NEZVYČAJNÝ PRÍPAD DLHODOBÉHO PREŽÍVANIA PACIENTKY S CHEMOREFRAKTÉRNYM MERKELOVYM KARCINÓMOM

UNUSUAL CASE OF LONG-TERM SURVIVAL OF THE PATIENT WITH CHEMOREFRACTORY MERKEL CELL CARCINOMA

MÁRIA REČKOVÁ[1], LAWRENCE H. EINHORN[2]

[1] ONKOLOGICKÁ KLINIKA, UNIVERZITA KOMENSKÉHO, NOÚ BRATISLAVA, SLOVENSKÁ REPUBLIKA
[2] INDIANA UNIVERSITY, 535 BARNHILL DRIVE INDIANAPOLIS, IN, USA

Súhrn
Prípad prezentuje 46-ročnú pacientku s Merkelovym karcinómom. V iniciálne lokalizovanom štádiu bola liečená chirurgickou resekciou s následnou adjuvantnou chemoterapiou. U pacientky došlo následne k opakovaným lokoregionálnym relapsom v krátkom časovom odstupe od adjuvantnej chemoterapie a nakoniec k relapsu vo vzdialenej lokalizácii. Distantný relaps bol liečený chirurgickou liečbou vzhľadom k predpokladanej chemorefrákternosti ochorenia. Pacientka je po ukončenej liečbe bez známok recidívy ochorenia v trvaní 16+ mesiacov. Prípad poukazuje na významnú úlohu chirurgickej liečby chemorefraktérneho ochorenia. Pretože vzdialený relaps ochorenia bol diagnostikovaný na základe kontrolných rádiografických vyšetrení u asymptomatickej pacientky, má okrem sledovania pacientov fyzikálnym vyšetrením význam aj rádiografické sledovanie, aspoň v určitých prípadoch.

Kľúčové slová: Merkelov karcinóm, chemorefraktérny, rádiografické sledovanie.

Summary
The case report presents a 46-year old patient with Merkel cell carcinoma. Initial treatment of localized disease consisted of surgery followed by adjuvant chemotherapy. Shortly after the adjuvant chemotherapy completion she relapsed several times locoregionaly and ultimately in a distant location. The distant relapse was treated surgically as the disease was considered to be chemorefractory. Since the last treatment, the patient has been disease-free for 16+ months. The case shows the importance of surgical treatment of chemorefractory disease. Because distant relapse was diagnosed by radiographic studies at the time when no other symptoms were presented, radiographic follow-up, at least in some cases, plays a very important role in addition to follow-up with physical examination.

Key words: Merkel cell tumor, drug resistance, radiography, follow-up studies.

Introduction

Merkel cell carcinoma (MCC) is a rare neuroendocrine carcinoma of the skin first described by Toker.1 The natural history of MCC varies. In some patients, the course of disease may be indolent with only localized disease that is well controlled by local excision only. However, MCC is potentially aggressive and usually warrants aggressive therapy. The combination of wide local excision (WLE), therapeutic lymph node dissection, and radiotherapy (RT) has been suggested for treatment of regional disease.2 However, if the initial presentation is not cured, relapses usually occur outside the field of locoregional therapy. Although distant metastases can respond to chemotherapy, the duration of response is brief, similar to the response achieved in extensive small cell lung cancer.

The following case presents a patient with unusual long-term survival of chemorefractory MCC following distant relapse.

Case Report

This is a case of L.E., Caucasian woman diagnosed with MCC. This 46-year old female first presented at Indiana Cancer Center with a 3-week of progressive growth of a blue-reddish nodule localized in the infraorbital region of her left cheek in February 2003. The nodule was 1.5 cm in diameter and was minimally tender on palpation. Short course of antibiotics was administered without improvement. The mass rapidly increased to 3cm in size. In March 2003, excision biopsy revealed Merkel cell carcinoma with positive surgical margins. The patient was referred to plastic surgery for definitive surgical treatment with reconstruction. In April 2003, she underwent wide re-excision with 2cm margin along with left parotidectomy and modified left neck dissection. Metastatic work-up included CT of the chest, abdomen and pelvis. No distant metastases were revealed. She was then treated with 4 courses of adjuvant chemotherapy consisting of cisplatin and etoposide. In September 2003, shortly after the 4th cycle of adjuvant chemotherapy, she relapsed locoregionaly and in the left

cervical lymph nodes. The Merkel cell tumor relapse was confirmed by biopsy. She was treated with a complete surgical resection. However, margins from left neck dissection were positive for malignant cells. Following resection, local radiotherapy with concurrent docetaxel was administered. She finished the treatment in November 2003. The treatment was complicated with weight loss secondary to mucositis and mouth pain, plus an episode of herpes zoster over her left upper extremity and chest.

In April 2004, she suffered a second locoregional relapse in her right supraclavicular lymph nodes that was confirmed by fine needle aspiration. Radiotherapy started in May 2004 and initially included right face and right neck. Again she showed excellent response to the radiation, nevertheless, halfway through the treatment a right tonsillar mass was noticed. Tonsillar biopsy revealed Merkel cell tumor. Radiotherapeutic fields were then adjusted to cover the right tonsillar fosse as well. Radiotherapy was completed in June 2004.

In March 2005, a distant relapse with large pelvic mass was diagnosed during her regular follow-up. CT scan revealed a large ovarian mass and an adrenal lesion. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy and laparoscopic right adrenalectomy. The ovarian mass and the right adrenal demonstrated involvement with Merkel cell carcinoma. She was asymptomatic at the time of distant relapse.

Since the abdominal operation she has remained disease free for 16+ months. PA and lateral chest X-ray and abdominal/pelvic CT scan as well as history and physical exam were all normal in July 2006.

Discussion

MCC is a rare, aggressive neuroendocrine carcinoma with male-to-female ratio of 1:0.9-1.1 and involves more whites than blacks.3 The tumor is usually localized at sun-exposed areas of head and neck (45-55%) or extremities (30-40%) but does occur in the trunk, genitalia, and perianal region with a random distribution.3 More frequent occurrence was reported in immunocompromised people. MCC stains with immunohistochemistry for neuron specific enolase, synaptophysin and chromogranin. It is felt to represent a small cell carcinoma of the skin. Unlike small cell lung cancer there is no direct correlation to cigarette smoking. MCC has a high propensity for local recurrence (20% to 75%), regional node metastases (31% to 80%), and distant metastases (26% to 75%), and approximately one-third of patients eventually die of the disease.4 Although MCC is a highly aggressive and potentially lethal cancer, spontaneous regression has been reported. The disease is staged according to presence of localized disease (stage I), locoregional metastases (stage II) or distant metastases (stage III). Recommended management usually consists of wide local excision (WLE) with 1 cm to 3 cm margins. However, treatment guidelines are not well defined because of tumor rarity, which makes randomized clinical trials with sufficient power difficult. Reported recurrence rates after primary therapy for MCC with surgery alone are between 22% and 100%.4 Elective lymph node dissection and adjuvant radiotherapy decreases the rate of locoregional recurrence, however has no marked influence on overall survival.2 Patients with involved nodes or clinically aggressive disease are usually treated with WLE, locoregional radiation therapy and chemotherapy regimens utilized in small cell lung cancer, such as cisplatin or carboplatin and etoposide.5-10 High-risk MCC was defined as having at least one of the following criteria: primary size greater than 1cm, node involvement, recurrence following initial surgery (the recurrence has to be outside of the previous radiation field), gross residual disease after surgery, or occult primary with involved lymph nodes.8 Like other neuroendocrine tumors the Merkel cell tumors are highly chemosensitive. Although distant metastases can respond to chemotherapy, the duration of response is brief, similar to what is achieved in extensive small cell lung cancer.

In this report, the patient relapsed locoregionally shortly after the end of initial systemic adjuvant treatment with cisplatin and etoposide, and thus her disease was considered chemorefractory. She experienced two locoregional nodal and tonsillar relapses within 5 months of chemotherapy completion. These were successfully controlled with radiotherapy. Then she developed distant visceral relapse with a 15x20 cm ovarian mass and a 6.4 cm adrenal mass. These were resected and she remains progression free for 16+ months.

Conclusion

The case of L.E. is unusual because of the long disease free interval (16+ months) of chemorefractory disease following both locoregional and distant relapse. The case shows the important role of surgical treatment in chemorefractory disease. Because the distant relapse was diagnosed by radiographic studies (CT scans) at a time when no symptoms were presented, radiographic follow-up, at least in some cases, appears to play a very important role in addition to follow-up by physical examination.

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Correspodence:
MUDr. Mária Rečková
Onkologická klinika, Univerzita Komenského, národný onkologický ústav,
Klenova 1, 833 10 Bratislava Slovenská republika
tel: +421 903544558, e-mail: maryrecka@gmail.com

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