Ipilimumab Therapy for Melanoma: A Mimic of Leptomeningeal Metastases

We have recently observed that patients with malignant melanoma on treatment with ipilimumab can demonstrate leptomeningeal enhancement on brain MR imaging mimicking metastatic disease. In Fig 1 is shown one such case of a 40-year-old man presenting with subacute onset of headaches, right-sided facial hemiparesis, and facial paresthesias. He also showed evidence of tongue deviation on neurologic examination suggestive of cranial neuropathy. The patient had a history of stage IIIC melanoma from an unknown primary site with metastasis to the axilla and was undergoing therapy with ipilimumab. MR imaging demonstrated multifocal leptomeningeal and cranial nerve enhancement. Lumbar puncture revealed CSF lymphocytosis and mildly elevated proteins (findings that can be seen with inflammatory processes) and cultures and cytology negative for infection and malignancy, despite repeat examinations. Following drug discontinuation and high-dose steroid therapy, the patient gradually recovered. Lymphocytosis in the CSF also resolved.

To our knowledge, these brain imaging findings have not been shown in the literature. Ipilimumab, also known as MDX-010, is a human monoclonal antibody that augments T-cell-mediated immunity by blocking inhibitory signals that suppress T-cell function (more specifically, it blocks cytotoxic T lymphocyte antigen-4).[1] It is approved for the treatment of late-stage melanoma and is currently undergoing clinical trials for other cancers. Manousakis et al[2] reported a case of an inflammatory multifocal radiculoneuropathy during ipilimumab therapy with a lumbar spine MR image in their article showing leptomeningeal enhancement along the cauda equina nerve roots. Their patient also had clinical evidence of cranial neuropathies with facial nerve enhancement, though the brain MR images were not included in the article. Carpenter et al[3] showed 3 cases of hypophysitis associated with ipilimumab, which was also thought to represent an immune-mediated response. Our case shows leptomeningeal enhancement and perivascular enhancement in the cerebral hemispheres and pons, findings perhaps analogous to an inflammatory process such as neurosarcoidosis or chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS). Prominent perivascular enhancement may therefore be a subtle clue to an inflammatory process rather than metastatic disease, though supportive clinical and laboratory findings are needed to make a confident diagnosis.

As immunotherapeutics are increasingly used as antineoplastic agents, neuroradiologists must be aware of their unusual adverse effects and imaging findings. Brain MR imaging to evaluate for metastatic melanoma is not an uncommon study, and oncologists may plan chemotherapy or radiation treatment without histologic or CSF cytologic proof of intracranial metastasis. We should therefore be aware of this potential pitfall and are reminded to be cognizant of the specific chemotherapeutic agents our patients are receiving when providing interpretations.

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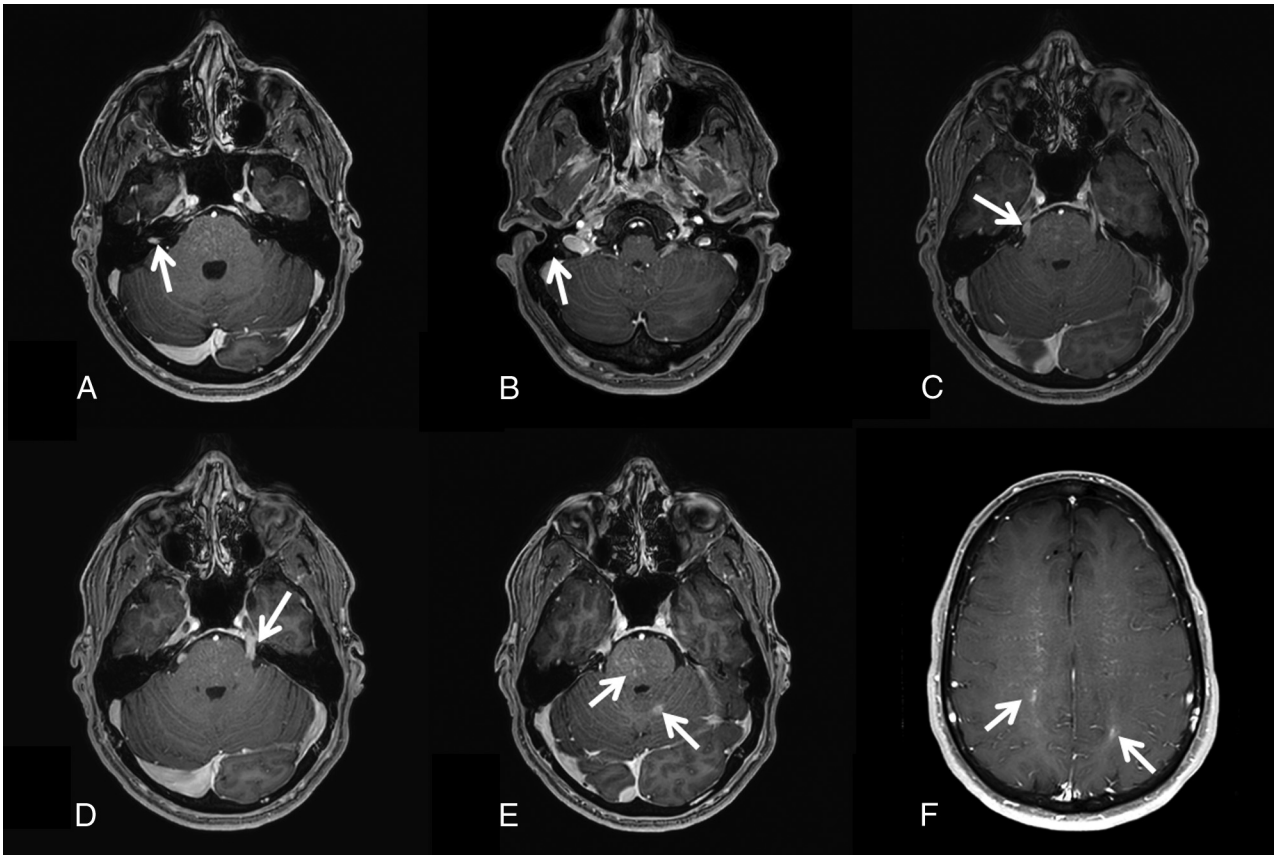

FIG 1. Postcontrast T1-weighted images demonstrate nodular enhancement involving the right facial nerve in the meatal (*A*) and mastoid (*B*) segments and the bilateral trigeminal nerves (*C* and *D*). Leptomeningeal enhancement along the cerebellar surface (*E*) and abnormal enhancement along the perivascular spaces in the pons and cerebral hemispheres (*E* and *F*) are also seen.