Case Report-II

Merkel Cell Carcinoma of Skin

JANAKI MG, KIRTHI KOUSHIK, REKHA BABY, VENKATESH KEMPIAH.

ABSTRACT

Merkel cell carcinoma is a rare neuroendocrinal tumour of the skin. It is noted for its typical aggressive nature unlike other skin tumours. Because of the rarity, the treatment is not standardised. Radiotherapy in the postoperative setting is effective in improving the loco regional control. A case of merkel cell carcinoma treated with postoperative radiotherapy is reported. Pertinent literature is reviewed.

INTRODUCTION

Merkel cell carcinoma of skin is a rare but aggressive tumour with higher lymph nodal spread and has poor outcome to the treatment.

CASE A sixty five year old frail lady presented with a left mid thigh swelling measuring 4 x 4 cms in posterior aspect of six months duration. The growth was proliferative and bled on touch (Fig 1). There were multiple left inguinal nodes measuring two to three cm. Biopsy from the growth revealed a malignant small round cell tumour with features of merkel cell tumour (Fig 2). A chest X-ray and an ultrasound of abdomen were normal. The patient underwent a wide excision of the tumour with a left inguinal lymph node dissection. Histopathology revealed a merkel cell carcinoma with the overlying squamous epithelium showing basisquamous carcinoma. The tumour was positive for CD 99 and cytokeratin. Multiple inguinal nodes showed metastatic deposits. With a final diagnosis of merkel cell carcinoma with basisquamous component and metastatic lymph nodes, the patient was treated with postoperative radiotherapy to the tumour bed with a five cm margin through parallel opposed lateral fields in prone position. A thick bolus of one cm wax was also used to avoid skin sparing effect of cobalt. Inguinal region was treated with a direct anterior portal prescribing at three cm depth. A dose of 50 Gy was delivered in 25 sittings over five weeks on a telecobalt machine. Following treatment, she was advised close follow up.

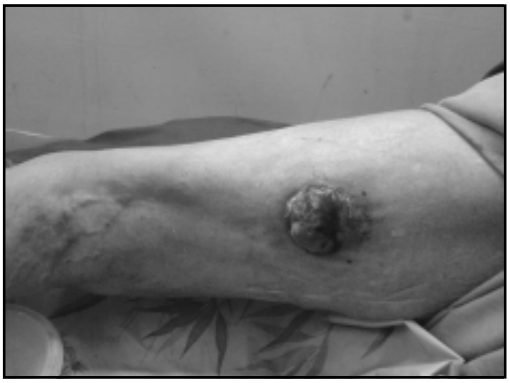

Fig 1: clinical photograph showing left thigh nodular ulcerated growth

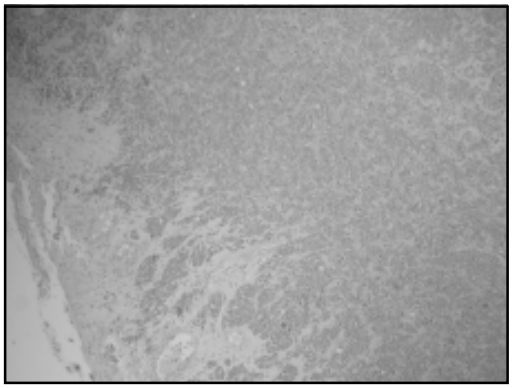

Fig 2: Histopathology showing round to oval cells in the dermis extending to the subcutaneous layer

Nine months later, patient presented with a left supraclavicular lymph node. Further investigations revealed widespread disease in the form of mediastinal, para aortic lymphadenopathy, multiple liver metastasis and

Department of Radiotherapy, M S Ramaiah Medical College, Bangalore - 560054, India.
Correspondence to: **KIRTHI KOUSHIK**
Email: kirthi.koushik@gmail.com

bone marrow infiltration. There was no loco regional recurrence. In view of her poor performance status, she was advised supportive treatment

DISCUSSION

Merkel cell carcinoma (MCC) of skin is a primary cutaneous neuroendocrine tumour arising from the merkel cells located in the basal layer of the epidermis and hair follicle.[1] Fredrick Sigmund Merkel discovered a particular round cell in the basal layers of the epidermis in 1875 and observed that these cells were associated with terminal nerve endings. However, Merkel cell carcinoma was first described by Toker in 1972 as an uncommon cutaneous neuroendocrine tumour. It is generally seen in the sun exposed areas of skin of elderly men. MCC occurring in patients who have undergone organ transplantation suggests its association with the immunocompromised status.

Differential diagnosis include cutaneous lymphoma, amelonotic melanoma, basal cell carcinoma and metastasis from noncutaneous neuroendocrine tumour. Careful clinical correlation guided by the immunohisto-chemistry markers will helps to differentiate MCC from other tumours. CD 99 could be positive in MCC[2] as well as in neuroendocrine tumour whereas MCC shows characteristic para nuclear dot pattern with CK 20 and also stains positive for neuron-specific enolase, chromogranin, and synaptophysin. MCC could be weakly positive for S100 and may also stain for kit receptor tyrosine kinase (CD 117).[1,3]

Staging is based on the extent of the tumour. Localized tumour of any size without in-transit metastasis is classified as stage I a lesion of less than 2 cms is associated with good prognosis. Presence of in-transit disease and/or regional lymph nodal disease is classified as stage II whereas any disease beyond regional lymph nodes including distant metastasis is staged as III. Regional lymph node involvement is the single most important prognostic factor.

Unlike squamous and basal cell carcinoma, MCC is an aggressive and fatal cancer. As far as the local recurrence, in transit, regional spread and distant metastasis are considered MCC behaves akin to cutaneous melanoma. The basic difference is its sensitivity to radiation. MCC is highly sensitive to radiation with a low surviving fraction of 0.37 versus 0.57 of melanoma cells. It means that following a single fraction of 2 Gy, 37% of merkel cancer cells survive whereas 57% of melanoma cells will survive. Thus radiotherapy has found an integral place in the initial management of MCC. Like any other cutaneous tumours, MCC is best treated with electrons which takes care of superficial disease and at the same time spares deep situated normal structures. Since we did not have the facility at that point of time, we treated on telecobalt with a bolus.

Due to its rarity, there are no set guidelines of treatment. Literature review suggests local recurrence rate of 22% after excision and distant metastasis in 70% of the patients.[4] Surgical excision with 3 cms margin is the standard treatment for primary tumour; role of lymphadenectomy is controversial.[5] Complete lymph node dissection (CLND) is preferred for gross nodes at presentation and clinically negative nodes are addressed with sentinel lymph node biopsy (SLNB). SLNB negative cases carry a better prognosis and are spared of the morbidity of additional surgery or radiotherapy. With the available limited data and multidisciplinary consensus, positive SLNB cases are offered CLND. Alternatively when the morbidity of CLND is considered unacceptable by the patient or the multidisciplinary tumour board radiotherapy is used to treat the lymphnode basin.[3] Following CLND, postoperative radiotherapy is definitely indicated when multiple nodes and/or perinodal spread are documented.

Postoperative adjuvant radiotherapy to primary site delays median time to first recurrence (24.2 Vs 11.8 months). However this is not translated to a better survival. Radiotherapy is also proved beneficial in postponing the median time to nodal recurrence (46.2Vs 11.3 months). In a Meta analysis by

Lewis et al, a total of 1254 patients treated with surgery alone or with radiation over a period of 38 years were analysed. There was a significant reduction in local (hazard ratio [HR], 0.27; P < .001) and regional (HR, 0.34; P < .001) failure with combined modality compared with surgery alone.[6] Overall survival rates 87% (1 year) and 49% (5 years) observed was not statistically significant. However, this study included only patients with stage I disease and no chemotherapy was administered. It is interesting to note that our patient remained disease free at primary as well as nodal sites. Radiotherapy is best avoided in select favourable tumours of less than two cms with negative margins and negative nodes.

Considering the neuro endocrine origin and its metastatic potential, there is a definite role of chemotherapy. Individual trials have shown a response of 65-75 %, however survival seems to be unaffected and hence is routinely not practiced and is reserved for metastatic disease with good performance status. Cyclophosphamide, doxorubicin, vincristine with or with out prednisone or etoposide and carboplatin are the most commonly used regimen.[7] Since immunological factors are associated with the occurrence of merkel cell carcinoma, their manipulation may offer additional therapeutic options in the future.

REFERENCES:

1) *Vincent.T.Devita, Jr Theodore S Lawrence, Steven.A.Rosenberg: Cancer; Principles and practice of oncology; 8th Edition, 2008:878-1879*

2) *Nicholson SA, McDermott MB, Swanson PE, Wick MR: CD99 and cytokeratin-20 in small-cell and basaloid tumours of the skin; Appl Immunohistochem Mol Morphol. 2000;8(1):37-41*

3) *Bichakjian CK, Lowe L, Lao CD, Sandler HM, Bradford CR, Johnson TM, and Wong SL: Merkel cell carcinoma: critical review with guidelines for multidisciplinary management; Cancer 2007;110:1–12.*

4) *Boyle F, Pendlebury S, Bell D: Further insights into the natural history and management of primary cutaneous neuroendocrine (Merkel cell) carcinoma.. Int J Radiat Oncol Biol Phys. 1995;31(2):315-23*

5) *Jabbour James, Cumming Robert, Richard A. et. al. Merkel Cell Carcinoma: Assessing the Effect of Wide Local Excision, Lymph Node Dissection, and Radiotherapy on Recurrence and Survival in Early-Stage Disease—Results From a Review of 82 Consecutive Cases Diagnosed Between 1992 and 2004; Ann Surgical Oncology 2007;14:1943-1952.*

6) *Lewis KG, Weinstock MA, Weaver AL, Otley CC: Adjuvant local irradiation for merkel cell carcinoma; Arch Dermatology, 2006;142(6):693-700*

7) *Tai PT, Yu E, Winquist E, et. al. Chemotherapy in neuroendocrine/Merkel cell carcinoma of the skin: case series and review of 204 cases; J clin Oncol 2000;18(12):2493-9.*