CHAPTER 120

# Merkel Cell Carcinoma

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Merkel cell carcinoma (MCC) is a neuroendocrine carcinoma of the skin. Although it is 40 times less common than malignant melanoma, it has a higher mortality (33 percent) than melanoma (15 percent). From 1986 to 2001 there was a rapidly increasing incidence in reported cases of MCC, with a tripling in the rate over this 15-year period. Management of MCC is challenging and optimal therapy is controversial, at least in part due to a lack of quality data on which to base treatment decisions.

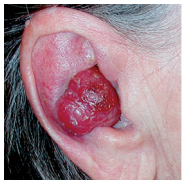
MCC is a relatively recently described entity, although the Merkel cell was described more than 100 years ago. In 1875, human Merkel cells were first described by Friedrich S. Merkel (1845–1919). He named these cells *Tastzellen* (touch cells) assuming that they had a sensory touch function within the skin due to their association with nerves. In 1972, Toker described five cases of "trabecular cell carcinoma of the skin." In 1978, Tang and Toker found dense core granules on electron microscopy that were typical of Merkel cells and other neuroendocrine cells. In 1980, the name *MCC* was first applied to this tumor. In 1992, antibodies to cytokeratin-20 allowed for the first time specific and relatively easy diagnosis of MCC to be made through immunohistochemistry. Since that time, electron microscopy is essentially no longer used to make the diagnosis. Most recently, in 2004, an elegant transgenic mouse model was used to isolate normal Merkel cells from mouse skin and find that they possessed excitable calcium channels and were capable of neurotransmitter release, suggesting that they do indeed play a role in touch sensation within the skin.[1]

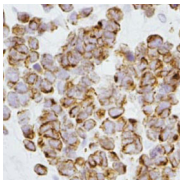
## EPIDEMIOLOGY

Over the 15-year period between 1986 and 2001, the incidence of MCC tripled from 0.15 per 100,000 to 0.44 per 100,000.[2] There are likely two factors that contribute to this increase in incidence that is more rapid than that of any other type of skin cancer. One factor is an increase in the accurate diagnosis of this malignancy through the routine use of cytokeratin-20 immunohistochemistry and the improved recognition of this malignancy by dermatopathologists. In the past, many MCCs were no doubt mischaracterized as lymphoma, melanoma, or undifferentiated carcinoma in the era before immunohistochemistry. A second likely reason is an increase in the number of people over age 65 years with extensive sun exposure history and prolonged immune suppression. Each of these factors is a known risk factor for MCC and several will be discussed in the section Etiology and Pathogenesis.

Recent studies have indicated that the number of MCC cases within the United States is between 600 and 1000 cases per year depending on the particular tumor registry analyzed.[3,4] This cancer is far more common in whites than in blacks, consistent with a known role for ultraviolet radiation in the pathogenesis. Specifically, the rates in whites have been reported as 0.23 per 100,000 as compared to 0.01 per 100,000 for blacks.[5] Although not specifically reported, rates in Hispanics and Asians are likely intermediate between those in blacks and whites. MCC tends to be more common in men than in women (2:1 in ratio).[3]

## MERKEL CELL CARCINOMA AT A GLANCE





- Higher mortality (33 percent) than melanoma (15 percent).
- Incidence tripled from 1986 to 2001.
- Affects elderly/whites/immunosuppressed.
- Consider in differential diagnosis of any rapidly growing, nontender nodule on sun-exposed area.
- Sentinel lymph node biopsy, surgery and radiation are indicated in most cases.
- Imaging (computed tomography/magnetic resonance/positron emission tomography): poor sensitivity and specificity at time of diagnosis and in early stages.
- Management: challenging; therapy is unique and controversial.
- Avoid over-aggressive surgery: adjuvant radiation therapy highly effective.
- Adjuvant chemotherapy: high morbidity, no proven benefits.
- Optimum care: multidisciplinary coordination between dermatologists, surgeons, radiation, and medical oncologists.

## ETIOLOGY AND PATHOGENESIS

There are several known risk factors for MCC that will likely continue to lead to an increase in the incidence of this disease.

### Age Greater than 65 Years

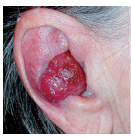
The median age for diagnosis of MCC is 70 years, and there is a five- to ten-fold increase in incidence after age 70 as compared with age less than 60 years, as shown in Fig. 120-1. Indeed, only about 5 percent of MCC cases present in patients under age 50 and it is extremely rare in childhood.[6]

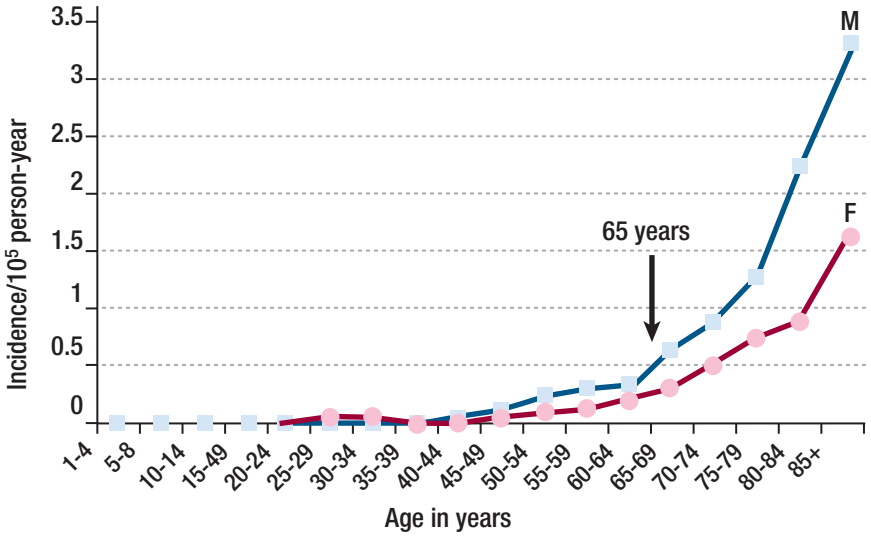
### Sun Exposure

Sunlight, prolonged ultraviolet exposure and photochemotherapy are all associated with an increased risk of MCC. The vast majority of MCC present on sun-exposed skin. It is clear, however, that sun is not required for MCC to develop. MCC cases can occur on sun-protected skin, including buttocks and vulva as well as portions of the scalp that are covered by hair.

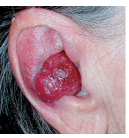
### Immune Suppression

The role of the immune system in preventing and fighting MCC is apparent within several different populations of immune-suppressed patients. Solid organ transplant recipients make up approximately 8 percent of all MCC cases.[7] There is thus approximately a 10-fold increase in MCC in the solid organ transplant population as compared to a control population.[5] In organ transplant recipients, the median age of presentation of MCC is far younger with almost half of patients presenting at less than 50 years of age as compared to only 5 percent in the typical population.[6] In transplant recipients, MCC is more aggressive than melanoma with 68 percent of these patients developing lymph node metastases as compared to 20 percent for melanoma.[6] The death rate due to MCC in this population is 60 percent as compared to 29 percent for melanoma.[6,7] The ratio of post-trans-






▲ **FIGURE 120-1** The most significant risk factor for Merkel cell carcinoma is age. Frequency of Merkel cell carcinoma by age and sex. M, male (■); F, female (●). (Reprinted from Agelli M, Clegg LX: Epidemiology of primary Merkel cell carcinoma in the United States. *J Am Acad Dermatol* **49**:832-841,2003, with permission.)



plant melanoma to MCC is 6:1 as compared to 65:1 in the general population,[5] indicating the relative importance of the immune system in suppressing MCC as compared to melanoma.

Several of the drugs used to suppress the immune system in transplant recipients, including cyclosporine, have previously been shown to act directly on certain tumor cells to augment their growth and aggressive behavior. Data from several other populations suggest, however, it is likely the immune suppression itself that is most important for MCC and not the direct effects of drugs such as cyclosporine acting on the tumor. Specifically, among HIV-positive patients, there is a relative risk of 13-fold for the development of MCC as compared to the general population.[8] Similar to solid organ transplant recipients, in HIV-positive patients, this disease also behaves more aggressively and presents at a younger age than in the general population. An increased incidence has also been noted in patients with chronic lymphocytic leukemia which is well known to cause profound and prolonged immune suppression, particularly in the T lymphocyte arm of the immune system.

### Molecular Genetics

At the molecular level, virtually nothing is known about MCC. It shares histologic features with another neuroendocrine carcinoma, small cell lung cancer, but it is unclear if these similarities at the histologic level extend to the genetic level as well. Thus far there is no clear tumor suppressor gene or oncogene that has been conclusively implicated in MCC. Diverse chromosomal abnormalities have been reported, including in chromosomes 1, 6, 7, 11, 12, and 18, but these are low-resolution genetic abnormalities and the specific tumor suppressors, or oncogenes, associated with these have not been identified. The p53 gene has been studied in MCC and no significant elevation in p53 mutations has been noted, suggesting that p53 mutation does not play an important role in the development or progression of MCC.[9]

## CLINICAL PRESENTATION OF MERKEL CELL CARCINOMA

Although there have been no large studies to describe the clinical presentation of MCC, based on our observations among over 100 cases,[13] we have generated a list as shown in Table 120-1. In distinction to melanoma, there are no clear "ABCD" features that alert a clinician to whether they are looking at an MCC or not. However, if several of the features shown in Table 120-1 are present, it is clearly appropriate to carry out a biopsy to evaluate for MCC or a separate malignant process. In our population,[13] we have analyzed the biopsy reports of more than 70 patients in which the clinician had submitted a presumed diagnosis at the time of biopsy. Strikingly, the clinician listed as clinical impression a benign diagnosis in over one half of cases. In particular, a cyst or acneiform lesion was the single most common of these (Box 120-1 and Figs. 120-2A and B) and non-melanoma skin cancer was also relatively frequent as a presumptive diagnosis (Fig. 120-2C).

**TABLE 120-1**
**Clinical Features of Merkel Cell Carcinoma**

| |
|---|
| Firm; red, purple or skin-colored, nontender papule or nodule (see Fig. 120-2A and B) |
| Most lesions are <20 mm in diameter at diagnosis |
| Rapid growth within 1–3 mo |
| Usually on a sun-exposed location (but not always) |
| Ulceration is rare |
| Locally aggressive, with local discontinuous and distant lymphatic spread (see Fig. 120-2B) |

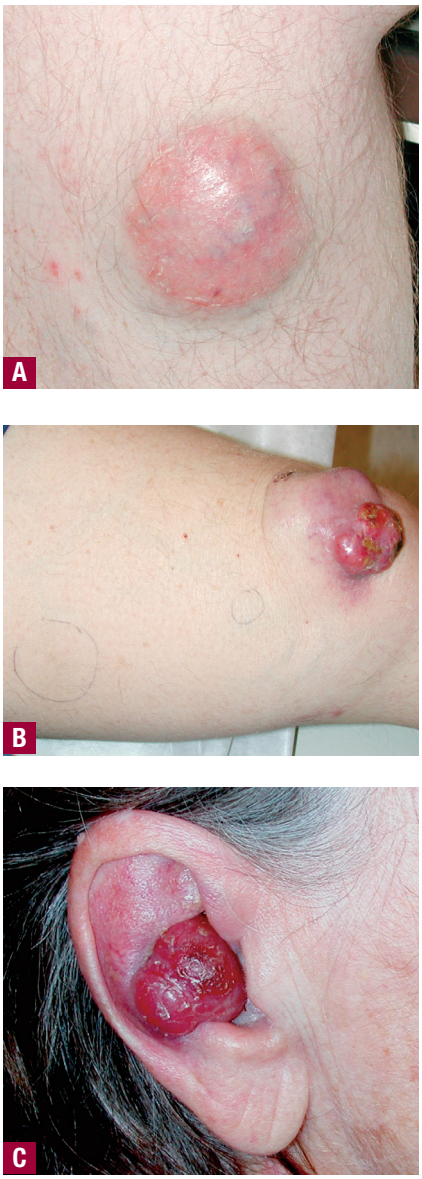
## PATHOLOGY

Merkel cells are thought to be mechanoreceptors involved in fine touch located within the basal epidermis. This is based on their close association with cutaneous nerves as well as recent data that shows Merkel cells are excitable cells with calcium channels and capable of release of neurotransmitters.[1] Although it has not been formally shown, it is widely agreed that Merkel cells in the skin are the precursor cells to MCC. As shown in Fig. 120-3A, the classic histologic features of MCC include sheets of small basophilic cells with scant cytoplasm, fine chromatin and no nucleoli. There are numerous mitotic figures and occasional individual necrotic cells. Lymphovascular invasion is a very common feature and often can be found when it is specifically searched for even in a "negative" margin. This helps to ex-

**Box 120-1**
**Differential Diagnosis of Merkel Cell Carcinoma**

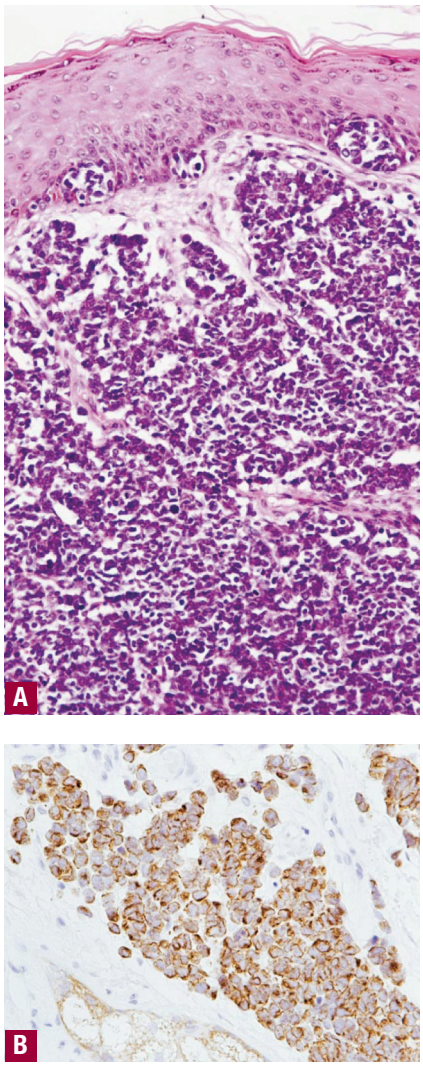
***Most Likely***
- Cyst
- Basal cell carcinoma
- Squamous cell carcinoma (see Fig. 120-2C)
- Amelanotic melanoma
- Cutaneous lymphoma
- Adnexal tumor

***Consider***
- Metastasis
- Dermatofibromasarcoma protuberans
- Keratoacanthoma
- Neuroblastoma




▲ **FIGURE 120-2** Clinical appearance of Merkel cell carcinoma (MCC). **A.** MCC frequently has a "cyst-like" appearance. This is reflected in the differential diagnoses given by clinicians at the time of the biopsy, with cyst/acneiform lesion being the most common clinical impression. **B.** MCC on the knee of a 70-year-old woman with chronic lymphocytic leukemia. For 6 months this lesion was thought to be a "cyst"; consequently, diagnosis and treatment was delayed. Pen marks indicate palpable satellite metastases that developed several months after the primary lesion, presumably tracking via lymphatics. **C.** MCC on the ear of an 87-year-old woman. The lesion grew rapidly and was nontender. After approximately 3 months, it was biopsied by a clinician who listed squamous cell carcinoma as the presumptive diagnosis.

plain the high local recurrence rate in MCC for narrow or even relatively wide margin excision when adjuvant radiation therapy is not given.




▲ **FIGURE 120-3** Merkel cell carcinoma pathology. **A.** Hematoxylin and eosin. There is diffuse dermal as well as intraepidermal involvement with Merkel cell carcinoma. This case was seen in consultation, with an initial diagnosis of cutaneous T-cell lymphoma. **B.** Cytokeratin-20. Showing the pathognomonic "perinuclear pattern" of cytokeratins (cam5.2). Reprinted from Nghiem P, Mckee P, Haynes H: Merkel cell (cutaneous neuroendocrine) carcinoma, in *Skin Cancer, Atlas of Clinical Oncology*, edited by A Sober, F Haluska, American Cancer Society, 2001, with permission.

## Hematoxylin and Eosin Stain

Three histologic patterns have been described up to now and none is clearly associated with a better or worse prognosis. The most common type is the "intermediate type." This has uniform small cells with minimal cytoplasm, pale nuclei, and a dispersed chromatin appearance. On hematoxylin and eosin staining, the differential diagnosis for this presentation is that of the small, blue-cell tumors including melanoma and lymphoma. The second most common pattern is the "small cell type." This takes its name from small cell lung carcinoma, which is the principal differential diagnosis for this pattern. It shows irregular, hyperchromatic cells with scant cytoplasm and malignant cells that are arranged in linear patterns infiltrating stromal structures. The least common but perhaps most histologically distinctive type is the "trabecular" type. This is the pattern originally described by Toker in 1972. It has a lattice-like, or network appearance, and the differential diagnosis includes metastatic carcinoid tumor.

## Immunohistochemical Stains

The use of antibody-based stains has greatly facilitated the ease and specificity of MCC diagnosis (Table 120-2). The single most useful of these stains to rule in MCC is cytokeratin-20.

## Cytokeratin-20

Intermediate filament protein is expressed in MCC as well as in adenocarcinomas of the colon, stomach, and pancreas. Within the skin, however, the expression of cytokeratin-20 is limited to Merkel cells. A "perinuclear dot" pattern of cytokeratin is essentially pathognomonic for MCC (see Fig. 120-3B).

## Antibodies to CAM5.2

CAM5.2, a cocktail of antibodies that detects multiple human cytokeratin epitopes, typically reacts with both MCC and small cell lung carcinoma. Although it is useful as an initial screening tool to detect tumors of squamous origin, its lack of selectivity relative to cytokeratin-20 means that it cannot be used to definitively diagnose MCC.

## Thyroid Transcription Factor-1

Thyroid transcription factor-1 is negative in MCC and positive in small cell lung cancer and thus useful for the differential diagnosis between these two tumors that can look identical by routine histology.

## Cytokeratin-7

Cytokeratin-7 has the same staining pattern as thyroid transcription factor-1, that is, negative in MCC and positive in

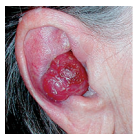
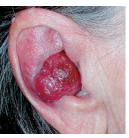


**TABLE 120-2**
**Immunohistochemistry Panel**

| | Cytokeratin-20 | Cytokeratin-7 and thyroid transcription factor-1 | Leukocyte common antigen | S-100 |
|---|---|---|---|---|
| Merkel cell carcinoma | + | – | – | – |
| Small cell lung carcinoma | – | + | – | – |
| Lymphoma | – | – | + | – |
| Melanoma | – | – | – | + |

small cell lung carcinoma; it is also expressed in epithelial cells of the lung, ovary, and breast.



### Neuron-Specific Enolase

Neuron-specific enolase is positive in MCC and other neoplasms derived from neural or neuroendocrine tissue. In some cases, neuron-specific enolase is released by neuroendocrine carcinomas including MCC and can be detectable in the blood.

### Leukocyte Common Antigen

Leukocyte common antigen is useful to differentiate between lymphomas and carcinomas, as it is positive in lymphomas and negative in carcinomas including MCC.

### S-100

S-100 is positive in most melanomas and glial cell tumors and negative in MCC.

Before cytokeratin-20 and cytokeratin-7, many MCC cases were misdiagnosed as lymphoma, small cell lung carcinoma metastases, or undifferentiated carcinoma. Currently, if immunohistochemistry is carried out properly, MCC diagnosis is typically definitive.

## STAGING AND PROGNOSIS

According to the American Joint Committee on Cancer, there are four clinical stages for MCC based on features at time of presentation. Localized disease is either Stage I (primary lesion ≤ 2 cm) or Stage II (primary lesion > 2 cm). Nodal spread of MCC is stage III, whereas patients presenting with metastatic disease beyond the local node bed have Stage IV disease. Survival after a diagnosis of MCC is highly dependent on the stage at presentation. Patients with truly local only disease have a greater than 90 percent chance of survival, which decreases to approximately 60 percent with nodal involvement, and below 10 percent among those presenting with metastatic disease. Unlike malignant melanoma, if MCC recurs it tends to do so rapidly with 90 percent of recurrences occurring within 3 years of diagnosis (Fig. 120-4A).[10]

### Sentinel Lymph Node Biopsy and Staging of Merkel Cell Carcinoma

Over the past 20 years, sentinel lymph node biopsy (SLNB) has become quite common in staging malignant melanoma presenting with a depth of greater than 1 millimeter. More recently, several studies have indicated that SLNB is also a sensitive test for detecting MCC spread to the lymph nodes.[11–13] SLNB clearly has less morbidity than an elective lymph node dissection. Interestingly, MCC has a much higher rate of involving the lymph nodes (approximately 30 percent of all cases) than melanoma (approximately 5 percent of all cases). If a SLNB is to be carried out properly, it needs to be performed at the time of the wide resection as opposed to after the wide excision when local lymphatics have been disturbed. The importance of SLNB in determining prognosis in MCC can be seen by comparing Figs. 120-4B and 120-4C. The essential difference is that one-third of patients with local only disease as determined by clinical palpation of lymph nodes, in fact have microscopic disease in the lymph nodes that very much affects their subsequent survival.[13] The 5-year survival rate of pathologically staged node-negative patients was 97 percent compared with 5-year survival of node-positive patients of 52 percent [10].

### Radiologic Imaging Studies

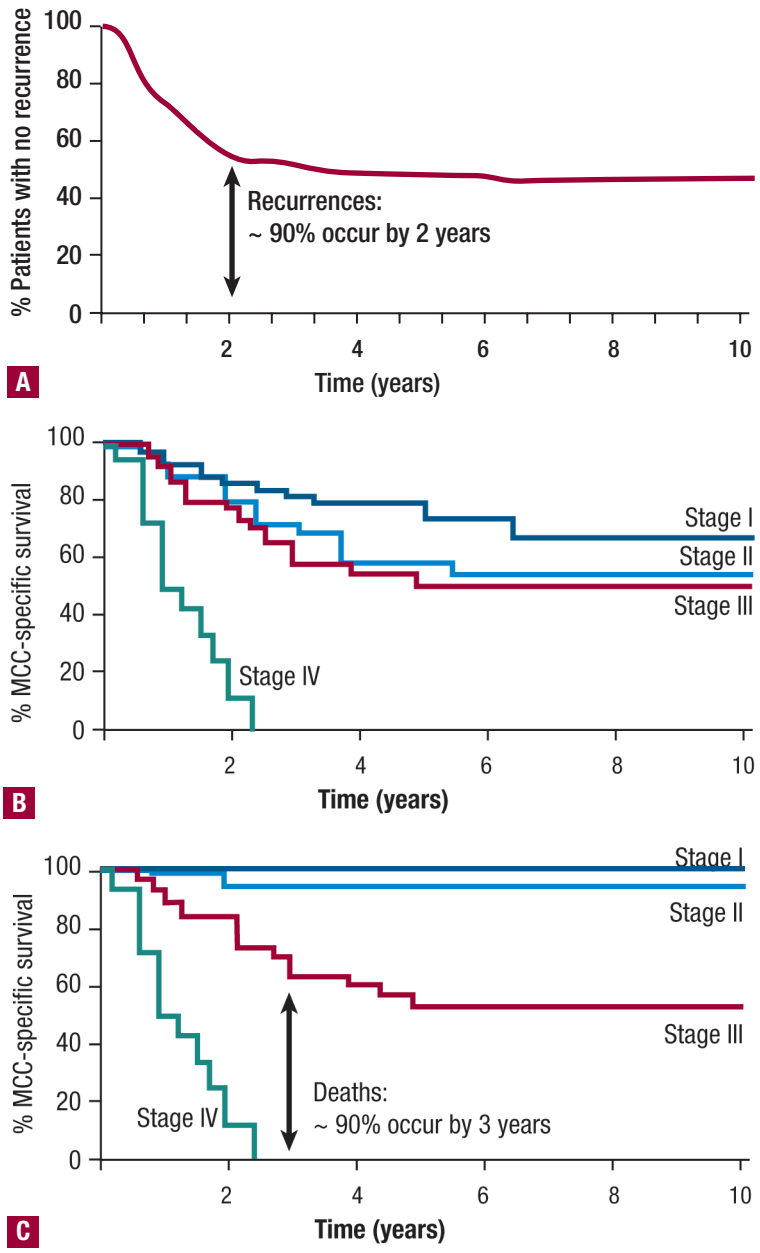
Although most patients who present for management of MCC have not had a SLNB, the majority have had computed tomographic (CT) scans. We studied our own series of patients to determine the sensitivity and specificity of CT scans in patients presenting with MCC.[13] We found that scans were not sensitive at all (missing 90 percent of positive cases) in terms of detecting nodal involvement of MCC as compared with SLNB. Among patients who had low-risk disease (negative sentinel lymph nodes or very small primary tumors) all of the "positive" scan results were, in fact, false positives.[13] We therefore reserve CT scans for patients presenting with more advanced disease, such as positive nodal involvement or clinical evidence of metastatic disease.

## TREATMENT

Optimal therapy for MCC is controversial and there is no broad consensus on how to manage this disease. One summary of multi-institution management is available through the National Comprehensive Cancer Network (http://www.nccn.org). The NCCN generates a treatment algorithm for MCC with annual updates. The best outcome for MCC is clearly obtained when multidisciplinary management is carried out by an experienced team. Each major treatment modality is summarized below.

### Surgery at Primary Site

The initial management in almost all cases of MCC is surgical excision of the tumor. When carried out without subsequent adjuvant radiation, surgery has a relatively high recurrence rate depending on the margins chosen. Surgery alone with 0.5 centimeter margins resulted in a 100 percent recurrence rate in 38 patients.[14] When wide local excision was carried out with 2.5 centimeter margins, the recurrence rate fell to 49 percent.[15] For Mohs surgical excision, the local recurrence rate was 16 percent, which was reduced further to 0 percent in patients who had adjuvant radiation therapy as well.[16] There are no data to suggest that extremely wide excision margins improve overall survival. Depending on the location of the tumor, significant morbidity can result when 2 to 3 centimeter margins are taken. Numerous studies show that if surgery is the sole treatment, recurrence rates are significantly higher than if radiation therapy is added to the regimen. Excision with narrow but clear margins (carried out at the time of SLNB) followed by adjuvant radiation therapy is a reasonable approach to management. Overly aggressive surgery, including amputation, or very wide margins in cosmetically sensitive areas, decreases quality of life, increases morbidity, delays time to initiation of adju-

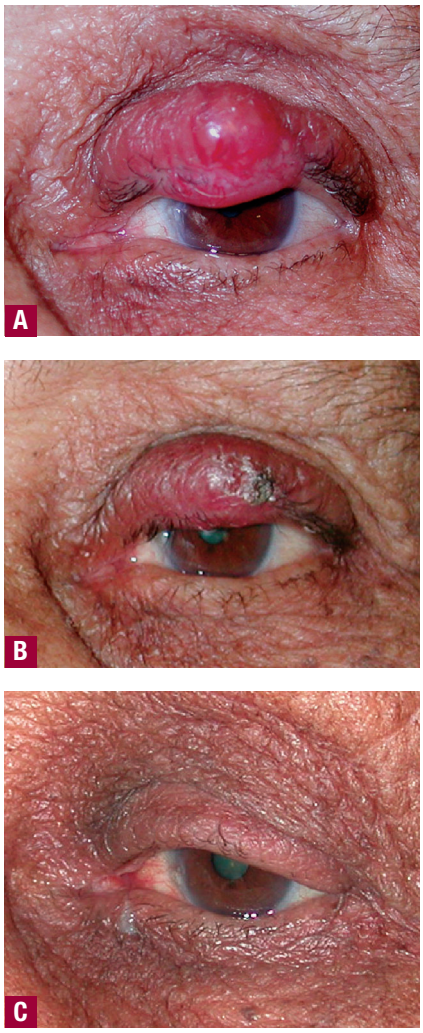



▲ **FIGURE 120-4** Prognosis of Merkel cell carcinoma depends on stage at presentation. **A.** Fraction of patients with Stage I, II, or III disease with no recurrence. Approximately 90 percent of patients who experienced a recurrence did so within 2 years of diagnosis (n, 237 patients). **B.** Disease-specific survival for patients who underwent clinical staging only. Clinical node staging does not provide optimal information for prognosis and treatment (n, 180 patients). MCC, Merkel cell carcinoma. **C.** Disease-specific survival for patients who underwent pathologic staging. Pathologic staging can be done by sentinel lymph node biopsy or other lymph node surgery. At 5 years, patients with no lymph node disease (Stage I or II) had a 97 percent survival rate. Those with lymph node disease (Stage III) had a 52 percent survival at 5 years (n, 145 patients). (Adapted from Allen PJ et al: Merkel cell carcinoma: prognosis and treatment of patients from a single institution. *J Clin Oncol* **23**:2300, 2005, with permission.)

vant radiation, and does not appear to improve survival or local cure rates.

## Surgery at the Draining Node Bed

The role of completion lymphadenectomy is controversial. It is typically carried out if there is gross involvement of the draining node bed clinically or if the SLNB is positive. One study showed a benefit of elective lymph node dissection in decreasing nodal recurrences but this was not associated with overall improved survival and clearly has significant morbidity associated with it.[17,18] The relatively greater morbidity of completion lymphadenectomy in combination with relatively frequent nodal recurrences after

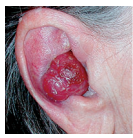


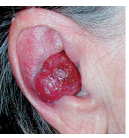

▲ **FIGURE 120-5** **A.** Merkel cell carcinoma on the eyelid arising 3 months before biopsy. The lesion was initially presumed to be a chalazion or cyst. **B.** Using a thin lead shield to protect the globe, the eyelid, the surrounding tissues, and draining lymph node bed were treated with radiation monotherapy. **C.** The patient remains recurrence-free at 2.5 years after diagnosis, and thus has a greater than 95 percent chance of cure at this point.

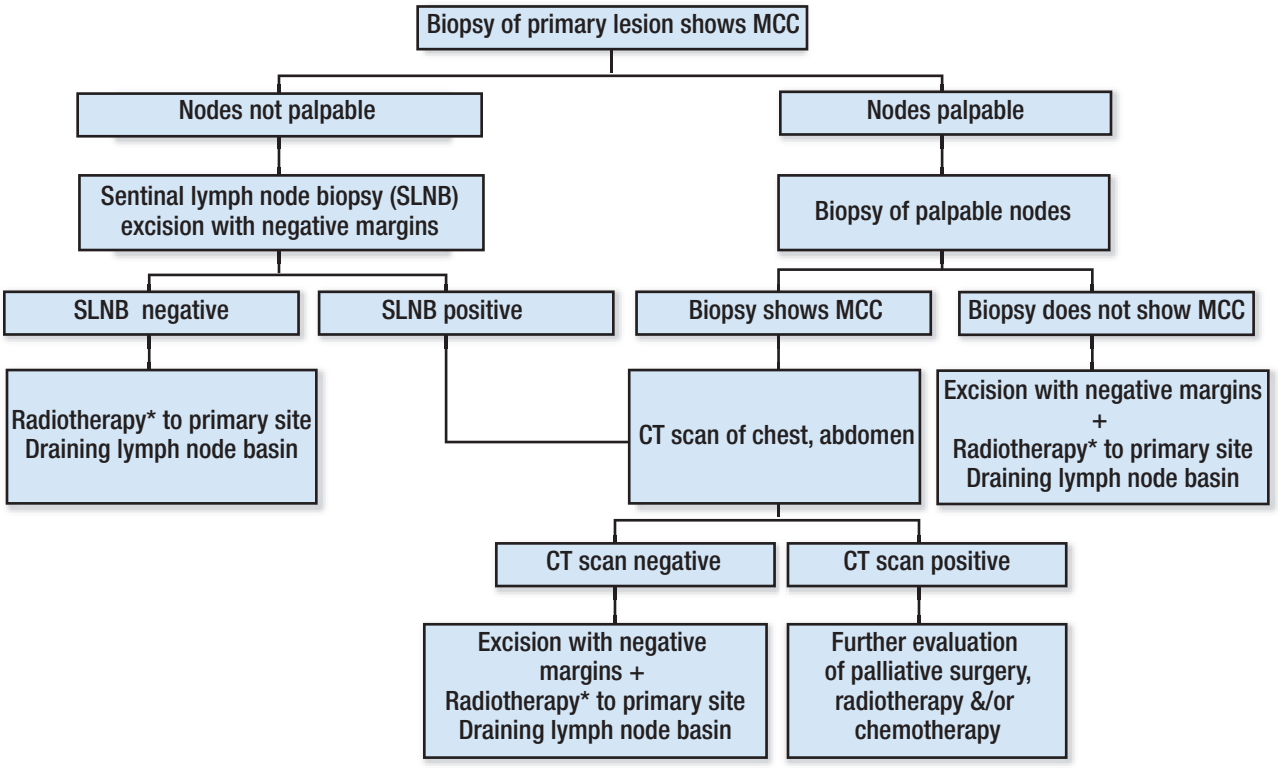
complete nodal dissection has led us to favor radiation therapy to the lymph node bed rather than surgical therapy.

## Radiation Therapy

MCC is an unusually radiosensitive tumor.[14,19] Recently, there have been reports of successful treatment of MCC with radiation as monotherapy. With a 3-year median follow up, there was 0 percent disease recurrence in 9 patients treated with radiation monotherapy.[19] One case treated with radiation monotherapy is shown in Fig. 120-5. In most of these cases, the lesion was felt to be inoperable and radiation was given for palliation, but








▲ **FIGURE 120-6** Approach to the patient with Merkel cell carcinoma (MCC). *Recommended radiation therapy dose (National Comprehensive Cancer Center Guidelines for MCC, 2006): 45–50 Gy for primary site with negative excision margins and node bed with no palpable disease. 55–60 Gy for primary site with positive excision margins and node bed with palpable disease. Radiation therapy given in 2-Gy fractions, 5 times/week over 4–6 weeks.

resulted in at least local cure in almost all cases. Data to support radiation as monotherapy remains very scant at this time.

The much more common use of radiation is as an adjuvant to surgery. Adjuvant radiation clearly is critical if surgical margins are positive or if margins are relatively narrow. Adjuvant radiation therapy to the draining node bed is an excellent means of treating sentinel lymph node-positive patients. Numerous studies, although mostly retrospective case studies, indicate a statistically significant improved local and nodal rate of control in this cancer if radiation is added.[20] The typical doses of radiation for MCC are shown in the legend of Fig. 120-6. Acute side effects from radiation therapy include erythema at the site and mild-to-moderate fatigue that peaks towards the end of radiation and usually resolves within 1 to 2 months of completing a 5-week course. Chronic radiation skin changes include temporary or permanent alopecia within the irradiated field, epidermal atrophy, loss of adnexal structures leading to skin or mucosal dryness, and risk of subsequent secondary skin cancers in the irradiated region in patients with a life expectancy of greater than 20 years after the radiation treatment. Perhaps the most significant potential side effect is lymphedema. This is more commonly an issue in lower extremities, when radiation therapy is given to the inguinal lymph nodes, especially after surgery has also been carried out in that region.

## Chemotherapy

The most commonly used regimen in MCC is the combination of carboplatin and etoposide. Chemotherapy is without a doubt useful in palliation for symptomatic disease that is otherwise inoperable. Most patients who have not received chemotherapy yet have a significant response with shrinkage of the tumor. Unfortunately, in almost all cases, the tumor grows back and is resistant to chemotherapy even if entirely different agents are used on a subsequent round of chemotherapy. After careful analysis of the literature, we currently do not recommend adjuvant chemotherapy for patients whose MCC has been treated with surgery, radiation therapy, or both. There are six reasons why we currently do not recommend adjuvant chemotherapy.

1. Mortality: there is a 4 to 7 percent acute death rate due to adjuvant chemotherapy in MCC partly due to the fact that these patients are often elderly.[21,22]
2. Morbidity: Neutropenia occurs in 60 percent of patients with fever, and sepsis in 40 percent.[23]
3. Decreased quality of life: this is quite severe in this older population, including fatigue, hair loss, nausea, and vomiting.
4. Resistance to chemotherapy: MCC that recurs after chemotherapy is less responsive to later palliative chemotherapy.
5. Immunity: Chemotherapy suppresses immune function and this is known in general to be very important in preventing and controlling MCC.
6. Apparent poorer outcomes: Among patients with nodal disease, there was a 60 percent survival if chemotherapy was not given among 53 patients. In contrast, survival was only 40 percent among node positive MCC patients who did receive adjuvant chemotherapy .[10] Although this is not a randomized trial and was not statistically significant, it certainly does not suggest a survival benefit for administrating adjuvant chemotherapy.

## Optimal Treatment for Merkel Cell Carcinoma

In general, optimal treatment for MCC should involve obtaining pathologically

clear margins by surgery, typically with 1- to 2-centimeter margins as possible, depending on the site. More narrow margins or even positive margins can often be effectively treated by local radiation, typically extending 3- to 5-centimeters beyond the tumor bed. We also recommend treating the draining lymph node bed, likely with radiation therapy, for patients with high-risk disease including a positive SLNB, immune suppression, or a tumor greater than 2 centimeters in diameter. Fig. 120-6 summarizes a treatment plan for patients with MCC.

## CLINICAL COURSE AND COMPLICATIONS

In more than 90 percent of cases, MCC is an unanticipated diagnosis at the time the pathology results become known. Most commonly, the lesion in question was thought to be a cyst or acneiform lesion. Although most patients and physicians are not familiar with this disease or its specific management, this disease can be lethal and there is a need to initiate therapy rapidly. Because of the rarity of this cancer, patients and physicians increasingly resort to the internet for medical information. One website, http://www.merkelcell.org, is devoted to aiding patients and physicians by presenting current data and referral center availability.

Among patients who experience a recurrence of their MCC, 90 percent of these happen within 2 years of diagnosis. The most common site of recurrence is the draining nodal basin or adjacent skin.[10] The chance of developing metastasis and subsequent death is highly associated with the stage of disease at presentation, varying from greater than 95 percent chance of cure to less than 10 percent chance of cure. For those who have recurrences, the locations and frequencies are skin (28 percent), lymph nodes (27 percent), liver (13 percent), lung (10 percent), bone (10 percent), brain (6 percent), bone marrow (2 percent), pleura (2 percent), and other sites (4 percent).[22] Once MCC has spread to viscera, it is essentially incurable.

Fortunately, for more than 50 percent of patients, a good outcome can be anticipated. Those who have had no recurrences for 3 to 5 years, unlike melanoma, are considered cured. The complications for those who do not experience a metastasis depend very much on the therapy they received. We believe that treatment with surgical excision and radiation therapy as outlined in this chapter has relatively minimal complication rates and the best possible chance of cure based on current literature. However, for those who receive very aggressive surgical excision, amputation or chemotherapy for low-risk disease, complication rates tend to be higher without improved outcomes.

## KEY REFERENCES

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