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A Case Report and Literature Review of Merkel Cell Carcinoma of the Face

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Case Report

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Abstract

Background:

Merkel cell carcinoma (MCC) is a rare and highly aggressive cutaneous neuroendocrine carcinoma that predominantly occurs in elderly Caucasians, with few reports in Asian populations. This report describes a case of MCC in a patient from North China, highlighting the lack of specific clinical manifestations and the considerable diagnostic challenges. The diagnosis was confirmed by systematic immunohistochemical examination, which revealed CK20 perinuclear dot-like positivity, TTF-1 negativity, and positivity for neuroendocrine markers, with negativity for melanoma and lymphohematopoietic markers. The tumor showed an extremely high Ki-67 proliferation index of approximately 84% and intravascular tumor emboli, indicating strong invasiveness. Fluorescence in situ hybridization showed no C-MYC amplification or TP53 deletion. Based on these findings and clinical-pathological features, the tumor was classified as the ultraviolet-driven subtype.

Case presentation:

We present an 84-year-old Han male patient with a right facial mass, who was pathologically diagnosed with MCC of the face based on histological examination, immunohistochemical staining, and fluorescence in situ hybridization (FISH).

Conclusions:

This case contributes valuable clinicopathological insights into MCC in Chinese populations, emphasizing that MCC should be considered in the differential diagnosis of relevant nodular lesions in non-Caucasian populations, particularly in regions with significant ultraviolet exposure. It also underscores the necessity of a multimodal diagnostic approach for accurate diagnosis and prognostic evaluation of such rare tumors.

Introduction

MCC is a rare, highly aggressive cutaneous malignancy. Epidemiologically, it predominantly affects elderly Caucasian males worldwide, with Merkel cell polyomavirus (MCPyV) infection, excessive ultraviolet exposure, and immunosuppression being well-recognized major risk factors[1]. Clinically, MCC typically presents as a painless nodule or plaque on sun-exposed areas such as the head, neck, and extremities, often with rapid growth.

Histologically, MCC is classified as a “small round blue cell tumor”, which poses considerable diagnostic challenges and necessitates differential diagnosis from multiple malignant neoplasms, including metastatic small-cell lung carcinoma, various lymphomas, melanoma, and round-cell sarcomas[2]. Immunohistochemical staining is therefore the core method for MCC confirmation. The key diagnostic indicators distinguishing MCC from its mimics are perinuclear dot-like positivity for CK20, negative TTF-1

expression, positive neuroendocrine markers, and negative melanoma- and lymphohematopoietic-related markers[3]. Notably, detection of C-MYC gene amplification and TP53 gene deletion in this case not only improved the accuracy of diagnosis but also provided valuable clues for exploring the molecular pathogenesis of MCC.

MCC reports in Asian populations are relatively rare, especially among Chinese patients. Most existing studies focus on European and American populations, resulting in insufficient clinical data to support the clinicopathological characteristics, pathogenesis, and prognosis of MCC in Chinese individuals[4]. These distinct epidemiological differences across regions and ethnicities underscore the significant clinical and scientific value of reporting MCC cases in Chinese populations. This case not only confirms that MCC can occur in non-Caucasian individuals but also suggests that in regions of China with relatively high ultraviolet exposure, clinicians should include MCC in the differential diagnosis of rapidly growing facial masses, even in the absence of other definite risk factors, to avoid misdiagnosis or missed diagnosis. Although MCPyV-related detection was not performed in this case, the tumor occurred at a sun-exposed site and exhibited typical morphological and immunophenotypic features, providing a typical example for the study of the pathological mechanism of ultraviolet-driven MCC.

In conclusion, this study reports a rare case of MCC in a Chinese patient, emphasizing the importance of improving clinicians' awareness of the disease and conducting systematic and standardized pathological evaluation. This report enriches the relevant literature in the field of MCC, provides practical reference for Chinese clinicians in the diagnosis and treatment of MCC, and plays a positive role in optimizing clinical diagnosis and treatment strategies and improving patient prognosis.

Case presentation

The patient was an 84-year-old Han Chinese male who presented with a two-month history of a gradually enlarging, painless mass on the right face. He first noticed a soybean-sized lesion two months prior, which had progressively increased in size without pain and had undergone spontaneous ulceration. He denied any history of trauma or prior surgery. The patient was a long-term resident of North China. Physical examination revealed normal development, good nutritional status, normal posture, clear consciousness, and no other remarkable abnormalities.

Special Examination: A mass measuring 2 cm × 2 cm × 2 cm was observed in the right infraorbital region, protruding above the skin surface. It was soft to palpation with cystic consistency, no induration at the base, and no enlarged submandibular lymph nodes were palpable.

Preliminary Diagnosis: Right facial tumor.

Treatment: After exclusion of surgical contraindications, excision of the right facial mass was performed under local anesthesia with continuous electrocardiographic monitoring.

Pathological Examination: Microscopically, the tumor was composed of small, round cells with scant cytoplasm, vesicular chromatin, and prominent nucleoli. Mitotic figures were frequently observed. The neoplastic cells were arranged in cords, sheets, or disorganized patterns within a scant, highly vascular stroma. Lymphovascular tumor emboli were identified (Fig. 1).

Molecular pathological examination showed the following immunohistochemical results:CD117 (+), CD99 (+), Syn (+), Vimentin (+), Ki-67 (84%), P53 (+), CD56 (focal +), CgA (focal +), CK20 (perinuclear dot-like +), CK (perinuclear dot-like +), CD45 (-), CK5/6 (-), TTF-1 (-), Melanoma (-), HMB45 (-), P63 (-), S-100 (-) (Fig. 2).

Postoperative FISH examination: The postoperative tumor tissue of this patient was tested using FastProbe C-MYC gene amplification dual-color probe and FastProbe P53 (17p13)/CEP17 gene dual-color probe, respectively.

Detection conclusion: The FISH status of both C-MYC gene amplification (Fig. 3) and P53 (17p13) gene deletion (Fig. 4) was negative in this sample. Please make a comprehensive judgment combined with clinical and other diagnostic findings.

Pathological diagnosis: Combined with multiple test results, the final diagnosis of this case is facial Merkel cell carcinoma.

Discussion

1. Epidemiology

MCC was first reported by Toker in 1972[5]. The present case shows significant differences in epidemiological background. Globally, MCC predominantly affects elderly Caucasian males, with a high incidence in North America, Oceania, and Europe. The incidence of MCC has appeared to increase over the past two decades; in the United States, the annual incidence increased by 2.66% from 1992 to 2013[6]. In addition, variations in the pathological diagnostic standards for MCC may influence the reported incidence in certain regions. A nationwide multicenter study from Korea confirmed that the epidemiological characteristics of MCC in Asian patients, such as a higher proportion of females, differ from those in Western countries[7], further highlighting the value of this case in supplementing MCC data for Asian populations.

2. Etiology and Pathogenesis

Two core etiological factors are widely recognized: MCPyV infection and ultraviolet-induced mutagenesis. Other major risk factors include organ transplantation, previous malignancies, human immunodeficiency virus infection, advanced age, and long-term use of immunosuppressive drugs[8]. In June 2025, the International Agency for Research on Cancer of the World Health Organization upgraded MCPyV from Group 2A to Group 1 carcinogen, confirming its causal association with MCC[9]. A history of previous skin cancers, including basal cell carcinoma, squamous cell carcinoma, and malignant

melanoma, is also associated with an increased risk of MCC[10–12]. MCPyV-positive cases account for approximately 80% of MCC. MCPyV commonly causes asymptomatic infection in childhood, with a high skin carriage rate in adults[13]. MCPyV-positive MCC usually harbors wild-type TP53 and RB1, whereas MCPyV-negative MCC often contains inactivating mutations in TP53 and RB1. When the viral genome integrates into the host genome and undergoes a truncating mutation of the large T antigen (LT), the virus loses its replicative capacity but retains the N-terminal LxCxE motif, which continuously binds and inhibits pRb, driving cell proliferation and tumorigenesis without binding p53[14]. Although MCPyV testing was not performed in this case, the tumor occurred on the facial skin of a patient from North China with chronic sun exposure, and immunohistochemistry showed high expression of P53 protein. These features favor classification as an MCPyV-negative MCC subtype, likely associated with ultraviolet radiation. FISH analysis revealed no TP53 gene deletion; however, strong positive expression of P53 protein still suggests other abnormalities in the TP53 pathway, which is partially consistent with the molecular profile of MCPyV-negative MCC.

3. **Clinical Manifestations**

MCC typically occurs on sun-exposed sites of the head, neck, and extremities, involving the facial skin and oral mucosa. It has a high recurrence rate and frequent regional lymph node and distant metastasis, with reported metastases to the testis, liver, lung, and heart; spontaneous regression is occasionally observed[15–17]. The tumor usually presents as a solitary solid nodule, purple or red in color, most commonly in elderly and immunocompromised individuals. Typical skin lesions are solitary, firm, painless red or violaceous nodules or plaques with rapid growth, smooth surface, and telangiectasia. Some patients already have lymph node involvement at initial diagnosis, and a minority present with unexplained lymphadenopathy without obvious primary skin lesions. MCC is highly aggressive, prone to recurrence and metastasis. Prognosis is closely related to tumor size, depth of invasion, lymph node metastasis, distant metastasis, and immune status. Heath et al. described the clinical manifestations of MCC using the mnemonic "AEIOU": Asymptomatic/lack of tenderness, Expanding rapidly, Immunosuppression, Older than 50 years, and Ultraviolet-exposed site on fair skin[18].

4. Immunohistochemical Markers

Immunohistochemistry is essential for the auxiliary diagnosis of MCC. Markers mainly include neuroendocrine, epithelial, and cell proliferation indicators. Typical findings are positive neuroendocrine markers, positive cytokeratins, and **characteristic perinuclear dot-like positivity for CK20, which are key for diagnosis and differential diagnosis[14–16]. Occasionally, MCC shows negative CK20; in such cases, diagnosis can be confirmed by positive NF, NSE, and negative TTF-1, S-100, CD45[17–23]. CD117 and SOX2 may also be positive, while CK7, P63, and LCA are usually negative[24–27]. This panel effectively excludes morphologically similar tumors such as basal cell carcinoma, squamous cell carcinoma, lymphoma, and metastatic small cell carcinoma.

5. Clinical Diagnosis

The 5-year overall survival rate for early-stage MCC ranges from 60% to 80%, but declines sharply to merely 11%–25% in patients with distant metastasis[28]. Therefore, early and accurate diagnosis is paramount for improving patient outcomes. The diagnosis of MCC is established through a comprehensive multimodal approach, encompassing clinical manifestations, imaging studies, histopathological examination, and immunohistochemical analysis. Clinically, MCC should be suspected in individuals over 50 years of age with a history of immunosuppression or chronic ultraviolet exposure, who present with rapidly enlarging, painless, reddish-purple firm nodules on sun-exposed areas, particularly the head and neck. Regional lymph node ultrasonography is valuable for assessing metastatic involvement. Positron emission tomography-computed tomography (PET-CT) has progressively supplanted conventional CT and MRI as the primary imaging modality, offering superior staging accuracy. Notably, among MCC patients staged by PET-CT, 16.8% were upstaged compared with only 6.9% when CT alone was employed[29]. Histopathologically, MCC is characterized by sheets of uniform, small, round basophilic cells arranged in trabecular, nested, or cord-like patterns, featuring scant cytoplasm, finely granular nuclear chromatin, and frequent mitotic figures with apoptotic activity. Immunohistochemistry serves as the cornerstone of diagnosis; however, given that certain specific markers may yield negative results, ancillary investigations such as karyotyping, comparative genomic hybridization, or multiplex FISH are warranted. In the present case, although FISH was negative, the diagnosis of MCC was confirmed based on characteristic clinical features and positive immunohistochemical findings. This illustrates that MCC diagnosis necessitates integration of multiple diagnostic modalities; reliance on any single method risks misdiagnosis and subsequent inappropriate therapeutic management.

6. Differential Diagnosis

MCC is frequently associated with other malignancies and is often overlooked due to its non-specific clinical manifestations. It must be differentiated from metastatic small cell lung cancer (SCLC), malignant melanoma, blastic lymphoma, squamous cell carcinoma (SCC), basal cell carcinoma (BCC), and other atypical neuroendocrine tumors.

(1) Metastatic Small Cell Lung Cancer

SCLC (oat cell carcinoma) may exhibit spindle-shaped nuclei and occasional "streaming" polarity. DNA released from tumor cells may form a cuff-like distribution around blood vessels. Immunohistochemically, SCLC is typically positive for TTF-1, ATOH1, TFAP2B, and CEACAM6, with CK20 positivity in less than 10% of cases. In contrast, MCC characteristically demonstrates perinuclear dot-like CK20 positivity and is negative for TTF-1. These morphological and molecular pathological features enable reliable distinction between the two entities.

(2) Malignant Melanoma

Melanoma displays considerable morphological heterogeneity, including small round cells, clear cells, nevus-like cells, and epithelioid cells, with variable melanin content and eosinophilic or amphophilic

cytoplasm. It frequently invades the epidermis and shows necrosis. MCC, conversely, consists predominantly of uniform basophilic small round cells, typically without epidermal involvement or pigment production. Immunohistochemically, melanoma expresses HMB45, S-100, Melan-A, SOX10, MITF, and tyrosinase. In the present case, negativity for HMB45, S-100, and Melan-A excluded melanoma.

(3) Lymphoma

Although histologically similar, MCC and lymphoma originate from distinct lineages. Lymphomas express T/B-cell markers (CD3, CD4, CD79a, CD20, LCA, CD45) and are negative for cytokeratins. MCC expresses neuroendocrine markers (NSE, CD56, CgA, Syn) and low-molecular-weight cytokeratins (CK8, CK18, CK19, CK20). In this case, negativity for CD45, partial positivity for CgA and CD56, and positivity for CK20 and Syn facilitated differentiation from lymphoma.

(4) Cutaneous Squamous Cell Carcinoma

SCC demonstrates variable histology depending on differentiation status. Well-differentiated tumors are composed of large polygonal cells with abundant cytoplasm and keratin pearls, whereas poorly differentiated tumors consist of small spindle cells with scant cytoplasm and hyperchromatic nuclei. SCC is positive for CK5/6 and p63 and negative for TTF-1. In this case, negativity for CK5/6 and p63 excluded SCC.

(5) Basal Cell Carcinoma

MCC may present as translucent nodules resembling BCC; however, it lacks the characteristic peripheral palisading. BCC is positive for CK5/6 and p63 and negative for CK20. In this case, negativity for CK5/6 and p63, combined with perinuclear dot-like CK20 positivity, excluded BCC.

7. Treatment

Treatment of MCC is determined by clinical stage and tumor location. The main therapeutic modalities include wide local excision with postoperative margin assessment and adjuvant radiotherapy[30]. Postoperative radiotherapy is generally recommended for patients with positive margins or lymphovascular invasion, provided it is tolerated, to improve survival outcomes. The efficacy of chemotherapy remains controversial, particularly with regard to tolerability in elderly patients. MCC is considered an immunogenic tumor, with robust interactions between tumor cells and the immune system being closely linked to its pathogenesis. Research on novel therapies has focused on immune checkpoint inhibitors, with combined immune checkpoint blockade representing a promising direction for future development[31].

Conclusions

The diagnosis and management of this case exemplify the diagnostic complexity and inherent risk of misdiagnosis associated with MCC. As a small round blue cell tumor, MCC exhibits significant histological overlap with metastatic SCLC, lymphoma, melanoma, Ewing sarcoma, desmoplastic small round cell tumor, and other malignancies, rendering morphological assessment alone insufficient for definitive diagnosis. Accurate diagnosis in this case was achieved through a comprehensive immunohistochemical panel. The characteristic perinuclear dot-like staining pattern for CK20, coupled with negative TTF-1 expression, served as critical discriminators from SCLC—the most common morphological differential diagnosis. Positive neuroendocrine markers (synaptophysin, chromogranin A, and CD56) substantiated neuroendocrine differentiation, whereas negative melanocytic markers (HMB45, Melan-A, and S-100) and the leukocyte common antigen (CD45) effectively excluded melanoma and hematolymphoid neoplasms, respectively. Notably, this panel—comprising CK20, CD117, CD56, pan-cytokeratin, CD99, synaptophysin, vimentin, chromogranin A, CK5/6, TTF-1, Melan-A, HMB45, S-100, CD45, p53, p63, and Ki-67—was substantially more extensive than those employed in previous reports of MCC in Chinese patients.

Consequently, the establishment of a standardized immunohistochemical diagnostic algorithm is imperative to circumvent diagnostic pitfalls and ensure accurate subtyping of MCC.The clinicopathological and prognostic features of this case carry significant educational and clinical implications. The tumor demonstrated rapid growth, an elevated Ki-67 proliferation index of 84%, and unequivocal intravascular tumor emboli—all established histological correlates of aggressive biological behavior and adverse prognosis. Ki-67 serves not only as a fundamental grading criterion for neuroendocrine neoplasms but also demonstrates robust correlation with tumor biology; elevated proliferation indices typically portend increased metastatic potential and inferior clinical outcomes. Fluorescence in situ hybridization analysis revealed neither MYC amplification nor TP53 deletion. Although negative, these findings possess diagnostic and molecular relevance, suggesting that tumorigenesis in this case may proceed independently of these canonical driver alterations. This observation aids in narrowing the differential diagnosis and indirectly supports classification as a UV-induced molecular subtype of MCC, which characteristically exhibits more complex genomic profiles.

In conclusion, we present a case of facial MCC in a Chinese patient, with detailed documentation of its clinicopathological characteristics to augment the existing Chinese MCC database. Through comprehensive literature review, we synthesize the clinicopathological manifestations, diagnostic methodologies, and therapeutic strategies for this rare malignancy in the Chinese population, thereby providing a reference framework for pathologists in the accurate diagnosis of MCC.

This case report is subject to several limitations. First, as a single-institution case report, the generalizability of our conclusions is constrained. Second, the absence of MCPyV testing precludes definitive determination of virological status and precise molecular subtyping. Third, the lack of long-term follow-up data impedes assessment of ultimate prognosis, recurrence patterns, and metastatic behavior. Nevertheless, this case retains substantial educational and clinical value. It enhances

understanding of MCC in the Chinese population, systematically illustrates a standardized diagnostic pathway, and contributes to the refinement of clinical diagnosis and management.

Abbreviations

Merkel cell carcinoma	MCC
Merkel cell polyomavirus	MCPyV
Small-cell lung cancer	SCLC
Positron emission tomography-computed tomography	PET-CT
squamous cell carcinoma	SCC
basal cell carcinoma	BCC

Declarations

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Authors' contributions

Jiao Long: Manuscript drafting and revision, data analysis and interpretation; Yaoqiang Liu: Material support, implementation of the research protocol, and data collection; Minhai Nie: Guidance on manuscript drafting, administrative and technical support; Dan Li: Technical and material support; Yunling Liu and Dan Qin: Material support, assistance with data filing and collation; Xuqian Liu: Study design and manuscript revision, acquisition of research funding, technical and material support, critical review of the intellectual content of the article.

Availability of data and materials

Data will be made available on request.

Ethics approval and consent to participate

This study was approved by the Institutional Ethics Committee of Southwest Medical University, in compliance with the relevant local laws and regulations. Written informed consent was obtained from the participant of this case report as well as for all accompanying images. The participant had signed the written informed consent form prior to being enrolled in the study.

Consent for publication

Written informed consent for publication of this case report and any accompanying images was obtained from the patient.

Competing interests

The authors have declared that no competing interests exist.

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Figures

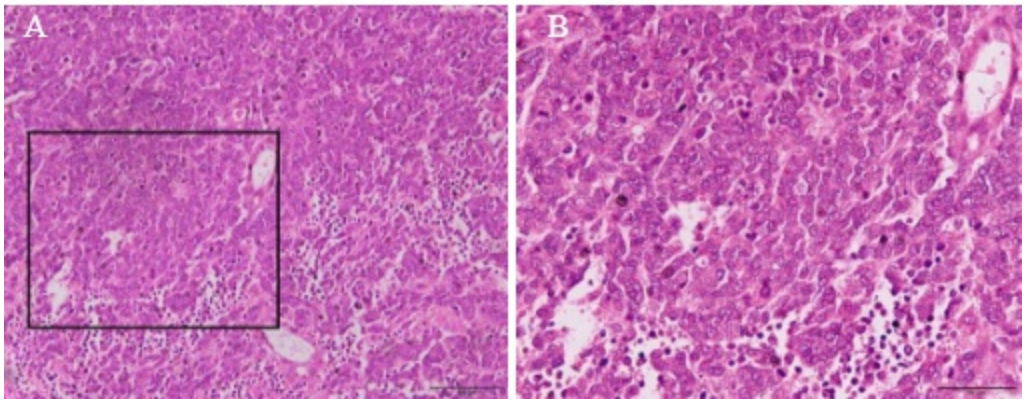


Figure 1

Hematoxylin and eosin (HE) staining of Merkel cell carcinoma (MCC) specimens (A: ×200; B: ×400).

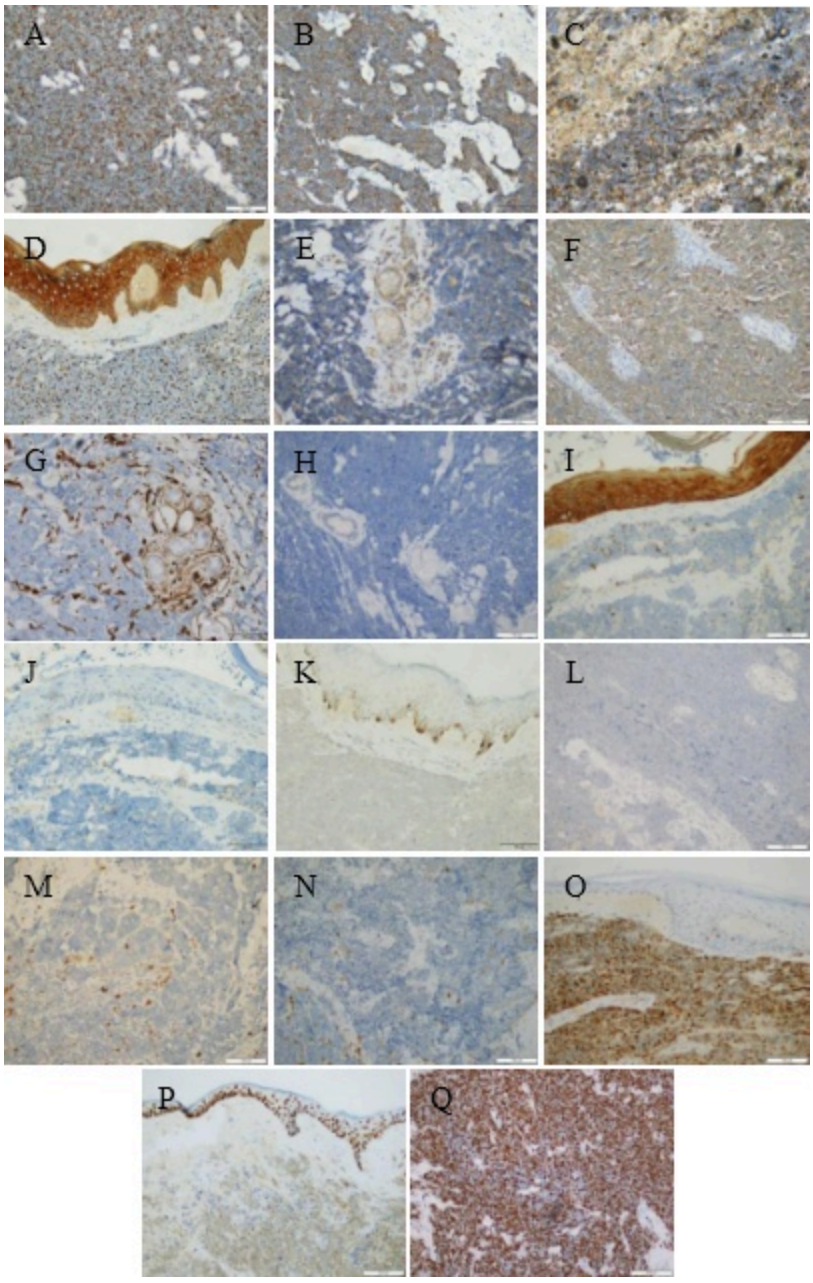


Figure 2

Immunohistochemical staining of MCC specimens

Note: The immunohistochemical markers of each map are A: CK20; B: CD117; C: CD56; D: CK; E: CD99; F: Syn; G: Vimentin; H: CgA; I: CK5/6; J: TTF-1; K: Melanoma; L: HMB45; M: S-100; N: CD45; O: P53; P: P63; (A~P: 200×)

Q: Ki67; (Q: 100×)

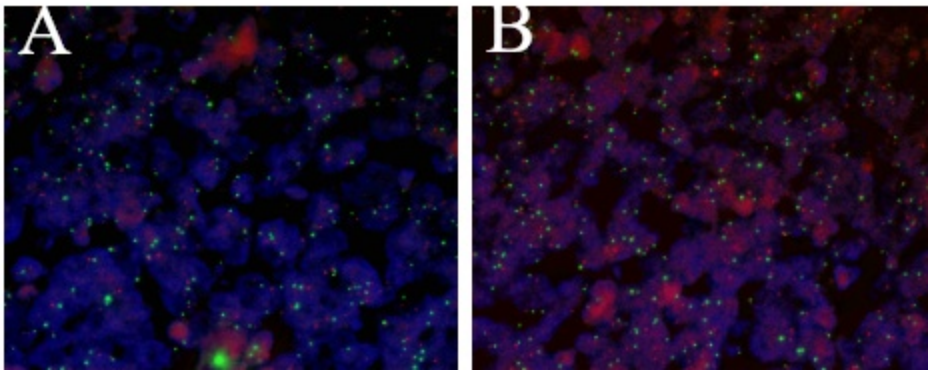


Figure 3

(Test results: 100 tumor cells counted; total number of C-MYC signals: 203, average copy number of C-MYC: 2.03; total number of CEP8 signals: 196, average copy number of CEP8: 1.96; C-MYC/CEP8 ratio: 1.04; Test conclusion: The FISH status of C-MYC gene amplification in this sample is negative. A comprehensive judgment should be made in combination with clinical findings and other diagnostic results.)

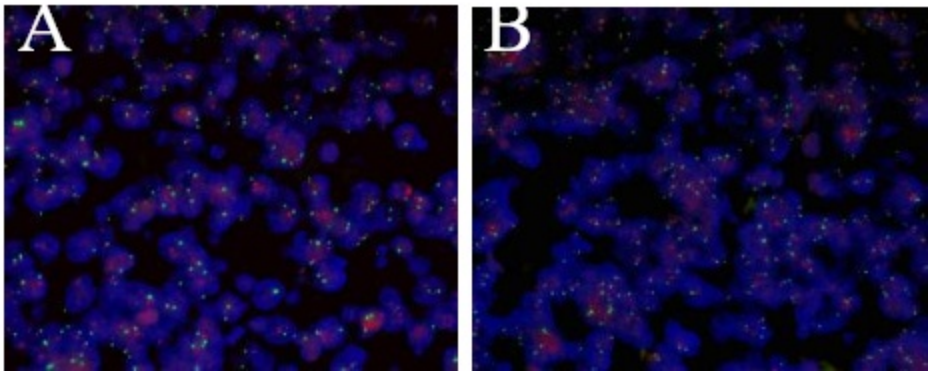


Figure 4

(Test results: 200 cells counted; 12% 1R1G cells, 4% 1R2G cells, 18% 2R1G cells, and 66% 2R2G cells; Test conclusion: The FISH status of P53 (17p13) gene deletion in this sample is negative. A comprehensive judgment should be made in combination with clinical findings and other test results.)