Cisplatin unfit bladder cancer patient with liver metastasis and CPS 100

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Introduction/Background

Standard 1st-line therapy for urothelial cancer (UC) of the bladder and upper urinary tract (UTUC) is cisplatin based combination chemotherapy (CT) [1,2]. Alternatively, carboplatin based chemotherapy is used for patients ineligible for cisplatin. Gemcitabine/Carboplatin (GCa) showed an objective response rate (ORR) of 38% [3,4].

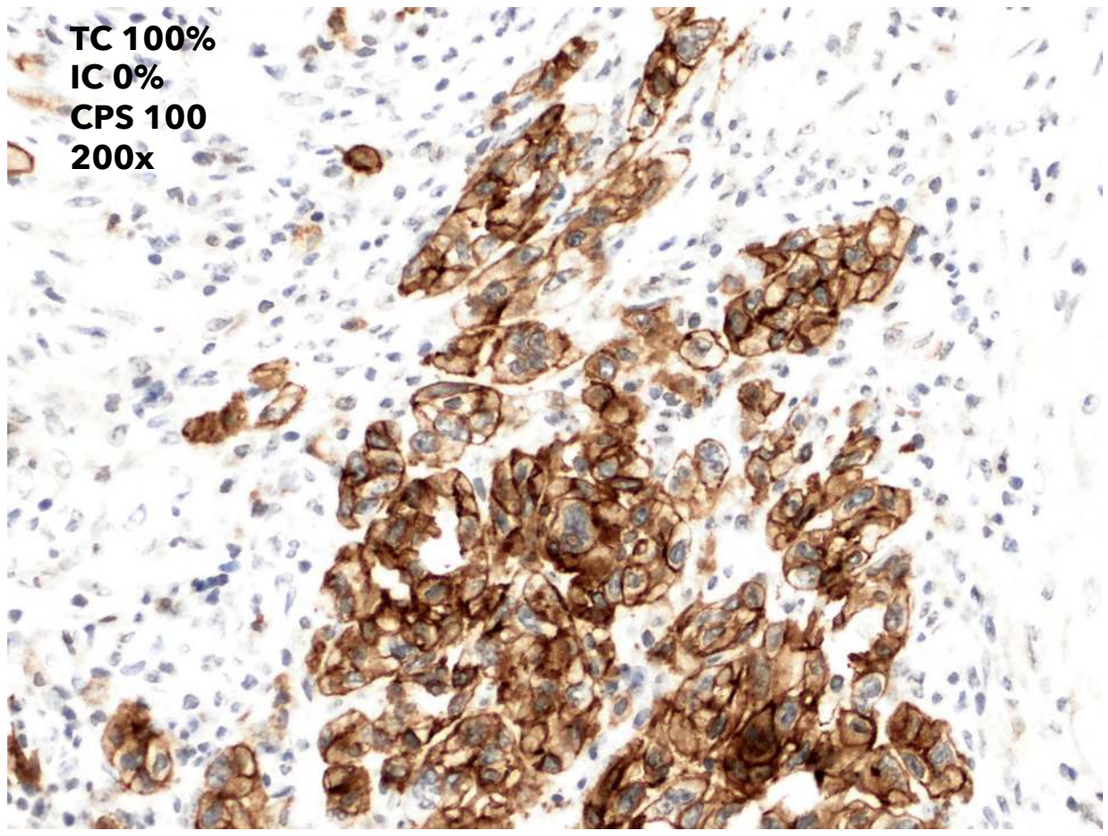
In 2017, pembrolizumab and atezolizumab were approved also for cisplatin ineligible patients in the first line setting based on ORRs of ~24% and promising overall survival in two uncontrolled phase II trials [5,6]. Recently, the indication for both checkpoint inhibitors (CPI) in the first line was restricted to patients with a positive PD-L1 status (“high levels of PD-L1”) based on preliminary and still unpublished results from ongoing phase III trials [7,8].

History

B is a 61 year old male bus driver. Work up of gross hematuria showed UC of the right upper urinary tract. Surgery was performed externally. Pathological review of the nephroureterectomy specimen showed urothelial cancer, G3, pT3b, pN1.

Diagnostic work-up

B first presented at Charité in January 2019 for consultation concerning adjuvant CT. Renal function was low (GFR 35ml/min) and performance status was good (PS1). Thus, 4 cycles of GCa were recommended. Five days later the patient presented at our emergency department with an acute abdomen.



PD-L1 immunohistochemical staining using E1L3N® (Cell Signaling Technology, Danvers, USA), Comment: Only tumor cells are stained but no immune cells

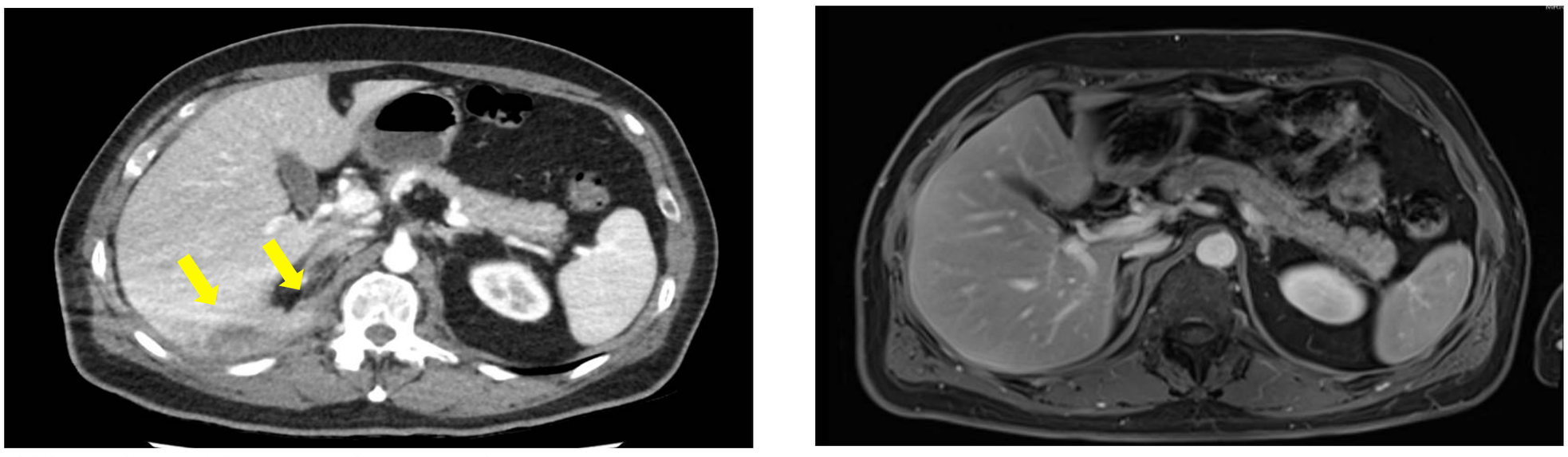
Immediate laparoscopic appendectomy revealed local and pelvic reccurrence of UC and further imaging showed a central necrotic liver metastasis which was rapidly progressing. PD-L1 status was requested and surprisingly showed IC 0% and CPS 100.

Treatment

The contradictory PD-L1 results, the lower response rate of CPI compared to GCa and the presumably better tolerability of immunotherapy were weighed against each other and discussed with the patient. Finally, pembrolizumab was started in 02/2019.

Outcome & Follow-up

The patient showed an immediate clinical improvement, PS 0 at 3 months and a complete response 6 months after CPI initiation.



CT Scan before and MRI 6 months after initiation of pembrolizumab
Comment: Complete remission

[1] von der Maase H, Sengelov L, Roberts JT et al. Long-Term Survival Results of a Randomized Trial Comparing Gemcitabine Plus Cisplatin, With Methotrexate, Vinblastine, Doxorubicin, Plus Cisplatin in Patients With Bladder Cancer. J Clin Oncol. 2005; 23: 4602–8. [2] Rouprêt M, Babjuk M, Compérat E. European Association of Urology Guidelines on Upper Urinary Tract Urothelial Carcinoma: 2017 Update. Eur Urol. 2018; 73: 111–22.[3] De Santis M, Bellmunt J, Mead G et al. Randomized Phase II/III Trial Assessing Gemcitabine/Carboplatin and Methotrexate/Carboplatin/Vinblastine in Patients With Advanced Urothelial Cancer Who Are Unfit for Cisplatin-Based Chemotherapy: EORTC Study 30986. J Clin Oncol. 2012; 30: 191–9. [4] De Santis M, Bellmunt J, Mead G et al. Randomized Phase II/III Trial Assessing Gemcitabine/ Carboplatin and Methotrexate/Carboplatin/Vinblastine in Patients With Advanced Urothelial Cancer “Unfit” for Cisplatin-Based Chemotherapy: Phase II–Results of EORTC Study 30986. J Clin Oncol 2009; 27: 5634–9. [5] Balar A V, Castellano D, O’Donnell PH et al. First-line pembrolizumab in cisplatin-ineligible patients with locally advanced and unresectable or metastatic urothelial cancer (KEYNOTE-052): a multicentre, single-arm, phase 2 study. Lancet Oncol. 2017; 18: 1483–92. [6] Balar A V, Galsky MD, Rosenberg JE et al. Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm, multicentre, phase 2 trial. Lancet. 2017 ; 389: 67–76. [7] Suzman DL, Agrawal S, Ning Y et al l. FDA Approval Summary: Atezolizumab or Pembrolizumab for the Treatment of Patients with Advanced Urothelial Carcinoma Ineligible for Cisplatin–Containing Chemotherapy. Oncologist. 2019; 24: 563–9. [8] EMA Press office. EMA restricts use of Keytruda and Tecentriq in bladder cancer [Internet]. Available from https://www.ema.europa.eu/en/news/ema-restricts-use-keytruda-tecentriq-bladder-cancer [cited 2019 Aug 15]