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Case Report
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A Case of Dermatomyositis in a Patient with Merkel Cell Carcinoma

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Abstract

Dermatomyositis is associated with numerous types of malignancies. To the best of our knowledge, the association of dermatomyositis with Merkel Cell Carcinoma has not yet been reported in the English Medical literature. We herein report a case of dermatomyositis in a patient with Merkel cell carcinoma.

Keywords: Dermatomyositis; Merkel cell carcinoma; CK20

Introduction

Dermatomyositis is an inflammatory disease characterized by muscle weakness and a skin rash. The condition mostly affects adults in the late 40s to early 60s and children between the ages of 5 and 15 [1]. It is more frequent in females than males. The exact cause of dermatomyositis is unknown; however, it shares many of the characteristics of an autoimmune disease. Inflammatory cells encircle the blood vessels in muscular tissue and lead to the progressive destruction of muscle fibers. Dermatomyositis has been shown to be associated with other autoimmune diseases such as Rheumatoid Arthritis, Systemic lupus erythematosus, Systemic sclerosis, as well as with malignancies [1-2].

The most common cancers associated with Dermatomyositis include cancer of the cervix, lungs, pancreas, breasts, ovaries, and gastrointestinal tract. Malignancy can develop before or after the development of Dermatomyositis [1]. The risk of cancer developing decreases three years after being diagnosed with dermatomyositis. Herein, we describe a patient with Dermatomyositis associated with Merkel Cell Carcinoma (MCC).

Case Presentation

A 54-year-old gentleman with past medical history significant for hypertension and hyperlipidemia was admitted with a one-month history of upper and lower limb weakness. His weakness worsened 2 days prior to his hospital admission and was accompanied with difficulty swallowing. The patient had also noticed a left axillary mass that has been increasing in size over several months prior to his admission. He suffered from a 50-pound weight loss over 3 months prior to his admission. Physical exam was remarkable for a patient being cachectic and ill appearing, Gottron's papules on dorsal Metacarpophalangeal (MCP) joints and Proximal Interphalangeal (PIP) joints, as well as proximal upper and lower extremity weakness (3/5). Laboratory tests revealed an elevated Creatine Phosphokinase (CPK) of 1674 U/L. With question of Dermatomyositis the patient was treated with intravenous corticosteroids (Methyl Prednisolone 100 mg to 200 mg daily) with minimal improvement in muscle weakness.

Computed tomography of the abdomen and pelvis revealed five solid-appearing, rim-enhancing lesions in the liver measuring up to 2.7 cm, suspicious for metastatic disease. Also present was left axillary lymphadenopathy as well as left retropectoral lymphadenopathy. The dominant lymph node was 5.6 cm × 3.3 cm. Magnetic resonance imaging of the thoracic spine with and without contrast showed epidural metastatic lesions with cord compression and cord edema at T6 and T11 vertebral bodies. There was also heterogeneous marrow signal intensity at T1 to T4 vertebral bodies. T10 and T11 vertebral bodies were compatible with metastatic lesions.

Excision of the left axillary mass revealed a high-grade neuroendocrine tumor. The tumor was Cytokeratin, (CK) 7 negative, CK20 positive, thyroid transcription factor (TTF)-1 negative, synaptophysin positive, chromogranin negative, and an immuno-profile suggestive of Cell

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Carcinoma significant for metastatic high-grade neuroendocrine carcinoma. Thus, the MCC was accompanied by metastasis to the liver, chest, and spine. The patient was transferred to the oncology floor for chemotherapy and radiation therapy.

He was treated with 3 cycles of chemotherapy with Cisplatin as an inpatient (for a total of six cycles), completed spinal radiation therapy as well as physical therapy needed for his muscle weakness. The patient had clinically improved but had significant muscle weakness due to ongoing dermatomyositis.

Discussion

To the best of our knowledge, the association of dermatomyositis with MCC has not yet been reported in the English Medical literature. The unresponsiveness of the weakness to high doses of corticosteroids was supportive of this being a paraneoplastic cause of dermatomyositis.

MCC is an aggressive neuroendocrine skin carcinoma with a high risk of metastasis. It is a rare skin condition with approximately 1500 cases per year in the United State. MCC usually presents as a firm, painless, nodule (up to 2 cm diameter) or mass (>2 cm diameter), but it may not have a distinct appearance [3]. Merkel-cell cancers tend to invade locally, infiltrating the underlying subcutaneous fat, fascia, and muscle, and typically metastasize early in their natural history, most often to the regional lymph nodes. MCC also spreads aggressively through the blood vessels to many organs, as was the case in our patient, particularly to liver, lung, brain, and bone. Definitive diagnosis of MCC requires examination of biopsy tissue. Histologically anastomosing red or blue trabecula and cell nests develop on the skin [4]. Sunlight exposure is thought to be one of the causes of MCC. Factors strongly linked to the development of MCC including older ages >65, fair skin, history of excessive sun exposure, and chronic immunosuppression from heart or kidney transplant or HIV [5].

This frequently metastatic disease has a 33% to 46% mortality rate and is most often caused by monoclonal integration of Merkel Cell Polyomavirus (MCPyV) [6]. The remainder of MCC cases is usually caused by exposure to UV light and its consequent somatic mutations. MCPyV is the only known human oncovirus in polyomavirus family. This asymptomatic infection usually manifests in the skin and its prevalence increases with age [6]. The host cell of MCPyV is still not known. Because benign Merkel cells are not numerous enough in patients with MCC, other possible host cells have been proposed. These include peripheral blood monocytes, dermal fibroblasts, and HEK 293 cells. The latter two are the only cells in which viral infection has been reproduced *in vitro* [6]. MCPyV replication occurs by three mechanisms: the E3 ligase targeting phosphorylated Large T antigen (LT), feedback inhibition by LT on its own promoter, and inhibition of LT production by viral micro RNA. After the virus enters into a host cell and viral replication is inhibited by these three subsequent actions, the virus then defaults to a latent, non-replicative state after infection [6]. MCPyV becomes cancerous through the integration of the viral genome into the host genome and truncation of LT to cause viral genome to be incapable of replication [6]. The very low probability of this kind of oncogenic transformation contributes to the rareness of MCC.

Even though MCC is most typically found in the dermis, it can arise in any skin layer. However, concrete evidence on the exact cell of origin of MCC is insufficient. Despite MCC cells displaying immunophenotypic and structural similarities to benign Merkel cells, the regions with highest Merkel cell density are not the most recurring sites of MCC. What is more probable is that MCCs originate in a cell population that is almost identical to the Merkel cell differentiation pathway. Due to the fact that virus negative MCCs have UV mutational distinctions while virus-positive MCCs do not, MCC tumors may arise from distinct cells of rigid with different levels of DNA photo-damage. Taking the above information into account, possible candidates for the origin of MCC identified are the following: pro-B cells or pre-B cells, fibroblasts, dermal mesenchymal stem cells, epidermal progenitor cell populations, HPV-infected epithelial stem cells, and mesothelial cells [6].

Confirming a diagnosis of MCC requires a series of histopathological and immunohistochemical tests. To prevent a misdiagnosis of MCC as basal cell carcinoma, it is crucial to use neuroendocrine markers as part of the investigation. The markers of MCC include Chromogranin A, synaptophysin, and Cytokeratin 20 (CK20) that were checked in our patient. The combination of CK20 expression and paranuclear dot-like pattern of intermediate filament staining is highly suggestive of MCC [6].

Prognostic findings of MCC are associated with the physical manifestation of the tumor. The two main prognostic parameters for MCC are tumor size and presence of locoregional or distant metastases. The larger the primary tumor size, the higher the risk of metastatic disease. In addition, VN-MCC patients typically have a worse prognosis than VP-MCC patients [6]. However, both VP-MCCs and VN-MCCs can have clinically aggressive and fatal courses.

The case described herein is unique due to the lack of skin lesions consistent with MCC. Numerous studies found that MCC patients who have no known history of a primary cutaneous lesion/tumor displayed improved survival than patients in the same stage with a primary presentation [7]. They have shown to have an intact immune system, higher oncoprotein antibody titers, as well as a higher mutational burden than those with a primary lesion contributing to their increased survival rates [8].

Surgical excision with 1 cm to 2 cm margins is usually the first treatment that a patient undergoes for MCC, especially for the primary tumor, however, our patient was not found to have a primary skin tumor. Chemotherapy may be used to treat both primary and metastatic MCC. Although the definitive role of chemotherapy is unknown chemotherapy plays a role in the treatment. Because of MCC's aggressive metastatic behavior, radiotherapy was used to treat the cancer. It has been shown to be effective in reducing the rates of recurrence and in increasing the survival of patients with MCC [9]. Other systemic therapies that are provided today include platinum-based drugs, taxanes, anthracyclines, and etoposoide. These have been found to be more palliative in nature than distinctly responsive to the targeted cancer. Anti-PD-L1 antibody avelumab has been recently approved as therapy for metastatic MCC [6].

Conclusion

In conclusion, our patient, who was devoid of a primary lesion, may have had a more robust immune system, than seen in many other patients, thus, eliminating the primary tumor before it was recognized. Besides the mere validation of additional therapeutic options for MCC, urgent questions still plague this cancer's research. For instance, there is a supremely distinguishable molecular dichotomy that exists between VP-MCC and VN-MCC [6]. In

addition, the cancer's cell of origin remains unknown. Awareness of MCC is very low compared to malignant melanoma, contributing to why most patients, as was the case in our patient, who was diagnosed with stage IV metastatic MCC, are seen with an advanced stage of disease. Awareness to this rare cancer can provide the key to early diagnoses and improved prognoses.

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