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SIMULTANEOUS PRIMARY MALIGNANT MELANOMA OF FOOT AND SQUAMOUS CELL CARCINOMA OF TONGUE : A RARE CASE REPORT.

Pathology

Dr. Jayanti Chandrakar	Associate Professor, Department of Pathology, Pt.JNMMC, Raipur, C.G.
Dr. Bhavana Thakur*	Assistant Professor, Department of Pathology, Pt.JNMMC, Raipur, C.G. * Corresponding Author
Dr. Vanita Bhaskar	Assistant Professor, Department of Pathology, Pt.JNMMC, Raipur, C.G.
Dr. Apurva Agrawal	Assistant Professor, Department of Pathology, Pt.JNMMC, Raipur, C.G.
Dr. Jyoti Choudhary	3rd year Post Graduate Student, Department of Pathology, Pt.JNMMC, Raipur, C.G.

ABSTRACT

A 53 year old male patient presenting with ulcerative growth over left foot since 2-3 years, inguinal lymph node swelling since 2-3 months, multiple chest wall swellings since 2-3 months and growth over right lateral border of tongue since 2-3 months. On histopathological examination a diagnosis of combined Squamous cell carcinoma of right lateral border of tongue and Malignant melanoma of left foot with cutaneous metastasis was made. The presence of two malignancies with different histopathologies at anatomically distinct sites suggests the diagnosis of dual primary malignancy which being a rare phenomenon prompted us to report this case.

KEYWORDS

Malignant melanoma, squamous cell carcinoma, dual primary malignancy.

Introduction:

The presence of multiple primary cancers in a single patient was first reported more than 100 years back. Since then, this phenomenon has been identified with increasing frequency, in part due to the increase in life expectancy of cancer survivors—a boon of advancements in cancer therapeutics—and to the more comprehensive screening protocols used in cancer patients. The two cancers are either detected at the same time (synchronous) or one may follow the other after a period of time (metachronous).[1] Skin cancer patients are primarily at increased risk of developing subsequent skin cancers of the same type. Shared risk factors might also increase the occurrence of a different type of subsequent skin cancer. [2]

Squamous cell carcinoma (SCC) and malignant melanoma (MM) are very prevalent and rapidly increasing malignancies. [3-5] Two or more kinds of tumors with different biological behaviour and histopathologic entities could be seen in one patient. [6] Herein, we present one case of combined primary malignant melanoma (MM) in foot and squamous cell carcinoma (SCC) of tongue.

Case Report :

A 53 year old male patient was admitted in our hospital with complaints of ulcerative growth over left foot since 2-3 years, inguinal lymph node swelling since 2-3 months, multiple chest wall swellings since 2-3 months and growth over right lateral border of tongue since 2-3 months. Biopsy was taken from ulceroproliferative growth over right lateral border of tongue under local anaesthesia and sent for histopathological examination. H and E stained sections showed features of well differentiated squamous cell carcinoma. At the same time, fine needle aspiration from swelling over chest wall as well as inguinal lymph node swelling was done. On cytological examination, smears showed dispersed population of pleomorphic cells with abundant cytoplasm. Nuclei were hyperchromatic showing marked anisokaryosis and prominent nucleoli. Binucleate and multinucleate cells were also seen. Melanin pigment was seen intracytoplasmic, in macrophages as well as dispersed in background. Cytomorphological features were suggestive of metastatic deposits of malignant melanoma.

The past history of the patient revealed that he was a chronic bidi smoker since 10 years. He noticed a small blackish swelling (mole) over left foot 3 years back which was excised by local doctor, but no histopathology was done. One year later again recurrence occurred at the same site with increase in size and ulceration and then biopsy was done from the site. The histopathological features were of Malignant melanoma. The patient then came to our hospital and was admitted in oncosurgery department. He received 6 cycles of chemotherapy following which radiotherapy was started.

The patient was now given diagnosis of combined Squamous cell carcinoma of right lateral border of tongue and Malignant Melanoma of left foot with cutaneous metastasis.

MRI Left Ankle Joint showed evidence of a relatively large sized subcutaneous mass like lesion noticed along the inferior or lateral aspect of heel region, appearing hyperintense on T2 and iso to faintly hypointense on T1 weighted images, measuring 7.1x4.1x6.2 cm in size (APxTRxCC). This subcutaneous lesion showed diffusely infiltrating margins with central ulceration and irregular everted superficial margins with infra calceneum soft tissue extension. Findings favoring a neoplastic pathology.

CECT FACE AND NECK showed ill defined irregular heterogeneously enhancing soft tissue mass noted involving right lateral border of tongue, measuring approx 1.8x 1.6 cm. There were few subcentimetric bilateral submandibular lymph nodes suggestive of nodal metastasis. Features were suggestive of neoplastic mass of right lateral border of tongue with nodal metastasis.

We received wide local excision of carcinoma left leg, left inguinal lymph node mass, right partial hemiglossectomy specimen and right level IA, IB, IIA, IIB and III lymph nodes. Sections from tissue labelled as "wide local excision of carcinoma left leg" showed features of Malignant Melanoma. Section from base, circumferential skin margins and circumferential soft tissue margins were free from tumour. Sections from tissue labelled as "left inguinal lymph node mass" consisted of single matted lymph node with attached 05 lymph nodes showing metastatic deposit of Malignant Melanoma. Attached skin and fibrofatty tissue were free from tumour.

Sections from tissue labelled as "right partial hemiglossectomy" showed features of Well Differentiated Squamous Cell Carcinoma. Two out of six lymph nodes of right level I A showed metastatic deposit of the tumour. Other lymph nodes were free from tumour. No lymphovascular or perineural invasion was identified. All the surgical margins (anterior surgical margins, posterior surgical margins and


Figure 1

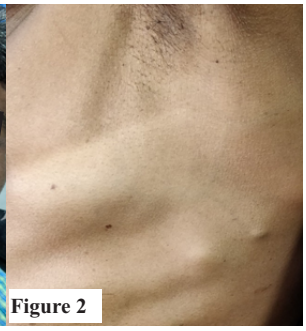
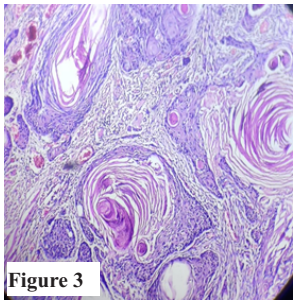


Figure 2

Figure 1: Ulceroproliferative growth over lateral border of tongue.
Figure 2: Multiple chest wall swellings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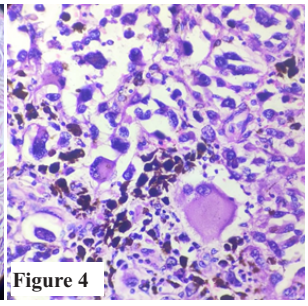
Figure 4

Figure 3: High power view (40X, H&E staining) showing well differentiated squamous cell carcinoma.
Figure 4: High power view (40X, H&E staining) showing malignant melanoma composed of large cells with abundant eosinophillic cytoplasm, marked atypia with pleomorphic nuclei and large eosinophillic nucleoli. Prominent melanin pigmentation is also demonstrable.

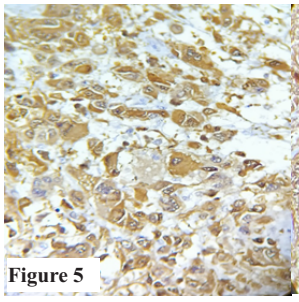
Figure 5

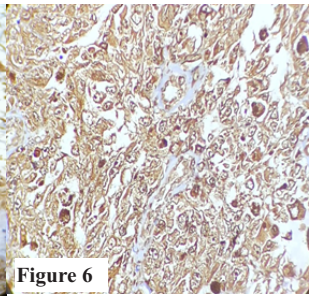
Figure 6

Figure 5: High power view of Immunohistochemical staining demonstrating S100 positivity.
Figure 6: High power view of Immunohistochemical staining demonstrating HMB 45 positivity.

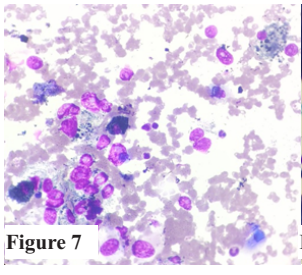
Figure 7

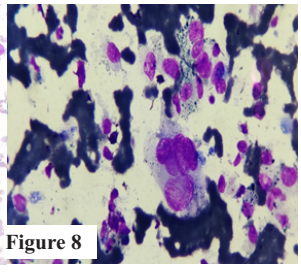
Figure 8

Figure 7 and 8: showing cytological features of malignant melanoma with dispersed population of pleomorphic cells having abundant cytoplasm. Binucleate and multinucleate cells are also seen. Melanin pigment is seen intracytoplasmic, in macrophages as well as dispersed in background.

DISCUSSION:

Squamous cell carcinoma (SCC) and Cutaneous malignant melanoma (CMM) are among the most prevalent [7] and rapidly increasing malignancies in white populations worldwide. [8] The major environmental risk factor for all skin cancers is ultraviolet radiation (UVR) from sunlight. [9] The type of UVR exposure (e.g. intermittent versus accumulated) appears to differ for SCC and CMM. [10] In addition, individual characteristics such as skin type, eye and hair color, nevi and immune suppression are important predictors of individual susceptibility to skin cancer. [11,12] High socioeconomic status is also associated with CMM.[13]

During the last fifteen years, several studies have suggested that a history of skin cancer increases the risk for a new primary cancer, both of the skin and other sites. Many of these studies were based on cancer registry data, with high quality case ascertainment but lacking data on individual risk factors that might explain this.

Robsahm et al examined the risk of a new primary cancer following an initial skin cancer and assessed risk factors associated with second primary cancers. During follow-up, 9608 new primary cancers occurred after an initial skin cancer. SIR analyses showed 50% and 90% increased risks for any cancer after CMM and SCC, respectively ($p < 0.01$). The logistic regression model suggested even stronger increase after SCC (130%). The highest risk was seen for subsequent skin cancers, but several non-skin cancers were also diagnosed in excess: oral, lung, colon, breast, prostate, thyroid, leukaemia, lymphoma and central nervous system. Factors that were associated with increased risk of subsequent cancers include male sex, older age, lower residential latitude, being married and low education and income. Parental cancer did not increase the risk of a subsequent cancer after SCC, but was a significant predictor among younger CMM survivors. [14]

Multiple primary malignancies in a single patient were first described in 1879 by Billroth. [15] The neoplasms may be limited to a single organ or involve multiple and anatomically separate organs. The North American Association of Central Cancer Registries (NAACCR) classifies multiple primary tumors into two categories: (1) *Synchronous*, in which the cancers occur at the same time (the Surveillance Epidemiology and End Results Program (SEER) definition is within two months) and (2) *Metachronous*, in which the cancers follow in sequence, that is, more than two months apart. [16] Metachronous primary malignancies are becoming increasingly common because of an increase in the number of elderly cancer survivors, greater awareness, and improved diagnostic modalities. In comparison, synchronous tumors occur uncommonly, with the most common site for synchronously existing multiple tumors being the breast. Whether the second lesion is truly a primary or represents metastases is difficult to decide and for this the Warren and Gates criteria (1932) are used which proposed that a diagnosis of multiple primary malignancies requires the following:

(1) each tumor should present a definite picture of malignancy;
(2) each tumor should be histologically distinct;
(3) the possibility that one is a metastasis of the other must be excluded. [1]

Tang et al reported one case of combining primary malignant melanoma (MM) in gingival mucosa and scalp squamous cell carcinoma (SCC) and reviewed the literature. They reviewed articles from 1953 to 2016 that contain the keywords “Squamous Cell Carcinoma” and “Malignant Melanoma” in the PubMed and MEDLINE databases. There were 58 articles in English about combining MM and SCC, including 928 cases combining cutaneous MM and cutaneous SCC and 4 cases combining mucosal MM and mucosal SCC. 5 cases were of combined mucosal MM and cutaneous SCC including their own case. [17]

The pathophysiology behind the occurrence of multiple primary malignancies has been theorized to be common carcinogen induced multiple cancers in an exposed epithelial surface, called “field-cancerization” as seen in head-neck tumours, as a late side effect of treatment used to treat the first tumour, and a genetic predisposition to neoplasia.[18] Other possible causal factors include persistent carcinogen exposure from environment, progressive ozone depletion and effects of ionizing radiation, increased use of organ transplant, and the increasing use of newer treatment modalities like hormonal manipulation, target therapies, genetic manipulation, and immunomodulators. [19]

CONCLUSION:

Metachronous primary malignancies are becoming increasingly common because of an increase in the number of elderly cancer survivors, greater awareness, and improved diagnostic modalities.

This metachronous presentation of dual primary malignancy of skin at two different sites prompted us to report this case.

It should also be noted that individuals who are at a high risk of skin cancer may have other risk-taking behaviour related to their increase in risk of a second primary cancer such as UV exposure, smoking, dietary intake and physical activity levels. Therefore increased awareness may help in identifying individuals at high risk for subsequent cancers and for whom particular attention ought to be directed.

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