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Case Report

Acute Anemia from Fungating Axillary Merkel Cell Carcinoma

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Abstract

Merkel cell carcinoma is a rare form of skin cancer. It is usually very aggressive and metastasizes rapidly with a high mortality rate. This type of carcinoma is often diagnosed when metastatic spread has already occurred in addition to local invasion. Common sites of metastasis include the brain, liver, lungs, and bones. We discuss an unusual presentation of 65-year-old female who presented with anemia secondary to blood loss from an exceptionally large fungating axillary mass due to metastatic Merkel cell carcinoma requiring multiple transfusions.

Keywords: Merkel cell carcinoma; Fungating axillary mass; Polyomavirus; Anemia; Blood transfusion; Nivolumab; Ipilimumab.

Introduction

Merkel cell carcinoma, also known as neuroendocrine carcinoma of the skin, most commonly occurs on the head, neck, and sun-exposed regions of the body. About 65% of cases present with local disease [1]. Merkel cells are specialized cells that lie in the basal layer of the epidermis and are responsible for tactile and light touch sensation. Merkel cell carcinoma, albeit the name, has been theorized to originate in epidermal or dermal stem cells as opposed to differentiated Merkel cells. Known risk factors for development of this carcinoma include advanced age, ultraviolet exposure, and immunosuppression. Evidence has also shown the presence of the Merkel cell polyomavirus in majority of Merkel cell carcinoma cases highlighting its association [1]. Merkel cell polyomavirus is ubiquitous and usually asymptomatic in healthy individuals, however, risk factors such as immunosuppression can lead to carcinogenic qualities. While skin biopsy confirms the diagnosis, additional sentinel lymph node biopsy is recommended due to the aggressiveness of spread. Complications include end organ dysfunction of metastatic sites. Merkel cell carcinoma is a rare and rapidly progressing cancer; therefore, prognosis is usually poor.

Case Presentation

A 65-year-old female with a history of metastatic Merkel cell carcinoma, gastrointestinal bleed, NSTEMI, diabetes mellitus, hyperlipidemia, hypertension, deep venous thrombosis status post IVC filter presented to the emergency department with complaints of fatigue and lightheadedness. Two months prior to arrival patient underwent a laparoscopic small bowel resection due gastrointestinal bleeding secondary to a metastatic mass and small bowel intussusception within the jejunum. Furthermore, four months prior to the current visit, patient suffered from an NSTEMI and had a drug-eluting stent placed.

Routine complete blood count (CBC) performed one day prior to arrival to the emergency department showed a hemoglobin of 7.6 g/dL, however repeat CBC upon arrival showed a downtrending hemoglobin measured at 7.1 g/dL. Upon physical examination, a fungating mass of the left axillary region was noted with active bleeding. Recent CT Chest showed large heterogenous enhancing, necrotic left axillary mass involving the overlying skin, seen in Figure 1.

Gross images of the axillary mass were unable to be obtained, however the Chest X-ray, shown in Figure 2, illustrates the extent of the mass.

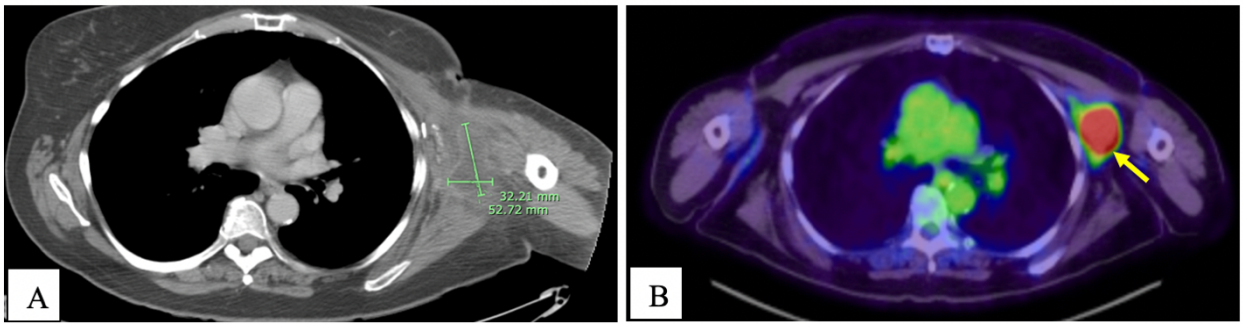

Figure 1: A) illustrates CT thorax with contrast, with measured left axillary mass; B)illustrates a PET scan showing hypermetabolic region (yellow arrow).

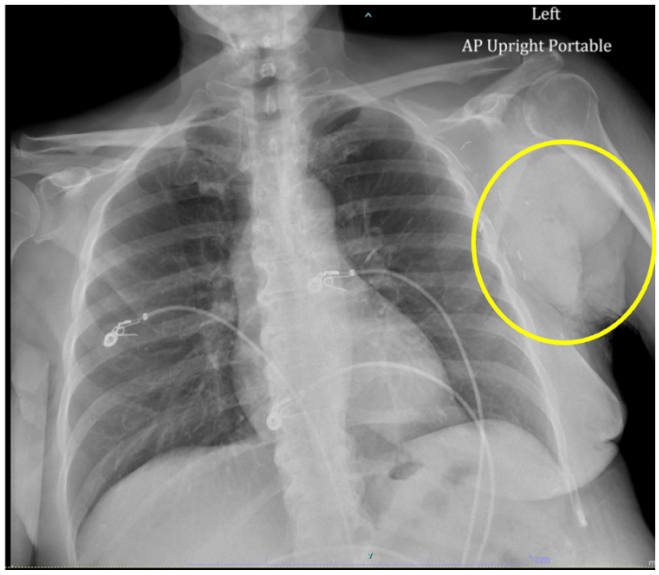

Figure 2: Chest X-ray illustrates the size of the fungating left axillary mass (yellow circle).

Patient required previous blood transfusions due to episodes of extensive bleeding of the left axillary tumor in the past. Gastroenterology and hematology services were consulted for input on the anemia given recent history of intestinal bleeding couple months prior to this presentation. NM GI bleeding scan showed evidence of intrajejunal bleeding, after which patient underwent a balloon enteroscopy and laparoscopy small bowel resection. During this admission, however, the fecal occult blood test was negative. Recent esophagogastroduodenoscopy and colonoscopy prior to emergency room visit were unremarkable for acute pathology or active bleeding hence no gastroenterological intervention was recommended during this admission.

The patient was diagnosed with symptomatic anemia secondary to both anemia of chronic disease and acute blood loss from the left axillary mass. One unit of packed red blood cells was transfused with good improvement in hemoglobin. Subsequent complete blood cell counts displayed stable hemoglobin levels around 8 g/dL. General surgery was consulted due to difficulty maintaining hemostasis bleeding fungating mass. Hemostasis was finally achieved at bedside with sustained wound pressure and surgicel bolstered with gauze. The patient's oncologist recommended discontinuing anticoagulation during the hospital stay due to increased risk of prolonged bleeding and low clot propagation risk. Prior to arrival clopidogrel, statin, and antihypertensive medications were continued during her hospital course.

Earlier in the year positron emission tomography (PET) CT scan showed a hypermetabolic mass in left axilla, standardized uptake value (SUV) max 13.05. In PET CT scan, red represents high metabolic activity usually seen in brain and malignancy, green represents moderate metabolic activity and blue represents low metabolic activity.

As seen in Figure 3, left axillary mass has high metabolic activity given malignancy. In standard practice, SUV > 2.5 have been considered malignant [2]. Sentinel lymph node biopsy showed that two out of eleven lymph nodes were positive for Merkel cell carcinoma with perinodal tissue extension.

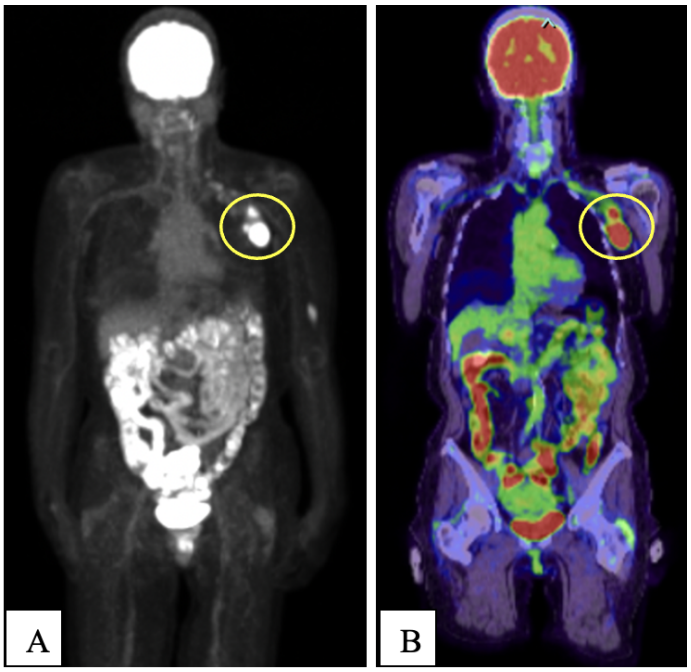

Figure 3: PET CT full body showing hypermetabolic left axillary nodules (yellow circle) and lymphoid masses; In 4B, red represents high metabolic activity, green represents moderate metabolic activity and blue represents low metabolic activity. As seen in this image, left axillary mass has high metabolic activity given malignancy.

Pathologic analysis confirmed metastatic Merkel cell carcinoma. Previous biopsies showed tumor cells express CK20 and are positive for CM2B4, or polyomavirus large T antigen. Furthermore, immunohistochemical studies showed the tumor to be immunoreactive with CAM5.2 (perinuclear dot like), CK AE 1 and CK AE3, PAX8, Synaptophysin, chromogranin, and CD56 while negative for CK7, CK 5/6, TTF-1, Napsin A, CDX2, WT-1, GATA3, p40, ER, CD45, S100. Surgical removal of axillary mass was considered, however deemed too risky due to recent NSTEMI, need for antiplatelet therapy, and complexity of the procedure. Patient was continued on treatment with an immunotherapy trial of Nivolumab and Ipilimumab for metastatic Merkel cell carcinoma as there was radiographic evidence of decreased hypermetabolic nodules and interval decrease in size.

Aspirin was stopped per cardiology recommendations and the primary team recommended that the patient follow up with their oncologist and gastroenterologist before restarting medications. All other prior to arrival medications were continued upon discharge including clopidogrel. Prior to discharge, wound care was consulted. The team discussed at length with the patient and family to maintain hemostasis and previous further bleeding complications from fungating mass.

Discussion

Complete surgical excision with wide margins of the primary tumor is the gold standard treatment for Merkel cell carcinoma. Radiotherapy can be used as primary treatment if the patient is a poor surgical candidate. Chemotherapy is also an option that can be considered. However, further immunosuppression with chemotherapy can lead to even worse prognosis due to the high rate of recurrence of Merkel cell carcinoma. Immunotherapy has shown promising results in cases of metastatic disease. Anti-PD-1 and PD-L1 antibodies have been utilized to boost the patient's immune system to provide enhanced tumor surveillance [3]. Thorough pathologic analysis of the tumor must be conducted when immunotherapy is initiated to evaluate for tumor responsiveness. The overall goal of immunotherapy is to regain the body's T cell function and effectiveness to slow tumor growth [1].

Merkel cell carcinoma is more common in older adults, males, and fair skinned individuals. Merkel cell carcinoma is often underdiagnosed and mistaken for other forms of skin cancer. Increasing incident rates have been thought to be due to improved diagnostic testing, such as enhanced biomarker detection and knowledgeable pathologist, and increased exposure to risk factors.

The pathophysiology of Merkel cell carcinoma is still a topic of debate and many mechanisms remain unclear. Although there is connection to Merkel cell polyomavirus, immunocompromised states are a major factor in oncogenesis [1]. When the immune system is not able to function correctly, it allows cell mutations to propagate leading to increased chance of tumorigenicity. T cells are lymphocytes that play a role in active immunity [4]. More specifically it has been proposed that the pathophysiology of Merkel cell carcinoma is related to T lymphocyte exhaustion by overexpression of programmed cell death ligand-1 (PD-L1) leads to disrupted immune surveillance. Each program cell death 1 (PD-1) or PD-L1 inhibitor is coupled with a specific antibody [5]. The combination of drugs ipilimumab (trade name: Yervoy) and nivolumab (trade name: Opdivo) aim to stimulate the immune system to fight cancer [6]. These medications are the current standard of care for unresectable, recurrent, or metastatic Merkel cell carcinoma [7].

Conclusion

Due to the rapid onset of metastatic spread in Merkel cell carcinoma, it is important to have definitive diagnosis at early

stages. Differentiation is crucial as other skin cancers and diseases share clinical characteristics and risk factors with Merkel cell carcinoma. Rapid progression and metastasis can lead to more complications and decreased 5-year survival rate.

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Patient consent statement: Patient provided written consent for publication of this case report. It is available upon request. This case report is written with patient privacy and confidentiality.

Clinical Trial Registration: Not applicable.

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