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Analysis of treatment options for Merkel cell carcinoma of the eyelid

Анализа терапијских приступа код Меркеловог карцинома капка

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Анализа терапијских приступа код Меркеловог карцинома капка

SUMMARY

Introduction Merkel cell carcinoma (MCC) is a clinically rare primary neuroendocrine carcinoma of the skin, which is more prevalent in the head and neck but rare in the eyelid. In clinical practice, it is characterised by a high misdiagnosis rate, high degree of malignancy and extremely poor prognosis. At present, there is no matured and effective treatment plan for MCC.

Case outline This case study retrospectively reports a patient experiencing MCC of the eyelid in Tangshan Ophthalmology Hospital. One month after tumour resection, the patient experienced cervical lymph node spread on the same side. Following chemotherapy, no abnormal lesions were found during a follow-up of two years and three months.

Conclusion The case study demonstrates that MCC is diagnosed mainly based on pathological examination and treated with surgical resection as the preferred option. In addition, postoperative adjuvant systemic chemotherapy and local radiotherapy have an inhibitory effect on the disease's metastasis and recurrence. Immunotherapy and molecular targeted drugs are the new development trends.

Keywords: Merkel cell carcinoma; malignant tumour; eyelid; surgery combined with chemoradiotherapy

САЖЕТАК

Увод Карцином Меркелових ћелија (МЦЦ) је клинички редак примарни неуроендокрини карцином коже, који се чешће јавља на глави и врату, али се ретко јавља на капку. У клиничкој пракси, карактеристике овог тумора су: веома честа погрешна иницијална дијагноза, висок степен малигности и изузетно лоша прогноза. Тренутно не постоји дефинитиван и ефикасан план лечења МЦЦ-а.

Преглед случаја У овом приказу случаја је ретроспективно приказан пацијент који је у нашој болници лечен због МЦЦ очних капака. Месец дана након ресекције тумора, дошло је до ширења тумора у лимфне чворове врата на истој страни. Након хемотерапије нису пронађене патолошке лезије током праћења од две године и три месеца.

Закључак Наш приказ студија показује да се МЦЦ дијагностикује углавном на основу патолошког прегледа и лечи се хируршком ресекцијом као пожељном опцијом, а постоперативна адјувантна системска хемотерапија и локална радиотерапија имају инхибиторни утицај на настанак метастаза и рецидиве. Имунотерапија и молекуларно циљани лекови су нови трендови у третману МЦЦ.

Кључне речи: карцином Меркелових ћелија; малигни тумор; очни капак; хирургија комбинована са хемиотерапијом

INTRODUCTION

Merkel cell carcinoma (MCC) is a rare primary neuroendocrine carcinoma of the skin [1]. Malignant neuroendocrine tumours of the skin originating from epidermal stem cells are more prevalent in areas exposed to sunlight, mainly occurring in the head, neck and limbs of the elderly. In one study, head and neck cases accounted for 50%, with unique ultrastructural changes and immunohistochemical staining characteristics [1]. Immunohistochemistry often shows chromogranin A (CgA [+]) and synapsin (Syn [+]). A primary lesion located in the eyelid region is rare (5–10% of cases) [2, 3], and may easily lead to misdiagnosis. To enhance

the understanding of MCC, this case study reports a patient experiencing MCC of the eyelid, including her clinical manifestations and treatment, as well as a review of the relevant literature.

CASE REPORT

Case data

A 62-year-old female patient was admitted to Tangshan Ophthalmology Hospital with a protuberant mass on the left upper eyelid. Ophthalmic examination showed a purplish-red mass-like protrusion of 5 × 5 × 3 mm (Figure 1A). Fundus examination revealed transparent cornea, clear anterior chamber, normal depth, turbid lens and no obvious congestion on the surface of the palpebral conjunctiva or obvious abnormalities. One month after local hot compress and application of erythromycin eye ointment, the mass exhibited progressive growth. In January 2021, the patient was hospitalised for mass resection. The resected mass was submitted to Tangshan Union Medical College Hospital for pathological examination.

Surgical method

First, chest and orbital computed tomography (CT) scans and abdominal and neck colour Doppler ultrasound were performed. On 28 January 2021, the patient underwent extended resection on the left upper eyelid combined with blepharoplasty. The entire upper eyelid was intraoperatively resected and the hard palate mucosa was taken as a substitute for the tarsus (Figure 1B), as per the National Comprehensive Cancer Network clinical practice guidelines (version 1.2020). Eyelid reconstruction was achieved by transplanting the excised hard palate

mucosa's inferior border to the lower eyelid's tarsal sulcus and transferring the upper eyelid skin flap (Figure 1C).

Pathological and immunohistochemical results

Postoperative pathological results suggested a malignant small round-cell tumour with diffuse tumour cells and abundant interstitial blood vessels (Figure 2A). Immunohistochemical results (Figure 2B) showed cytokeratin (CK) (+), vimentin (−), S-100 (−), cluster of differentiation (CD)56 (+), Syn (+), Neuron-Specific Enolase (NSE) (−), CD34 (+) vessels, CD7 (+) T cells, TDT (−), Pax-5 (+) B cells, CD20 (+) B cells, CD79a (+) B cells, CD3 (+) T cells, CD45Ro (+) T cells, CD10 (−), CD21 (−), Bcl-6 (−), Mum-1 (−), CD5 (+) T cells, cyclind1 (−), Ki-67 (approximately 60% +) and Bcl-2 (+). The patient was diagnosed with MCC of the left eyelid.

Postoperative treatment plan

On March 1, 2021, the patient was readmitted for further postoperative treatment. Plain and contrast-enhanced CT scan of the neck displayed multiple lymph nodes. Ultrasound-guided lymph node biopsy revealed metastatic MCC (Figure 2C). Immunohistochemistry showed vimentin (−), CK (−), CD56 (weakly +) scattered cells, CK20 (+) and Ki-67 (30% +) (Figure 2D).

The radiotherapy regimen included electron beam radiotherapy for the left eyelid using fractionated doses of 200 cGy for a total of 3,000 cGy, and conformal radiotherapy for left periclavicular lymph nodes using fractionated doses of 200 cGy for a total of 5,000 cGy five times weekly. A total of six courses of chemotherapy treatment were conducted based on

etoposide combined with carboplatin regimen (20 days per course). Three months after hard palate mucosa transplantation, the palpebral fissure was incised. The size, opening and closing of the left palpebral fissure were all normal (Figure 1D). Following chemotherapy, whole-body physical examination was performed once quarterly, and then once every 6 months. There were no significant complications observed on the eyeball following electron beam radiotherapy.

Ethics: This study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of Tangshan Peoples Hospital (No. rmyy-Ilks-151). All methods were carried out in accordance with relevant guidelines and regulations.

DISCUSSION

Merkel cell carcinoma, also known as cylindrical cell carcinoma, is aggressive and mainly affects the elderly, with an average onset age of 68 years [4]. It has a local recurrence rate of 25%, lymph node metastasis incidence of 52%, distant metastasis proportion of 34% and mortality rate of 14%–52%. Due to its low incidence, a unified and matured treatment plan is yet to be developed. Generally, tumors < 2 cm have better prognosis than those > 2 cm [5].

Extended tumor resection and lymph node dissection are the mainstay of treatment, and the optimal efficacy can be achieved when combined with chemoradiotherapy. However, there is no unified standard for the specific range of surgical resection, as the tumour is prone to recurrence and metastasis due to lymph node spread. Currently, most scholars advocate for active surgical resection and adjuvant radiotherapy, as their combination is significantly more effective than radiotherapy alone.

In the case reported here, the postoperative pathological report indicated total resection and no tumour cells at the tumour edge. First, the patient was treated with complete resection under a

microscope and then intraoperatively. The entire upper eyelid was resected at a distance of 1.2 cm from the outer margin of the mass, and the hard palate mucosa was taken as a substitute for the tarsus.

The most typical clinical manifestation of MCC is a rapidly enlarging red or purplish-red nodule in the short term, which is also non-specific and may be accompanied by pain or ulcers. Early diagnosis of MCC is challenging and prone to misdiagnosis, based on histopathological and immunohistochemical examinations. Under microscope examination, the majority of MCCs are found within the dermis, revealing a round or oval nuclei, clear nuclear membranes, thin and scattered chromatin, unclear nucleoli, few endochylema and visible karyokinesis. On immunohistochemistry, MCCs mostly display neuroendocrine features. Cytokeratin 20 is a sensitive and specific biomarker of MCC, which is usually located near the nucleus in a comma or cap-like shape. In addition, tumor cells are diffusely positive for synaptophysin and CgA, and constantly positive for CD56. Komatsu et al. [6] reported a case of MCC of the lower eyelid in a 37-year-old non-immunocompromised female patient. The patient presented with normal vision at initial presentation with an eyelid tumor measuring 12 × 10 mm with a violaceous surface that was firm and immobile. Pathological results showed that the tumor cells exhibited small round-cell infiltration. Immunohistochemical examination indicated that the tumor cells exhibited a positive reaction to synaptophysin, CgA and CK 20, whereas thyroid transcription factor-1 showed a negative reaction. The final diagnosis of MCC was confirmed. This article highlights the importance of considering MCC as a differential diagnosis of eyelid tumors in younger patients, even in the absence of immune compromise.

In recent years, advances in immunotherapies, particularly immunotherapies involving the programmed cell death protein 1 and programmed cell death ligand 1 pathways have greatly prolonged the survival of patients with metastatic diseases. Immunotherapy agents such as

avelumab and famotidine have shown great efficacy in treating metastatic MCC. Research [7] has shown that patients with surgically incurable locally advanced MCC can be treated with intratumoral injection of talimogene laherparepvec. Several MCC treatment alternatives, such as MLN0128 and pazopanib, continue to be researched.

Merkel cell carcinoma is mainly treated with surgical resection as the preferred option; however, postoperative adjuvant systemic chemotherapy and local radiotherapy inhibit its metastasis and recurrence. The application of immunotherapy and molecular targeted drugs remains critical for effective treatment of MCC.

Merkel cell carcinoma is a rare and highly aggressive neuroendocrine carcinoma, often presenting with non-specific clinical manifestations, such as a rapidly enlarging red or purplish-red nodule. This non-specificity, combined with its rarity, frequently leads to misdiagnosis in clinical practice. Early diagnosis relies heavily on pathological examination and immunohistochemical staining. Immunotherapy and molecular targeted drugs represent emerging treatment trends, offering hope for further improving the prognosis of MCC. However, the high misdiagnosis rate of eyelid MCC highlights the need for increased awareness among clinicians and pathologists, as well as the development of more specific diagnostic markers and standardized treatment protocols.

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article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Availability of data and materials: The datasets used and analyzed during the current study are available from the corresponding author on reasonable request

Conflict of interest: None declared.

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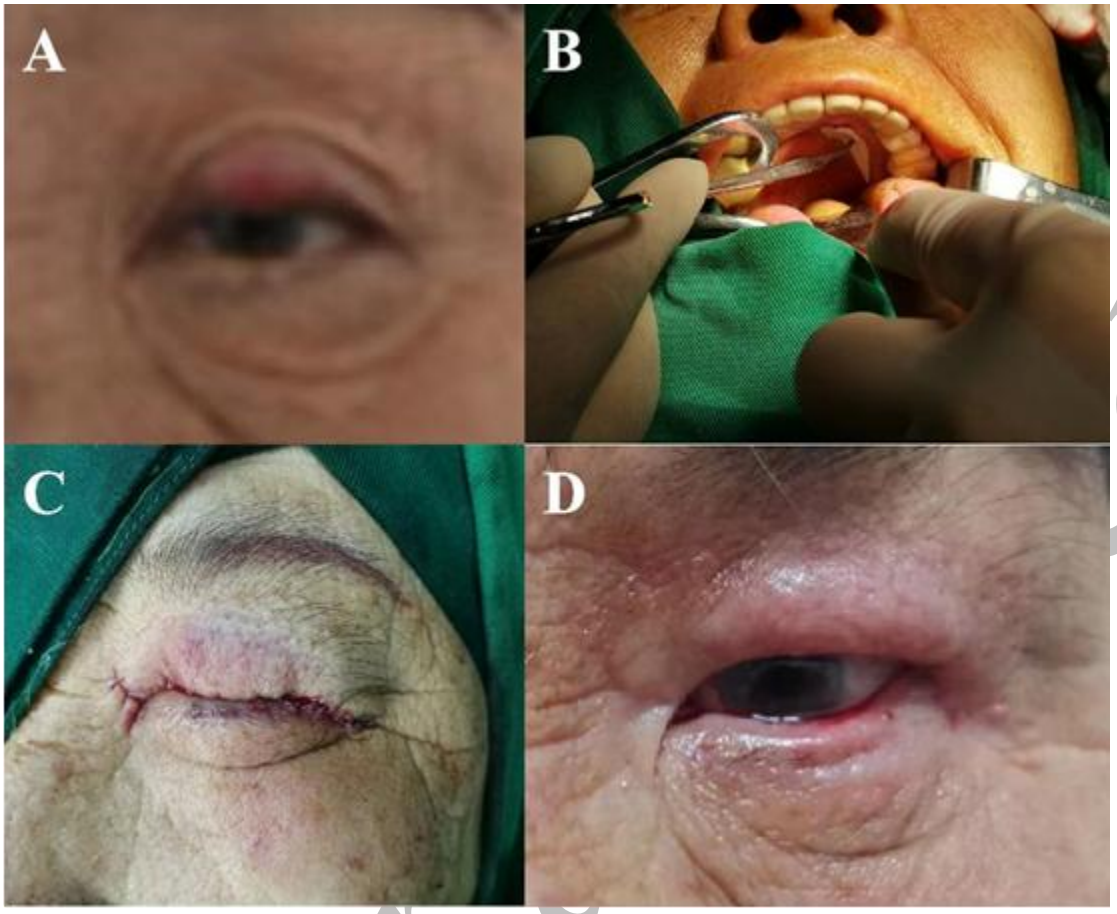

Figure 1 Photographs of a left eyelid mass, surgical process and postoperative outcome; A – a red mass-like protrusion was observed in the center of the left upper eyelid, with a size of 1.0 mm × 0.8 mm × 0.5 mm; B – the hard palate mucosa was taken; C – the eyelid was reconstructed; D – three months after hard palate mucosa transplantation, the palpebral fissure was incised; the size, opening and closing of the left palpebral fissure were all normal

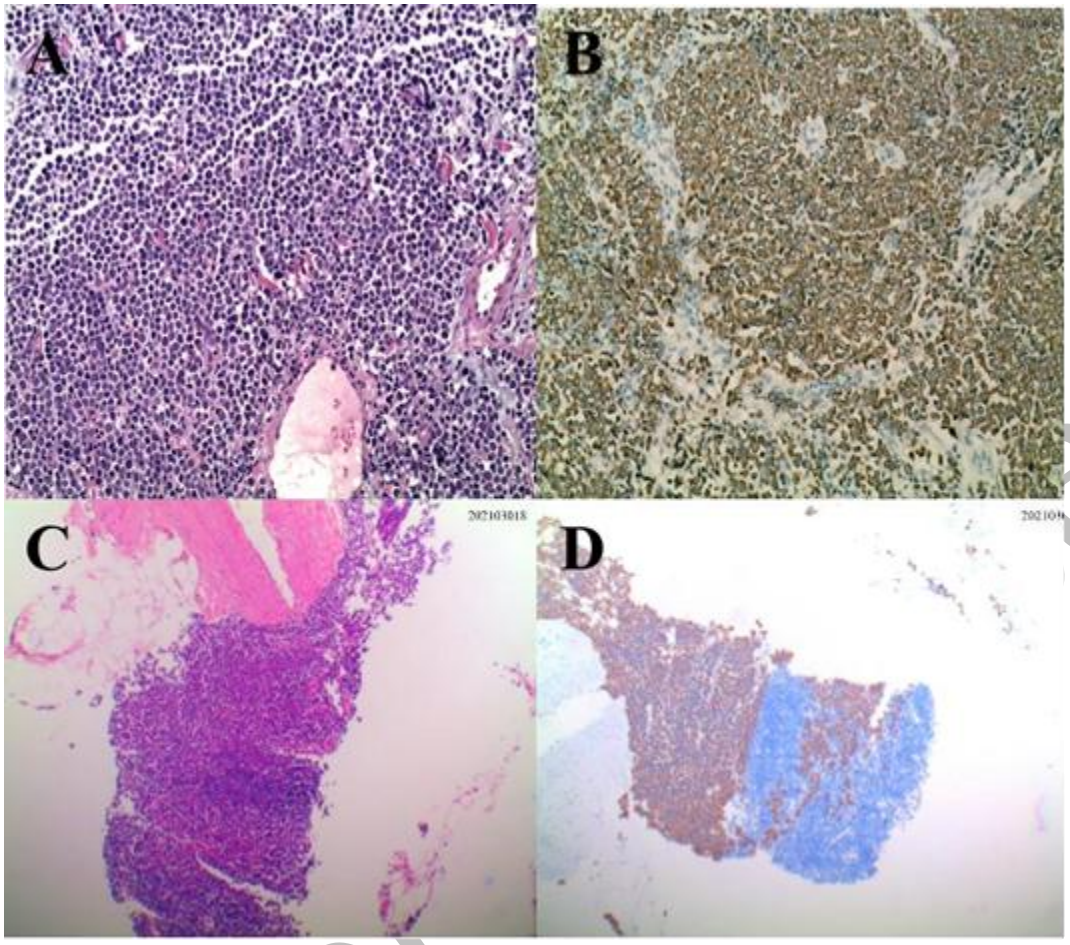

Figure 2 Pathological and immunohistochemical results; A – left upper eyelid, HE 20 × 10; B – left upper eyelid, immunohistochemistry, CK20, 20 × 10; C – left supra-clavicular lymph nodes, HE, 10 × 10; D – left supra-clavicular lymph nodes, CK20, 10 × 10

