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Tolerance and Efficacy of Pembrolizumab
Stage IV Melanoma Patient Undergoing Hemodialysis

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Introduction

Patients with **severe renal insufficiency** present challenges in oncology medication prescription, as most anti-cancer drugs and their metabolites are eliminated through the kidneys.

The product summaries (SmPCs) rarely mention the possibility of using these drugs or dosage adjustments for such patients.

Hemodialysis or end-stage renal disease patients (GFR < 15 mL/min) are **often excluded from clinical trials.**

Pembrolizumab is a monoclonal anti-PD-1 antibody that enhances T cell responses, including anti-tumor activity. It has proven efficacy in patients with metastatic melanoma and has been FDA-approved since 2014.

We report the rare case of a hemodialysis patient with a GFR < 5 mL/min in complete remission after pembrolizumab treatment.

Observation

A 74-year-old male patient with the following medical history:

Medical history:
Hypertension (HTA)
End-stage renal disease (GFR 6 mL/min), on hemodialysis three times a week since 2016
Cardiac arrhythmia
Insulin-requiring diabetes

History:
May 2018: Pigmented lesion on the left eyelid, evolving over 1 year (2.5x2x1 cm ulcerated, pigmented tumor).
Extension workup: multiple pulmonary opacities.
➔ Stage IV melanoma (AJCC8 classification), LDH 344 UI/L.
June 2018: Initiation of anti-PD1 treatment and clean-up surgery of the primary tumor to avoid a mutilating procedure.

Melanoma Characteristics
Breslow thickness: 5 mm
Ulcerated, BRAF wild-type

Treatment :

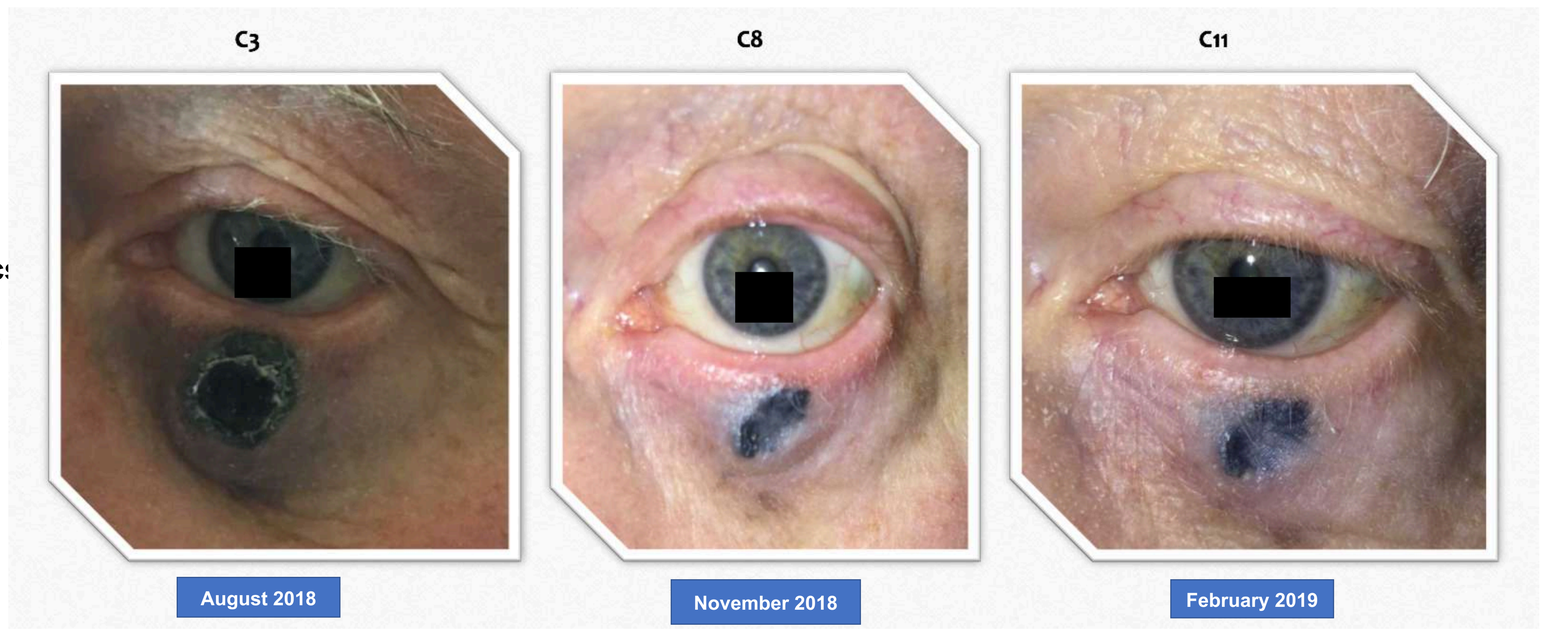
Pembrolizumab was initiated on July 3, 2018, at the standard dose of 2 mg/kg every three weeks, without dose adjustments.
The patient received pembrolizumab infusions on the same day, in the afternoon, after his hemodialysis sessions.
The patient did not experience any side effects, and there was no impact on his renal function.

Reevaluation in February 2019 after 13 cycles: Complete remission (CR) on thoraco-abdominal-pelvic CT scan, clinical evaluation, and PET scan.

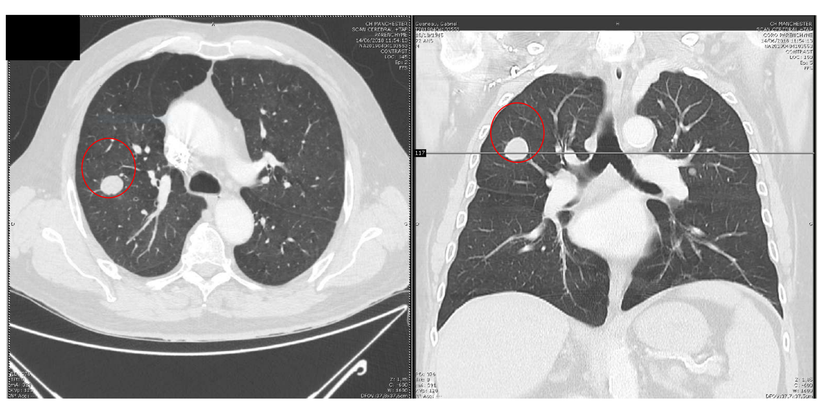
Diagnostic Staging Workup: Thoraco-abdominal-pelvic CT scan and brain MRI:
Multiple infra- and juxta-centimetric nodular lesions in both lung fields, suggestive of secondary metastases.
There was no involvement of the eyeball by the mass on the lower eyelid.

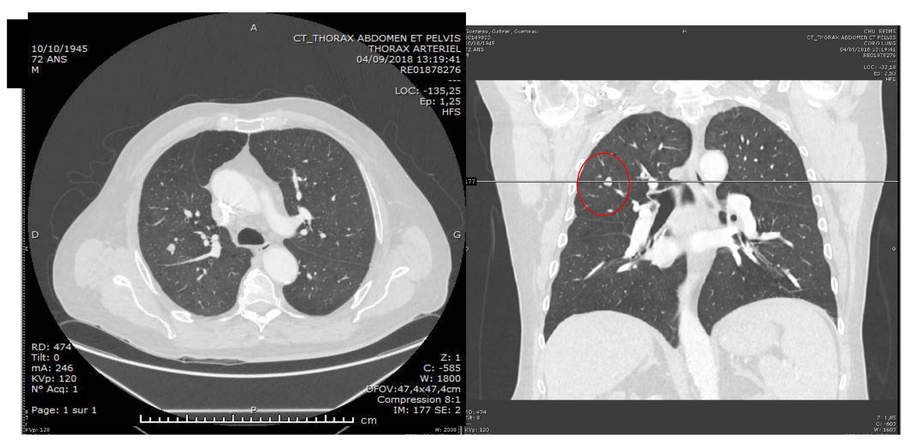
In summary:
Stage IV melanoma M1b
LDH 344 U/L.

➔ **June 2018 MDT (Multidisciplinary Tumor Board):** Initiation of anti-PD1 treatment in order to avoid excessively debilitating surgery.



Residual pigmentation, non-indurated lesion:
Surgical intervention (reconstruction with palatal mucosa graft) scheduled for June 2019


CT SCAN 2018 : C4 Pembrolizumab



CT SCAN : C8 Pembrolizumab


PET SCAN C10 Pembrolizumab :
Complete Response

Discussion

The product characteristics summaries for Pembrolizumab indicate that **no dose adjustment is necessary** for patients with mild to moderate renal impairment, but it has not been studied in patients with severe or end-stage renal failure on hemodialysis.

The main consideration for hemodialysis patients is the **risk of reduced exposure to the treatment due to hyperfiltration**.

Most medications are administered after dialysis sessions. Studies show that monoclonal antibodies or similar molecules are not dialyzable due to their molecular weight. This suggests that **Pembrolizumab can be administered without considering the timing of hemodialysis**.

In our case, our patient received Pembrolizumab every 3 weeks after his hemodialysis sessions, which occurred every 2 days.

➔ A recent study showed that the use of anti-PD1 in patients with severe organ dysfunction at the start of treatment resulted in a rate of side effects similar to patients without organ dysfunction.

Conclusion

Our case suggests that Pembrolizumab can be used safely and has shown efficacy in a hemodialysis patient with end-stage renal failure.

Limitations: our case is unique as we do not have pharmacokinetic and pharmacodynamic data regarding the use of Pembrolizumab in hemodialyzed patients.

A study involving a larger population of hemodialyzed patients is therefore necessary.

Given the increasing prevalence of type 2 diabetes and hypertension in the general population, the number of hemodialysis patients is expected to continue rising.

The prescription of immunotherapies in hemodialyzed patients will become more common, and it seems more than necessary to obtain clear guidelines on the use of these drugs in this population.