Summary of MMIG Meeting and MCC Forum
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American Academy of Dermatology Annual Meeting
San Antonio, TX

MMIG Working Group: Friday February 1, 2008
MCC Forum: Sunday February 3, 2008

Below are highlights of topics presented at these meetings. Please note that these are unpublished data and are provided to help MMIG members manage their patients and give an overview of what is being done at different centers.

Organized by topic (details below):

1. **Goals of MMIG**
2. **Proposed AJCC Staging System**
3. **Correlation of Breslow Thickness with SLNB Positivity**
4. **Histopathologic Features of MCC Correlating with Survival**
5. **XRT to Primary Tumor Site: Management & Outcomes at Different Centers**
6. **Node Bed Treatment After Positive SLNB: CLND vs XRT**
7. **Merkel Cell Polyomavirus Paper in *Science***
8. **Collection of Patient Data and Material for Studies**

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1. Goals of MMIG (Merkel cell carcinoma Multicenter Interest Group)

- Promote communication and collaborative studies on MCC
- Enhance access to patient data and specimens
- Expand evidence-based care for MCC

MMIG is funded in part by a grant from the Jerry Wachter Fund of the American Cancer Society (www.jw.org).

2. Proposed AJCC staging system

The proposed AJCC MCC staging system was presented by Dr. Lemos. The major change from existing systems is inclusion of substages for method of nodal evaluation (clinical evaluation vs. pathologic evaluation). The proposed staging system is as follows:

Stage I: Local, < 2cm
Ia: Nodes microscopically negative and not clinically detectable
Ib: Nodes not clinically detectable

Stage II: Local, ≥ 2cm
IIa: Nodes microscopically negative and not clinically detectable
IIb: Nodes not clinically detectable
IIc: Primary tumor invading bone/muscle/fascia/cartilage

Stage III: Regional Nodal Disease
IIIa: Micrometastasis
IIIb: Macrometastasis (clinically detectable)

Stage IV: Distant Metastatic Disease

3. Correlation of Breslow Thickness with SLNB Positivity

Drs. Cherpelis (Moffitt) and Bichakjian (U of MI) both presented unpublished data from their institutions showing a correlation between thicker tumors (Breslow thickness) and increased likelihood of positive sentinel lymph node biopsy. Both centers found no clear correlation between tumor diameter and sentinel lymph node involvement. **Thus, Breslow thickness of primary tumor may be a better predictor of SLN involvement than primary tumor diameter.**

It is strongly suggested that MCC clinicians speak with their pathologists and request that Breslow thickness be recorded routinely for MCC in "mm of thickness" for primary MCC tumors. If the base of the lesion has been transected, "at least _____mm" should be noted. Criteria for measuring thickness are identical to those for melanoma. The College of American Pathologists (CAP) will list Breslow thickness as a recommended parameter for reporting when reading out MCC pathology (as well as lymphovascular invasion and tumor infiltrating lymphocytes).

4. Histopathologic Features of MCC Correlating with Survival

Dr. Klaus Busam (MSKCC) presented unpublished data correlating histopathologic parameters with survival. Lymphovascular invasion, infiltrative (not circumscribed/nodular) growth pattern, tumor thickness (Breslow), and size were statistically associated with poorer outcomes in univariate analyses. Number of mitoses is not useful in MCC, as nearly all tumors have many mitoses.

5. XRT to Primary Tumor Site: Management & Outcomes at Different Centers

Dr. Bichakjian presented data from his series of patients and the treatment algorithm used at the University of Michigan. For primary tumors ≤2cm, WLE is performed (1cm margins if <1cm, 1-2cm margins if 1-2cm). Adjuvant XRT is only given if angiolymphatic invasion is present or if surgical margins are close. For tumors >2cm, adjuvant XRT follows WLE in all cases. While duration of follow-up is limited (median ~1 year), they have had excellent local control, with no local recurrences in 48 patients; 3 patients had in-transit recurrences.

Summary of varying protocols for adjuvant XRT:
(Note: all sites report excellent local control)
Memorial Sloan Kettering Cancer Center: no XRT following WLE in majority of cases
Univ Washington: XRT to primary site following WLE in almost all cases
Univ California, San Francisco: XRT to primary site following WLE in almost all cases
Univ Michigan: XRT only if >2cm primary or if angiolymphatic invasion or close surgical margins are present

6. Node Bed Treatment After Positive SLNB: CLND vs XRT

Dr. Bichakjian presented additional data from his series of patients regarding treatment of a nodal basin following a positive SLNB. At the University of Michigan, most patients undergo a completion LN dissection (CLND) without XRT. Adjuvant XRT is reserved for patients who have extranodal extension or >2 nodes involved after CLND, or XRT is given to the node bed for patients who are not surgical candidates for CLND.
Dr. Nghiem presented data from an MCC patient series in Seattle showing no nodal recurrences following XRT monotherapy to the involved LN basin for SLNB-positive cases.

Treatment of the involved nodal basin (positive SLNB) varies by center:
Univ Michigan: CLND in all cases; adjuvant XRT if >2 nodes involved or if extranodal extension present
Memorial Sloan Kettering Cancer Center: XRT monotherapy in most cases
Univ Washington: XRT monotherapy in most cases
Univ California, San Francisco: XRT monotherapy in most cases

7. Merkel Cell Polyomavirus Paper in *Science*

Dr. Nghiem presented a summary of a recent Science paper describing a new virus, Merkel cell polyomavirus. The authors (Drs. Moore and Chang, who previously identified and described the Kaposi's sarcoma herpesvirus) used sophisticated techniques to identify a new virus which they called Merkel cell polyomavirus (MCV). MCV was detected in 8 of 10 MCC tumors and only in 16% of normal skin samples. In 6 of the tumor samples positive for the virus, the virus was integrated into the host genome. Only 3 other known polyomaviruses infect humans, but none of those integrate into the genome or cause cancer. Viral integration into the host genome is a feature seen in cancer-causing polyomaviruses in animals. While MCV is certainly not necessary or sufficient to cause MCC, it may play a role in oncogenesis of a subset of MCCs. This is an exciting finding that opens the opportunity for further research and may help to explain the increased risk of MCC in immune compromised patients.

8. Collection of Patient Data and Material for Studies

It was emphasized that all centers should ideally collect patient data and specimens for their own future research purposes. The University of Washington group has IRB approval to collect data and specimens on MCC patients and is happy to provide sample documents to other centers.

MMIG Speakers: February 1, 2008
Chris Bichakjian, University of Michigan
Basil Cherpelis, Moffitt Cancer Center, University of South Florida
Bianca Lemos, University of Washington
Paul Nghiem, University of Washington

Forum Speakers: February 3, 2008
Chris Bichakjian, University of Michigan
Klaus Busam, Memorial Sloan-Kettering Cancer Center
Bianca Lemos, University of Washington
Kevan Lewis, Brown University
Tara Miller, University of California, San Francisco
Paul Nghiem, University of Washington

In attendance at the MMIG meeting:
Chris Bichakjian (Michigan)
Clara Curiel (Arizona)
Basil Cherpelis (Moffitt)
Tim Johnson (Michigan)
Sheela Kerstetter (MGH)
Peter Lee (Minnesota)
Bianca Lemos (UW)
Nanette Liegeois (Hopkins)
Paul Nghiem (UW)
Clark Otley (Mayo)
Brian Rothschild (Colorado)
Chrys Schmults (DFCI)
Thomas Stasko (Vanderbilt)
Martina Ulrich (Berlin)
Richard Wang (UTSW)
Nathalie Zeitouni (Roswell Park)