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Merkel Cell Carcinoma of the Skin: An Exceptionally Rare Entity with Unique Locality-Related Characteristics

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Abstract

Background: Merkel cell carcinoma (MCC) is a rare, aggressive cutaneous neuroendocrine tumor, which is often misdiagnosed, resulting in most cases presenting with early metastasis. The present study aimed to highlight the incidence, clinical and diagnostic features, pathological characteristics, treatment, and outcomes of MCC.

Method: This is a retrospective single-center cohort study that included MCC patients who referred to our center between January 2008 and December 2024. Continuous variables were expressed as median values with interquartile ranges or mean values with standard deviation. Categorical variables were presented as frequencies and percentages. Statistical significance was set at $P < 0.05$.

Results: A total number of nine patients were included (three males, six females). The mean age at diagnosis was 66.3 ± 6.2 years. The lower limb was the most common tumor location (eight patients), and the mean tumor diameter was 54 ± 28 mm. Of these, six patients (66.7%) had clinically positive lymph nodes, and three (33.3%) had distant metastasis at presentation. Only one patient did not undergo surgery for the primary tumor. Also, four patients (44.4%) underwent regional lymphadenectomy. Adjuvant radiotherapy and chemotherapy were administered to 3 (33.3%) and 2 (22.2%) patients, respectively. During follow-up, one patient developed local recurrence, and two patients developed distant metastasis. Eventually, three patients died (33.3%), while six patients (66.7%) were lost to follow-up. The mean disease-free survival value was 4.6 ± 4.1 months, while the mean overall survival was 9.6 ± 9.1 months.

Conclusion: MCC exhibited distinct characteristics in our locality, particularly in tumor location and size. Early diagnosis and radical surgical intervention may improve outcomes.

Keywords: Merkel cell carcinoma, Neuroendocrine, Skin neoplasms, Prognosis

Introduction

Merkel cell carcinoma (MCC) is a rare, aggressive cutaneous neuroendocrine tumor.[1] It accounts for less than 1% of all skin malignancies with life-threatening potential. MCC primarily affects sun-exposed areas of the body.[2] Due to its rarity, the infinitesimal number of cases, and the lack of detailed clinical data, it is often misdiagnosed, resulting in the majority of cases presenting with early metastasis; thus, the timely diagnosis of MCC is critical.[3]

Confirming the diagnosis typically requires combining patient history with clinical and radiological findings, histopathology (which exhibits a small-cell neuroendocrine appearance), and immunohistochemistry (specifically CK20 positivity and TTF-1 negativity).[4] The pathogenesis is associated with key risk factors, including old age, ultraviolet (UV) radiation, and immunosuppression, as well as the Merkel cell polyomavirus, which results in a distinct pattern of numerous DNA mutations.[5]

The first-line treatment is surgical excision; for unresectable tumors, radiotherapy is an effective alternative. On the other hand, metastatic disease usually needs systemic treatment with immune checkpoint inhibitors (ICIs).[6]

This study aimed to highlight the incidence, clinical and diagnostic features, pathological characteristics, treatment modalities, and outcomes of MCC, seeking to provide an algorithm for management of such cases and to investigate if the characteristics of MCC patients presenting to our tertiary center differ from established international norms.

Methods

Study design and setting

This is a retrospective single-center cohort study conducted at the Oncology Center, Mansoura University. We analyzed the data of pathologically confirmed MCC patients who presented to our center between January 2008 and December 2024.

Ethics approval and consent to participate

All procedures performed in the study involving human participants followed the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. IRB approval was obtained from the Institutional Research Board at the Faculty of Medicine, Mansoura University, under the number R.25.05.3174. As this was a retrospective study, consent to participate in the study is waived as per the IRB policy.

Inclusion criteria

1. Histopathologic confirmation of cutaneous MCC
2. Adequate clinical documentation
3. Minimum follow-up of 6 months unless the patient died earlier

Exclusion criteria

1. Extracutaneous primary MCC
2. Neuroendocrine carcinoma of unknown origin
3. Incomplete records

Variables

The demographic, clinical, therapeutic, and prognostic data were collected, including the following data:

- Demographics
- Clinical presentation
- Histopathology
- Staging and imaging
- Treatment
- Outcomes

Pathologic review

Available histological slides and immunohistochemistry were re-reviewed by an expert pathologist to ensure consistent reporting of key features such as mitotic count, lymphovascular, and perineural invasion (Figures 1-3).

Outcomes

- Local recurrence
- Regional recurrence
- Distant metastasis

- Overall survival (OS)
- Disease-free survival (DFS)

Statistical analysis

Descriptive statistics were used to summarize patient demographics, clinical features, treatment modalities, and outcomes. Continuous variables were expressed as median values with interquartile range or mean values with standard deviation, depending on distribution. Categorical variables were presented as frequencies and percentages. Kaplan-Meier survival analysis, including subgroup analysis, was planned for OS and DFS, but it was omitted later as 6 out of 9 patients were lost to follow-up. Statistical significance was set at $P < 0.05$.

Results

A total of nine patients with pathologically proven MCC over a 17-year period were included in the final analysis. The cohort comprised three male and six female patients with a mean age at diagnosis of 66.3 ± 6.2 years. The mean body mass index was 40 ± 5 kg/m^2. Seven patients (77.8%) were hypertensive, and 5 (55.6%) were diabetic. The most common tumor location was the lower limb (8 patients, 88.9%), and the mean tumor diameter was 54 ± 28 mm. Six patients (66.7%) presented with clinically positive lymph nodes, and 3 (33.3%) had metastatic disease at presentation. Basic clinical, epidemiological, and therapeutic characteristics are summarized in Tables 1 and 2.

Immunohistochemical (IHC) analysis supported the diagnosis in all included cases. CK20, synaptophysin, and chromogranin were positive in all specimens tested. TTF-1 was negative in all three cases tested, effectively ruling out a lung origin. The Ki-67 proliferation index was high in all tested cases, showing percentages of 25%, 70%, and 80%. A summary of the IHC results is presented in Table 3.

Six patients (66.7%) underwent wide local excision (WLE), while 2 (22.2%) had excision only. One patient did not undergo surgery for the primary tumor. Four patients (44.4%) underwent regional lymphadenectomy with a mean number of 12 lymph nodes harvested, and 4 positive lymph nodes identified. Adjuvant radiotherapy and chemotherapy were administered to 3 (33.3%) and 2 (22.2%) patients, respectively. None of the included patients received target or immune therapy.

During a median follow-up period of 6 months, one patient (11.1%) developed local recurrence, and two patients (22.2%) developed distant metastasis. Eventually, three patients died (33.3%), while six patients (66.7%) were lost to follow-up. The mean DFS was 4.6 ± 4.1 months, while the mean OS was 9.6 ± 9.1 months.

Discussion

This study included nine patients with MCC. The mean age at diagnosis was 66.3 years. The lower limb was the most common tumor location (8 patients), and the mean tumor diameter was 54 mm. Six patients had clinically positive lymph nodes, and three patients had distant metastatic disease at presentation. Six patients underwent WLE, while two patients had excision only. One patient did not undergo surgery for the primary tumor. Four patients underwent regional lymphadenectomy. Adjuvant radiotherapy and chemotherapy were administered to three and two patients, respectively. During follow-up, one patient developed local recurrence, and two patients developed distant metastasis. Eventually, three patients died, while six patients were lost to follow-up. The mean DFS was 4.6 months, while the mean OS was 9.6 months.

MCC is a rare, aggressive form of neuroendocrine carcinoma that presents as a rapidly growing, painless, irregular erythematous cutaneous or subcutaneous

nodule.[5, 6] Chronic exposure to UV light is a crucial risk factor for MCC. Thus, the typical presentation involves sun-exposed areas of the skin, such as the head and neck, in immunosuppressed elderly patients.[5] Those features are represented by the AEIOU acronym: A = asymptomatic, E = expanding rapidly, I = immune suppression, O = older than 50 years, and UV-exposed site.[6] However, covered body areas such as the extremities and the trunk may also be affected. Mucosal surface involvement is exceptionally rare.[5] In our locality, MCC appears to be rarer than expected. Only nine patients over 17 years in a tertiary referral cancer center serving millions of people is an extremely small number. In addition, almost all of the included patients (8 out of 9) had their tumors in the lower limb, not in sun-exposed areas. This suggests different disease epidemiology, risk factors, and presentation in our locality.

In a study that included 5722 patients with available tumor size information, the median tumor size was 1.7 cm (0.1-7.0 cm).[7] This also confirms the hypothesis that the disease characteristics in our locality are different. The median tumor size in the included patients was 54 (± 28) mm, ranging from 36-110 mm.

At presentation, MCC is often confined to its primary site. However, MCC spreads first to regional lymph nodes, followed by distant metastases to non-regional lymph nodes, skin, pleura, lungs, bones, or liver.[8,9] In our cohort, two-thirds of the patients already presented with regional nodal metastasis, while one-third (three patients) had distant metastatic disease at the time of presentation.

The diagnosis of MCC usually starts with clinical suspicion, especially in fair-skinned elderly patients, often presenting with a rapidly expanding, firm, red violaceous dome-shaped or plaque lesion, most commonly appearing on sun-exposed areas.[4,10] Although dermoscopy can show features like polymorphous vascular patterns, milky-red globules, and linear irregular vessels, these findings are neither specific nor sensitive enough to confirm a diagnosis of MCC.[11]

Definitive diagnosis is achieved through an excisional or punch biopsy that samples the full dermis and subcutaneous fat. Microscopic examination with hematoxylin and eosin (H&E) staining typically reveals dense sheets of small basaloid cells featuring neuroendocrine-type "salt-and-pepper" chromatin, minimal cytoplasm, a high mitotic rate, and frequent crush artifact.[11] According to American Joint Committee on Cancer/ College of American Pathologists (AJCC/CAP) guidelines, Synoptic reporting should include tumor diameter (clinically measured), depth, margin status, lymphovascular invasion, growth pattern, mitotic rate, and immune infiltrate.[12]

Definitive diagnosis relies on IHC: MCC typically expresses cytokeratin 20 (CK20) with a characteristic perinuclear dot-like pattern (~70%–100 % of cases), pancytokeratins, and neuroendocrine markers such as synaptophysin, chromogranin A, CD56, NSE, and INSM1; it is uniformly negative for TTF-1, S 100/HMB45, CK7, CDX2, and lymphoid markers.[12,13] In our cohort, CK, CK20, synaptophysin, and chromogranin were the most commonly used IHC markers, and they showed positivity in all specimens tested. In contrast, TTF-1 showed negativity in all specimens tested.

After confirming diagnosis, a thorough clinical examination of the skin and regional lymph nodes should be followed by imaging—ultrasound of nodal basins and computed tomography or positron emission tomography–computed tomography to assess regional and distant metastasis.[14]

Management decisions in MCC are guided by multiple factors, including the tumor stage, anatomical site, regional lymph node

status, and the patient's general condition.[15] The first-line treatment for primary tumors is WLE with free pathological margins. However, WLE is not always feasible due to functional and cosmetic limitations, particularly in head and neck tumors. Mohs micrographic surgery can be a suitable surgical option for such a patient. Patient comorbidities and the risk of postoperative complications may also restrict surgical options. Therefore, it is crucial to balance these limitations against the potential clinical benefit.[14,15] Sentinel lymph node biopsy is recommended even for clinically node-negative cases, since approximately 26 % will have occult nodal involvement.[16] As the included patients in our cohort were treated over a long time period and two-thirds showed positive lymph node involvement at presentation or even metastasis, sentinel lymph node biopsy was not a routine procedure for patients with negative lymph nodes. Consequently, only four patients underwent surgical inguinal lymph node dissection, and four patients did not undergo lymph node surgery.

Radiotherapy plays an important role in management, either as an adjuvant treatment in high-risk cases or as a primary option in non-operable patients, with favorable success rates.[4] Delays in initiating adjuvant radiotherapy beyond 8 weeks post-surgery increase the risk of recurrence. For advanced MCC, immunotherapy plays a significant role in treatment due to the increased association of developing the disease with immunocompromised patients. At present, three ICIs have been approved by the Food and Drug Administration (FDA): Avelumab (anti-PD-L1 monoclonal antibody), Retifanlimab, and Pembrolizumab (anti-PD-1 monoclonal antibodies). ICIs have significantly improved outcomes in metastatic MCC, with durable responses in 30–60% of patients.[16-18] Chemotherapy - usually carboplatin plus etoposide- is now used only with palliative intent, with a good success rate. Alternative regimens include cyclophosphamide, doxorubicin, and vincristine.[4,19] In our cohort, three patients received adjuvant radiotherapy, and two patients received adjuvant chemotherapy, while none of the included patients received immunotherapy, either due to presenting in the early study period or due to the absence of sufficient financial capabilities.

The prognosis of MCC is primarily determined by clinical stage at diagnosis.[20] Modern strategies for local control have resulted in 5-year disease-specific survival rates of up to 90% in patients with localized MCC.[21] In contrast, managing node-positive disease remains challenging, with reported 5-year survival rates falling below 60%, and approximately 13.5% for distant metastases.[20-22] Interestingly, patients presenting with nodal metastases and no detectable primary tumor often demonstrate improved survival, possibly due to immune-mediated regression of the primary lesion.[18] Host-related factors significantly influence prognosis. Older age (≥70 years), male sex, and immunosuppression are associated with more advanced disease at presentation and reduced survival.[22-24] Immunosuppressed individuals also have shorter responses to therapy.[24] Histopathological features associated with poor prognosis include lymphovascular invasion, high mitotic rate, tumor thickness >10 mm, and sheet-like growth patterns in nodal metastases.[22] In our cohort, three of the patients died (33%), while six (66%) were lost to follow-up. No patient was reported alive and on regular follow-up.

Our study has several limitations: it is retrospective, which introduces potential selection bias and insufficient data; the number of included patients is extremely small; and two-thirds of the patients were lost to follow-up, limiting the accuracy of statistical analysis. Nevertheless, the study offers a significant contribution to the field as

it is the first to report this disease entity in our locality, revealing different patient characteristics, tumor features, and incidence patterns, and providing insight into a tertiary cancer referral center's 17-year experience.

Conclusion

MCC is an exceptionally rare cutaneous neuroendocrine tumor that exhibits aggressive behavior and a high propensity for lymph node and distant metastasis. Despite its extremely rare incidence, it showed different characteristics in our locality, especially regarding the tumor location and size. IHC stains are a cornerstone in establishing the diagnosis, and radical surgical resection with negative margins in the early stages is the primary strategy for improving outcomes.

Availability of Data and Material

All the clinical, radiological, and pathological data used in this manuscript are available on the Mansoura University medical system (Ibn Sina Hospital Management System): http://srv137.mans.edu.eg/mus/newSystem/

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Authors' Contributions

OH: conceptualization, supervision & revision. **RT:** Editing and revision of the pathology part. **AE, EG, EE, KB:** data collection & writing, **MB**: revision & editing All authors have read and approved the manuscript.

Conflict of Interest

None declared.

References

1. Singh N, McClure EM, Akaike T, Park SY, Huynh ET, Goff PH, et al. The evolving treatment landscape of Merkel cell carcinoma. *Curr Treat Options Oncol.* 2023;24(9):1231-58. doi: 10.1007/s11864-023-01118-8. PMID: 37403007; PMCID: PMC11260505.
2. Lewis DJ, Sobanko JF, Etzkorn JR, Shin TM, Giordano CN, McMurray SL, et al. Merkel cell carcinoma. *Dermatol Clin.* 2023;41(1):101-15. doi: 10.1016/j.det.2022.07.015. PMID: 36410971.
3. Badiu IM, Korecka K, Orzan AO, Spadafora M, Longo C, Forsea AM, et al. A review of non-invasive skin imaging in Merkel cell carcinoma: Diagnostic utility and clinical implications. *Cancers (Basel).* 2024;16(21):3586. doi: 10.3390/cancers16213586. PMID: 39518026; PMCID: PMC11545219.
4. Gauci ML, Aristei C, Becker JC, Blom A, Bataille V, Dreno B, et al. Diagnosis and treatment of Merkel cell carcinoma: European consensus-based interdisciplinary guideline - Update 2022. *Eur J Cancer.* 2022;171:203-31. doi: 10.1016/j.ejca.2022.03.043. PMID: 35732101.
5. Becker JC, Stang A, DeCaprio JA, Cerroni L, Lebbé C, Veness M, et al. Merkel cell carcinoma. *Nat Rev Dis Primers.* 2017;3:17077. doi: 10.1038/nrdp.2017.77. PMID: 29072302; PMCID: PMC6054450.
6. Patel P, Hussain K. Merkel cell carcinoma. *Clin Exp Dermatol.* 2021;46(5):814-9. doi: 10.1111/ced.14530. PMID: 33252781.
7. Iyer JG, Storer BE B, Phillips JL, Bichakjian CK, et al. Relationships among primary tumor size, number of involved nodes, and survival for 8044 cases of Merkel cell carcinoma. *J Am Acad Dermatol.* 2014;70(4):637-43. doi: 10.1016/j.jaad.2013.11.031. PMID: 24521828; PMCID: PMC3959572.

8. Siqueira SOM, Campos-do-Carmo G, Dos Santos ALS, Martins C, de Melo AC. Merkel cell carcinoma: epidemiology, clinical features, diagnosis and treatment of a rare disease. *An Bras Dermatol.* 2023;98(3):277-86. doi: 10.1016/j.abd.2022.09.003. PMID: 36870886; PMCID: PMC10173065.
9. Schmults CD, Blitzblau R, Aasi SZ, Alam M, Amini A, Bibee K, et al. NCCN Guidelines® Insights: Merkel Cell Carcinoma, Version 1.2024. *J Natl Compr Canc Netw.* 2024;22(1D):e240002. doi: 10.6004/jnccn.2024.0002. PMID: 38244274.
10. Lugowska I, Becker JC, Ascierto PA, Veness M, Blom A, Lebbe C, et al. Electronic address: clinicalguidelines@esmo.org. Merkel-cell carcinoma: ESMO-EURACAN Clinical Practice Guideline for diagnosis, treatment and follow-up. *ESMO Open.* 2024;9(5):102977. doi: 10.1016/j.esmoop.2024.102977. PMID: 38796285; PMCID: PMC11145756.
11. Brickley SA, Franco A, Somers K. Skin cancer: Back to basics-merkel cell carcinoma. *J Dermatol Nurses Assoc.* 2021;13:102-5.
12. Bichakjian CK, Olencki T, Aasi SZ, Alam M, Andersen JS, Blitzblau R, et al. Merkel cell carcinoma, version 1.2018, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw.* 2018;16(6):742-74. doi: 10.6004/jnccn.2018.0055. PMID: 29891526; PMCID: PMC9440150.
13. Rutkowski P, Owczarek W, Nejc D, Jeziorski A, Wysocki WM, Słowińska M, et al. Expert recommendation on diagnostic-therapeutic management in skin carcinomas. *Oncol Clin Pract.* 2022;18:69-91.
14. Lebbe C, Becker JC, Grob JJ, Malvehy J, Del Marmol V, Pehamberger H, et al. Diagnosis and treatment of Merkel cell carcinoma. European consensus-based interdisciplinary guideline. *Eur J Cancer.* 2015;51(16):2396-403. doi: 10.1016/j.ejca.2015.06.131. PMID: 26257075.
15. Fojnica A, Ljuca K, Akhtar S, Gatalica Z, Vranic S. An updated review of the biomarkers of response to immune checkpoint inhibitors in Merkel cell carcinoma: Merkel cell carcinoma and immunotherapy. *Cancers (Basel).* 2023;15(20):5084. doi: 10.3390/cancers15205084. PMID: 37894451; PMCID: PMC10605355.
16. Nghiem PT, Bhatia S, Lipson EJ, Kudchadkar RR, Miller NJ, Annamalai L, et al. PD-1 blockade with pembrolizumab in advanced Merkel-cell carcinoma. *N Engl J Med.* 2016;374(26):2542-52. doi: 10.1056/NEJMoa1603702. PMID: 27093365; PMCID: PMC4927341.
17. Lipson EJ, Vincent JG, Loyo M, Kagohara LT, Luber BS, Wang H, et al. PD-L1 expression in the Merkel cell carcinoma microenvironment: association with inflammation, Merkel cell polyomavirus and overall survival. *Cancer Immunol Res.* 2013;1(1):54-63. doi: 10.1158/2326-6066.CIR-13-0034. PMID: 24416729; PMCID: PMC3885978.
18. Zwijnenburg EM, Lubeek SFK, Werner JEM, Amir AL, Weijs WLJ, Takes RP, et al. Merkel cell carcinoma: New trends. *Cancers (Basel).* 2021;13(7):1614. doi: 10.3390/cancers13071614. PMID: 33807446; PMCID: PMC8036880.
19. Pedersen EA, Verhaegen ME, Joseph MK, Harms KL, Harms PW. Merkel cell carcinoma: updates in tumor biology, emerging therapies, and preclinical models. *Front Oncol.* 2024;14:1413793. doi: 10.3389/fonc.2024.1413793. PMID: 39136002; PMCID: PMC11317257.
20. Harms KL, Healy MA, Nghiem P, Sober AJ, Johnson TM, Bichakjian CK, et al. Analysis of prognostic factors from 9387 Merkel cell carcinoma cases forms the basis for the new 8th edition AJCC staging system. *Ann Surg Oncol.* 2016;23(11):3564-71. doi:

10.1245/s10434-016-5266-4. PMID: 27198511; PMCID: PMC8881989.
21. Farley CR, Perez MC, Soelling SJ, Delman KA, Harit A, Wuthrick EJ, et al. Merkel cell carcinoma outcomes: Does AJCC8 underestimate survival? *Ann Surg Oncol.* 2020;27(6):1978-85. doi: 10.1245/s10434-019-08187-w. Erratum in: *Ann Surg Oncol.* 2020;27(Suppl 3):983. doi: 10.1245/s10434-020-08871-2. PMID: 32103415.
22. Zaggana E, Konstantinou MP, Krasagakis GH, de Bree E, Kalpakis K, Mavroudis D, et al. Merkel cell carcinoma-Update on diagnosis, management and future perspectives. *Cancers (Basel).* 2022;15(1):103. doi: 10.3390/cancers15010103. PMID: 36612102; PMCID: PMC9817518.
23. Mohsen ST, Price EL, Chan AW, Hanna TP, Limacher JJ, Nessim C, Set al. Incidence, mortality and survival of Merkel cell carcinoma: a systematic review of population-based studies. *Br J Dermatol.* 2024;190(6):811-24. doi: 10.1093/bjd/ljad404. PMID: 37874770.
24. Moshiri AS, Doumani R, Yelistratova L, Blom A, Lachance K, Shinohara MM, et al. Polyomavirus-negative Merkel cell carcinoma: A more aggressive subtype based on analysis of 282 cases using multimodal tumor virus detection. *J Invest Dermatol.* 2017;137(4):819-27. doi: 10.1016/j.jid.2016.10.028. PMID: 27815175; PMCID: PMC5565758.

Table 1. Basic numerical variables of the included patients with MCC (mean, minimum, and maximum values)

Variable	Mean (± SD)	Minimum	Maximum
Age	66.3 (± 6.2) years	58	77
BMI	40 (± 5) kg/m^2	35	47
Tumor largest diameter	54 (± 28) mm	36	110
Operative time (n = 6)	137.5 (± 51.5) minutes	45	240
Number of harvested lymph nodes (n = 4)	12 (± 4)	8	17
Number of positive lymph nodes (n = 4)	4 (± 2)	2	8
DFS	4.6 (± 4.1) months	0	12
OS	9.6 (± 9.1) months	2	31

SD: Standard deviation; BMI: Body mass index, DFS: Disease free survival, OS: Overall survival; n: Number; MCC: Merkel cell carcinoma

Table 2. Basic categorical variables of the included patients with MCC (frequency and percentage)

Variable	Frequency	Percentage (%)
Gender		
Male	3	33.33
Female	6	66.66
Medical comorbidities		
Diabetes mellitus	5	55.55
Hypertension	7	77.77
Chronic liver disease	1	11.11
Tumor location		
Head and neck	1	11.11
Lower limb	8	88.88
• Gluteal	3	33.33
• Thigh	2	22.22
• Leg	2	22.22
• foot	1	11.11
Lymph node status at diagnosis		
Positive	6	66.66
Negative	3	33.33
Distant metastasis at diagnosis		
Positive	3	33.33
Negative	6	66.66
Surgery type		
Wide local excision	6	66.66
Excision	2	22.22
Not done	1	11.11
Lymph node surgery		
Lymph node dissection	4	44.44
Core needle biopsy	1	11.11
Not done	4	44.44
Postoperative complications (n=8)		
Yes (wound dehiscence)	2	22.22
No	6	66.66
Pathological characteristics		
Lymphovascular invasion	5	55.55
Perineural invasion	4	44.44
Necrosis	6	66.66
Adjuvant radiotherapy		
Yes	3	33.33
No	6	66.66
Chemotherapy		
Yes	2	22.22
No	7	77.77
Recurrence		
Yes	1	11.11
No	5	55.55
N/A	3	33.33
Metastasis		
Yes	2	22.22
No	6	66.66
N/A	1	11.11
Status at last follow-up		
Dead	3	33.33
Lost to follow-up	6	66.66

N/A: not available; MCC: Merkel cell carcinoma; n: Number

Table 3. Summary of IHC results of the pathological specimens of included MCC patients

Marker	Positive	Focal Positive	Negative	Not done
CK	4	0	0	5
CK20	5	2	0	2
TTF-1	0	0	3	6
Chromogranin	4	1	0	4
Synaptophysin	5	0	0	4
CD99	2	0	2	5
Ki-67 (percent)	3	—	—	6

IHC: Immuohistochemical; MCC: Merkel cell carcinoma

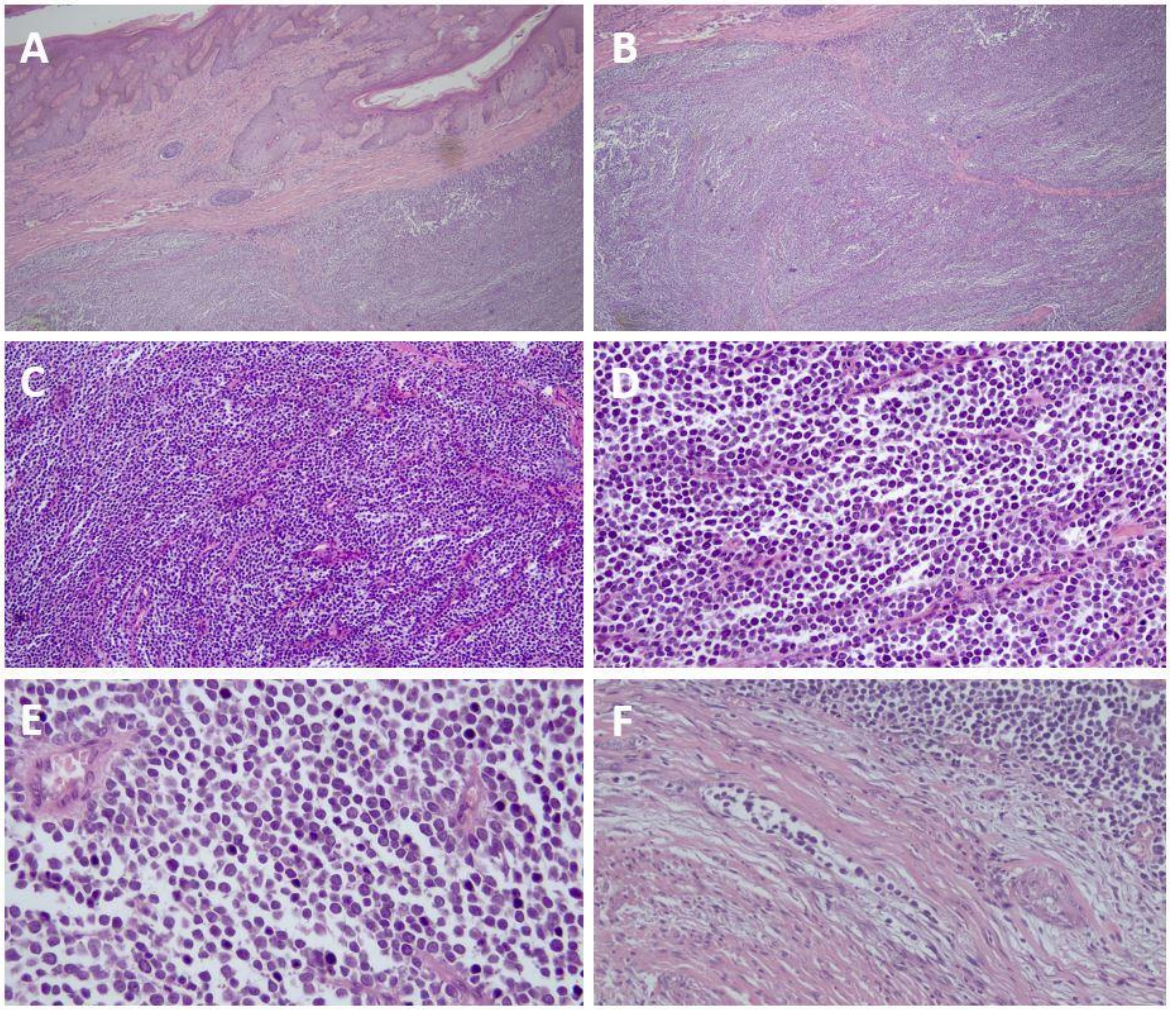

Figure 1. This figure shows the microscopic examination of Merkel cell carcinoma by Hematoxylin and Eosin (H&E). A: Merkel cell carcinoma with poorly circumscribed tumor growth pattern involving dermis (H&E, ×4 objective); B: Merkel cell carcinoma with nodular and sheet-like growth pattern (H&E, ×4 objective); C: Round small blue uniform tumor cells with high Nuclear/Cytoplasmicratio, hyperchromatic nuclei and scant cytoplasm (H&E, ×10 objective); D: Uniform small blue rounded tumor cells with indistinct cell borders, rounded hyperchromatic nuclei with nuclear molding, characteristic salt-and-pepper chromatin pattern and mitosis (H&E, ×20 objective); E: High power magnification showing malignant round small blue cells with hyperchromatic nuclei with frequent apoptotic bodies and detected mitotic figures (H&E, ×40 objective); F: Lymphovascular tumor emboli in Merkel cell carcinoma (H&E, ×40 objective).

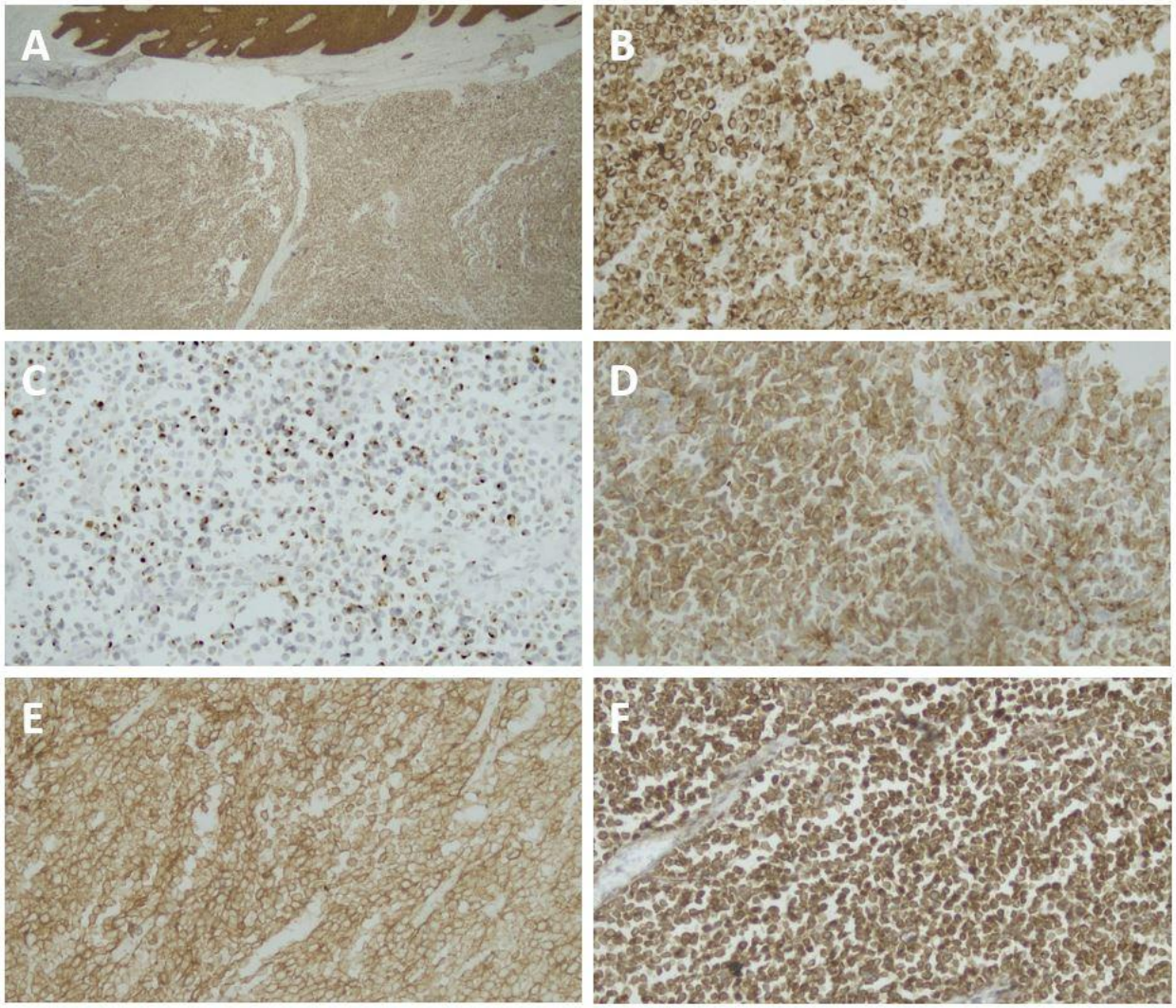

Figure 2. This figure shows positive immunohistochemical staining in Merkel cell carcinoma. A: Diffuse cytoplasmic and membranous positivity for CK in Merkel cell carcinoma (×4 objective); B: Diffuse cytoplasmic and membranous positivity for CK20 in Merkel cell carcinoma (×20 objective); C: Typical dot-like paranuclear pattern of CK20 expression in Merkel cell carcinoma (×20 objective); D: Diffuse cytoplasmic chromogranin positivity in Merkel cell carcinoma (×20 objective); E: Diffuse membranous positivity for CD56 in Merkel cell carcinoma (×20 objective); F: Diffuse cytoplasmic positivity for BCL2 in Merkel cell carcinoma (×20 objective).

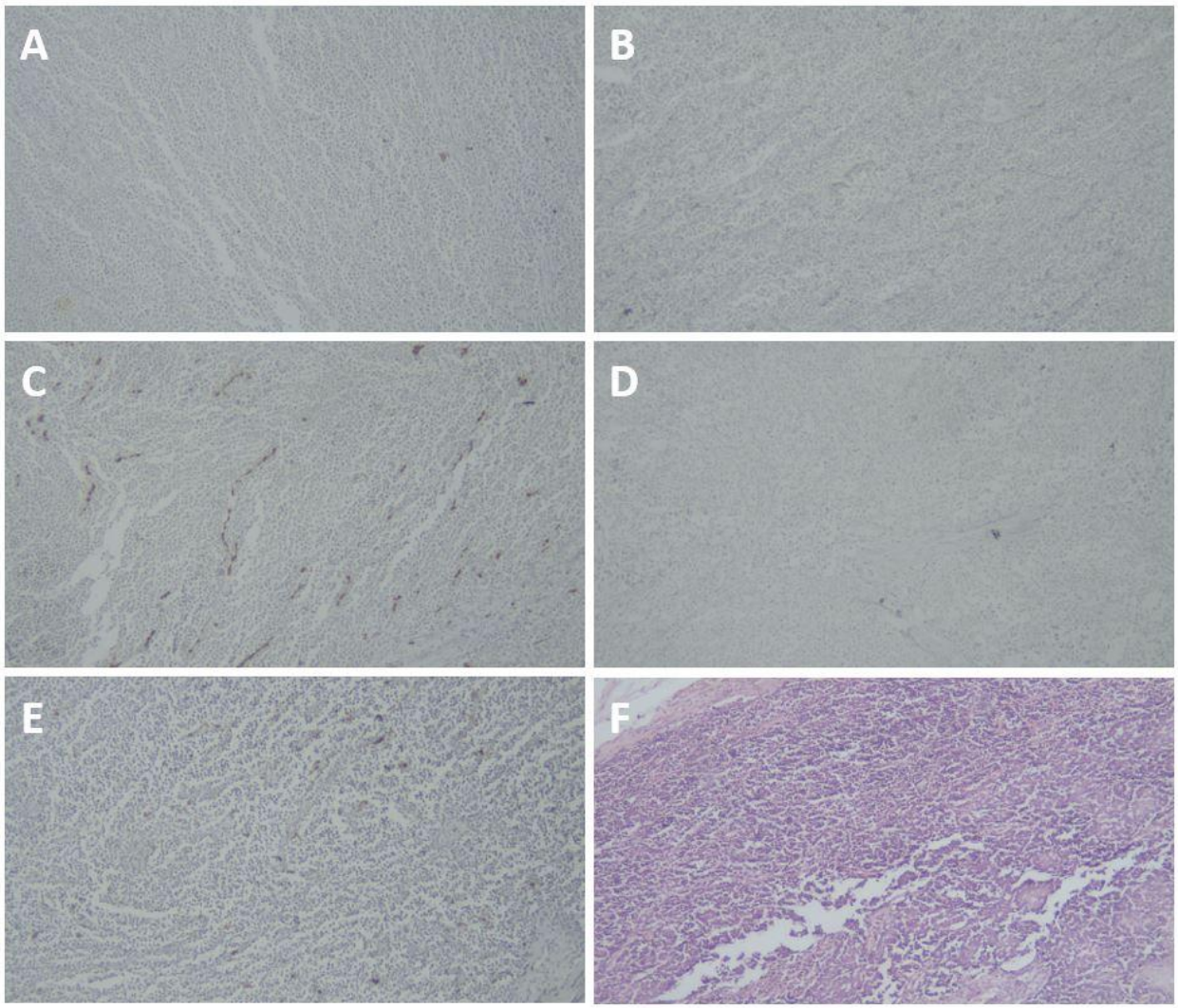

Figure 3. This figure shows the negative IHC in MCC, a microscopic picture of lymph node (LN) metastasis. A: Negative reaction for cluster of differentiation (CD)20 in tumor cells of Merkel cell carcinoma (×10 objective); B: Negative reaction for myogenin in tumor cells of Merkel cell carcinoma (×10 objective); C: Negative reaction for (erythroblastosis transformation-specific related gene 1) (ERG1) in tumor cells of Merkel cell carcinoma (with positive internal control) (×10 objective); D: Negative reaction for Desmin in tumor cells of Merkel cell carcinoma (×10 objective); E: Negative reaction for leukocyte common antigen (LCA) in tumor cells of Merkel cell carcinoma (×10 objective); F: Lymph node positive for tumor metastasis in Merkel cell carcinoma (H&E ×10 objective)