between t-SNPC and *BRCA1/2* mutations should be further clarified in future. In addition, capturing more precise molecular data would allow tracing the molecular evolution of this disease and therefore, hopefully, lead to earlier detection and intervention.

Conclusion

t-SNPC is a very aggressive phenotype and the early detection of this transformation and pathological diagnosis may improve patient survival when genetic mutations, including *BRCA 1/2*, are detected.

AUTHOR CONTRIBUTIONS

Taku Naiki: Conceptualization; data curation; writing – original draft. Aya Naiki-Ito: Conceptualization; writing – original draft. Tatsuya Kawai: Data curation; writing – review and editing. Hirokazu Komatsu: Data curation; writing – review and editing. Ryutaro Nishikawa: Data curation; writing – review and editing. Masakazu Gonda: Data curation; writing – review and editing. Maria Aoki: Data curation; writing – review and editing. Yosuke Sugiyama: Data curation; writing – review and editing. Yoshihiko Tasaki: Data curation; writing – review and editing. Takahiro Yasui: Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

The ethics committees of Nagoya City University Graduate School of Medical Sciences gave approval for this study (#60-22-0134) and written informed consent was obtained in accordance with the World Medical Association Helsinki Declaration.

Informed consent

Written informed consent was obtained from the patient for publication of this article and accompanying images.

Registry and the Registration No. of the study/trial

Not applicable.

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Editorial Comment

Editorial Comment from Dr Sekino and Dr Hinata to A case of metastatic treatment-emergent small cell/neuroendocrine prostate cancer with BRCA2 mutation diagnosed by liver biopsy

Treatment-emergent small cell/neuroendocrine prostate cancer (t-SNPC) mainly occurs in the advanced or metastatic castration-resistant prostate cancer that is caused by the transformation of prostate adenocarcinoma after androgen deprivation therapy (ADT).[1] t-SNPC is an aggressive disease with a poor prognosis. The ADT treatment is ineffective, and the combined chemotherapy strategy of etoposide plus cisplatin/carboplatin was effective for patients with t-SNPC.[2] Therefore, early diagnosis and treatment play an important role in the survival in the patient with t-SNPC. This case report by Naiki *et al*. showed that metastatic t-SNPC with BRCA2 mutation diagnosed by liver biopsy.[3]

In this case report, the patient was diagnosed as t-SNPC by the pathological findings of liver metastasis. The

incidence of t-SNPC may rise with the widespread use of new androgen receptor-targeted therapies.[1] However, the incidence of t-SNPC may be underestimated because there is currently no criteria to perform a biopsy for t-SNPC. Additionally, the secondary biopsies are not routinely performed, leading to miss the opportunity to diagnose t-SNPC. The clinicians should consider the second biopsies when examining patients with the atypical and aggressive clinical courses.

In this case report, FoundationOne® CDx (Foundation Medicine, Cambridge, MA, USA) was used for cancer-related gene profiling using liver tumor specimen, and a BRCA2 mutation was identified. BRCA2 is a key player in DNA damage repair (DDR). A recent study reported that DDR aberrations were rare in t-SNPC. In contrast, alterations in DDR were identified in patients with de novo NEPC.[4] In this case report, BRCA2 mutation was found after chemotherapy treatment. However, there was no time to use PARP inhibitor treatment because of the rapid and aggressive clinical course. This indicates that clinicians should consider gene profiling examinations, such as FoundationOne® CDx, at an early stage for the treatment options when seeing patients with t-SNPC.

Yohei Sekino M.D., Ph.D. and Nobuyuki Hinata M.D., Ph.D.
Department of Urology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan
akikosekino@gmail.com

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Editorial Comment from Dr Kato to A case of metastatic treatment-emergent small cell/neuroendocrine prostate cancer with BRCA2 mutation by liver biopsy

Most urologists in clinical practice encounter suspected treatment-emergent small cell/neuroendocrine prostate cancer (t-SNPC) with rapid progression of disease. Post diagnosis, the treatment of these patients is difficult due to limited options; due to a poor prognosis, patients inevitably die prematurely during the course of treatment. The expression of typical markers for neuroendocrine differentiation including synaptophysin, NSE (neuron specific enolase), and chromogranin A is seen in majority of patients,[1] while these are not expressed in other patients. However, rapid disease progression is seen in all patients. Treatment options for t-SNPC are very limited and resistance to platinum-based therapies develops quickly. Urologists in charge should start exploring therapies for late stage treatments for t-SNPC; genetic diagnoses established in recent years would be a valuable resource in the discovery of new therapies. One of the genetic diagnosis methods, namely, Foundation One is being widely used in cancer hospitals across the world. The detection ratios of druggable gene mutations are low; however, there is still hope for both patients and urologists in finding available treatment options. Despite this new proposed genetic diagnostic approach, limitations existing within institutions currently prevent urologists from referring patients for genome analysis.

First, not inaccurate diagnosis of the disease state and referring patients to the genome diagnostic outpatient department and delay in consultation from the genome diagnosis department. These situations leave cancer patients at a great disadvantage when trying to develop and tailor specific treatment regimens in a timely manner. It is obvious that consultation with the genome diagnosis department is key in developing treatment regimens to improve patient care. However, there are some other limitations in Japanese hospitals. For example, a urologist cannot not directly order the exhaustive genomic testing, such as Foundation One, without an expert panel and counseling for the patients. Not all institutes have an expert panel and counseling for the patients, only few certified institutes have these systems. This difference among institutes lead a difficulty for urologists to search treatment options of aggressive prostate cancer. Currently, urologists believe that the ratio of positive detection for *BRCA* mutation is up to 10% and that there is a very low positive rate among castration-resistant prostate cancer patients to achieve treatment goals despite the efficacy of olaparib for the inhibition of Poly (ADP ribose) polymerase for the treatment of prostate cancer cells with