Merkel Cell Carcinoma: Epidemiological Study with Special Reference to Polyomavirus and Vascular Factors in Pathogenesis

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Heli Kukko defended her PhD thesis in Helsinki on 13 May 2011. The thesis was supervised by Associate Professor Tom Böhling, Department of Pathology and HUSLAB, University of Helsinki and Helsinki University Hospital and Associate Professor Virve Koljonen, Department of Plastic Surgery, Helsinki University Hospital, Helsinki, Finland. The opponent was Professor Hans-Günter Machens, University of München, Germany. The thesis is available at: http://urn.fi/URN:ISBN:978-952-10-6940-6.

Merkel cell carcinoma (MCC) is a rare cutaneous malignancy that occurs predominantly on sun-exposed areas of skin. A new polyomavirus (MCPyV) was identified in MCC tumour tissues in 2008, suggesting that viral infection may be an aetiological factor. A typical MCC is a rapidly-growing painless purple nodule. In its early stage it can be misjudged by its appearance as a cyst or abscess. Recurrences are common, and approximately half of the patients will develop lymph node metastases and one-third of the patents will have distant metastases. It mostly affects elderly persons, with an average age of 70 years at the time of diagnosis. MCC was first described in 1972 and the first patient with MCC in Finland was identified in 1983. MCC has been poorly recognized, but increased awareness and better diagnostic accuracy has increased the reported incidence.

In this study, all cases with a notation of MCC during 1979–2008 were obtained from the Finnish Cancer Registry. Based on this data, the incidence is 0.11 for men and 0.12 for women, which is similar to that in other Nordic countries, but lower than in the USA. For clinical series, the files of patients diagnosed with MCC during 1983–2004 were reviewed, and the tissue samples were re-evaluated, if available (n=181). One-third of the patients were men, and the most common site of the primary tumour was the head and neck (53%). The majority of patients (86%) presented with a clinically node-negative (Stage I or II) disease, but the disease recurred in 38% of them.

The treatment schemes were heterogeneous. No additional benefit from a wide margin (≥ 2 cm) was found compared with a margin of 0.1–1.9 cm, but intralesional excision was more often associated with local recurrence. None of the patients with Stage I–II disease who had received postoperative radiotherapy had local recurrence during the follow-up period. The 5-year relative survival ratio for Stage I disease was 68%, for Stage II 67%, for Stage III 16%, and for Stage IV 0%. The relative excess risk of death was significantly lower among women than among men.

Some of the tissue samples were further analysed for vascular invasion (n=126) by immunohistochemistry using vascular endothelial markers CD-31 and D2-40. Vascular invasion was seen in 93% of the samples and was observed in very small tumours (<5 mm). The tissue samples were also analysed for the presence of MCPyV, using polymerase chain reaction (PCR) and quantitative PCR. MCPyV DNA was present in 80% of 114 samples studied. The patients with virus-positive tumours had better overall survival than patients with virus-negative tumours.

Fig. 1. Heli Kavola (formerly Kukko) defended her PhD thesis in Helsinki, Finland on 13 May 2011. The opponent was Professor Hans-Günther Machens (*left*). Professor Erkki Tukiainen (*right*) acted as custos.

Immunohistochemical analyses were performed for the expression of VEGFR-2 (n=21) and endostatin (n=19), but they had no prognostic value.

Our results support the concept of treating MCC with margin-negative excision and radiotherapy to the tumour bed to reduce local recurrence.

The finding of a high frequency of lymphovascular invasion reduces its value as a prognostic factor, but emphasizes the role of sentinel node biopsy even in very small primary MCC.