

Spinal Metastasis from Merkel Cell Carcinoma in an Elderly Male

Abstract

Merkel cell carcinoma is a cutaneous neuroendocrine malignancy that has an aggressive nature. Classically, it affects the elderly Caucasian population with a predilection for the sun-exposed areas of the body. Pathogenesis has been linked to ultraviolet radiation, immunosuppression, and the Merkel cell polyomavirus. Definitive diagnosis entails histologic evaluation and immunohistochemical staining. With its generalized appearance and tendency for metastasis, a high index of suspicion must be utilized. In this case, we present the unique presentation of Merkel cell carcinoma as a rapidly enlarging lymph node with metastatic disease to the spinal column presenting as new-onset low back and radicular pain.

Keywords: Elderly, merkel cell carcinoma, spinal metastasis

Introduction

Merkel cell carcinoma (MCC) is an aggressive skin neoplasm, neuroendocrine in origin, also known as small cell carcinoma of the skin. Classically, MCC occurs on the chronically exposed, sun-damaged skin of the face, neck, and the upper and lower extremities in the elderly,^[1] but it has occurred in younger populations, especially those that are immunocompromised.^[2-8] Pathogenesis has been related to many factors, more recently being the Merkel cell polyomavirus.^[2-6,9] The common cutaneous manifestation includes a violaceous papule or nodule with a smooth, shiny surface.^[1] Although variations of the cutaneous manifestations of MCC include pedunculated masses, chalazions, and granulation tissue.^[10-12] The incidence in the United States is projected around 1500 cases each year^[2] with increases seen, in part, to diagnostic and staining techniques. Even with early recognition, MCC has a dismal prognosis given the high rate of recurrence and early metastasis. While literature has evaluated many of the common and unique metastatic sites, there is limited information regarding involvement of the spinal column and surrounding tissue. In this case, we offer a look into the unique clinical presentation of metastatic disease to a lymph node and spinal column

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without a known primary cutaneous tumor.

Case Report

In February of 2015, a 75-year-old man was evaluated by his primary care physician for an asymptomatic left neck nodule that would “move around.” There did not appear to be any overlying skin changes, but the patient was concerned given the rapid increase in size over a couple of weeks’ duration. A thorough history and physical examination did not reveal any acute abnormalities. The patient was referred to surgery where a lymphadenectomy was performed. The specimen removed measured 1.3 cm and was submitted for flow cytometry, histology, and immunohistochemical staining. The pathology revealed small blue cells 2–3 times the size of nearby lymphocytes, arranged in nests [Figure 1] with a staining pattern most consistent with MCC, thyroid transcription factor-1 negative, AE1/AE1 positive, synaptophysin strongly positive, and cytokeratin 20 strongly positive [Figure 2].

After a negative positron emission tomography-computed tomography (PET/CT) scan, the patient was evaluated using the National Comprehensive Cancer Network (NCCN) guidelines and labeled Stage 1. The patient was offered chemotherapy but declined due to concerns about quality of life. His treatment included

How to cite this article: Jockisch K, Abdeen Y, Alderink C, Flippin T, Kuru S, Shaaban H. Spinal metastasis from merkel cell carcinoma in an elderly male. *Asian J Neurosurg* 2020;15:128-31.

Submission: 11-01-2018 **Accepted:** 30-09-2019
Published: 25-02-2020

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Access this article online

Website: www.asianjns.org

DOI: 10.4103/ajns.AJNS_5_18

Quick Response Code:



adjuvant radiotherapy (RT) postlymphadenectomy. This was completed on May 27, 2016. Shortly after, however, the patient began experiencing bilateral shoulder, cervical neck, and lower back pain. This was evaluated with multiple X-rays and an open-air MRI which came back negative. After failure of medical therapy by orthopedics for pain, the patient was eventually referred to neurosurgery. The physical evaluation revealed diminished sensation in the distal right upper extremity and asymmetric reflexes among the right and left arms. There was also significantly diminished muscle strength in the right deltoid labeled a 1 of 5. An MRI was then ordered and completed in August. The results showed multiple areas of tumor in the cervical, thoracic, and lumbar spine. In the cervical spine, there was a diffuse abnormal signal in the C5 vertebra with epidural extensions posterior to the C4 vertebra and C5 causing canal stenosis. There was also tumor in the neural foramina on the right of C5 with extension to the inferior aspect of C6. The thoracic level yielded an anterolateral paraspinous tumor up to 35 mm at the level of T3, with minimal involvement of the T4 vertebra. There was also a paraspinous mass noted on the left at the level of L4–L5 measuring up to 57 mm. This involved the L4–L5 L5–S1 foramina with destruction of the lateral bony elements. There was a 64 mm tumor abutting the lumbosacral plexus at the right side of vertebral level S2. This was also evaluated using a PET/CT [Figures 3-4].

The patient was treated with a combination of chemo-radiation therapy consisting of carboplatin/etoposide. Unfortunately, he was unable to complete therapy due to a significant decline in function from bilateral deep venous thrombosis and an episode of cardiac arrest. The patient and his family ultimately decided to retire to hospice care given the poor prognosis and inability to handle the treatment regimen.

Discussion

The MCC case presented here represents a very unique clinical manifestation given its primary isolated lymph node involvement and later spinal column metastasis. At presentation, most cases of MCC develop as a rapidly growing, painless, violaceous, or skin-colored papule or nodule.^[1,6-8,13,14] This is typically seen in the elderly Caucasian male population, most commonly observed on the skin of the face (27%), the upper limbs, and the shoulders (22%), followed by the lower limbs and hips (15%), according to a study by Albores-Saavedra *et al.*^[7] Notably, the study also addressed common sites of extracutaneous isolated tumor involvement, such as lymph nodes. Indeed, studies have shown as much as 14% of those with nodal disease to have no associated cutaneous finding.^[7,8,10,11,13,14]

With MCC's lack of distinctive characteristics and assorted presentations, clinical suspicion is often underutilized. That is why past studies have suggested the use of the AEIOU

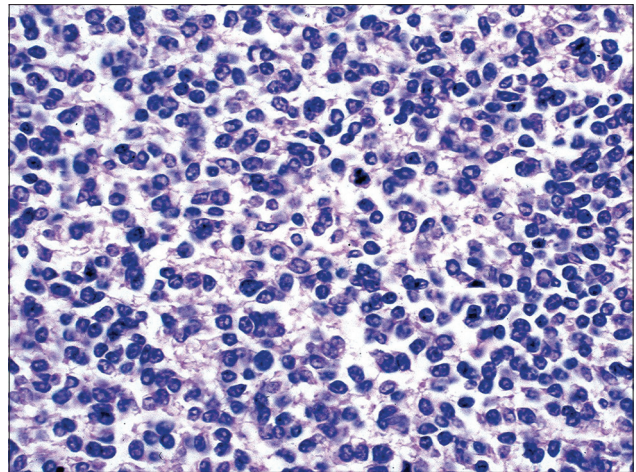


Figure 1: Microscopic section showing a lymph node with near replacement by coalescing nests of malignant cells. The individual tumor cells have hyperchromatic nuclei and surrounding scant cytoplasm with abundant mitotic activity

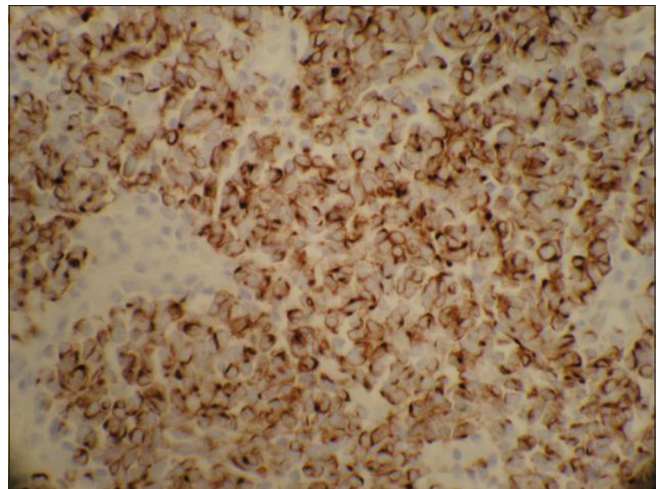


Figure 2: Cytokeratin 20 staining is strongly positive

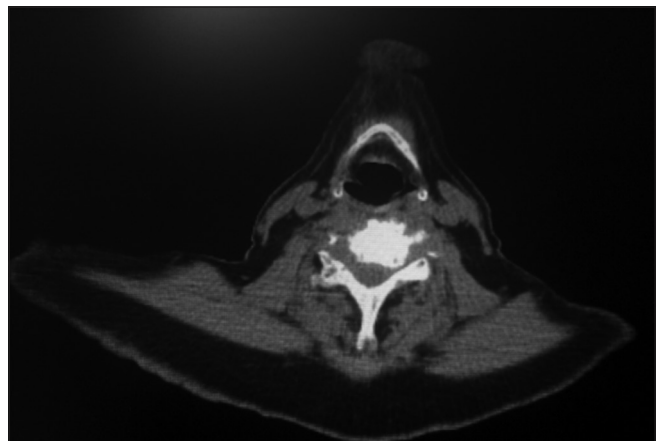


Figure 3: Whole-body positron emission tomography-computed tomography with contrast revealing hypermetabolic activity in the C5 vertebral body, in the left anterolateral soft tissue, as well as in the left foramen with a standardized uptake value of 5. There is also some suggestion of asymmetric soft-tissue attenuation of concern for a paraspinous mass



Figure 4: Pictured is a hypermetabolic paraspinal soft-tissue mass at the level of L4 that extends caudally. The mass is posterior to the left psoas muscle and measures 3.5 cm × 4.8 cm. This may be contiguous with another portion extending into the left paraspinal muscle measuring 3.9 cm × 4 cm. There is also an extension into the foramen at the L4–L5 and the L5–S1 levels, with some probable bony destruction of the L5 transverse process

system – asymptomatic/lack of tenderness, expanding rapidly, immune suppression, older than 50 years of age, and ultraviolet (UV) exposure-for initial evaluation.^[7,8,13] When applied to this case, the patient characteristics meet four of the five criteria, thereby demonstrating its possible utility. This is unsurprising given that the system’s formulation resulted from the five most common clinical features that were observed among the MCC group studied. While this system may be beneficial for increasing the clinical threshold of suspicion, definitive evaluation with histology and staining is necessary.^[4] This is due to the somewhat broad clinical differential of similar appearing conditions such as basal cell carcinoma, amelanotic melanoma, and epidermoid cyst.^[15]

MCC is described as one of the “small blue cell tumors” that is neuroendocrine in origin. It is thought to arise from mechanoreceptors at the dermal-epidermal junction, with about 10% arising from the epidermis.^[6] Histological evaluation presents in three main architectural patterns: trabecular, intermediate, and small cell. The primary distinguishing factor of MCC from other cancers, namely other small blue cell tumors, is its unique immunohistochemical staining pattern. This is due to the presence of both epithelial and neuroendocrine components that can be targeted for identification. The two markers commonly used, as done in this case, are synaptophysin and cytokeratin 20.^[14,16]

Several factors have been implicated in the pathogenesis of MCC without any single etiology being identified. Increased risk has classically been associated with chronically damaged sun-exposed skin. This becomes evident with the increased rates of MCC seen among Caucasians, with very few cases seen in the African American population.^[7] In addition, nearly 81% of MCC develops on the sun-exposed areas of the body.^[1] An increased incidence has also been seen in psoriatic patients receiving psoralen and UVA

phototherapy.^[3] Other likely contributing factors include the Merkel cell polyomavirus, which has been identified in up to 80% of MCC cases^[9,16-19] and immunosuppression with MCC reported in younger populations secondary to conditions such as organ transplant.^[18]

The natural course of MCC often results in rapid growth and early metastasis. Some of the common sites described are the lymph nodes, distant skin, bones, liver, and lung.^[8,13,14] While distant metastasis is common, there is limited information regarding metastasis to the spinal column, especially in the setting of nerve complication. With the symptoms of back pain, dermatomal sensory loss in the upper right extremity, weakness, and asymmetric reflexes, the patient’s presentation in this case was consistent with radiculopathy. This presentation has rarely been seen in the literature. These findings underscore the need for prompt diagnostic evaluation of new-onset radicular pain in those patients with a history of MCC.

For staging and comprehensive therapeutic approaches, current practices use the NCCN for guidelines. Each treatment plan employed is dependent on the stage at diagnosis. The current approach for localized disease is resection with negative margins and RT.^[20] Although, RT may be the sole option for treatment for those who are poor surgical candidates. In advanced disease, a combination of RT and etoposide with platinum-containing agents is the accepted management.^[17,20,21] Even with the common use of these agents, outcomes have shown high rates of morbidity and mortality,^[19] and despite the radiosensitive nature of MCC, the prognosis is poor with the stage of the disease at diagnosis being the best predictor of overall survival.^[1,5-7]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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