CASE REPORT

Spontaneous regression and recurrence of stage III Merkel cell carcinoma

Sandra Catharina Petronella Jansen,¹ Christine P M Groeneveld-Haenen,² Paul J J M Klinkhamer,³ Rudi M H Roumen⁴

¹Department of Surgery, Maxima Medical Centre, Veldhoven, Noord-Brabant, The Netherlands

²Department of Dermatology, Máxima Medical Centre, Veldhoven, Noord-Brabant, The Netherlands

³Department of Pathology, PAMM, Eindhoven, Noord-Brabant, The Netherlands

⁴Department of Surgery, Maxima Medisch Centrum, Veldhoven, Noord-Brabant, The Netherlands

Correspondence to

Sandra Catharina Petronella Jansen, scp.jansen@student.maastrichtuniversity.nl

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SUMMARY

Merkel cell carcinoma (MCC) is a malignant neuroendocrine carcinoma originating in the skin. It is typically aggressive with a tendency to recur locally and metastasise. There have been several case reports about spontaneous regression of MCC over the past years, but to the best of our knowledge this is the first case of a regional lymph node metastasised MCC with complete spontaneous regression and recurrence. In addition, the primary tumour has an unusual localisation on the foot.

BACKGROUND

Merkel cell carcinoma (MCC) is a malignant neuroendocrine carcinoma originating in the skin. It is typically aggressive with a tendency to recur locally and metastasise frequently.¹ Despite its highly malignant character, spontaneous regression appears to be relatively common for MCC. This phenomenon was first described in 1986 by O'Rourke and Bell.² About 34 case reports have been written on this subject since then.^{3–14} Our case reports a complete spontaneous regression of a stage III MCC located on the left foot with regional metastatic spread to the lymph nodes in the left groin. After 9 months, nodal recurrence was diagnosed by ultrasound and cytology, and again histopathological examination of surgically removed nodes showed complete spontaneous regression. A follow-up 5 months later showed renewed enlargement of lymph nodes in the left groin with pathological nodes in the femoral, iliac and obturator field for which radiotherapy was applied.

Since the patient was first diagnosed with MCC, she was—over a period of several years—also diagnosed and treated for other dermatological conditions, namely actinic keratosis, morbus Bowen superficial spreading malignant melanoma and basal cell carcinoma.

CASE PRESENTATION

In June 2011, a 58-year-old Caucasian woman presented to the department of dermatology with a nodular lesion on her left foot, which had emerged 6 months earlier and was growing rapidly (figure 1). It was located at the medial side of the ankle, distal to the malleolus, with a diameter of 2.2 cm and a livid—red, firm and non-ulcerated aspect. A punch biopsy revealed dermal tumour proliferation of relatively small cells. Immunohistochemical staining was positive for anti-pan cytokeratin antibody KL1, CK20, synaptophysin, CD56, chromogranin and EMA (epithelial membrane antigen). No expression

was seen for CK7, S100, BerEp4, TTF-1 and CEA (carcinoembryonic antigen). These results supported a diagnosis of an MCC (figures 2 and 3).

Physical examination revealed an enlarged lymph node in the left groin. Ultrasound of the left groin showed two femoral and two superficial inguinal lymph nodes suspect for metastasis, ranging in size from 11 to 20 mm. Fine-needle aspiration (FNA) confirmed metastasis of the known MCC. Thoracic X-rays, PET and CT of thorax and abdomen showed no signs of metastasis elsewhere, and routine haematology tests and biochemical values were essentially normal. Consequently, the MCC was interpreted as stage III T2N1M0.¹⁵

One month later, the planned surgical excision of the primary tumour and lymph nodes of the left groin was cancelled because spontaneous regression of the primary lesion was observed by the patient. This was confirmed by the surgeon and dermatologist when comparing the present situation with pictures taken earlier (figure 4). Moreover, clinical palpation in combination with an ultrasound, which was performed immediately, pointed out regression of the previously enlarged nodes from over 20 mm to less than 10 mm. Further check-ups noted the regression staying progressive, eventually resulting in small nodes of less than 5 mm. A wide local excision of the primary tumour and a sentinel node procedure were planned about 6 months after the initial diagnosis, essentially because the patient insisted on such procedure. Surprisingly, histopathological study showed no tumour cells in the two samples, but only scar tissue and chronic inflammation (figure 5).

Figure 1 The initial presentation of the primary tumour, localised in the dermis on the medial side of the left foot. Note the biopsy lesion in red.

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Figure 2 The initial biopsy from the primary tumour on the left foot (H&E×100).

The patient remained under strict follow-up. Half a year later another ultrasound was performed because of a neuropathic pain caused by the surgical exploration of the groin. It showed a solitary, pathologically enlarged lymph node and the FNA cytological study again showed malignant cells, comparable to localisation of an MCC. Once again an examination of the groin was performed with excision of the lymph node, using guidance of ultrasound and a radioactive iodine seed to verify the correct node for removal. Remarkably, histopathology again showed no malignant cells.

One and a half years after primary diagnosis, the patient was referred to a medical oncologist and neurologist because of general weakness and backaches. In the proximity of enlarged and rapidly growing lymph nodes, metastatic disease was considered likely. Total spine MRI showed two possibly suspicious lesions, yet the bone scans were negative. A PET scan revealed only pathological activity in the left groin. A liquor sample did not show any malignant cells. The lesions on the MRI were ultimately diagnosed as haemangiomas.

Another open lymph node biopsy was performed, showing a small proliferation of atypical small cells in a miniature part of the lymph node. It was immunohistochemically positive for CK20 and anti-pan cytokeratin antibody KL1, and displayed the

Figure 3 Picture indicating the spontaneous regression of the lesion shown in figure 1 after about 4 weeks.

Figure 4 Immunoperoxidase staining for CK20 with characteristic dot-like positivity (×100).

characteristic dot-like staining pattern consistent with metastasis of the known MCC.

Finally, about 2 years after primary diagnosis, a superficial inguinal and deep femoral lymph node dissection was executed. During the procedure the resection appeared to be irradical, which was confirmed by histopathological examination. Two out of the four lymph nodes contained metastasis of the known MCC. The multidisciplinary oncology team decided to apply locoregional radiotherapy.

DISCUSSION

To the best of our knowledge, this is the first case report of complete spontaneous regression of a stage III MCC with repeated recurrence and regression of malignant lesions with an atypical localisation of the primary tumour on the foot. Currently about 34 case reports have been written on spontaneous regression of MCC (partial or complete), 10 of which cases concern lymph node metastasis (stage III). The common localisation of MCC is sun-exposed skin, mostly in the head and neck region. In the 34 published cases, a vast majority of the primary tumours was localised on the head. One was on the upper leg, three on the forearm and of one report, the position is not known. Median follow-up period was 28 months, ranging from 6 months to 15 years. In none of the cases a recurrence of the MCC was reported.

Despite the differences, our case also bears some similarities to the other cases. That is, in all cases the spontaneous

Figure 5 Biopsy after regression of the primary tumour on the left foot. Sclerosis of the dermis with no residual tumour cells.

regression started after an invasive biopsy procedure was performed. Moreover the histopathological findings after regression showed signs of what appears to be chronic inflammation, as was seen in the present case.

Although the mechanism of complete spontaneous regression of MCC is still poorly understood, several theories have been suggested. The first theory says that the so-called Merkel cell polyomavirus is implicated in the oncogenesis since immunosuppressed patients appear to have an increased risk for developing an MCC. On the other hand, it is suggested that some form of immune modulation may result in (complete) tumour regression. This theory is supported by the various histopathological observations in patients with complete spontaneous regression of MCC, which show signs of chronic inflammation with humoral and cellular immune responses leading to replacement of the original tumour cells.^{1 16} Since biopsy preceded the complete regression in all of the written case reports, it is plausible to conclude that this probably was the triggering mechanism.

Learning points

- ▶ Complete spontaneous regression of MCC can occur in a metastasised stage.
- ▶ After complete spontaneous regression, recurrence is possible (and as this case shows even repeated recurrence and regression can occur).
- ▶ Follow-up after complete spontaneous regression of the MCC is important.

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wrote the article, using the patient information given by CPMG-H, PJJMK and RMHR. CPMG-H, PJJMK and RMHR rectified the case report. SCPJ is the guarantor.

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Patient consent Obtained.

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