Am J Transl Res 2025;17(5):3554-3559
www.ajtr.org /ISSN:1943-8141/AJTR0162787

Case Report

Breast skin merkel cell carcinoma: a case report

Xinming Hou[1], Qian Lv[2], Zhaobao Lv[1]

[1]Department of Breast and Thyroid Surgery, The Second People's Hospital of Liaocheng, Linqing 252600, Shandong, China; [2]Department of Medicine, Linqing People's Hospital, Linqing 252600, Shandong, China

Received December 19, 2024; Accepted April 21, 2025; Epub May 15, 2025; Published May 30, 2025

Abstract: Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine skin malignancy characterized by high recurrence and metastasis rates. Here, we present a case of primary breast skin MCC in a 65-year-old female patient who initially presented with a peanut-sized lump on her right breast, which rapidly developed into a cauliflower-like mass accompanied by intermittent pain. The patient underwent radical surgery (right mastectomy and right axillary lymph node dissection), followed by postoperative chemotherapy. Immunohistochemical examination revealed positive staining for Cytokeratin 20 (CK20), Synaptophysin (Syn), Cluster of Differentiation 56 (CD56), and Chromogranin A (CgA), confirming the diagnosis of MCC. A subsequent Positron Emission Tomography - Computed Tomography (PET-CT) scan revealed secondary liver metastasis. Despite an initial effective response to chemotherapy, the patient developed severe bone marrow suppression, necessitating a switch to maintenance therapy with capecitabine.

Keywords: Merkel cell carcinoma, breast, skin, clinical pathology, immunohistochemistry

Introduction

Merkel cell carcinoma (MCC) is a rare, aggressive neuroendocrine skin malignancy with an incidence of 0.18-0.41 per 100,000 individuals annually [1]. MCC typically presents as a rapidly growing, painless nodule on sun-exposed areas such as the head, neck, or face in elderly patients, but its non-specific clinical features can make diagnosis challenging [2]. Despite advances in diagnostic techniques and therapeutic approaches, early detection and effective management of MCC remain significant challenges [3]. Here, we report a rare case of primary breast skin MCC in a 65-year-old female patient, who presented with a rapidly progressing tumor that ulcerated and discharged purulent material.

Clinical data

General information

The patient is a 65-year-old female who, in March 2023, incidentally discovered a lump on the surface of her right breast, approximately the size of a peanut, with red and yellow coloration. The lump ruptured, oozed fluid, repeatedly scabbed, and gradually increased in size, developing a yellow-white, cauliflower-like protrusion. The mass was accompanied by intermittent pain. In June 2023, she sought medical attention at the Second People's Hospital in Liaocheng. Her medical history was unremarkable, with no history of miscarriages or a family history of malignancies. Upon examination, the right nipple was absent, and a cauliflower-like mass measuring 15 × 15 cm was observed at the center of the right breast (**Figure 1**). The mass was prominently protruding, with purulent discharge on the surface, slightly limited mobility, and a 3.0 cm firm enlarged lymph node palpable in the right axilla. The preliminary diagnosis was a tumor of the right breast. The study was approved by the Institutional Review Board and Research Ethics Committee of the Second People's Hospital of Liaocheng, and conducted in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. The patient was fully aware of the potential risks of disclosing her personal health information, particularly concerning sensitive photo-

https://doi.org/10.62347/YFTJ3672

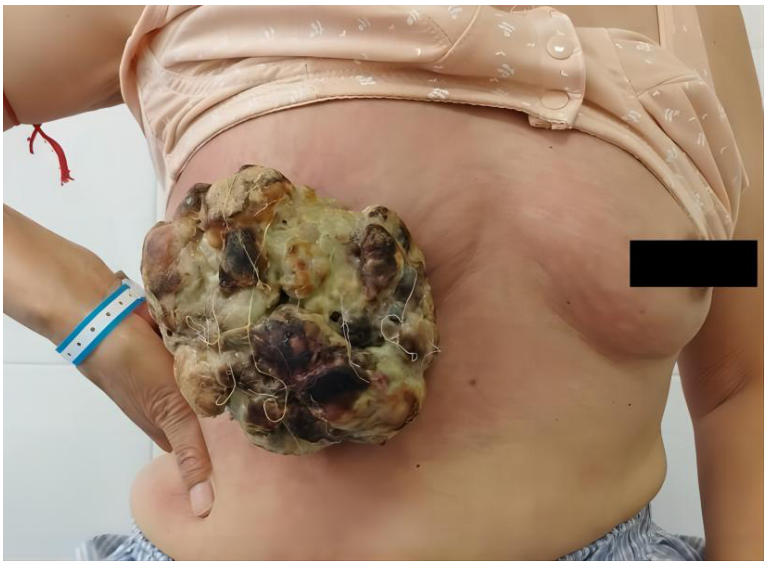

Figure 1. Breast skin Merkel cell carcinoma (MCC) lesion.

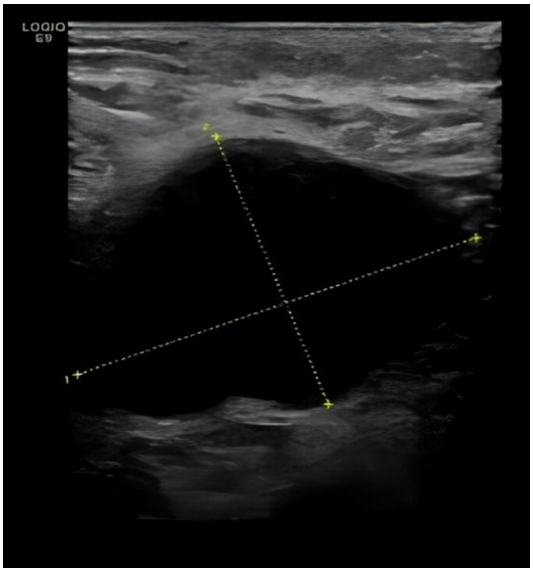

Figure 2. Right breast ultrasound image.

graphs. Special attention was given to ensure the privacy and dignity of the patient throughout this study.

Examination

On June 27, 2023, imaging studies revealed the following: (1) Breast ultrasound: Several lymph nodes with clear border and regular shapes were observed, with the largest measuring approximately 4.4 cm × 3.4 cm in the right axilla, displaying an unclear hilum structure (**Figure 2**); (2) Liver ultrasound: Cystic hypoechoic lesions were noted in the liver, with the largest located in the left lobe, measuring about 2.8 cm × 2.5 cm. These lesions had clear borders, regular shapes, and good through-transmission (**Figure 3**); (3) Chest computed tomography (CT): Ground-glass opacity nodules, measuring 7 mm and 12 mm, were observed in the posterior and apical segments of left upper lobe. These nodules had clear but slightly irregular borders, along with multiple part-solid ground-glass opacity (pGGO) nodules in the left upper lung, suggestive of adenocarcinoma in situ (AIS) or minimally invasive adenocarcinoma (MIA), warranting further evaluation.

Laboratory findings indicated mild anemia, with a hemoglobin level of 108 g/L (normal range: 110-150 g/dL for females). Iron therapy was initiated to address this condition. No abnormality was observed in biochemistry tests. Biopsy of the right breast and right axilla tissues revealed poorly differentiated malignant tumor cells (**Figure 4**). Following comprehensive auxiliary examinations, the patient underwent radical surgery for malignant breast tumor on June 30, 2023, including right mastectomy and right axillary lymph node dissection.

The postoperative pathological examination revealed a right breast skin MCC measuring 15 cm × 13.5 cm × 6 cm, involving subcutaneous tissue with vascular invasion but clear surgical margins. Lymph node metastasis was assessed as follows: In the first group of axillary lymph nodes (24 nodes examined), metastatic carcinoma was found in 2 nodes (2/24). In the third group (2 nodes examined), metastatic carcinoma was found in 1 node (1/2). For the second group (6 nodes examined), intermuscular region (1 node examined) and other areas of the right axilla (1 node examined), no metastatic carcinoma was detected (0/6, 0/1, and 0/1 respectively). These ratios indicate the number of metastatic lymph nodes out of the total number examined in each respective group. Im-

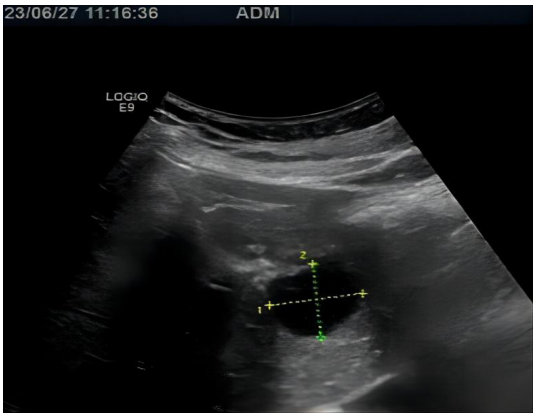

Figure 3. Liver ultrasound image.

munohistochemical examination results showed: partially positive for cytokeratin 20 (CK20) (**Figure 5D**), negative for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (Her-2), positive for synaptophysin (Syn) (**Figure 5A**), partially positive for cluster of differentiation 56 (CD56) (**Figure 5C**), focal dot-like positive for chromogranin A (CgA) (**Figure 5B**), positive for insulinoma-associated protein 1 (INSM1), faintly positive for thyroid transcription factor 1 (TTF-1), and 80% positive for Ki-67 antigen (Ki-67). Postoperative Positron Emission Tomography - Computed Tomography (PET-CT) identified a low-density lesion in liver segment S6 with increased glucose metabolism, consistent with metastasis (**Figure 6A**). A subsequent upper abdominal CT scan on July 20, 2023 revealed a slightly ill-defined low-density lesion of about 2.4 cm in the right posterior lobe of the liver, showing indistinct visualization in arterial phase and low density in residual phase (**Figure 6B**).

Diagnosis

Pathological diagnosis: Right breast skin MCC with secondary malignant liver tumor.

Treatment

Due to the advanced disease stage, the patient underwent salvage chemotherapy. Postoperatively, the following regimen was given: paclitaxel albumin-bound (200 mg on days 1 and 8), and carboplatin (500 mg on day 1) every three weeks. During chemotherapy, the patient developed thrombocytopenia and severe bone marrow suppression, leading to poor tolerance and necessitating extended follow-up intervals.

Treatment outcome, follow-up, and prognosis

The patient underwent regular outpatient follow-ups at our hospital. Liver metastases was confirmed with a shrinkage in size (from 2.4 cm to 1.3 cm) without new lesions detected (**Figure 6B**, **6C**). The treatment was effective, requiring continuation of chemotherapy. Due to poor tolerance, the regimen was changed to capecitabine (1.5 g twice daily) for maintenance therapy.

Discussion

Merkel cell carcinoma (MCC) is a rare, aggressive neuroendocrine malignancy with an incidence rate of 0.18-0.41 per 100,000 individuals, predominantly affecting sun-exposed areas in white patients over 65 years of age (such as the head, neck, and face) [4-6]. The exact pathogenesis of MCC remains unclear, but approximately 80% of cases are believed to be associated with Merkel cell polyomavirus (MCPyV) infection [7], while other cases may result from damage caused by ultraviolet radiation. MCC typically presents as a solid, painless, rapidly growing, reddish-purple, dome-shaped skin nodule. The lesions are usually non-specific and solitary, with ulcers being uncommon. MCC has the potential to metastasize to deep lymph nodes, lungs, brain, and other sites through lymphatic and hematogenous spread [3]. In this case, the patient developed MCC on the breast skin, which progressed rapidly and ulcerated, emitting purulent discharge - an atypical presentation of MCC.

Pathological diagnosis serves as the gold standard for confirming MCC. Microscopically, MCC typically appears as round or oval-shaped cells, relatively uniform in size and morphology, and may present as solid nests, interconnected trabeculae, or a lymphoma-like pattern. Immunohistochemistry (e.g., CK20, TTF-1, NF, CgA, Syn, NSE, CD56) is crucial, as the immunophenotype typically displays neuroendocrine characteristics, with CK20 positivity and TTF-1 negativity [8-10]. In this case, the pathological examination revealed tumor cells arranged in island-like, nest-like, small trabecular, or scattered patterns. The tumor cells were relatively

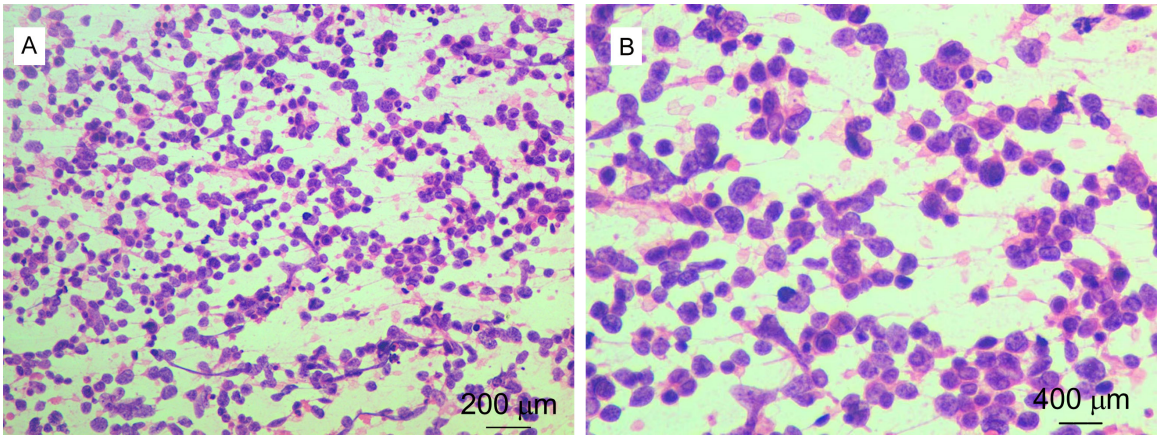

Figure 4. Hematoxylin and Eosin (HE) staining of cancer cells. A: magnification 200×; B: magnification 400×.

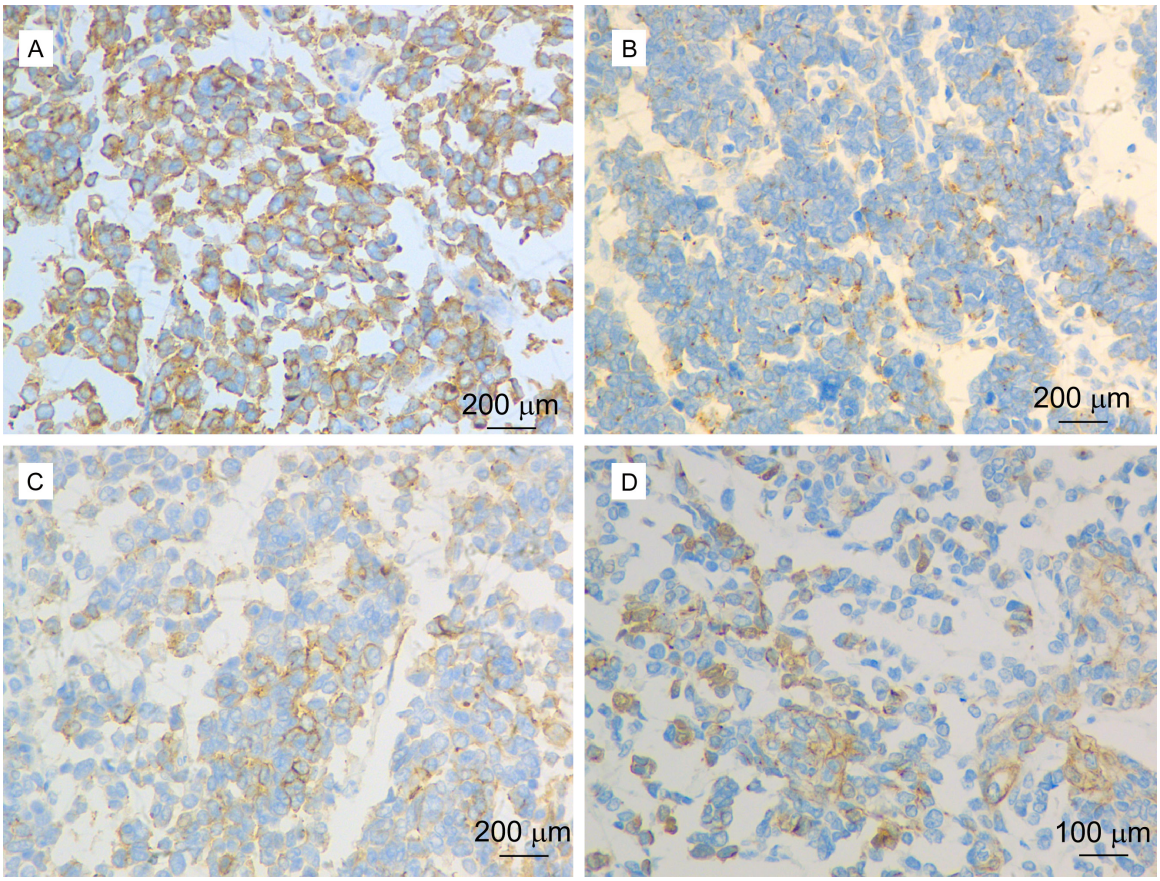

Figure 5. Immunohistochemistry images. A: magnification 200×, positive for synaptophysin (Syn); B: magnification 200×, partially spot positive for chromogranin A (CgA); C: magnification 200×, partially positive for cluster of differentiation 56 (CD56); D: magnification 100×, partially positive for CK20.

uniform in size, slightly larger than lymphocytes, with sparse acidophilic cytoplasm. Nucleoli were small and basophilic, with visible mitotic figures. The chromatin appeared as fine granules or dust-like particles [11], consistent with the histomorphology of MCC. Immunohistochemical examination showed characteristic cytoplasmic dot-like positivity for CK20, partial

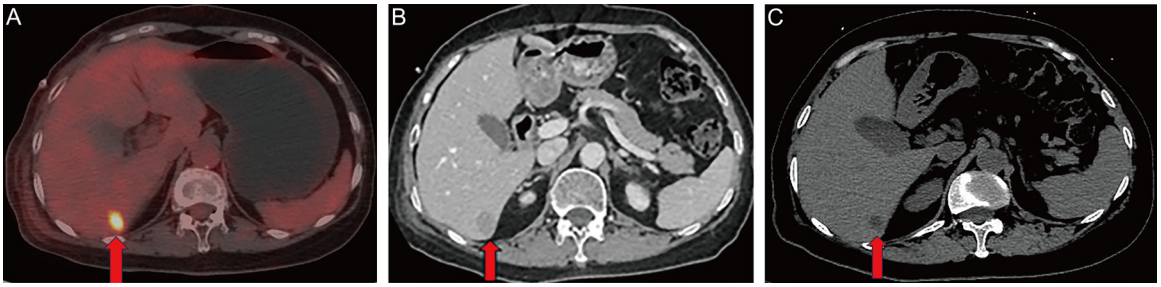

Figure 6. Upper abdominal positron emission tomography - computed tomography (PET-CT) and computed tomography (CT) scan image. A: Postoperative PET-CT scan image of the upper abdomen; B: Postoperative CT scan image of the upper abdomen; C: Post-treatment CT scan image of the upper abdomen.

positivity for CD56, indicative of skin origin. Electron microscopy revealed neuroendocrine granules within tumor cells, confirming neuroendocrine carcinoma and supporting the diagnosis of neuroendocrine tumors, with partial positivity for CgA and positive staining for Syn, aligning with neuroendocrine tumor characteristics.

Currently, there is no definitive treatment for MCC. Primary approaches include wide local excision, as outlined in the 2018 National Comprehensive Cancer Network (NCCN) guidelines [12]. For localized MCC, patients typically undergo wide excision and sentinel lymph node biopsy, with surgical margins usually set at 1-2 cm from the tumor edge. High-risk patients may require adjuvant radiotherapy at 50-66 Gy to the primary site after surgery. Radical radiotherapy may be considered for inoperable or unsuitable candidates, with recommended doses of 60-66 Gy.

For patients with metastatic MCC, the treatment mainly includes a combination of surgery, radiotherapy, and systemic therapy [13]. The objective response rate (ORR) of combination chemotherapy in metastatic MCC patients is approximately 61.5%, with a median progression-free survival (mPFS) of about 3 months [14]. With the rapid advancements of immunotherapy, studies have demonstrated that immune checkpoint inhibitors, used in phase I and II clinical trials for advanced MCC, offer response rates similar to chemotherapy but with longer durations of efficacy [15]. In this case, the patient's primary lesion was classified as stage T4, and liver metastases were discovered postoperatively. The patient initially received a chemotherapy regimen of paclitaxel combined with carboplatin, which was later switched to maintenance therapy with capecitabine at a dose of 1.5 g twice daily due to poor tolerance.

Looking forward, several promising avenues for MCC treatment are emerging. Novel immunotherapies are rapidly evolving, with ongoing clinical trials investigating new checkpoint inhibitors and combination therapies involving PD-1/PD-L1 blockade alongside other immune modulators, such as CTLA-4 inhibitors [16]. Targeted therapies are also being explored, particularly those aimed at specific molecular pathways indicated in MCC pathogenesis, such as PI3K/AKT/mTOR signaling and Wnt/β-catenin pathways [17]. Personalized medicine approaches, leveraging genomic and proteomic profiling to tailor treatments to individual patients, may further enhance therapeutic outcomes [18]. These advancements hold promises for improving both the efficacy and safety of MCC treatments, ultimately leading to better patient outcomes.

Overall, the prognosis for MCC remains poor, with high rates of distant metastasis, local lymph node infiltration, and local recurrence contributing to high mortality. It is imperative to enhance awareness of this condition to ensure early diagnosis and treatment, ultimately improving patient quality of life and extending survival.

Disclosure of conflict of interest

None.

Address correspondence to: Zhaobao Lv, Department of Breast and Thyroid Surgery, The Second people's Hospital of Liaocheng, No. 306 Health Street, Linqing 252600, Shandong, China. E-mail: lvzhaobao0708@163.com

References

[1] Paulson KG, Park SY, Vandeven NA, Lachance K, Thomas H, Chapuis AG, Harms KL, Thompson JA, Bhatia S, Stang A and Nghiem P. Merkel cell carcinoma: current US incidence and projected increases based on changing demographics. J Am Acad Dermatol 2018; 78: 457-463, e452.

[2] Dellambra E, Carbone ML, Ricci F, Ricci F, Di Pietro FR, Moretta G, Verkoskaia S, Feudi E, Failla CM, Abeni D and Fania L. Merkel cell carcinoma. Biomedicines 2021; 9: 718.

[3] Heath M, Jaimes N, Lemos B, Mostaghimi A, Wang LC, Peñas PF and Nghiem P. Clinical characteristics of Merkel cell carcinoma at diagnosis in 195 patients: the AEIOU features. J Am Acad Dermatol 2008; 58: 375-381.

[4] Hernandez LE, Mohsin N, Yaghi M, Frech FS, Dreyfuss I and Nouri K. Merkel cell carcinoma: an updated review of pathogenesis, diagnosis, and treatment options. Dermatol Ther 2022; 35: e15292.

[5] Sergi MC, Lauricella E, Porta C, Tucci M and Cives M. An update on Merkel cell carcinoma. Biochim Biophys Acta Rev Cancer 2023; 1878: 188880.

[6] Fidanzi C, Troaca SF, Fanelli GN, Romanelli M, Dini V, Viacava P, Marconcini R, Morganti R, D'Erme AM, Bagnoni G and Janowska A. Epidemiology of Merkel cell carcinoma in Tuscany (Italy), 2006-2021. Eur J Cancer Prev 2023; 32: 298-300.

[7] Yang JF and You J. Merkel cell polyomavirus and associated Merkel cell carcinoma. Tumour Virus Res 2022; 13: 200232.

[8] Komatsu H, Usui Y, Sukeda A, Yamamoto Y, Ohno SI, Goto K, Kuroda M, Nagao T and Goto H. Prevalence of merkel cell polyomavirus in primary eyelid merkel cell carcinomas and association with clinicopathological features. Am J Ophthalmol 2023; 249: 49-56.

[9] Gauci ML, Aristei C, Becker JC, Blom A, Bataille V, Dreno B, Del Marmol V, Forsea AM, Fargnoli MC, Grob JJ, Gomes F, Hauschild A, Hoeller C, Harwood C, Kelleners-Smeets N, Kaufmann R, Lallas A, Malvehy J, Moreno-Ramirez D, Peris K, Pellacani G, Saiag P, Stratigos AJ, Vieira R, Zalaudek I, van Akkooi ACJ, Lorigan P, Garbe C and Lebbé C; European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO) and the European Organization for Research and Treatment of Cancer (EORTC). Diagnosis and treatment of Merkel cell carcinoma: European consensus-based interdisciplinary guideline - update 2022. Eur J Cancer 2022; 171: 203-231.

[10] Stanoszek LM, Chan MP, Palanisamy N, Carskadon S, Siddiqui J, Patel RM, Harms KL, Lowe L, Fullen DR and Harms PW. Neurofilament is superior to cytokeratin 20 in supporting cutaneous origin for neuroendocrine carcinoma. Histopathology 2019; 74: 504-513.

[11] Mistry K, Levell NJ, Craig P, Steven NM and Venables ZC. Merkel cell carcinoma. Skin Health Dis 2021; 1: e55.

[12] Bichakjian CK, Olencki T, Aasi SZ, Alam M, Andersen JS, Blitzblau R, Bowen GM, Contreras CM, Daniels GA, Decker R, Farma JM, Fisher K, Gastman B, Ghosh K, Grekin RC, Grossman K, Ho AL, Lewis KD, Loss M, Lydiatt DD, Messina J, Nehal KS, Nghiem P, Puzanov I, Schmults CD, Shaha AR, Thomas V, Xu YG, Zic JA, Hoffmann KG and Engh AM. Merkel cell carcinoma, version 1.2018, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2018; 16: 742-774.

[13] Garcia-Carbonero R, Marquez-Rodas I, de la Cruz-Merino L, Martinez-Trufero J, Cabrera MA, Piulats JM, Capdevila J, Grande E, Martin-Algarra S and Berrocal A. Recent therapeutic advances and change in treatment paradigm of patients with merkel cell carcinoma. Oncologist 2019; 24: 1375-1383.

[14] Su J, Lai J, Yang R, Xu B, Zhu Y, Zhao M, Yang C and Liang G. Capecitabine plus bevacizumab versus capecitabine in maintenance treatment for untreated characterised KRAS exon 2 wild-type metastatic colorectal cancer: a retrospective analysis in Chinese postmenopausal women. BMC Gastroenterol 2019; 19: 17.

[15] Paulson KG, Iyer JG, Blom A, Warton EM, Sokil M, Yelistratova L, Schuman L, Nagase K, Bhatia S, Asgari MM and Nghiem P. Systemic immune suppression predicts diminished Merkel cell carcinoma-specific survival independent of stage. J Invest Dermatol 2013; 133: 642-646.

[16] Rubatto M, Sciamarrelli N, Borriello S, Pala V, Mastorino L, Tonella L, Ribero S and Quaglino P. Classic and new strategies for the treatment of advanced melanoma and non-melanoma skin cancer. Front Med (Lausanne) 2022; 9: 959289.

[17] Chamcheu JC, Roy T, Uddin MB, Banang-Mbeumi S, Chamcheu RN, Walker AL, Liu YY and Huang S. Role and therapeutic targeting of the PI3K/Akt/mTOR signaling pathway in skin cancer: a review of current status and future trends on natural and synthetic agents therapy. Cells 2019; 8: 803.

[18] Cassler NM, Merrill D, Bichakjian CK and Brownell I. Merkel cell carcinoma therapeutic update. Curr Treat Options Oncol 2016; 17: 36.