February 12, 2007

Brief summary of Merkel Cell Carcinoma Multicenter Interest Group (MMIG) meeting

Dear Colleagues:

For those of you who could not attend, we had a very interesting and lively discussion on Friday evening, February 2, in Washington DC, for our second annual MMIG meeting. What follows is a brief summary of the presentations and discussion.

Dr. Siegrid Yu, co-organizer of the meeting, welcomed people and thanked Schering for an unrestricted grant used to cover costs of the meeting room and refreshments.

As Dr. Michelle Heath was unable to attend due to illness, Dr. Paul Nghiem of University of Washington/Seattle Cancer Care Alliance gave a summary of findings relating to the clinical presentation of Merkel Cell Carcinoma. As is well known, risk factors include fair skin, UV exposure, immunosuppression, and age over 50. In addition, in our cohort we also found that over 80% of lesions were non-tender and roughly 70% had grown very rapidly within one month prior to biopsy. The single most common presumptive diagnosis was a cyst or folliculitis lesion. A possible mnemonic for the key MCC risk factors is: "AEIOU" as in the vowels:

Asymptomatic (non-tender)

Expanding rapidly

Immune suppressed

Older than 50 years of age

UV-exposed fair skin

Dr. Klaus Busam of Memorial Sloan Kettering Cancer Center (MSKCC) gave a beautiful presentation of the histologic features of Merkel Cell Carcinoma both in classical and atypical presentation settings. He noted that while cytokeratin 20 is a fantastic marker for Merkel Cell Carcinoma in general, there are rare cases of cytokeratin 20 negative Merkel Cell Carcinomas and also rare cases in which cytokeratin 20 may be in a diffuse pattern as opposed to the classic perinuclear dot pattern. Neither of these variants appears to have different biologic behavior. He also showed several examples of squamous cell carcinoma occurring in conjunction with Merkel Cell Carcinoma raising interesting questions about the etiology of Merkel Cell Carcinoma. He is analyzing the largest series of Merkel Cell Carcinoma histologic specimens in conjunction with outcomes data and hopes to have an update for us next year as to possible histologic prognostic factors in Merkel Cell Carcinoma. There was agreement now though that there is no established independent prognostic factor for Merkel Cell Carcinoma based on histology.

Dr. Dan Coit of MSKCC gave a fascinating summary of his most extensive experience with Merkel Cell Carcinoma at Memorial Sloan-Kettering Cancer Center where their numbers of patients now approach 500. As a pancreatic and gastric cancer

surgeon, Dan noted that survival for Merkel Cell Carcinoma is, relative to those diseases, extremely favorable and in his series, a good deal better than the retrospective literature. A major focus of discussion was the exceedingly low (approximately 10%) rate of local recurrence in his series of patients when treated essentially with approximately 1.1 centimeter margins on average and without radiation therapy in about 90% of cases. Dr. Coit pointed out that this was largely a prospective series and that retrospective series may bias towards worse outcomes...a point that Dr Robert Stern agreed was typically the case. Approximately 10% of Dr. Coit's patients were given adjuvant radiation...mostly those at the highest risk for recurrence.

Dr. Clark Otley of Mayo Clinic presented his recently published data on over 1,200 patients extracted from the literature who had a primary Merkel Cell diagnosed in the skin with surgical excision with clear margins who then underwent adjuvant radiation therapy or not. In this extremely large retrospective series, there was roughly a three-fold increase in local as well as regional nodal recurrences among patients who did not receive radiation therapy. This was highly statistically significant with $p > .001$. Clark also noted his own personal experience of carrying out Mohs surgery in the past on Merkel Cell Carcinomas only to find discontiguous tumor at margins that had previously been clear. This led him to largely shift away from using Mohs surgery for Merkel Cell Carcinoma and to be a proponent of local radiation therapy.

Dr. Paul Nghiem summarized the recent American Joint Committee on Cancer (AJCC) meeting at which it was decided that Merkel Cell Carcinoma would be staged independently of other nonmelanoma skin cancers. Currently, MCC is lumped into one chapter in the AJCC staging manual with 80 other skin cancer diagnoses. Under the leadership of Dr. Arthur Sober, the plan is that Merkel Cell Carcinoma will be considered separately with its own staging system per the AJCC. Currently, there are four published and conflicting staging systems (the most recent being from Mike Veness in Australia using 1 cm as the cutoff between Stage I and II.) Clearly these multiple staging systems complicate the literature for this disease.

The plan will be to gather existing database sources as rapidly as possible over the next few months to look at a rational staging system for MCC based on existing data. This will almost certainly mean that stages one and two will be local low risk and local high risk disease, respectively, stage three will be nodal disease and stage four will be metastatic disease. Having a dedicated staging system will assist in clarifying the literature in the future and also improve the quality of data that is captured by tumor registrars throughout the country when they are coding Merkel Cell Carcinoma. These data will then be available for future studies through the National Cancer DataBase.

Discussion was lively for all sections of this session and it was great fun to get a critical mass of people together to discuss this disease. We are actively trying to decide if we'll stick with an Ancillary format for next year's meeting (probably more likely), or potentially go to a daytime more 'official' session.

Summary by Paul Nghiem, MD, PhD