

## A Case of Penile Cancer with Germline BRCA1 mutation

국립암센터 내과<sup>1</sup>이준기<sup>1</sup>, 최원영<sup>1</sup>

**Introduction:** Penile squamous cell carcinoma (PSCC) is rare with an annual incidence of less than 1 case per 100,000 people. Although Human papillomavirus (HPV) infection is one of the etiologic factors, precise pathogenic mechanisms remain elusive. Here, we report a case of PSCC with a germline pathogenic variant (PV) of BRCA1, diagnosed with next-generation sequencing (NGS) of both the tumor and blood DNA.

**Case:** Description A 53-year-old man was diagnosed with penile cancer and underwent penectomy. Surgical pathology revealed PSCC without evidence of HPV infection. As the resection margin was positive for tumor cells, he underwent concurrent chemo-radiation therapy (CCRT) with cisplatin and fluorouracil. However, lung metastasis was identified during follow-up, and he was treated with palliative chemotherapy, including cisplatin and an oral fluoropyrimidine (S-1). NGS was performed with the resected tumor and the test revealed a mutation in the BRCA1 gene (L1790P) with an allele frequency of 71.4%. This variant occurs at the BRCA1 C-terminal (BRCT) domain impairing the DNA Damage Repair signaling, eventually leading to genomic instability and carcinogenesis. Since the high allele frequency was suggestive of a germline mutation, NGS was tested with his blood DNA which confirmed heterozygous BRCA1 mutation of L1790P. Collectively, this patient's PSCC was concluded to have been caused by the germline BRCA1 PV. The patient's lung nodule showed partial response to platinum-based chemotherapy, and he is currently maintaining S-1.

**Discussion:** Previous studies reported that BRCA1 PVs were associated with breast, pancreatic, and stomach cancers in males. However, this is the first report of penile cancer arising in the background of BRCA1 PV. With the implementation of NGS, we contemplate that more penile cancers with BRCA mutations will be diagnosed in the future. Cancers with BRCA mutation are known to have heightened sensitivity to platinum-based chemotherapy, and this case also showed a good response to a cisplatin-based regimen. PARP inhibitors could be an effective strategy, and this remains one of the potential options for this patient as subsequent therapy.

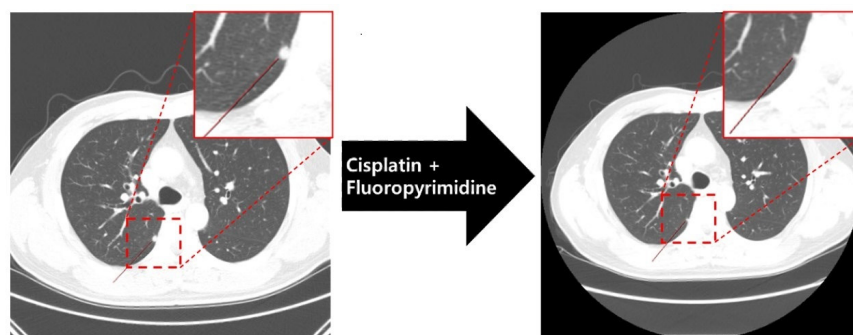


Figure 1. Chest CT showing tumor response after cisplatin and fluoropyrimidine chemotherapy

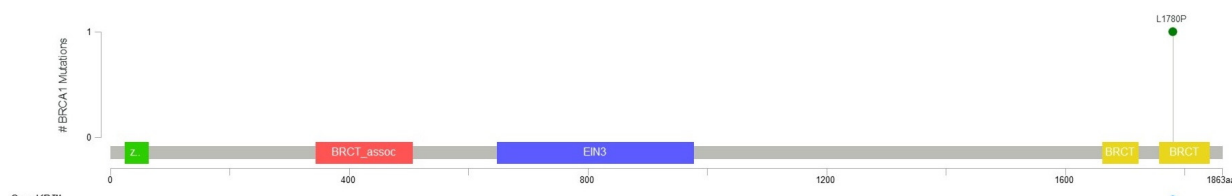


Figure 2. Germline BRCA1 pathogenic variants in this case patient confirmed by next-generation sequencing of both tumor and blood DNA.