16 and an association with HPV could not be ascertained (figure 3). The Ki-67 LI was 2.5% (figure 4). However, the patient died within a year following surgery. The immunohistochemical examination of case 2 revealed strongly positive p16 expression (figure 7) and Ki-67 LI of 27.3% (figure 8). The patient responded well to radiotherapy and chemotherapy, and is currently free of disease in the 3 years of follow-up.

DISCUSSION

BSCC is a rare bimorphic variant of SCC which occurs predominantly in elderly men.¹ Its occurrence has been associated strongly with the use of tobacco, alcohol, exposure to benzene and HPV 16.^{1 3 4} This has been proven with animal experiments, where activation of toxic metabolites that interact with the DNA lead to formation of covalent adducts.⁴ It has a high propensity to occur in the upper aerodigestive tract; however, there are reports of its occurrence even in the conjunctiva and the paranasal sinuses.¹ Nevertheless, the clinical picture is consistent to the presentation of SCC, the behaviour of this tumour is very aggressive and often lung is most common target for distant metastases.⁵ Histopathologically, a multifarious arrangement of tumour cells in the form of nests, lobules, trabecular, cribriform pattern with inspissation of mucinous material or

Figure 7 Highly positive expression of p16 (original magnification ×10).

hyalinised stroma,¹ jigsaw puzzle pattern³ and cystic spaces containing stellate granules or replicated basal lamina arranged in parallel stacks or globoid masses⁴ can be noted. Although both our cases corroborate well with the above histopathological findings, BSCC still goes unrecognised if a minor squamoid component is overlooked. Hence biopsies especially endoscopic, if superficial, may not sample both the squamoid and basaloid components.⁵ Nevertheless the occurrence of synchronous and metachronous SCC and BSCC have been reported.⁵ The presumably metastatic lesion in our second case could well be the metachronous occurrence of BSCC.

Owing to its classical histopathological diversity, it can mimic several other tumours like adenoid cystic carcinoma, small cell neuroendocrine carcinoma, basal cell carcinoma and SCC. BSCCs encompass 2–5% of all head and neck SCC.⁶ Most authors believe that BSCC can be stratified into the HPV-induced form and the classical form.⁶ The HPV-induced form occurs predominantly in the oropharynx, is poorly differentiated, exhibit non-keratinising morphology, show increased cervical node metastases, radiosensitive and has better prognosis. Hence, the detection of HPV serves as a powerful indicator of sensitivity to radiotherapy and improved survival regardless of the treatment type.^{3 6 7} Furthermore, several hypotheses like absence of field cancerisation, immune surveillance to viral specific tumour antigens and intact apoptotic response to radiation⁸ may have led to better prognosis in the oncogenic virus-induced

Figure 6 Tumour islands showed peripheral palisading of cells (H&E stain, original magnification, ×20).

Figure 8 Very high Ki-67 labelling index (original magnification ×10).

BSCC. Based on the clinical outcome these tumours could be categorised into those with better or worse prognosis based on the HPV status.

Previously conducted studies on p16, a surrogate marker of HPV, suggest that it detects HPV with 100% sensitivity and 76% specificity. The presence of p16 expression by immunohistochemistry markedly correlated with the presence of HPV by in situ hybridisation in all oropharyngeal BSCC cases.⁹ Yet, there are few histopathological parameters like a combination of pure basaloid pattern and comedo necrosis, only basaloid patterns and prominent stromal hyalinisation which dictate the prognosis and rate of metastasis in these tumours. On the contrary, patients with vascular, lymphatic and perineural invasion had no distant metastases and survival of 100%.⁵

Because our first case showed negative p16 expression, it could be categorised as the HPV negative form or the classical form. Incidentally, the first patient did not survive for long following treatment. Additionally, the histopathological finding of predominant basaloid pattern, comedo necrosis and abundant hyalinisation could have contributed to a poor prognosis. With regard to our second case, strong positive p16 immunoreactivity suggested its strong association with HPV. In spite of remarkably high Ki-67 LI, the patient responded better to radiotherapy and chemotherapy, which is usually true for HPV-associated BSCC cases.

Based on these observations, we could draw three possibilities from our second case: (1) the lesion on the gingiva could be the unnoticed primary site, which is further supported by the fact that lung is a common site for distant metastasis; (2) the lung carcinoma treated with surgical and radiotherapy could have induced the occurrence of a second primary on the gingiva¹⁰; and (3) the occurrence of synchronous and metachronous lesion cannot be ruled out.

This unique variant of SCC is reported in many sites and organs and presents with exceptional pathological and clinical features. The immunoprofile of these tumours are helpful to distinguish them from a wide range of other malignant neoplasms. Radical excision followed by locoregional radiation and chemotherapy is a logical approach to control the disease. It is advisable that patients with metastatic disease should undergo a thorough systemic work-up. This will aid in streamlining treatment, recognising finest therapeutic strategies, allowing patient stratification in clinical trials thereby contributing to decreased morbidity and mortality to the patients. The importance of HPV16 status as a prognostic indicator warrants unambiguous separation of HPV-positive and HPV-negative BSCCs.

Learning points

- ▶ Basaloid squamous cell carcinoma (BSCC) has propensity to occur in the upper aerodigestive tract.
- ▶ BSCC carries the risk of distant metastases, which is sixfold more than oral SCC.
- ▶ Based on its behaviour BSCC could be classified into HPV-induced form and the classical types.
- ▶ HPV-induced form BSCC is radiosensitive and has better prognosis.

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Competing interests None.

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