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CORRESPONDENCE

Malignant melanoma of inner canthus with long-term survival after resection of brain metastasis and treatment with ipilimumab

Malignant melanoma with distant metastases has been recently treated with immune checkpoint inhibitors (ICIs) or BRAF inhibitors. These inhibitors were able to improve the prognosis of malignant melanoma. However, the prognosis for patients with brain metastasis is still poor.[1]

A 45-year-old Japanese woman presented to our department with black nodule in her inner canthus that developed 4 years ago and was gradually enlarging. Physical examination showed a 30×27 mm-sized, pale red to blackish purple nodule protuberating as polyps with peripheral telangiectasias (Figure 1A). We clinically diagnosed it as malignant melanoma. No lymph nodes and distant metastasis was detected by FDG-PET. The tumor was resected with 1 cm margin and sentinel lymph node biopsy was performed. Pathological findings revealed atypical tumor cells with

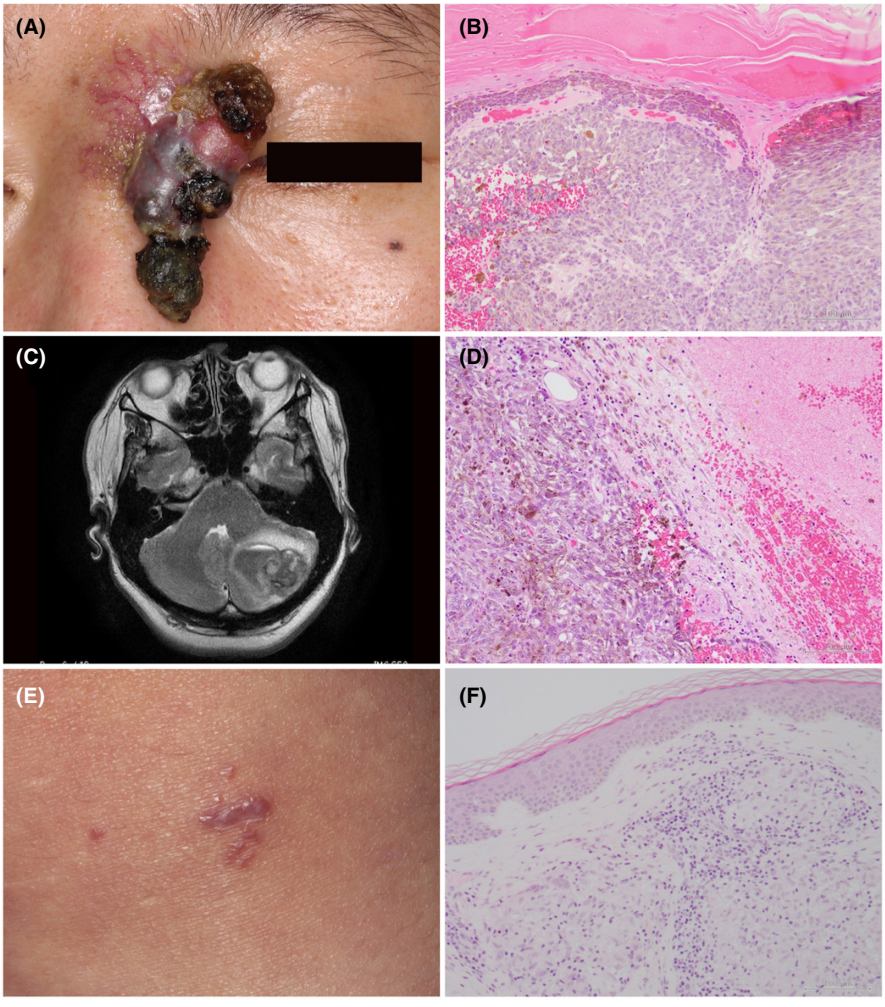

FIGURE 1 (A) Physical examination showed a pale red to blackish purple nodule with peripheral telangiectasias in the inner canthus. (B) Pathological findings of the resected tumor demonstrated proliferating of atypical tumor cells with melanin in the dermis (hematoxylin–eosin [H&E], original magnification ×200). (C) Brain MRI, T2-weighted image showed mostly low signals with a cystic appearance accompanied by high signal margins. (D) Pathological findings of the resected brain metastasis demonstrated proliferation of atypical tumor cells with necrosis and hemorrhage (H&E, ×200). (E) Aggregated red papules on the right knee. (F) Biopsy specimen showed epithelioid granulomas without caseous necrosis in the dermis (H&E, ×200)

melanin were proliferating in the dermis, accompanied by hemorrhage (Figure 1B). BRAF mutation was not detected. There was no evidence of metastasis in the neck sentinel lymph node. On the next day of the operation, she developed a headache and vomiting with loss of consciousness. A brain MRI revealed bleeding from metastasis in the cerebellum (Figure 1C). The hematoma and tumor were surgically removed. Histologically, atypical tumor cells invaded the brain tissue with necrosis and hemorrhage (Figure 1D). After the surgery, ipilimumab (4 times every 3 weeks) was administered. At that time, her ECOG Performance Status was 1 and LDH was 292 U/L. Hypophysitis and destructive thyroiditis developed 4 weeks after the treatment and were treated by prednisolone (70 mg/day). Additionally, Chest X-ray and CT revealed bilateral hilar lymphadenopathy. Six months later, reddish papules developed on the right knee (Figure 1E). The diagnosis of sarcoidosis was pathologically confirmed (Figure 1F). Currently, she is treated with hydrocortisone 20 mg/day and has no recurrence and metastasis 6 years after the first operation.

Treatments for brain metastases involve surgical resection, stereotactic radiosurgery, whole brain radiotherapy, and chemotherapy including ICIs.[2] The treatment strategy has not been established, which depends on patient's performance, neurological symptoms, location, size, and number of brain metastases. The efficacy of ICIs and BRAF inhibitors for brain metastases of malignant melanoma has been clarified. Our patient was treated with ipilimumab after surgical resection of the brain metastasis and achieved long-term survival. Surgical resection is a treatment option, when brain metastasis is solitary or limited number and localized to resectable region and has been reported to have a better prognosis.[3] Patients with brain metastases treated with immunotherapy alone were associated with an increased risk of death compared to those treated with surgery followed by immunotherapy (hazard ratio, 1.72; 95% CI, 1.00-2.99) in a retrospective study.[4] Our patient survived longer, compared to this study, which could demonstrate the efficacy of ICIs after resection of brain metastases. However, further prospective studies would be needed to confirm its efficacy. Notably, our patient developed hypophysitis and destructive thyroiditis, and sarcoidosis as immune-related adverse events. A previous study revealed that patients developing sarcoidosis by ICIs had an improved overall survival.[5] Combination therapy of surgical resection and ICIs is considered to be a noteworthy and effective treatment option.

DECLARATION SECTION

Approval of the research protocol: N/A.
Informed Consent: The patient provided written informed consent.
Registry and the Registration No. of the study/trial: N/A.
Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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