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Pathological complete response to preoperative avelumab treatment in a patient with advanced Merkel cell carcinoma

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To the Editor:

Merkel cell carcinoma (MCC) is an aggressive and rare skin cancer with neuroendocrine features. In patients with advanced MCC, the 5-year overall survival rates have been reported to be 35.4%, and 13.5% for those with nodal and distant metastatic disease, respectively [1]. Recently, avelumab, an anti-PD-L1 inhibitor, was approved for treating advanced MCC and has shown a complete response rate of 13.8% [2]. Herein, we report a patient with advanced MCC of the eyelid in which a pathological complete response to avelumab was confirmed.

A 67-year-old woman visited the clinic complaining of rapidly growing nodules in her lower eyelid. The previous physician had performed a biopsy and diagnosed MCC. Despite two resections, the tumor

was not completely removed and recurred rapidly. At the first visit to our hospital, a 4×3cm subcutaneous tumor was observed on the lower right eyelid (**Figure 1**). Lymph nodes in the periauricular and neck areas were swollen, and computed tomography showed that the tumor had invaded the orbit (**Figure 2**). The biopsy specimen showed monotonous small round cells (**Figure 3**). Immunohistochemical staining revealed that the tumor was positive for CK20 and Merkel cell polyomavirus.

The patient initially refused surgery because she was concerned about the poor cosmetic outcome of the surgery and eyelid dysfunction. Therefore, we

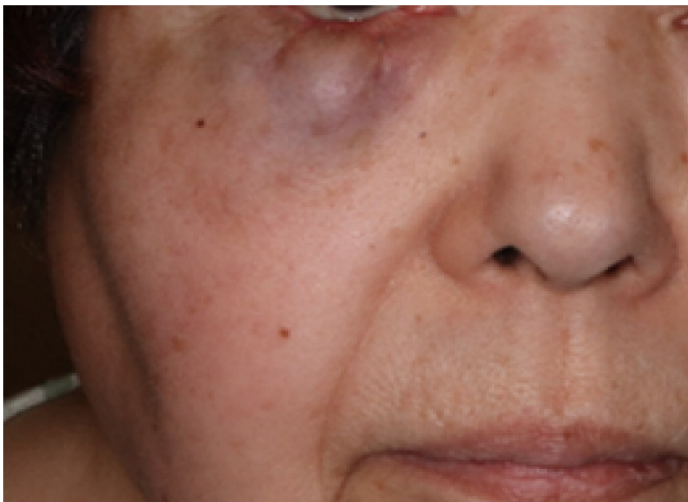


Figure 1 A 4×3cm subcutaneous tumor on the lower right eyelid.

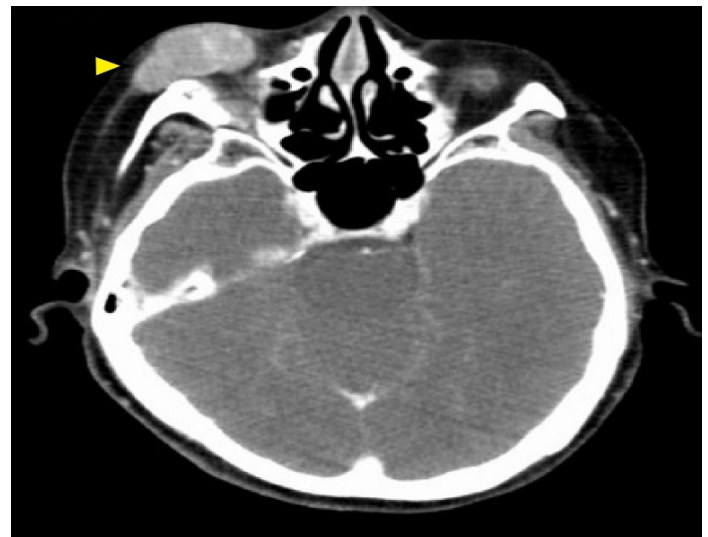


Figure 2 Computed tomography of the primary tumor invading the orbit (arrowhead).

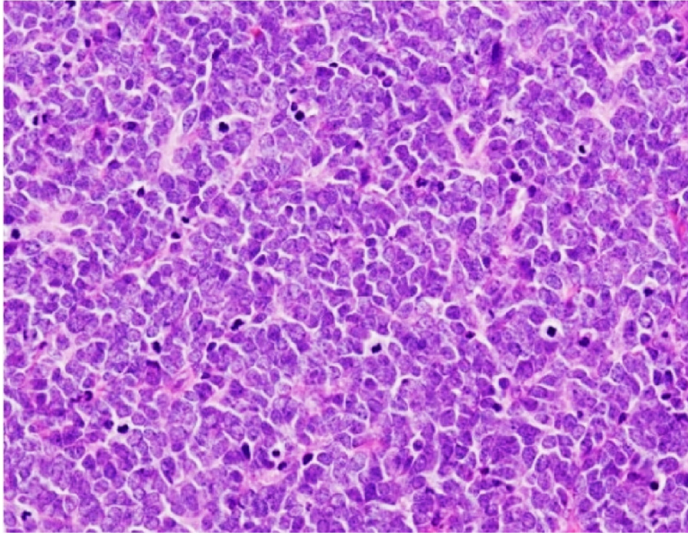


Figure 3 Pathological findings, H&E staining. The biopsy shows monotonous small round cells with nuclear enlargement and mitosis, 100 \times .

administered avelumab (10mg/kg every two weeks) to treat the tumor. After the second course of avelumab, the primary tumor and lymph node metastases shrank significantly (**Figure 4**). Then, as the patient opted to undergo surgery instead of continuing avelumab treatment, we performed wide excision and lymph node dissection. Pathologically, there were no viable tumor cells in the whole resected specimen of the primary site and lymph nodes and significant lymphocyte infiltration and macrophage proliferation were present (**Figure 5**). After the operation, we performed 4 cycles of

avelumab treatment and the patient was followed up thereafter. Currently, the tumor has not recurred for 20 months.

Conventional chemotherapy for MCC, including platinum-based regimens, etoposide, taxanes, and anthracyclines, either alone or in combinations, results in temporary tumor shrinkage. However, the responses are rarely durable and resistance develops quickly. The median progression-free survival of chemotherapy was only 94 days and the median overall survival was 9.5 months [3]. Conversely, treating naïve MCC patients with avelumab achieved an objective response rate of 62.1%, and 83% of these patients had response durations of at least 6 months [4]. In the present study, after our patient underwent surgery following the second course of avelumab, the resected specimen indicated a pathological complete response with numerous lymphocyte and macrophage infiltrations. It has been reported that the denser the intratumoral infiltration of lymphocytes, the higher the disease-specific survival rate in various solid tumors [5]. In our case, dense infiltration of lymphocytes was observed and no recurrence of tumor was observed within 20 months after radical resection. Therefore, the pathological response in a neoadjuvant setting could be a surrogate endpoint of improved patient outcomes in the treatment of several cancer types, including melanoma [5].



Figure 4 Computed tomography of the primary lesion after the second administration of avelumab.

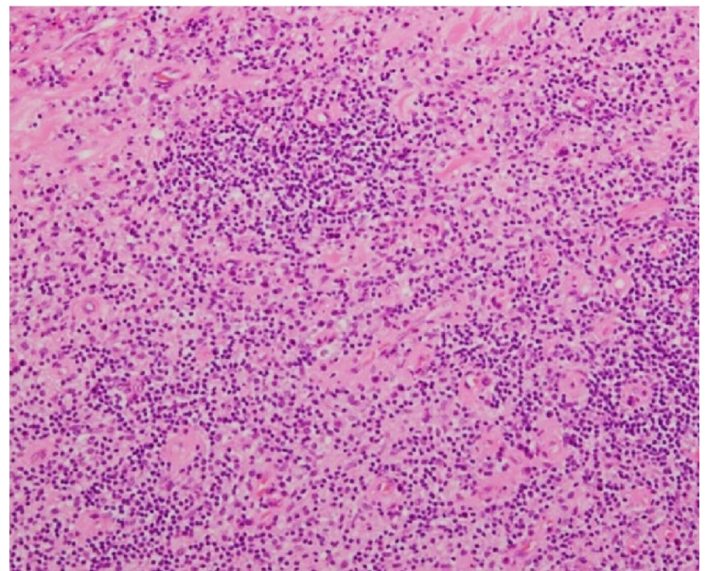


Figure 5 H&E staining: Dense infiltration of lymphocytes and macrophages is evident in the resected specimen, 100 \times .

In conclusion, neo-adjuvant avelumab therapy for advanced MCC has the potential to reduce tumor burden and likely reduce the extent of surgical resection as well as provide prognostic information.

Potential conflicts of interest

The authors declare no conflicts of interest.

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