CASE REPORT

Merkel cell carcinoma of the gluteal region: A rare case report and literature review

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Abstract

Merkel cell carcinoma (MCC) is a rare cutaneous neuroendocrine cancer that shows aggressive biological behaviour. Although it usually occurs on sun-exposed areas, it can sometimes be seen on non-sun-exposed sites. Here, we present the case of a 66-year-old woman with MCC arising from the right gluteal region that was treated with excision and adjuvant chemoradiotherapy. On follow-up after the 24 months, the patient was disease- and recurrence-free, representing the longest survival among patients with gluteal MCC. Early diagnosis and treatment are important to improve survival rates in patients with non-sun-exposed MCC.

Keywords: Merkel cell carcinoma, Non-sun-exposed, Skin, Radiology.

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Introduction

Merkel cell carcinoma (MCC) is a rare, aggressive, cutaneous neuroendocrine cancer, which is often seen in older and/or immunocompromised patients and on the sun-exposed areas of the body. Itis most commonly seen in the head and neck, upper limbs, lower limbs and trunk, but rare cases have been reported in vulva, penis, pharynx and oral mucosa. The patients usually present with a fast growing mass causing deformation on the skin. The diagnosis requires histopathological confirmation.[1,2]

To the best of our knowledge, only eight cases of gluteal MCC have been published in the English literature[3-10] (Table-1). Here, we report an additional case of gluteal MCC and discuss clinical characteristics and treatment options, by comparing our case with earlier cases.

Table-1: Comparison of the clinical characteristics of gluteal Merkel cell carcinomas.

	Age	Gender	Race	Immunosuppression or predictive factor	Metastatic sites	Treatment	Survival outcomes
Krejci et al. 2010	62	M	Not reported	Kidney and pancreas Tx	Pancreas, LN	Surgery, ChT	9 months
Perman et al. 2011	60	M	African-American	None	LN	Surgery, adjuvant RT	Not reported
Acab et al. 2016	76	M	Caucasian	None	LN, lung	Surgery, ChT	14 months
Shanbhag & Amonkar 2018	73	M	Not reported	None	LN,skin	Palliative care	Not reported
Howell et al. 2018	68	M	Caucasian	None	LN, skin	Surgery, adjuvant RT, ChT	Not reported
Türkkan et al. 2018	50	M	Not reported	Kidney tx	LN, lung	Surgery, adjuvant RT, palliative RT, ChT	≥15 months
Mulchan et al. 2019	80	M	African-American	None	LN	Surgery, adjuvant RT	3 months
Fernandez-Regueiro et al. 2019	85	M	Not reported	None	LN	Palliative care	1 month
The case presented here	66	F	Caucasian	None	LN	Surgery, adjuvant RT, ChT	≥24 months

ChT: Chemotherapy, RT: Radiotherapy, LN: Lymph node, Tx: transplantation.

Case Report

Written informed patient consent was obtained for the publication of the case report. The case was seen in July 2018 at Adiyaman Training and Research Hospital. A 66-year-old woman was admitted to the department of surgery with the complaint of painless swelling and redness of the skin in the right gluteal region. She had a history of diabetes mellitus, hypertension and coronary artery disease, as well as a history of endovenous laser therapy applied to the bilateral lower extremity veins. An 8cm mass in the right gluteal region, which caused discoloration of the skin, was observed during physical examination. Tru-cut biopsy of the lesion revealed a tumour consisting of cells with small-to-medium sized nuclei with fine chromatin and scant cytoplasm (Figure-1) which showed immunohistochemical positivity for pancytokeratin, cytokeratin 20, epithelial membrane

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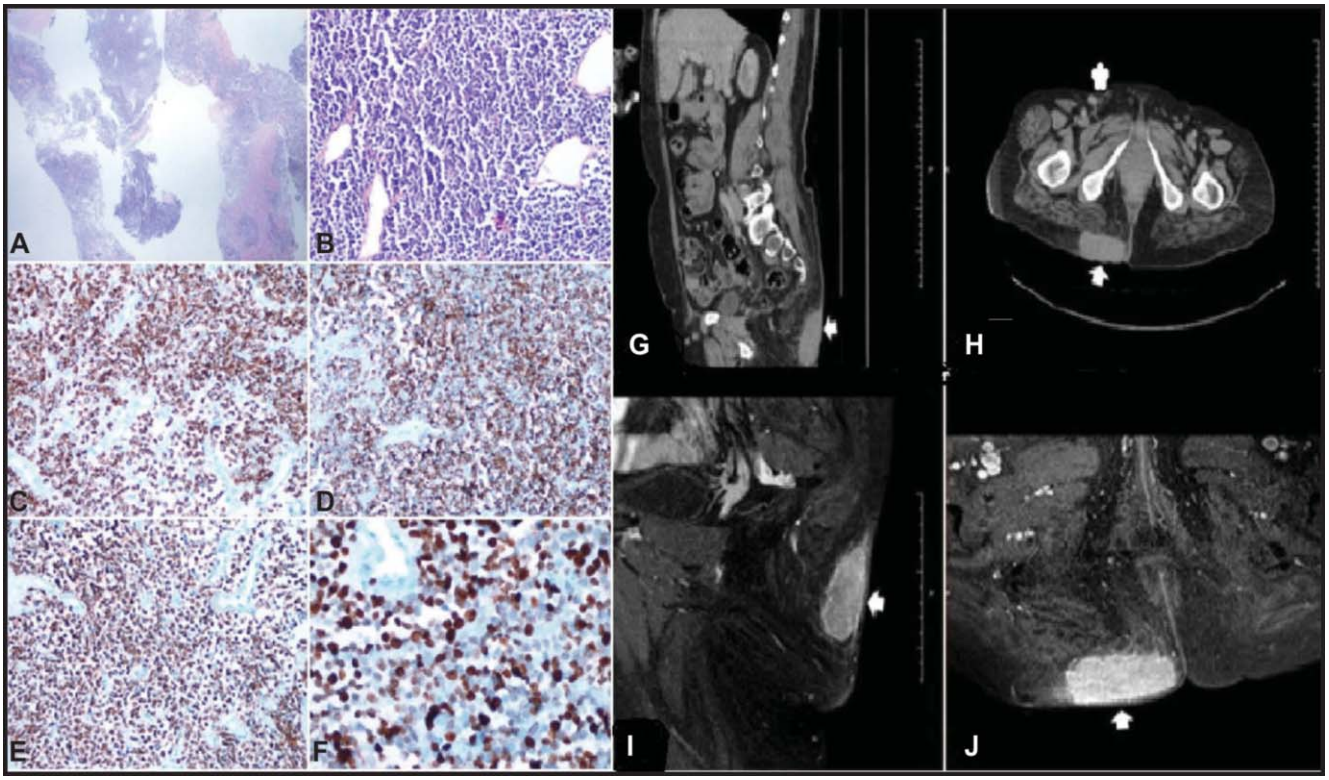

Figure: Histopathological/immunohistochemical findings of the tru-cut biopsy and imaging of the lesion. The tumour was composed of small-to-medium blue cells with fine chromatin and scant cytoplasm. Haematoxylin-eosin (A;original magnification x20) and Haematoxylin-eosin (B; original magnification x200). Immunohistochemically the neoplastic cells were positive for cytokeratin 20 (C; original magnification x200), EMA (D; original magnification x200), chromogranin (E; original magnification x200) and had high Ki-67 proliferation index (F; original magnification x400). Sagittal and axial enhanced computed tomography seen in the right gluteal mass (arrow), enlarged lymph nodes in the right inguinal region suspicious for metastasis (star) (G,H). The mass seen in sagittal and axial pelvic enhanced MRI is no relationship with the perianal region and other deep pelvic organs (I,J).

antigen [EMA], chromogranin and neuron specific enolase (NSE) (Figure). The tumour cells were also weakly positive for synaptophysin and CD99 and had a high Ki-67 proliferation index, but were negative for thyroid transcription factor-1 (TTF 1), cytokeratin 7, vimentin, HMB-45, S100, smooth muscle actin (SMA), desmin, myogenin and CD45. Therefore, the diagnosis of 'neuroendocrine carcinoma consistent with Merkel cell carcinoma'' was made.

Following the histopathological diagnosis, a thorough radiological examination was performed, including pelvic magnetic resonance imaging (MRI), thoracoabdominal computed tomography (CT), whole body positron emission tomography-computed tomography (PET/CT), in order to reveal the possible relationship of the deep part of the lesion with the perianal region and to investigate distant metastasis (Figure-1). Pelvic MRI showed no relationship with the perianal region and other deep pelvic organs. While nothing was found in the distant organs, metastasis was observed radiologically, as there were enlarged lymph nodes in the right inguinal region that were suspicious for metastasis. Although tru-cut biopsy of the suspicious lymph nodes were negative for malignancy, the possibility of partial tumoral involvement and/or micrometastasis could not be ruled out. It was decided to excise the mass with clean wide surgical margins and unilateral inguinal lymph node dissection followed by adjuvant radiotherapy and chemotherapy.

A 7.5x7x3cm white-to-tan tumour was detected in gross examination of the excised specimen, which was morphologically identical to the tumour in the initial tru-cut biopsy. No lymphovascular and/or perineural invasion was observed. Two of the 10lymph nodes were metastatic. The surgical margins were negative for malignancy.

The patient was evaluated as T3N1bM0 (Stage 3B) according to the criteria of the American Joint Committee on Cancer Staging System 8th Edition[11] and was administered radiotheraphy and chemotheraphy (four cycles of Cisplatin 25 mg/m^2 and Etoposide 100 mg/m^2). The patient was disease- and recurrence-free at 24-month follow-up.

Discussion

Merkel cell carcinoma (MCC) was first described by Dr. Toker in 1972 as trabecular carcinoma of the skin. It is thought to be caused by Merkel cells located in the basal layer in the epidermis. Several etiological factors such as exposure to ultraviolet light, exposure to arsenic and risk factors, such as history of chronic lymphocytic leukaemia, congenital dysplasia syndrome, viral infections (HIV, Merkel cell polyoma virus) and immunosuppression after organ transplantation, have been documented to date. Becker et al have reported that the incidence of MCC is 15 times higher in patients who have undergone immunosuppressive/organ transplantation, as compared to the normal population.[12] Our patient did not have any of these etiological and/or risk factors, however, the presence of Merkel cell polyoma virus could not be investigated.

MCC is a locally aggressive tumour with possibility of distant metastasis and is more likely to occur in areas that are mostly exposed to the sun. Although rarely, it can also be seen on areas not exposed to the sun. Marcoval et al have observed that patients without sun exposure have a worse prognosis than those with sun exposure.[13]

Local recurrence rate, regional lymph node metastasis rate, and distant organ metastasis rate is 27-60%, 45-91% and 18-52% respectively.[3] Five-year average survival in patients with MCC is 50-68%.[2]

Table-1 shows the characteristics of the patients diagnosed with gluteal MCC reported to date.

Many entities should be considered in differential diagnosis including basal cell carcinoma, melanoma, metastatic neuroendocrine carcinoma, Ewing's sarcoma, lymphoma and squamous cell carcinoma.[13] In our case, these entities were carefully excluded by immunohistochemical analysis.

After a histopathological diagnosis is made, due to its high metastatic feature, CT and MRI are frequently used to determine the stage of the disease in order to choose the appropriate treatment modality in a short time. PET-CT also has a notable clinical impact in determining the stage of the disease in these patients.

Meckel cell carcinoma is a rare disease and the surgical approach cannot be standardised due to its occurrence in different anatomical locations, which limits treatment options. However, there is consensus about the local excision of the tumour with a 1-2cm clear surgical margin. In patients with smaller tumours (<1cm), unfavourable prognostic factors such as lymphovascular invasion and immunosuppression are not expected and, therefore, wide excision is considered sufficient; on the other hand, for masses larger than 1cm and in patients with unfavourable prognostic factors, local lymph node dissection and adjuvant radiotherapy are recommended with wide excision.[3] The main method of treatment for metastatic disease is single agent or combination chemotherapy. Regimen with the combination of Cisplatin or Carboplatin with Etoposide, Cyclophosphamide with Doxorubicin, Vincristine are used. In addition, Avelumab, Nivolumab and Pembrolizumab can be given as immunotherapeutic agents as another treatment option in patients with metastatic MCC. Other than these treatment options, the use of Phosphoinositide 3-kinase inhibitors, the mammalian target of rapamycin [mTOR] pathway inhibitors, apoptotic inhibitors, receptor tyrosine kinase inhibitors and octreotide have also been used in the treatment of MCC.[14]

Due to the large size of the lesion in our patient, the tumour was removed with a wide excision and since there was suspicion of spread to the local lymph nodes, unilateral inguinal lymph node dissection was performed. Metastasis was confirmed histopathologically in two of the 10 dissected lymph nodes. Thus, we also recommend lymph node dissection, or at least sentinel lymph node sampling, in cases with radiological suspicion for metastasis.

Conclusion

We reported the ninth gluteal MCC case in the literature and to the best of our knowledge, the first female case of gluteal MCC. Lack of any significant risk factors in the aetiology is also noteworthy. Although the patient was evaluated as Stage 3B, disease-free and recurrence-free survival longer than 24 months could be achieved with a treatment strategy that included wide excision with local lymph node dissection and adjuvant chemoradiotherapy.

Patient Approval: An informed consent form was obtained from the patient for publishing of this paper.

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