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Case Report

Spontaneous Regression of Dermal Metastases in Merkel Cell Carcinoma

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Abstract

Introduction: Merkel cell carcinoma (MCC) or cutaneous neuroendocrine carcinoma is a rare and aggressive cutaneous malignancy. Interestingly, despite its aggressive nature, complete spontaneous regression of MCC has been reported, mostly of the head and neck sites, and after biopsy or fine-needle aspiration sampling. There has been speculation that the biopsy of MCC may trigger complete spontaneous tumor regression via stimulation of the immune system. Spontaneous regression of metastatic MCC lesions after the excision of the main lesion, however, has not been reported in English literature.

Presentation of case: We report an extremely rare case of MCC of the left gluteal region with left inguinal lymphadenopathy and metastatic dermal nodules who underwent excision of the main lesion and was noted to have spontaneous regression of his dermal metastases post-operatively.

Conclusions: Spontaneous regression of MCC remains a poorly understood phenomenon. Further research into the histopathological features and immunity status should be considered to elucidate the mechanism underlying this phenomenon, as it will potentially be life-saving for patients with this rare malignancy, whose median survival will otherwise be measured in months.

Keywords: Merkel cell carcinoma; spontaneous regression; metastasis

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Introduction

Merkel cell carcinoma(MCC) is a rare and aggressive cutaneous malignancy. First described in 1972 by Cyril Toker as “trabecular carcinoma of the skin,” it is also known as neuroendocrine carcinoma or small cell carcinoma of cutaneous origin [1].The 5-year disease-specific survival of MCC is reportedly between 56% to 64% and a mere 0% to 18% for those with metastatic disease at presentation [2, 3]. Interestingly, despite its aggressive nature, complete spontaneous regression of MCC has been reported [3, 4]. A rare and poorly understood phenomenon, it was first described in 1986 by O'Rourke and Bell [5]. Subsequently, sporadic cases of spontaneous regression have been described, with the largest single series of ten cases by Connelly *et al*. in 2000 [6]. Majority of these cases has been MCC of head and neck sites. In this article, we report an extremely rare case of MCC of the left gluteal region with left inguinal lymphadenopathy and metastatic dermal nodules who underwent excision of the main lesion and was noted to have spontaneous regression of his dermal metastases post-operatively.

Case Presentation

An 86-year old Chinese gentleman presented in January 2014 with a gradually-enlarging left gluteal lump. He denied any bleeding, pain or itch and had no constitutional symptoms. The patient sought medical attention as the enlarging lesion had caused him discomfort on sitting. On examination, a large exophytic mass measuring approximately 6cm by 6cm was seen over his left gluteal region. There was palpable left inguinal lymphadenopathy. No other lesions were noted.

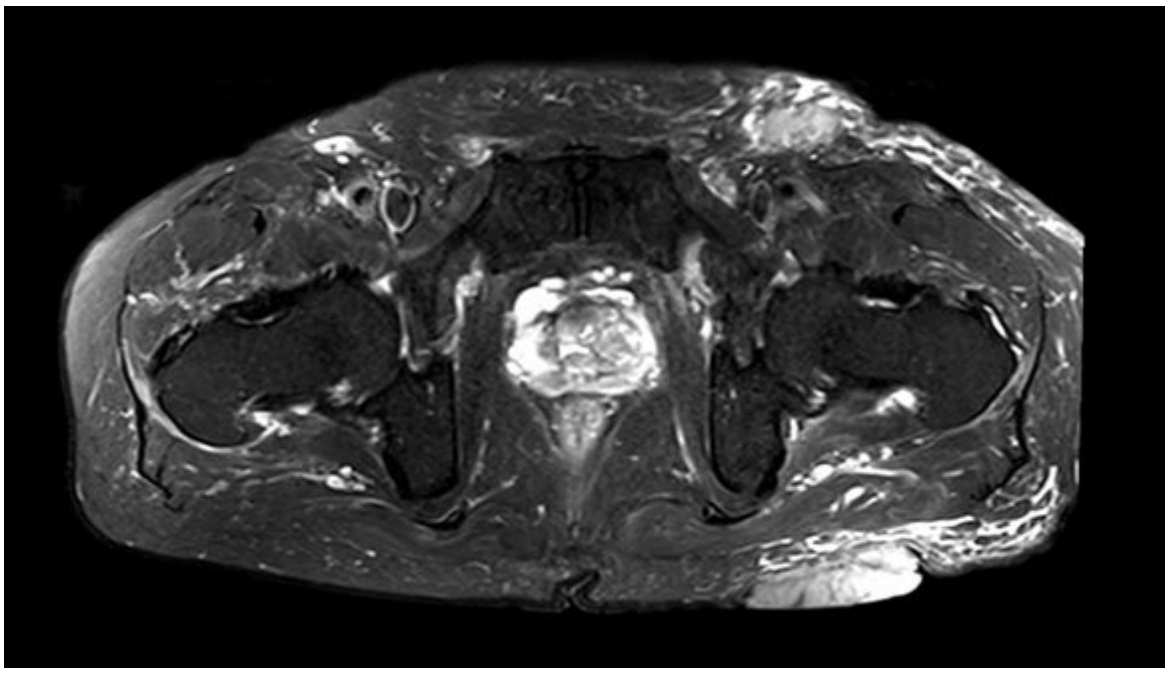

Figure 1 MRI showing a T2-hyperintense 5.2cm by 5.8cm by 1.9cm mass in the left gluteal region with left inguinal lymphadenopathy

Trucut biopsy of the gluteal lesion revealed neuroendocrine carcinoma which stained diffusely and strongly for pankeratins, Epithelial Membrane Antigen (EMA), synaptophysin and CD56. Fine

needle aspiration of the left inguinal lymphadenopathy returned as metastatic carcinoma. The patient then underwent magnetic resonance imaging (MRI) which showed a 5.2cm by 5.8cm by 1.9cm lobulated mass over the left gluteal region with extension into the underlying subcutaneous tissues but no obvious involvement of the gluteus muscles. Multiple enlarged lymph nodes were seen in the left inguinal region (Figure 1). Computed tomography of the chest, abdomen and pelvis were negative for metastases. After discussion at a multidisciplinary Sarcoma Board, curative surgical resection with lymphadenectomy was recommended. The patient then underwent pre-operative evaluation for his multiple medical comorbidities including hypertension, hyperlipidemia and chronic renal impairment. However, despite the expedited process, multiple new dermal lesions which were not previously present, developed during two-month interim period and were noted on the day of planned surgery (Figure 2a-c). Frozen section confirmed that these lesions were inkeeping with tumor involvement. Curative resection was then deemed infeasible in view of the inability to resect all satellite lesions. The patient was re-counselled and underwent palliative resection of the main lesion with a view for possible adjuvant radiotherapy to the metastaticdermal nodules and inguinal lymphadenopathy.

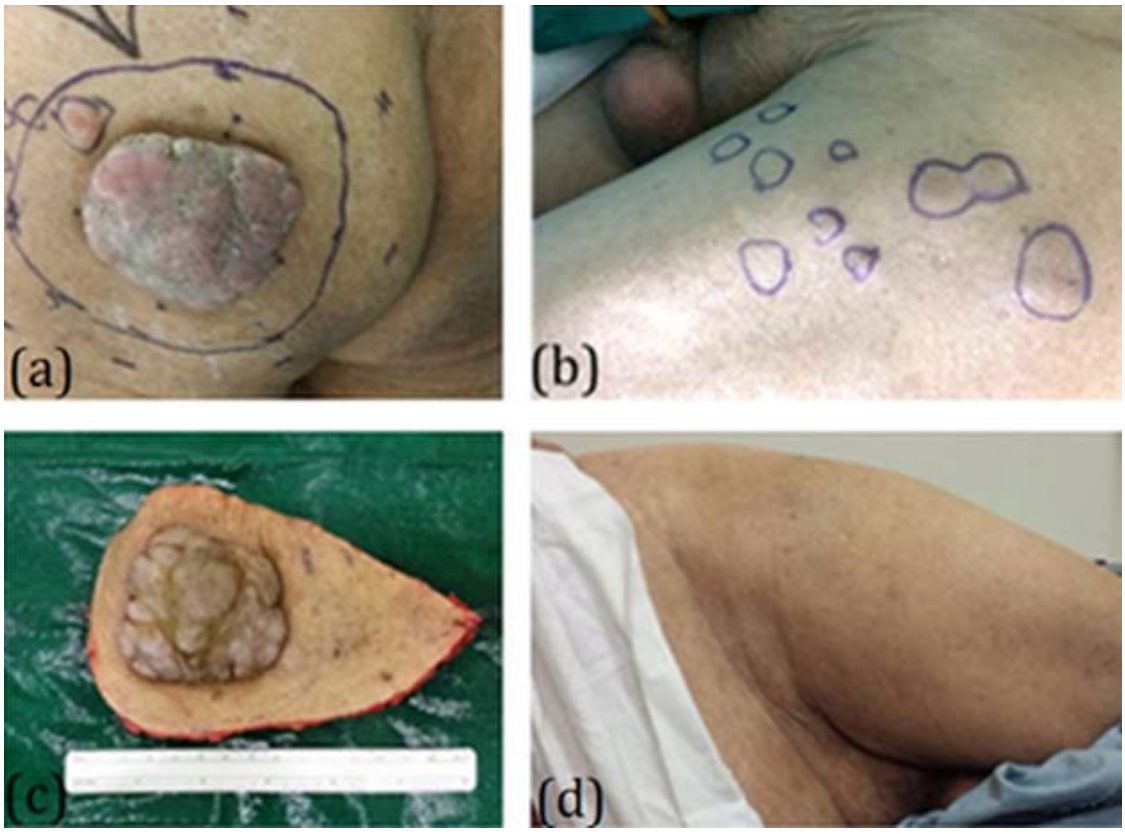

Figure 2(a) Main lesion – an exophytic purplish-red plaque over the left gluteal region, (b) Multiple dermal metastases, (c) Resected left gluteal tumor specimen and (d) Complete regression of dermal metastases seen at post-operative follow-up at 15 weeks

Excision of the left gluteal lesion with wide margins was performed and histology returned as neuroendocrine carcinoma featuring nested and irregular trabecular architecture, comprised of uniform cells with round to ovoid nuclei, finely granular chromatin with indistinct nucleoli, scant cytoplasm and frequent mitoses. The tumor cells stained diffusely positive for low molecular weight cytokeratin CAM 5.2 as well as synaptophysin.

Post-operative recovery was uneventful. Interestingly, at outpatient review two-month post-operatively, all metastatic dermal nodules had spontaneously regressed. The patient declined repeat imaging to assess his inguinal lymphadenopathy but remains well with no recurrence of any dermal lesion (Figure 2d).

Discussion

MCC is an aggressive cutaneous neuroendocrine malignancy originating from Merkel cells of the epidermis. Merkel cells function as mechanoreceptors and are sensitive to touch [7,8]. A rare entity with an estimated incidence of 0.6 per 100,000 person-years, it has seen a steady increase in recent years due in large part to improved detection as well as an increase in the prevalence of patients harboring risk factors for the disease. These include fair skin, elderly age, ultraviolet (UV) light exposure and immunosuppression [9]. Heath *et al*. previously summarized the clinical features of this condition using the acronym "AEIOU": Asymptomatic/lack of tenderness, Expanding rapidly (≤ 3 months), Immunosuppression, Older than age 50, and location on a UV-exposed site [10]. In 2008, Feng *et al*. identified a new human polyomavirus (Merkel cell polyomavirus, MCPyV) involved in the pathogenesis of MCC [11]. Subsequent studies have suggested that integration of the polyomaviral DNA into host DNA precedes tumorigenesis, rendering strength to the hypothesis of an infectious etiology[12, 13].

MCC frequently presents as a red or violaceous cutaneous lesion and predilection for head and neck sites has been well-documented [2, 10]. With a propensity for spread via dermal lymphatics, many patients present with satellite lesions at the point of diagnosis. Our patient did not have dermal metastases at the point of presentation but rapidly developed them over the short course of pre-operative evaluation, consistent with the known aggressive nature of MCC.

Spontaneous regression of MCC is an extremely rare phenomenon and was first reported in 1986 [5]. To date, majority of reported cases are of the head and neck sites. An extensive English literature search on PubMed revealed no prior reports of spontaneous regression of extremity dermal metastases after resection of the main lesion. To the best of our knowledge, our patient is the first-ever reported case of such a phenomenon.

There has been speculation that the biopsy of MCC may trigger tumor regression via stimulation of the immune system. Immune reconstitution in previously immunocompromised patients with MCC leading to spontaneous regression of MCC has also been reported [14, 15]. Supporting this hypothesis that the immune system plays a critical role in MCC regression, histopathologic studies have demonstrated lesion infiltration by CD4+, CD8+, and CD3+ T lymphocytes and macrophages, suggesting that T-cell-mediated immunity plays an important role in tumor regression [16-18]. Apoptotic events have also been reported to play an important role in spontaneous regression [19].

Conclusion

Spontaneous regression of MCC remains a poorly understood phenomenon. Further research into the histopathological features and immunity status should be considered to elucidate the mechanism

underlying this phenomenon, as it will potentially be life-saving for patients with this rare malignancy, whose median survival will otherwise be measured in months.

References

1. Toker C. Trabecular carcinoma of the skin. ***Archives of Dermatology***. 1972, 105:107-110
2. Santamaria-Barria JA, Boland GM, Yeap BY, *et al*. Merkel cell carcinoma: 30-year experience from a single institution. ***Ann SurgOncol***. 2013, 20:1365-1373
3. Allen PJ, Bowne WB, Jaques DP, *et al*. Merkel cell carcinoma: prognosis and treatment of patients from a single institution. ***J ClinOncol***. 2005, 23:2300-2309
4. Lemos BD, Storer BE, Iyer JG, *et al*. Pathologic nodal evaluation improves prognostic accuracy in Merkel cell carcinoma: analysis of 5823 cases as the basis of the first consensus staging system. ***J Am AcadDermatol***. 2010, 63:751-761
5. O'Rourke MGE, Bell JR. Merkel cell tumor with spontaneous regression. ***J DermatolSurgOncol***. 1986, 12:994-997
6. Connelly TJ, Cribier B, Brown TJ, *et al*. Complete spontaneous regression of Merkel cell carcinoma: A review of the 10 reported cases. ***Dermatol Surg***. 2000, 26:853-856
7. Tilling T, Moll I. Which are the cells of origin in merkel cell carcinoma? ***J Skin Cancer***. 2012, 2012:680410
8. Gould VE, Moll R, Moll I, Lee I, Franke WW. Neuroendocrine (Merkel) cells of the skin: hyperplasias, dysplasias, and neoplasms. ***Lab Invest***. 1985, 52: 334-353
9. Albores-Saavedra J, Batich K, Chable-Montero F, *et al*. Merkel cell carcinoma demographics, morphology, and survival based on 3870 cases: a population based study. ***J CutanPathol***. 2010, 37:20-27
10. Heath M, Jaimes N, Lemos B, *et al*. Clinical characteristics of Merkel cell carcinoma at diagnosis in 195 patients: the AEIOU features. ***J Am AcadDermatol***. 2008, 58:375-381
11. Feng H, Shuda M, Chang Y, Moore PS. Clonal integration of a polyomavirus in human Merkel cell carcinoma. ***Science***. 2008, 319:1096-1100
12. Stakaitytė G, Wood JJ, Knight LM, *et al*. Merkel cell polyomavirus: molecular insights into the most recently discovered human tumour virus. ***Cancers (Basel)***. 2014, 27: 1267-1297
13. Coursaget P, Samimi M, Nicol JT, *et al*. Human Merkel cell polyomavirus: virological background and clinical implications. ***APMIS***. 2013, 121:755-769
14. Richetta AG, Mancini M, Torroni A, *et al*. Total spontaneous regression of advanced merkel cell carcinoma after biopsy: review and a new case. ***Dermatol Surg***. 2008, 34:815-822
15. Kubo H, Matsushita S, Fukushige T, Kanzaki T, and Kanekura T. Spontaneous regression of recurrent and metastatic Merkel cell carcinoma. ***J Dermatol***. 2007, 34:773-777
16. Turk T, Orlic ZC, Smoljan I, *et al*. Spontaneous regression of Merkel cell carcinoma in a patient with chronic lymphocytic leukemia: a case report. ***J Med Case Rep***. 2009, 3:7270
17. Takenaka H, Kishimoto S, Shibagaki R, Nagata M, Yasuno H. Merkel cell carcinoma with partial spontaneous regression: an immunohistochemical, ultrastructural, and TUNEL labeling study. ***Am J Dermatopathol***. 1997, 19:614-618
18. Maruo K, Kayashima KI, Ono T. Regressing Merkel cell carcinoma-a case showing replacement of tumour cells by foamy cells. ***Br J Dermatol***. 2000, 142:1184-1189
19. Mori Y, Hashimoto K, Tanaka K, Cui CY, Mehregan DR, Stiff MA. A study of apoptosis in Merkel cell carcinoma: an immunohistochemical, ultrastructural, DNA ladder, and TUNEL labeling study. ***Am J Dermatopathol***. 2001, 23:16-23