Merkel Cell Carcinoma : An Indian Experience

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Abstract

Merkel cell carcinoma [MCC] is a rare neoplasm of skin with an aggressive behaviour and unfavourable prognosis. MCC mainly occurs in the elderly, in the sun exposed areas of skin. Indian's experiences regarding patients' profiles, clinical presentation, age of occurrence, pattern of tumour are very limited as well as challenging.This retrospective study was performed, in a tertiary care hospital in Paschim Medinipur, West Bengal, India, reviewing the cases of five patients.In our cases we try to elaborate data regarding the age of occurrences, presentation, and behaviour of tumour and prognosis of MCC.The patients' profiles, clinical presentation, age of occurrence the tumour characteristics including histopathological and immunohistochemical profiles are similar to the cases presented in other parts of world.

Index terms— merkel cell carcinoma, neuroendocrine tumour, skin tumour.

1 Introduction

erkel cell carcinoma(MCC) is a rare primary cutaneous neoplasm with epithelial and neuroendocrine differentiation and it has been first described by Toker in 1972 1 as the "trabecular carcinoma of the skin". This neoplasm arises from the neuronal crest cells-Merkel cells which is situated in the basal layer of the epidermis. Though the exact cause remains unkown, sunlight has been reported to be a major risk factor. Common associations include in situ or invasive squamous cell carcinoma, basal cell carcinoma indicating its origin from multipotent stem cells of ectodermal derivation. High occurance of this tumour in organ transplant receipients and in immunocopromised patients indicates the role of immunosuppression in its etiogenesis (2). The reported annual incidence of MCC ranges from 0.2 to 0.45 per 100000 3 . It is mainly a disease of the Caucasian race. The annual age-adjusted incidence of MCC is 0.23 per 100,000 for whites and 0.01 for blacks 4 . Age of occurrence in elderly with mean age at presentation being around 75 years 5 . Only a few cases reported before the age of 50, and are usually related to immunosuppression 6 . Many cases have been reported worldwide, majority of which are Caucasians, while Indian experience regarding incidence of MCC, clinical presentation, age of occurrence and pattern of tumour are very limited. So in this article we tried to share our experience of such few rare occurrences in a tertiary care hospital of eastern India.

2 II.

3 Material and Methods

4 Result

Patient characteristics, as detailed in table no 1, shows that during the study period 5 patients were came with a skin lesion, among them one was younger than 50 year, and others were older than 60 year. There was a slight male predominance with a ratio of 1.5:1 (60% male and 40% female). In this study all patients were Asian and farmer with history of occupational sun exposure. One patient had history of immunosuppresion due to pre-diagnosed CLL.

As mentioned in Table 2, most lesions appeared on sun-exposed skin. Most common site of the primary tumour was head & neck region (40%) and upper limbs (40%), followed by lower limbs (20%) (Fig- 1). Size of

the tumours were variable ranging from 1.5 cm to 4.6 cm. Primary tumour diameter of less than 2 cm was found in 3 cases and that of more than 2 cm in 2 cases. Four patients presented with a nodule covered by intact skin, while more advanced tumour form was found in one with ulcerating growth. The lesions were painless, firm, and non-tender. Regional lymph node metastasis found in two patients. Three patients of the group having no regional lymph node metastasis were clinically diagnosed as benign lesion. Other two patients with lymph node enlargement were clinically suspected as malignant.

All patients were subjected to excision followed by histopathological examination. The prepared H&E stained slides exhibited diffuse pattern of infiltration of dermis by small round cells with an intact epidermis (Fig 2a **??** 2b & 2c), cells having scanty eosinophilic cytoplasm and round vesicular nuclei with fine granular chromatin (Fig **??**d). In immunohistochemical examination, the tumor cells showed typical perinuclear dot like positivity for cytokeratin 20 (Fig- **??**a), negative for TTF-1 (Fig- **??**b), as well as immunoreactive for chromogranin (Fig- **??**c) and NSE (Fig- **??**d). On the basis of these histological and immunohistochemical features, diagnosis of Merkel Cell Tumor were established. Then additional excisions were performed to achieve margins 3 cm wide and 1-2 cm deep along with lymph node dissection. The patients were evaluated with a CT scan for staging. CT scan reports revealed regional lymph node metastasis in two patients having primaries more than 2 cm in size; others were negative for metastasis. All patients were treated with post-operative radiotherapy. The follow-up were done through CT scan. Two patients died 1 year later during the follow-up period.

5 Discussion

Merkel cell carcinoma is a rare neoplasm of skin with an aggressive behaviour and unfavourable prognosis 7 . Many reported cases found in literature are mainly in white 4 . Data regarding the occurrences, presentation, behaviour of tumour and prognosis is still limited in Indian subcontinent. In our study we found only five cases of MCC in three years of span (2009-2011). It is mainly a tumour of elderly 5 , few cases found before age of 50 years were associated with immunosuppression 6 . In our study, among five cases four (80%) were within age range of 60-80 years and one (20%) younger than 50 years, who had previously diagnosed CLL. According to Brenner et al incidence of CLL as second neoplasm is 15.9% & majority of this second neoplasm preceded the diagnosis of MCC 8 . Here the occurrence of MCC was slightly higher in male with M:F ratio of 1.5:1, which also follows Heath et al study 9 . Constant sun light exposure is obvious in all patients as they all are farmer by occupation. Also they presented with tumours involving head & neck, upper limbs and lower limbs, supporting the possible contributory role of sun light in development of MCC, as shown by Miller & Rabkin in their study that incidence of MCC is increased with the exposure of solar UVB ray 9,10 . Van Gele et al also shows a UV-B-induced C to T mutation in MCC cell line11, suggesting that sun exposure plays a leading role in the pathogenesis of this tumour. However, this does not provide a satisfactory explanation, because MCC has been reported in nonsun exposed sites.

MCC usually presented as a non-tender nodular growth, sometimes as an ulcerated lesion 7 . Most of the tumours are approximately 2 to 4 cm in diameter 12 . Clinically correct diagnosis is made rarely, because these lesions can resemble many other tumours. The clinical differential diagnosis often includes basal cell carcinoma, squamous cell carcinoma, pyogenic granuloma, keratoacanthoma, amelanotic melanoma, adnexal tumor, clear cell acanthoma, lymphoma, and metastatic carcinoma 13 .

On gross examination it shows grey coloured cut surface 14 (Fig- 1). Microscopically tumour occurs in the dermis, sometimes in subcutaneous tissue with an intact overlying epidermis 7 , though epidermal involvement by the tumour is also reported previously 15 . Tumours are composed of small round cells arranged in diffuse and sometimes in trabecular pattern. The cells have scanty eosinophilic cytoplasm and round vesicular nuclei with fine granular chromatin & multiple nucleoli. Mitotic count is high 16,17 . Immunohistochemically MCC are positive for low molecular weight keratin (CK20), chromogranin & neuron specific enolase 7,18 . The CK20 shows typical perinuclear dot like positivity 7 . MCC are negative for TTF-1 19,20 . In our present study all cases show similar above mentioned histological & immunohistochemical features.

Different types of chromosomal abnormalities have been reported in this tumour. Trisomy of chromosome 6 & 1 are most typical 21,22,23 along with partial & complete trisomy of chromosome 11 24,25 .

Due to rarity of the tumour there are multitudes of treatment protocols. The treatment depends on the stage of the tumour at the time of presentation. Patient with a localized tumour surgery with excision of 3 cm wide margins and 2 cm depth is considered as a gold standard method. 26,27 . Postoperative radiotherapy in patients without lymph node metastasis is still controversial. But due to high rate of local relapse, 45-60 Gy 26,28 is used routinely to the area of lesion to decrease the local recurrence 29 . The lymph node involvement is an important prognostic factor of this tumour. Its involvement decrease the survival rates from 88% to 50% and it is evident in 50% -70% of all patients within 2 years of diagnosis 30 . So sentinel node biopsy 31 and routine lymph node dissection 27,32 is strongly recommended along with postoperative radiotheraphy in case of its metastasis 33 . Other poor prognostic factors are tumour size >2 cm, male sex, age>60 years & immunosuppression 26,29,32 .

V.

6 Conclusion

We reported five cases of merkel cell carcinoma, arising in different parts of the body, from surrounding areas of Paschim Medinipur district in eastern India. Patients' profiles and tumour characteristics including histopathological findings & immunohistochemical patterns are similar to those presented in other parts of world. A strong clinical suspicion, clinicoradiological correlation and histopathological and immunohistochemical confirm-ation are required for proper evaluation along with wide margin resection with or without postoperative radiotheraphy & lymph node dissection.

7 VI.

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Figure 1: Figure 1 Volume

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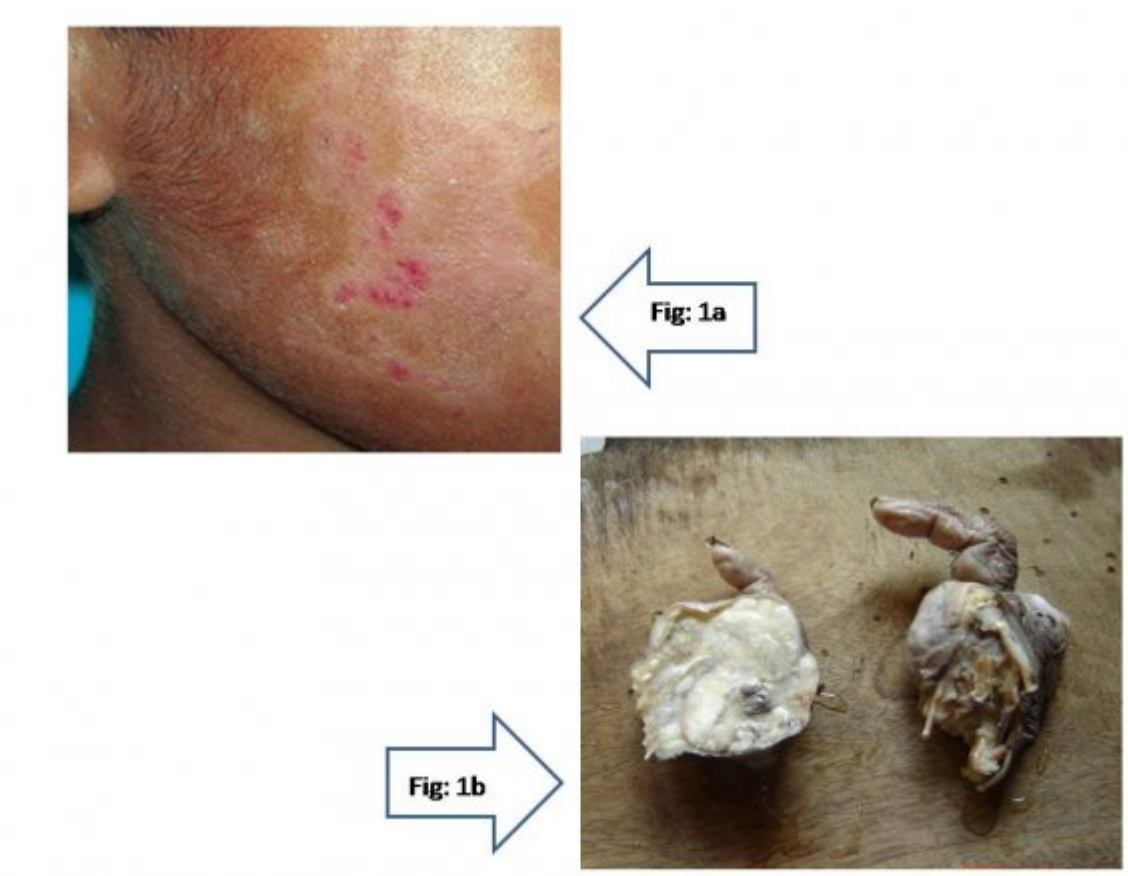

Figure 2:

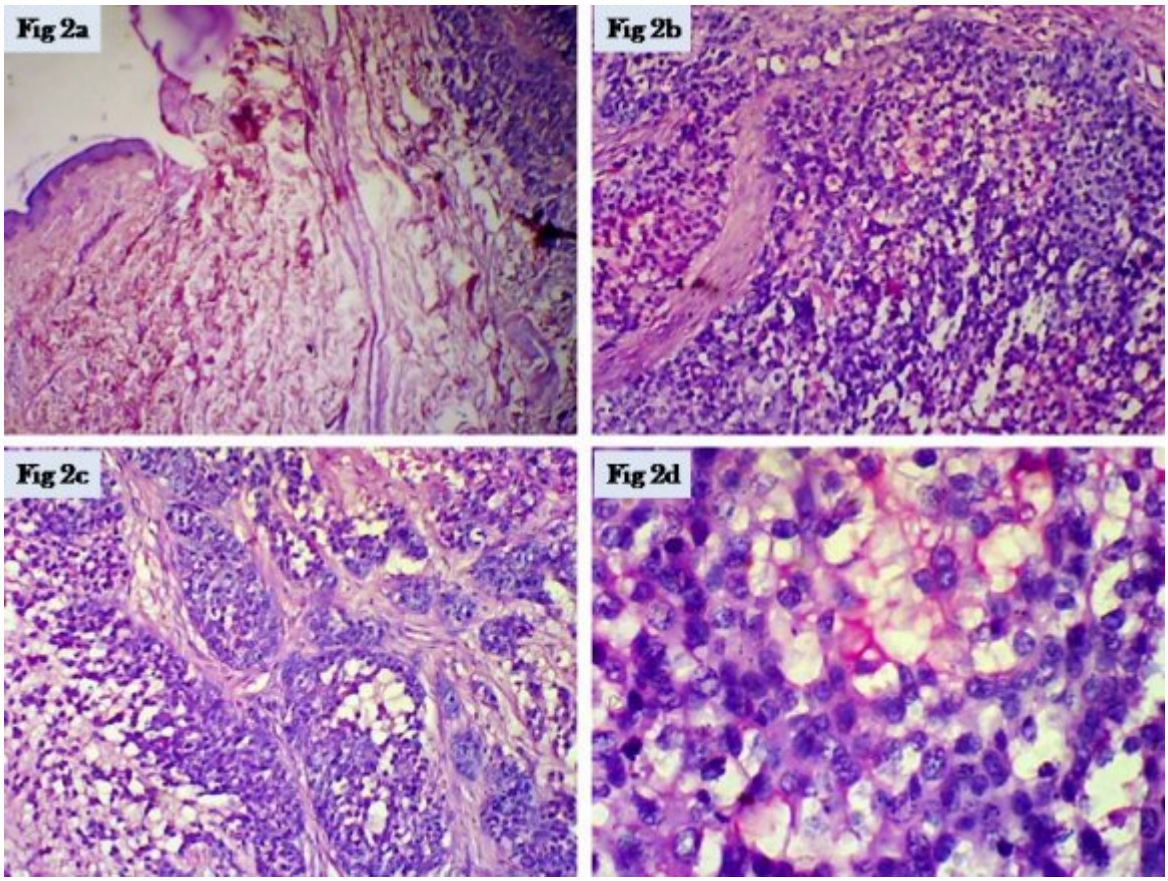

Figure 3:

2

Number of
cases (%)

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Figure 4: Table 2 :

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