A Case of Metastatic Basal Cell Carcinoma Treated with Cisplatin and Adriamycin

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A 72-year-old man was referred to our hospital for treatment of an ulcer that had been growing on his back for 10 years. Physical examination showed an ulcerated tumor from the neck to the back and swollen cervical lymph nodes. The tumor size was 12×9 cm. Histology of the biopsy showed a nodular and morpheic basal cell carcinoma (BCC). A chest computed tomography (CT) scan showed multiple lung tumors. CT-guided biopsy of the lung and the cervical lymph node revealed metastatic basal cell carcinoma (MBCC). The primary skin tumor was resected and a total of 10 courses of cisplatin (25 mg/m²/day ×75%) and adriamycin (50 mg/m² ×75%) were administered for metastatic basal cell carcinoma (MBCC). The patient died 5 years and 3 months after his first visit. Autopsy revealed MBCC in the lung, kidney, pancreas, several lymph nodes, liver and bone. A portion of the tumor cells were composed of squamoid cells with eosinophilic cytoplasm, large nuclei, lack of the characteristic peripheral palisading and retraction artifacts, and variable cytoplasmic keratinization. These pathological findings were compatible with basosquamous cell carcinoma. Chemotherapy was effective for MBCC in this patient. (J Nippon Med Sch 2017; 84: 286–290)

Key words: metastatic basal cell carcinoma, cisplatin, adriamycin, lung metastasis, lymph node metastasis

Introduction
Metastatic basal cell carcinoma (MBCC) is rare, ranging from 0.0028 to 0.55% of basal cell carcinoma (BCC) cases¹⁻³. No previous study has reported that MBCC can be effectively treated with a combination therapy of cisplatin and adriamycin. Evidence-based treatments for MBCC have not yet been established. Herein, we report a case of extensive MBCC in which an excellent response was achieved with chemotherapy.

Case Report
A 72-year-old man was referred to our hospital for treatment of an ulcer that had been growing on his back for 10 years. Physical examination revealed an ulcerated tumor from the upper part of the back to the cervical region, and swollen cervical lymph nodes (Fig. 1-a and b). The tumor size was 12×9 cm. A red nodule, 1 cm in diameter, on his neck was located 5 cm from the ulcerated tumor (Fig. 1-c). The biopsy of the ulcerated tumor showed a nodular and morpheic BCC histologically (Fig. 1-d and e). The red nodule was located in an area of subcutaneous tissue far from the primary tumor and was not continuous with the primary tumor pathologically, so we considered it to be a subcutaneous MBCC. Magnetic resonance imaging (MRI) showed a supraclavicular node and many enlarged cervical lymph nodes. A lymph node biopsy revealed BCC. Multiple bilateral lung nodules were detected by computed tomography (CT) (Fig. 2-a). A CT guided biopsy of the lung tumor revealed metastasis of the BCC. The primary ulcerated skin tumor was excised with a 1 cm margin, and total excision of the left cervical lymph node and subcutaneous tumor on the...
Metastatic Basal Cell Carcinoma

Fig. 1 (a, b) Physical examination revealed an ulcerated tumor from the upper part of the back to the cervical region and swelling of the patient's cervical lymph nodes. (c) A red tumor 1 cm in diameter was located 5 cm from the ulcerated tumor. (d)–(e) Histopathology of the biopsy specimen (hematoxylin-eosin stain). (d) Tumor islands of basaloïd cells can be seen in the dermis. (e) Linear cords and strands are intermingled with sclerotic collagen.

Fig. 2 (a) Chest CT scan before chemotherapy. (b) After one course of chemotherapy, the chest CT scan showed a 63.6% unidimensional reduction in the size of the lung nodules. (c, d) A chest CT scan revealed no reduction in their size of the lung nodules one month after 5 cycles of therapy. (e) The lung nodules located in the lower lobe had again progressed 5 months after 5 cycles of therapy. (f) The size of the lung nodules was reduced on the chest CT scan 1 month after 7 cycles of therapy. Yellow circles show metastatic lesions in the lung.

back of the head was undertaken. The histopathological examination revealed BCC and a diagnosis of MBCC to the lung, lymph nodes, and subcutaneous region was made.

The patient received a regimen of cisplatin, 25 mg/m²/day × 75% (35 mg), via an intravenous bolus from day 1 to day 3; adriamycin, 50 mg/m²×75% (70 mg), via an intravenous bolus from day 1. After 1 course of chemother-
apy, a follow-up chest CT scan showed a 63.6% reduction in the size of the lung nodules (Fig. 2-b). Although a partial response was achieved after the 3 courses (Fig. 2-c and d), there was a recurrence of lung nodules in the lower lobe within 15 months (Fig. 2-e). Following treatment with 8 courses of the therapy, the size of the nodules had not remarkably changed, and the chemotherapy was temporarily discontinued (Fig. 2-f). A total of 10 courses of chemotherapy later, the lung nodules progressed and a chest CT showed osteosclerotic changes in the left tenth rib and left shoulder joint and osteolytic changes in the right shoulder joint, indicating bone metastases. The patient died 51 months after his first visit. Autopsy revealed metastasis of the BCC to the lung, kidney, pancreas, several lymph nodes, liver and bone, a portion of which were compatible with basosquamous cell carcinoma (BSC) or metastatic SCC. They showed several nests composed of squamoid cells with eosinophilic cytoplasm, large nuclei, lack of the characteristic peripheral palisading and retraction artifacts, and variable cytoplasmic keratinization except in the lung and bone (Fig. 3). Immunohistochemical staining of the metastatic lesions, except in the lung, was positive for epithelial membrane antigen (EMA, monoclonal, Roche, Indianapolis, USA) and negative for anti-epithelial antigen (Ber-EP4, monoclonal, DAKO, Kyoto, Japan), whereas the primary skin lesion, lung metastatic lesion, and left cervical lymph node stained positive for Ber-EP4 and negative for EMA (data not shown). Diffuse alveolar damage was determined to be the cause of death.

Discussion

The important characteristics of our case were as follows: 1) BCC metastasis to the lung, lymph nodes and bone; 2) The chemotherapy was effective in that it prolonged the life of the patient; 3) Autopsy revealed metastasis of BCC to several organs, a portion of which were compatible with BSC or metastatic SCC. Beadles first described a patient with MBCC, Cortran, Lattes and Kessler described the diagnostic criteria for this condition, and our case was compatible with these criteria.

In Japan, to our knowledge, 58 cases were reported in the literature from 1980 through 2017. This original data was obtained from MEDLINE searches using PubMed or the Japan Medical Abstracts Society (ICHUSHI) database. We compared the characteristics of these 58 Japanese
cases of MBCC with those of 1,227 cases of non-MBCC from 2001 to 2005 that Ansai et al. described. The male/female ratios were 1.1:1 for MBCC and 1:1.3 for non-MBCC. The ages at diagnosis of the primary lesion were approximately 66.4 ± 14.2 years for MBCC and 70.1 ± 13.9 years for non-MBCC. These were similar to those in reports by Ashley et al. and von Domarus and Stevens. MBCC occurred in the trunk (43%), head and neck (46%) and extremities (9%), whereas non-MBCC occurred mostly in the face (69.1%). Histopathologically, MBCC was comprised of the infiltrative/morpheic type (53%), nodular and solid type (46%), and nonsuperficial type, whereas non-MBCC was comprised of the nodular type (77.3%), superficial type (9.8%) and morpheic type (9.7%) BCC. The BCCs most commonly metastasized to the regional lymph nodes (63%), lungs (36%), bone (19%), and skin (12%). Seventy-four percent of the primary tumors were larger than 5 cm, the interval between the onset of tumor and metastasis was approximately 8.5 years, and the time to death after diagnosis of metastasis was approximately 28 months. BCC tumors more than 5 cm in diameter showed a 25% incidence of metastasis, which increased to 50% for lesions more than 10 cm in diameter.

In this case, the histopathology of the primary skin tumor and lung and cervical lymph node metastases confirmed BCC, but the kidney, pancreas, several lymph nodes and liver had features of BSC or metastatic SCC. Although the lymph nodes showed BCC at biopsy, they showed BSC or metastatic SCC features in the autopsy diagnosis. Moreover, there were no primary SCC lesions in several organs. Iarrobino et al. reported a similar case whose patient had metastatic SCC in an axillary lymph node after treatment of MBCC with vismodegib and combination therapy of cisplatin and adriamycin although lymph nodes before therapy revealed BCC histologically. In addition, Ransohoff et al. underwent exome sequencing and compared primary BCC and lymph node BCC before vismodegib administration and lymph node SCC after vismodegib administration. They found that recurrent lymph node SCC had a similar mutation and genomic identity to the original BCC. They also concluded the possibility of alterations in signaling of the BCC to squamous differentiation. Although our patient was not treated with a target therapy, we have suggested that BCC can mutate to SCC, potentially as a mechanism of tumor escape or resistance to chemotherapy.

The first report of successful treatment for MBCC was published in 1978 in a phase I trial of cisplatin. Guthrie et al. reported that combination therapy using cisplatin and adriamycin with MBCC was highly effective in 1985. In addition, the same authors reported good results with the same combination therapy in a larger scale study in 1990. The median time to progression was 36.8 months.

We searched for MBCC case reports in the literature that were treated with cisplatin and adriamycin using PubMed or the ICHUSHI database. In Japan, 8 MBCC patients received cisplatin and adriamycin combination therapy or carboplatin and epirubicin therapy with few side effects. A total of 4 patients had partial responses. In 1 patient the disease progressed, but the details of the other 3 are unknown, and the median progression time was 39 months. Those findings indicated that this therapy was effective in prolonging life for patients with MBCC, compared with the median survival time, which has been found to be as short as 8 months after the onset of metastatic disease without chemotherapy.

In our case, a total of 10 courses of therapy were effective in slowing the progression of an MBCC tumor and extending the patient’s life. Based on our patient, and past literature reviews, cisplatin and adriamycin combination therapy remains a key treatment with potential usefulness for at least some patients with MBCC.

Conflict of Interest: The authors declare no conflicts of interest.

References

10. Snow SN, Sahl W, Lo JS, Mohs FE, Warner T, Dekkinga...


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