

Hematologic malignancy induced by cancer immunotherapy and cytotoxic chemotherapy

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Immunotherapy, including anti-PD-1/L1 inhibitors, suppresses tumors via modulation of immune-tumor cell interactions. Although they offer promising benefits, they also lead various immune-related adverse effects. Here, we report a rare case of secondary hematologic malignancy potentially induced by cytotoxic chemotherapy or immunotherapy. A 53-year-old man without past medical history, presented to Severance Hospital with a neck mass. A sono-guided biopsy was performed and pathologic diagnosis revealed “metastatic poorly differentiated carcinoma with necrosis, suggesting large cell neuroendocrine carcinoma (NEC)”. He was subsequently diagnosed with a NEC stage IV, with metastases to right adrenal and multiple lymph nodes. He initially received 19 cycles of etoposide-cisplatin chemotherapy from 2020.8.4 to 2021.9.8, along with palliative radiotherapy. Next-generation sequencing (NGS) of a metastatic lymph node was performed, and revealed high-tumor mutational burden (TMB) of 53.1/mb, a predictive biomarker for immunotherapy in various cancers. After progression on first-line etoposide-cisplatin, he started anti-PD-L1 inhibitor, Atezolizumab in clinical trial setting (2021.10.19). Since the thrombocytopenia grade 3 sustained, he had to stop the Atezolizumab after the 9th cycle (2022.03.15). Best objective response was partial response. Owing to the sustained thrombocytopenia, a bone-marrow study was performed in November 2022. The BM aspirate and biopsy showed 40% of myeloid blast cells. Karyotype analysis revealed 46,XY,del(6)(p22),t(11;19)(q23;p13.1)[20]. As a result, he was diagnosed with treatment-related acute myeloid leukemia (AML). The patient was treated with standard 7+3 (Cytarabine + Idarubicin) chemotherapy. He achieved complete remission and was consolidated with high dose cytarabine (HiDAC) and allogeneic hematopoietic stem cell transplantation.(2022.11.22). Following AML treatment, NEC was stable as of 2023.04. Secondary malignancy is a rare event both for cytotoxic chemotherapy and immunotherapy; however, caution is needed for solid tumor patients when sustained thrombocytopenia is observed.

