Merkel cell carcinoma in a 17-year-old boy, report of a highly aggressive fatal case and review of the literature

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Abstract

Merkel cell carcinoma is a rare tumor frequently involving the skin with an aggressive behavior and fatal outcome. It occurs mostly in the caucasian race between 60-80 years of age and it is rare in children. Herein we report our experience with a highly aggressive fatal Merkel cell carcinoma in an immunocompetent 17-year-old boy. Its characteristics and treatment modalities will be also discussed.

Introduction

Merkel cell carcinoma (MCC) is an uncommon neuroendocrine cutaneous tumor which is highly aggressive.[1] The median age at presentation is 60-80 years and mostly affects sun-exposed regions of head and neck. It usually presents as a rapidly growing painless single red cutaneous nodule or indurated papule.[2] Therefore in general MCC is a tumor of the elderly with a lethal outcome in more than 30% of the patients.[3]

Herein we report an extremely rare case of MCC in a 17-year-old boy presented with a small occipital nodule which had grown rapidly over 3 months to a huge size of 20-cm.Unfortunately he died after operation in the intensive care unit.

Case Report

A 17-year-old boy presented with a small nodule, measuring 2×2 cm in occipital area which was excised by a local surgeon. The pathologic specimen was sent to our center for further studies. At the beginning, he was well and in good general condition. Physical examination was unremarkable with normal blood pressure (120/80 mmHg), pulse rate (80/min), respiratory rate (12/min) and temperature (37°C). Laboratory examination was also unremarkable i.e. normal complete blood count and biochemical indices. The received pathology specimen consisted of an elipse of skin and subcutaneous tissue with a subcutaneous nodule of about 2.0 cm in diameter. Microscopic findings showed a dermal based lesion composed of strands and nests of relatively uniform, small and round cells with scant cytoplasm, round to oval nuclei, and powdery dispersed chromatin as well as inconspicuous nucleoli (Figure 1a,b,c). The tumor showed extension to the reticular dermis and subcutis, sparing the papillary dermis, epidermis and adnexa. There were numerous mitotic figures in the sections examined.

The immunohistochemistry results of malignant cells showed reactive cytokeratin (dot like), epithelial membrane antigen (EMA), Cytokeratin 20 (dot like), CD 56, neuron specific enolase (NSE), synaptophysin, neurofilament and CD99 (Figure 2a). These cells were negative for leukocyte common antigen (LCA), Thyroid transcription factor-1 (TTF-1), desmin and vimentin. Ki-67 was positive in 100% of the tumor cells (Figure 2b). The primary diagnosis of cutaneous neuroendocrine neoplasm (Merkel cell carcinoma) was made. Chest and abdominal CT scan were unremarkable and no mass was identified, so it was concluded that the tumor was a primary neuroendocrine carcinoma of skin. Immunologic test including immunoglobulin levels and CD4 count were normal. HIV antibody was also negative. The patient was referred for chemoradiation, but refused treatment and he didn't start the therapy. After 3 months he came back with a huge malodorous 20 cm occipital mass with ulceration, extensive necrosis and bleeding (Figure 3). Skull and chest CT scan and MRI were performed. Underlying skull bone was involved by tumor and also there were multiple lung metastases. Physical examination of the head and neck failed to show any lymphadenopathy.

Considering the huge size and bleeding of the tumor, a decision was made to excise the tumor as completely as possible, and start chemoradiation after surgery.

During the operation, the patient developed severe hypotension, down to 30 mmHg (systolic pressure). However he was rescued and the main bulk of the mass was excised. He left the operation room to repair the site of excision by a distant free flap after a couple of days. Unfortunately after 3 days in intensive care unit (ICU) despite of normal blood pressures, he suffered a cardiorespiratory arrest and expired.

The received specimen in the pathology laboratory was a huge irregular necrotic mass, measuring 20×17×5 cm, covered by ulcerated skin. Microscopy of the mass was the same as the original biopsy and repeated immunohistochemical studies showed the same results of the initial biopsy.

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Discussion

MCC is a rare, highly aggressive and usually cutaneous neuroendocrine tumor which was first described by Toker in 1972 as a trabecular carcinoma.[4] In 1978 the same author described the presence of dense core granules in the cytoplasm of these tumor cells and proposed the possible origin from cutaneous Merkel cells.[5] In 1980 the entity was called Merkel cell carcinoma.[6] The pathogenesis of MCC is not fully understood. Recently reports have been published about a possible viral oncogenesis of MCC. These studies resulted in the discovery of a new polyoma virus, the Merkel cell polyomavirus.[7] MCC is usually a carcinoma of the elderly with the most common location on the sun-exposed areas of head and neck. It usually presents as a rapidly growing red to violaceous firm nodule.[8] The most common clinical features of MCC have been summarized as AEIOU: i) A for asymptomatic/lack of tenderness ii) E for expanding rapidly in <3 months iii) I for immunosuppression iv) O for older than 50 years and 5) U for UV exposed location. Over 90% of the patients meet 3 or more of the AEIOU criteria.[9] Our patient didn't have 2 of the criteria i.e. he was very young and there was no evidence of any immunosuppression. MCC in the immunosuppressed patients such as an AIDS victims or organ transplant patient occurs at a significantly younger age. About 50% are younger than 50 years of age.[7] Although our patient didn't have any underlying disease or predisposing risk factor.

Due to uncharacteristic features of MCC, the diagnosis in most cases is first made on the basis of histopathologic features as was our case.[7]

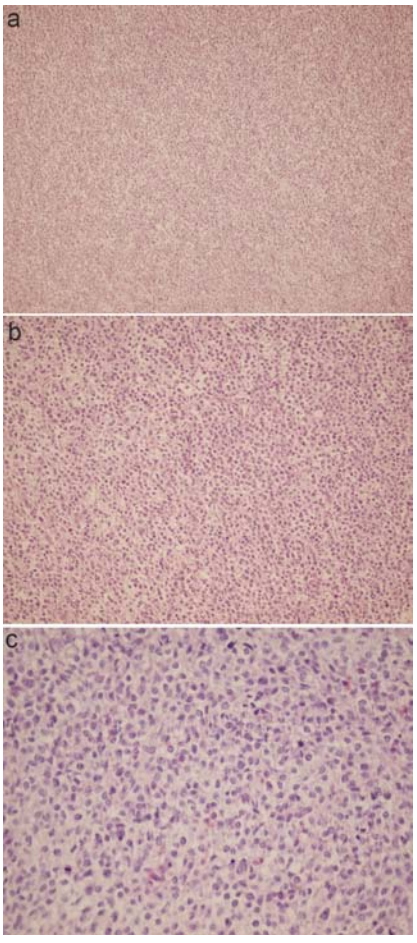

Figure 1. Sections from occipital subcutaneous mass show hypercellular tumor composed of small cells with powdery chromatin and high mitotic rates in different magnifications. (a) X100; (b) X250; (c) X400.

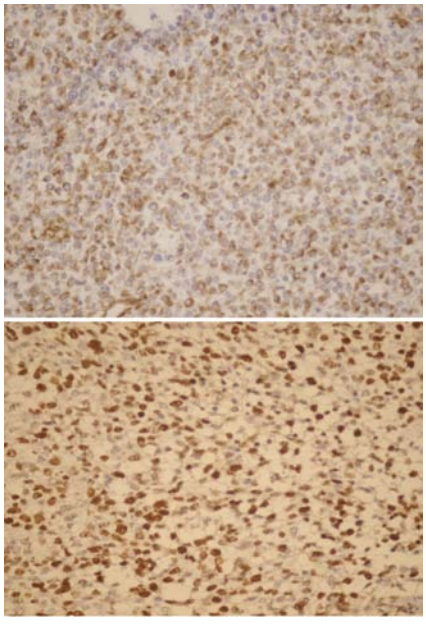

Figure 2. (a) Immunohistochemistry of the sections from the mass show positive CK20 with dot like appearance; and (b) ki-67.

MCC is a dermal-based tumor composed of nests and cords of small round cells with round to oval nuclei and inconspicuous nucleoli. These histologic subtypes are small cell, intermediate and trabecular variant. However, these variants are clinically insignificant.[10] Our case was of intermediate variant which is the most common type, composed of solid nodules and diffuse sheets of basophilic cells with round to oval relatively pale nuclei and indistinct cytoplasmic borders as well as inconspicuous nucleoli. MCC is a very rapidly growing tumor and the proliferative index, as well as the amount of mitotic activity is very high.[11]

The histologic differential diagnoses in this tumor are malignant melanoma, small cell carcinoma of lung, lymphoma and Ewing's sarcoma/ Primitive neuroectodermal tumor (PNET), all of which can be excluded by immunohistochemistry.[10] Negative HMB45, TTF-1 and CD 45 exclude tumors such as malignant melanoma, small cell carcinoma of lung and lymphoma respectively. Dot like cytoplasmic CK and CK20 are against the diagnosis of Ewing's sarcoma/PNET.[7-9] Positive CD99, TdT (Terminal deoxynucleotidase), paranuclear dots by neurofilament (NF) and c-kit have also been reported in MCC.[10-13] Wide surgical excision has been reported as the only effective treatment, followed by adjuvant chemoradiation.[14,15] The unique point about this patient was sudden severe and intractable hypotension (30 mmHg) during surgery and excision of the tumor, which has not been reported previously, but seems to be due to release of vasoactive intestinal peptide (VIP) from the tumor cells into the blood circulation (although we couldn't evaluate the level).[16]

According to the prognosis, ten-year survival has been revealed to be different in the tumors less and above 2 cm. 10-year-survival rate for tumors larger than 2 cm was reported as about 39%.[17] Tumor staging has been extensively introduced in previous reports.[18] Stage of the tumor has been reported to correlate with 10-year survival.[18] MCC has a propensity to metastasize to many sites, particularly lymphnodes, lung, liver, brain and bone.[19,20] To the best of our knowledge just 2 MCCs have been reported in the children in the English literature.[21,22] As a conclusion, our case was a remarkable one, because of his age, absence of immunosuppression and intraoperative hypotension, which can be life-threatening.

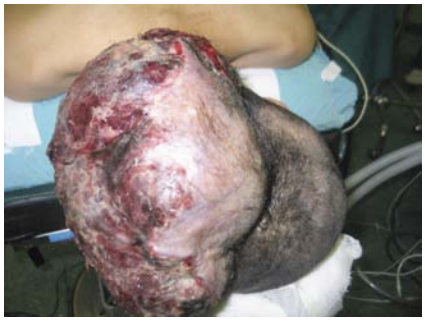

Figure 3. Gross picture of the scalp mass, before operation.

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