Chemotherapy for a BRCA2 mutant-NEPC patient

Editorial Comment

Editorial Comment to Prominent response to platinum-based chemotherapy in a patient with BRCA2 mutant-neuroendocrine prostate cancer and MDM2 amplification

In this issue, Daimon et al. reported on the efficacy of platinum-based chemotherapy in patients with neuroendocrine prostate cancer harboring BRCA2 mutations. Docetaxel administered after progression to castration-resistant prostate cancer (CRPC) initially suppressed disease progression, but prostate-specific antigen (PSA) levels remained constantly elevated during the subsequent administration of enzalutamide and cabazitaxel. Eventually, the patient was pathologically diagnosed as adenocarcinoma with neuroendocrine differentiation. After

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BRCA2 mutation with MDM2 amplification and loss of heterozygosity of RB1 were identified by targeted next-generation sequencing, the patient is currently undergoing platinum-based chemotherapy, decreasing PSA level.

The patient was diagnosed with prostate cancer with a high Gleason score at the relatively young age of 55 years with no family history, although it is unknown whether this patient has germline or somatic mutation in BRCA2 gene. Because BRCA2 is essential to maintain genomic integrity by homologous recombination of double-strand breaks, BRCA2 mutations accumulate genomic errors and increase the risk of carcinogenesis. Recently, Nyberg et al. reported an increased incidence of prostate cancer among BRCA2 mutation carriers in a prospective cohort study (EMBRACE trial).

It has been reported that carriers of BRCA2 mutations respond well to platinum-based chemotherapy. Here, the patient carried BRCA2 mutation (p.N2345Qfs*20), which involves the DNA-binding domain, and suggested pathogenic by causing the homologous recombination deficiency. Poly (ADP-ribose) polymerase (PARP) inhibitor was developed for metastatic CRPC with BRCA1 or BRCA2 mutation. PARP inhibitors are expected to be effective in this case. However, there have been no reports on the efficacy of PARP inhibitors in patients treated with platinum drugs. Recently, BRCA reversion mutations restoring its function were reported as a mechanism obtaining resistance to PARP inhibitor as well as platinum-based chemotherapy. Therefore, subsequent report on this case after the use of PARP inhibitor would be important with sequential genomic analysis on BRCA2.

Conflict of interest
Masaki Shiota has received honoraria from AstraZeneca.

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