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Case Report

Merkel cell carcinoma presenting as a rapidly growing mass in an elderly Chinese lady

麥克爾氏細胞癌表現為年老患者的快速增大腫塊

PT Chan 陳寶德, SC Chiu 趙善存, FCS Leung 梁志珊

A 73-year-old Chinese lady presented with a rapidly enlarging submental mass that easily bled on contact. Incisional skin biopsy revealed Merkel cell carcinoma. CT scan of neck with contrast showed that the mass extended up to 10 mm deep to the platysma at the supraglottic and glottic level. There was no evidence of local invasion deep to the thyroid cartilage. Tiny lymph nodes were noted along both carotid spaces. The mass was removed with wide excisonal margin with no skin graft. The resection margins were clear. The patient was followed up regularly looking for recurrence.

患者為女性，73歲，中國人。首發表現為頦下快速增大腫塊，並常伴接觸性出血。切入式皮膚組織活檢確診為麥克爾氏細胞癌。頸部造影電腦掃描見腫塊於聲門及聲門下水平深達頸闊肌下10毫米。掃描至甲狀軟骨處未見局部侵蝕擴散。雙側頸動脈間隙有細小淋巴結。腫塊經闊緣手術切除，無需植皮。切口邊緣無浸潤。患者接受定期隨訪，以察復發。

Keywords: Merkel cell carcinoma, Chinese

關鍵詞：麥克爾氏細胞癌，中國人

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Introduction

Merkel cell carcinoma (MCC) is a rare cutaneous malignancy that usually affects the elderly population. In 1875, Friedrich Sigmund Merkel described a unique non-dendritic, non-keratinocytic epidermal cell. This cell, now bearing his name, was thought to be functioning as a touch receptor. In 1972, Toker described five cases of trabecular cell carcinoma, which were thought to be derived from the sweat gland.[1] However, in 1978, Tang and Toker found dense core granules typical of Merkel cells on electron microscopy study

of trabecular cell carcinoma.[2] Therefore the term Merkel cell carcinoma was proposed.[3] The following is a report of MCC occurring in an elderly lady.

Case report

The patient was a 73-year-old Chinese female who presented to the surgical unit with a two months' history of a rapidly enlarging mass over the submental area. There was no history of preceding injury over the affected site. The mass grew rapidly and bled easily after minor abrasion. Breathing and swallowing were not affected. The patient reported no weight loss, malaise or bone pain. Physical examination revealed a 4 cm diameter sessile haemorrhagic nodule with a lobulated surface, located at the submental area of the neck (Figure 1). The oral cavity was normal and the mass was not bimanually palpable. The cervical, axillary and groin lymph nodes were not enlarged. Liver and spleen were not palpable.

The differential diagnoses included primary skin malignancies like amelanotic melanoma, MCC, angiosarcoma, cutaneous B cell lymphoma and cutaneous infections like bacillary angiomatosis and mycobacterial infections. An incisional skin biopsy was performed which showed fragments of skin infiltrated by sheets of poorly differentiated tumour cells extending up to the dermoepidermal junction. The tumour cells possessed small amount of cytoplasm and hyperchromatic round nuclei with indistinct nucleoli, and frequent mitosis (Figure 2). Immunohistochemical study showed positivity for cytokeratin 20 (CK 20) and CAM 5.2 (Figure 3). The cells were negative for thyroid transcription factor 1 (TTF-1, lung and thyroid marker) and were

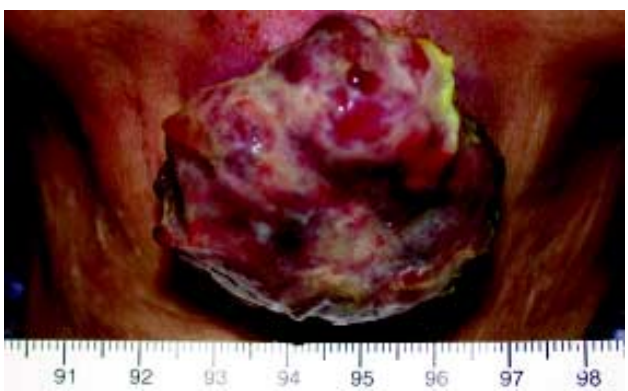

Figure 1. A fleshy and haemorrhagic nodule with lobulated surface is present on the submental area.

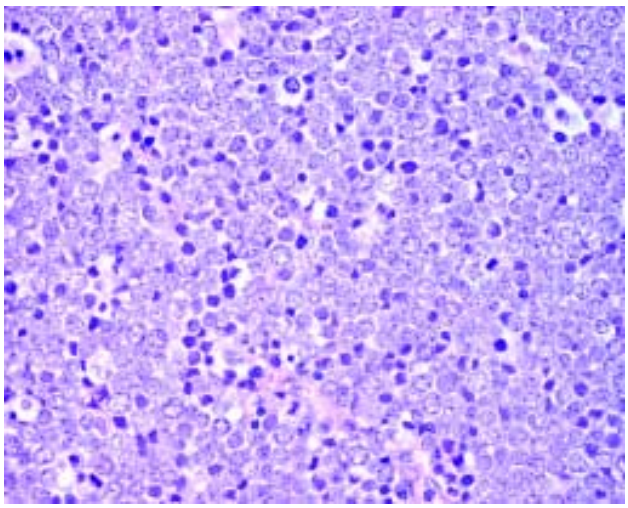

Figure 2. High power view of histologic features of Merkel cell carcinoma. The cells have hyperchromatic nuclei and scanty cytoplasm; several mitotic cells are present.

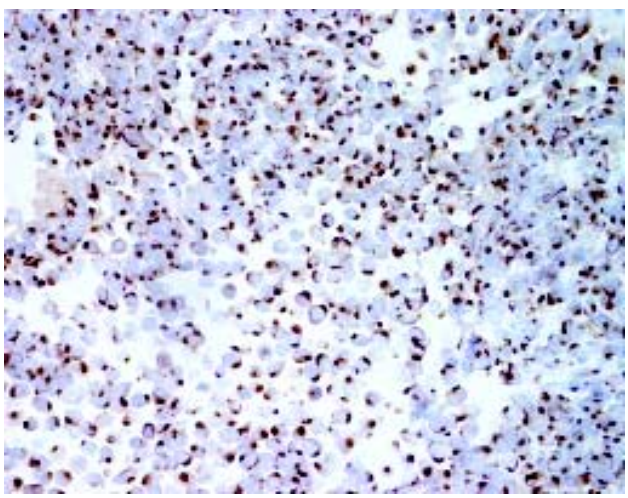

Figure 3. Immunohistochemical stain shows that the cells have dot like positivity with CAM 5.2.

weakly positive for synaptophysin and CD56. The features were those of MCC. Skin biopsy specimens for bacterial and mycobacterial cultures were all negative. Further staging investigations including chest X-ray and ultrasound abdomen did not reveal any metastasis. Computerised tomography of the neck with contrast showed a 41 x 31 x 39 mm non-calcified subcutaneous soft tissue mass in the midline of the anterior neck. The mass extended up to 10 mm deep to the platysma at the supraglottic and glottic level. There was no evidence of local invasion deep to the thyroid cartilage. Tiny lymph nodes were noted along both carotid spaces, with the largest one measuring up to 7 x 10 mm. Wide excision of the neck tumour was performed. The resection margins were clear. No adjuvant treatment was given to the patient after assessment by clinical oncologist.

Discussion

MCC is a rare cutaneous tumour. A retrospective epidemiological study of MCC in the United States has recently been reported.[4] It has an estimated age-adjusted incidence of 0.24 per 100,000 person-years and over 76% of the cases are age 65 years or older. In the United States, incidence of MCC in Whites is 11 times higher than in Blacks and 2.2 times higher than all other races. The male to female ratio is 2 to 1. In females, the sites of predilection of MCC are the head and extremities. The trunk and limbs are more commonly affected in male younger than 65 years, whereas localisation at the head becomes more common.

Patients with MCC often present with a flesh coloured cutaneous nodule that enlarges rapidly. The rapid growth of the mass, the location over head and neck region and our patient's age were typical for MCC. Sometimes, MCC presents with a plaque-like morphology. Besides its occurrence in sun-exposed area, it may rarely affect the oral mucosa, vulva and penis. The tumour spreads frequently and common secondary sites are the skin, lymph nodes, liver, lung, bones and brain.[3] On presentation, 70-80% of patients have localised disease, 10-30% of patients have regional lymph node involvement and 1 to 4% of patients have distinct metastases. A simple staging system has been proposed: stage I, localised skin disease (IA $\leq$2 cm, IB >2 cm); stage II, regional lymph node disease and stage III, metastatic disease.[5]

MCC is composed of small blue cells with hyperchromatic nuclei and minimal cytoplasm. These cells lie in the dermis and there is frequent subcutaneous extension. Epidermal involvement is rare. Mitosis and apoptosis are often widespread. Three histological patterns have been described: intermediate, small cell and trabecular.[3] They have no clinical significance and MCC most often contains an admixture of these patterns. In about 40% of MCC in one study, intimate association with epithelial lesions has been noted.[6] These include actinic keratosis, Bowen's disease, squamous cell carcinoma and basal cell carcinoma. Moreover, squamous and eccrine differentiations have been observed in MCC. Some authors, therefore, suggest that MCC may arise from primitive epidermal stem cells that are capable of differentiating into several phenotypic directions.[6] The diagnosis of MCC is aided by immunohistochemistry. MCC often expresses CK 20 but TTF-1 is usually negative.[7]

The aetiology of MCC is speculative. A significant correlation between logarithms of age-adjusted incidence of MCC and UVB radiation indexes in different geographical regions has been shown.[4] A 100-fold increase in incidence of MCC in patients treated with photochemotherapy has been described.[8] Arsenic exposure has also been implicated with a case report of coexisting Bowen's disease and MCC in a patient with chronic arsenic poisoning.[9] A number of chromosomal abnormalities have been reported including

trisomy 1,6,11,18 as well as deletion of chromosome 7 and 1p.[3] However, no conclusive gene candidates have been identified and it is not known whether there is any prognostic significance of the presence of chromosome abnormalities. The prognostic significance of expression of antiapoptotic gene bcl-2 and proapoptotic genes p53 and bax is still controversial.[10]

Due to its rarity, prospective clinical studies for treatment evaluation in MCC have not been done.[3] Surgical treatment is the primary therapy for localised disease. A two to three cm wide and two cm deep margins have been suggested. The role of radiotherapy is controversial. Although some studies have shown improved local control when adjuvant radiotherapy is given after initial surgery; these studies are nonrandomised retrospective analyses and a survival advantage has not been consistently demonstrated. The present case, therefore, did not receive any adjuvant therapy. Chemotherapy is often used in recurrent or metastatic MCC, its value as an adjuvant therapy as well as the optimal regimen remains undefined. The five-year survival of MCC in stage I, II and III diseases are 64%, 47% and 0% respectively.[3] Besides staging, other favourable clinical prognostic factors include tumour location in head and neck and female sex.[3] Pathologically, small cell size and high mitotic rate have been reported as predictors of low survival rate.[11]

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