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Successful metastatectomy for pseudo-progression in a melanoma brain metastasis after ipilimumab treatment

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Introduction

Immune checkpoint inhibitors are of major interest in oncology because they can achieve durable disease control. For example, > 20% of the metastatic melanoma patients treated with ipilimumab have an overall survival of at least 3 years¹. Since immune checkpoint inhibitors exert their effect via T cell mediated anti-tumor activity, one feature is initial pseudo-progression due to CD8 positive cytotoxic lymphocyte influx in metastases, which can initially lead to increase of tumor-related symptoms². In case of brain metastases, dexamethasone is a treatment option for neurological complaints. However, corticosteroids temper the potential immune response of immune checkpoint inhibitors. Therefore, immune suppression is rather avoided when possible³.

Case report

Here we present a 24-year-old man who was referred with metastatic melanoma and treated with 4 courses of 3 mg/kg ipilimumab. At the last course, he experienced no tumor-related symptoms anymore. However, 6 days thereafter he presented at the emergency

department with headache and vomiting. A MRI scan of his head showed a solitary brain metastasis in the left frontal lobe of 5.5 cm with peri-tumoral edema and midline shift. Response assessment revealed partial regression of the known metastases. Dexamethasone was started at a dose of 4 mg twice daily. In the next 2 days, he had two episodes of abrupt reduced consciousness accompanied with bradycardia without positive arguments for epileptic activity. Unfortunately, the patient collapsed and remained in a comatose state with light fixed pupils, hypertension and bradycardia. A brain CT scan showed increased mass effect and edema. Treatment with mannitol was initiated, intubation and sedation with propofol was started. Two hours later patient started to show signs of slight improvement with pupils reacting to light and later on obeying comments. Since the systemic metastases seemed to respond well to ipilimumab, the decision was made to perform an emergency craniotomy for metastatectomy. Pathological examination showed a melanoma metastasis with a high density of tumor infiltrating lymphocytes. Afterwards, the patient ameliorated quickly and was discharged one week later. The tumor cavity was post-operative treated with stereotactic radiotherapy. Initially, he complained of having double vision that resolved in time. Homonymous hemianopia on the right side due to occipital ischemia as a result of transtentorial herniation persists. He developed vitiligo and has currently, 3.5 years later, ongoing regression of his systemic metastases and persistent complete intracranial remission without further treatment.

Discussion

Sometimes unconventional decisions have to be made in the rapidly changing field T cell boosting therapies. Pseudo-progression caused by T cell influx has to be included in the decision-making process of patients treated with ipilimumab or other immune activating therapies.

Recently, the immune checkpoint inhibitors nivolumab and pembrolizumab and the combination of ipilimumab plus nivolumab demonstrated auspicious survival rates ⁴⁻⁶. In non-small cell lung cancer, nivolumab has a superior outcome compared to standard docetaxel ⁷. This ongoing improvement of immune checkpoint inhibition in melanoma, lung cancer and other tumor types likely amplifies the number of patients (successfully) treated with this novel drug class.

It should be considered standard of care to evaluate for brain metastases prior to immune checkpoint inhibition, also in asymptomatic patients. Still, it is unclear whether this kind of complications could be foreseen since not every tumor lesion goes through a period of clinically relevant pseudo-progression. The caveat is that pseudo-progression is difficult to differentiate on imaging from true progression.

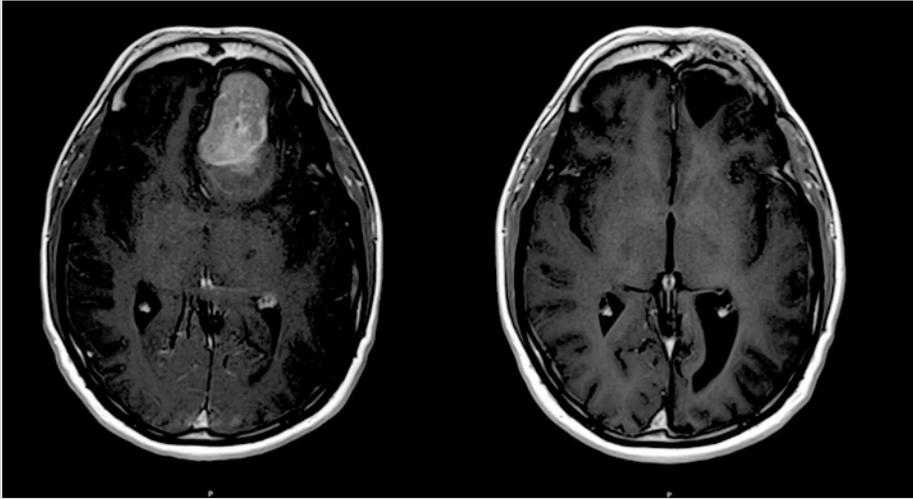


Figure 1: Radiological examinations.

On the left, the intracranial tumor is seen on a T1 weighted MRI image with contrast prior to surgery. On the right, a T1 weighted MRI image with contrast of the same brain region 1.5 years later is shown.

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