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BRCA mutation in Vietnamese prostate cancer patients: a mixed cross-sectional study and case series

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Abstract

Objectives: Prostate cancer features have been linked to mutations in the *BRCA1* and *BRCA2* genes. Assessing the status of *BRCA1* and *BRCA2* gene carriers in patients contributes to accurate diagnosis, disease prognosis as well as appropriate targeted treatment methods. This study evaluated the prevalence of these mutations in Vietnamese prostate cancer patients and assessed their correlation with clinical features.

Methods: A cross-sectional study was performed at Bach Mai Hospital between 2021 and 2022. We enrolled 60 prostate cancer patients. Next-generation gene sequencing was used to identify *BRCA1* and *BRCA2* mutations in formalin-fixed paraffin-embedded samples. Patients with somatic gene mutations underwent further germline mutation analysis. We also reported a case series following the British Medical Journal guidelines, detailing the clinical course of such patients.

Results: Patients with *BRCA2* pathogenic variants revealed no *BRCA1* mutations, although different mutations were identified. Two patients showed germline mutations. Patients with *BRCA* mutations were younger (average age: 66.2 years) than those with non-mutations (72.1 years) at diagnosis. High Gleason scores, lymph node metastases, and distant metastases were more prevalent in the mutation group. One patient with germline *BRCA* mutation had aggressive prostate cancer and early resistance to non-PARPi (Poly ADP-ribose polymerase inhibitors) treatments.

Conclusions: We provide preliminary data on *BRCA* mutations in Vietnamese patients with prostate cancer, suggesting that *BRCA2* mutations correlate with aggressive disease characteristics. Our findings further elucidate the clinical implications of these mutations.

Keywords: *BRCA1*; *BRCA2*; prostate cancer; Vietnamese patient

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Introduction

After lung cancer, prostate cancer is the second most common cancer in men globally. In 2020, there were 1,414,259 new cases of prostate cancer, which resulted in 375,304 fatalities (6.8 % of all male cancer-related deaths). The incidence rates vary worldwide. Australia and New

Zealand and countries from North America and Western and Northern Europe have the highest incidence rates of prostate cancer, while countries in South-Central Asia have the lowest. In Vietnam, 6,248 new cases (6.3 % of new cases in men) and 2,628 deaths due to prostate cancer were reported in 2020 [1]. At the Bach Mai Hospital, approximately 80 % of prostate cancer patients are initially diagnosed with advanced-stage cancer. Testing for *BRCA1* and *BRCA2* genes in prostate cancer helps select candidates suitable for poly ADP-ribose polymerase inhibitors (PARPi) therapy, determine the patient's prognosis, and plan for screening and early diagnosis of patients with *BRCA* germline mutation carriers [2, 3].

Genomic instability arises from the inability to effectively mend double-strand breaks through homologous recombination repair (HRR). Genes associated with HRR, including *BRCA1*, *BRCA2, ATM, CHEK2*, and *PALB2*, play a crucial role in this repair mechanism. *BRCA1* and *BRCA2* are important tumor suppressor genes that play key roles in DNA double-strand break repair [4–6]. Double-strand DNA breaks occur quite commonly in cells; a loss-of-function mutation occurring in the remaining gene in a carrier of a heterozygous *BRCA* mutation (loss of heterozygosity) leads to genomic instability and causes cancer [7, 8]. In a study by Pritchard et al., 25.3 and 0.9 % of male patients with metastatic prostate cancer showed *BRCA*2 and *BRCA1* mutations [9]. According to Ibrahim et al., men who carry a BRCA mutation have higher Gleason scores and elevated prostate-specific antigen (PSA) levels [10]. *BRCA1/2* mutations were linked in a large retrospective analysis to nodal involvement, a higher Gleason score, metastatic disease at diagnosis, and the T3–T4 stage [11]. Furthermore, *BRCA2* is a separate prognostic factor linked to unfavorable results. The 5-year cancer-specific survival and metastasis-free survival of patients with localized prostate cancer were considerably lower in *BRCA2* carriers compared to non-carriers (82 vs. 96 % and 77 vs. 93 %, respectively) [12, 13]. Studies worldwide have shown the occurrence of *BRCA1* and *BRCA2* gene mutations is related to these factors and the patient's prognosis [14–16]. Hence, assessment of such mutations may help determine the effectiveness of platinum chemotherapy and PARPi.

In addition, most studies have only used patient blood samples for testing. The genetic material from blood samples is of high quality; assessment of such material may only show the rate of germline mutations but may miss the rate of somatic mutations, which needs to be examined to determine the targeted treatment. Meanwhile, prostatectomy or biopsy specimens are stored in a formalin-fixed paraffin-embedded (FFPE) form, and the DNA isolated from these samples is fragmented and of poor quality owing to deamination and cross-linking during formalin fixation [17]. With great progress in science and technology, next-generation gene sequencing (NGS) has been proposed as an effective and viable alternative for detecting variants in these two genes [18, 19].

In Vietnam, some research facilities have been established to diagnose *BRCA1* and *BRCA2* mutations in breast and ovarian cancer patients [20–22]. However, existing data on the *BRCA1* and *BRCA2* mutation status in the prostate cancer population in Vietnam are not sufficient to support treatment and prognosis.

Thus, the study aimed to determine the rate of *BRCA1* and *BRCA2* gene mutations in prostate cancer patients using NGS and to analyze the correlation between *BRCA1* and *BRCA2* gene mutations and clinical characteristics in prostate cancer patients.

Methods

Study design

This mixed cross-sectional study and case series report were conducted at Bach Mai Hospital between 2021 and 2022. The flow chart of the study is presented in Figure 1.

Study process

The genetic analysis techniques used in the research were as follows.

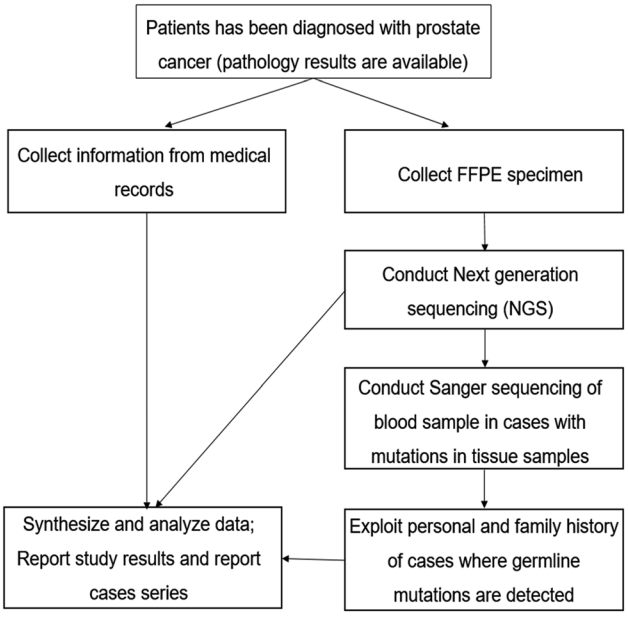

Figure 1: Flow chart of this study.

Next-generation sequencing: Pathological samples were obtained following tumor biopsy or resection to analyze the *BRCA1* and *BRCA2* mutation status. Tumor DNA was extracted from FFPE specimens using a QIAamp DNA Mini Kit (Qiagen, Germany). DNA fragmentation and library preparation were performed using the BRCAaccuTest™ (NGeneBio, Korea) following the manufacturer's instructions. Massive parallel sequencing was performed using an Illumina MiSeq system (Illumina, USA) with a minimum target coverage of 100×.

Sanger sequencing: Pathogenic mutations in blood samples were detected by Sanger sequencing [23]. The DNA sample was amplified with an appropriate bait at the mutation site that caused the disease. Sanger sequencing of purified PCR products was performed using POP-7 on a 3130xl gene analyzer system Polymer (Applied Biological Systems, USA). CodonCode Aligner software (v.9.0.1), UCSC Genome Browser (GRCh38, https://genome.ucsc.edu/cgi-bin/hgTracks?db=hg38&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType=default&virtMode=0&nonVirtPosition=&position=chr17%3A39723967%2D39723967&hgsid=18893927-20_SsSeOiexcTivQkjcblQsLNErTFxj), and National Center for Biotechnology Information Basic Local Alignment Search Tool (NCBI BLAST, https://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastn&BLAST_SPEC=GeoBlast&PAGE_TYPE=BlastSearch) were used to analyze the sequencing results to determine the mutation location and type.

Participants

The patients had been diagnosed with prostate cancer and underwent biopsy or surgery for the primary tumor, whose specimen was FFPE. Peripheral blood samples required for further analyses of germline gene mutations, complete medical record information, and consent for participation in the study were obtained from patients with somatic gene mutations in FFPE tissues.

The exclusion criteria were as follows: Patients whose specimens did not qualify for NGS (specifically, samples with low post-extraction DNA concentration and/or quality) were excluded.

In this study, we eliminated 38 cases due to insufficient concentration and quality of input DNA and sequencing library. We also eliminated eight cases without enough information in the medical record (the rate of exclusion from the study was 46/106 cases, accounting for 43.4 %).

Measures

The outcome variables included age, patient history, disease stage, metastatic status, serum total PSA level at diagnosis, Gleason score, and *BRCA1* and *BRCA2* variants [24]. Data on the medical records, pathology results, genetic test results, and patient statements (family history) were obtained (Table 1).

Sample size

The samples were collected using the entire sampling method. After collecting and eliminating patients with insufficient data on research indicators and tissue samples that did not meet the standards for conducting NGS, only 60 patients were included in the study.

Table 1: Define outcome variables and analysis variables.

Variables	Variable definition	Variable classification	Method of data collection
Age	Age of patient (unit: year)	Quantitative variable	Medical report
History	Family history Personal history	Categorical variable	Medical report and patient statements
Disease stage	I, II, III, IV	Qualitative variable	Medical report
Metastatic status	No metastasis, lymph node metastasis, distant metastasis	Qualitative variable	Medical report, pathology results
Serum total PSA level at diagnosis	Serum total PSA level at diagnosis (unit: ng/mL)	Quantitative variable	Medical report
Gleason score	2–10 scores	Quantitative variable	Medical report
BRCA1, *BRCA2* variants	Pathogenic Likely pathogenic Variants of uncertain significance (VUS) Likely benign Benign	Categorical variable	Genetic testing result (NGS and Sanger results)

Statistical analysis

Statistical analyses were performed using SPSS Statistics (version 20.0; IBM Corp., Armonk, NY). Continuous variables were expressed as the medians and interquartile ranges, while categorical variables were expressed as frequencies and percentages. Using Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables, we examined the between-group differences and the prevalence of related indicators. p-Values less than 0.05 were regarded as significant.

Ethics statement

This study was approved by the Ethics Committee of Bach Mai Hospital (approval number: 5362/BM-HĐĐĐ). Data on all research variables and indicators were collected accurately and scientifically. The patients consented to the research participation agreement and the research information statement. All personal patient information was kept confidential and used only for research purposes.

Results

Rate of detection of *BRCA* variants in the study group

After assessing the *BRCA1* and *BRCA2* gene mutation status in paraffin-embedded tumor tissue samples, we

Table 2: Some characteristics of five patients with *BRCA2* gene mutations detected.

Characteristics	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5
Age	66	64	61	66	75
Stage	T3aN0M1b	T3bN1M0	T3bN1M1b	T3bN1M1b	T3bN0M1b
Nucleotide change	8364G>A	7879A>T	2612C>G	9253del	1888_1889insAA
Protein change	Trp2788Ter	Ile2627Phe	Ser871Ter	Thr3085GlnfsTer19	Thr630LysfsTer15
Frequency (VAF %)	4 %	3.1 %	69.6 %	13.0 %	15.2 %
Biopsy sample	Bone	Prostate	Prostate	Prostate	Prostate
Molecular consequence	Nonsense	Missense	Nonsense	Deletion	Insertion
Clinical significance	Pathogenic (germline)	Pathogenic (somatic)	Pathogenic (germline)	Pathogenic (somatic)	Pathogenic (somatic)

VAF, variant allele frequency.

discovered that 5 of 60 patients (8.3 %) carried *BRCA2* pathogenic variants. None of the patients had pathogenic variants in the *BRCA1* gene. Moreover, 55 patients (91.7 %) did not carry mutations in the *BRCA1* or *BRCA2* gene (see Table S1).

In five patients who exhibited mutations in the *BRCA2* gene, five different gene variations were discovered at the mutation location. Two patients had nonsense mutations, one had a missense mutation, one had a deletion mutation, and one had an insertion mutation with variant allele frequencies (VAF) of 3.1–69.6 %.

We continued to investigate the germline mutation status in patients with *BRCA2* gene mutations in the tumor tissue samples. Currently, two patients showed germline mutations, two patients did not detect germline mutations on blood samples and one scheduled for blood sampling was inaccessible (Table 2).

Some clinical characteristics and *BRCA* gene mutation status

The average age of the study group was 71.7 ± 8.1; ranging from 54 to 90 years. Most patients were aged between 60 and 79 years (see Table S2).

The median PSA level at initial diagnosis was 202.10 ng/mL; the highest PSA level was 5,000.00 ng/mL, while the lowest level was 1.80 ng/mL. Most patients had a PSA level of >100 ng/mL at diagnosis (see Figure S1).

The average age at the time of diagnosis in the five patients with *BRCA* mutations was 66.2, which tended to be lower than that of patients without *BRCA* mutations (72.1). Five patients with *BRCA* mutations tended to have a higher Gleason grade group (80 % had Gleason grade group 4–5) than those of patients without mutations (78.5 %). The rates of regional lymph node metastasis and distant metastasis in patients who carried *BRCA* mutations were higher (60 and 80 % compared with 45.5 and 72.7 %, respectively) (Table 3).

Table 3: Correlation of clinical characteristics and *BRCA* gene mutation in 60 patients.

Clinical characteristics at diagnosis	*BRCA* mutated (n=5)		*BRCA* wild type (n=55)		p-Value
	n	%	n	%	
Age, median (IQR)	66 (63–66)		72 (65–78)		0.097[a]
Gleason grade group					
Grade group 1-3	1	20 %	12	21.8 %	0.705[b]
Grade group 4-5	4	80 %	43	78.2 %	
cT stage					
T1-2	1	20 %	10	18.2 %	0.651[b]
T3-4	4	80 %	45	81.8 %	
cN stage					
N0	2	40 %	30	54.5 %	0.435[b]
N1	3	60 %	25	45.5 %	
cM stage					
M0	1	20 %	15	27.3 %	0.730[b]
M1	4	80 %	40	72.7 %	
Serum total PSA (ng/mL), median (IQR)	153.40 (30.00–296.30)		214.90 (69.50–407.20)		0.385[a]
Serum total PSA level					
≤100 ng/mL	2	40 %	20	34.6 %	0.611[b]
>100 ng/mL	3	60 %	35	63.6 %	

[a]Mann-Whitney U test, [b]Fisher's exact test, PSA, prostate specific antigen; IQR, inter quartile range.

Cases series report

Case 1

Case presentation

Patient #1 is a 66-year-old male with no remarkable medical history. In April 2021, the patient presented with lower back pain, inadvertent weight loss, and prolonged fever over several weeks. Clinical examination revealed symptoms of bone metastasis and no suspicious infection. Computed tomography (CT) examination indicated multiple osteolytic bone metastases in the axial skeleton, no visceral metastases were observed (Figure 2).

Bone biopsy revealed adenocarcinoma metastasis originating from the prostate (Gleason score: 4 + 5 = 9). Further workup disclosed a serum total PSA level measuring 296.30 ng/mL. Prostate magnetic resonance imaging (MRI) delineated a lesion characterized by a Prostate Imaging-Reporting and Data System (PI-RADS) score of 5 within the left peripheral zone, accompanied by an absence of regional lymphadenopathy (Figure 3). In a patient diagnosed with high-risk, high-volume metastatic prostate cancer, a therapeutic regimen consisting of androgen deprivation therapy using goserelin, abiraterone acetate, prednisone, and bisphosphonate was administered. The patient responded favorably to the therapy, with notable improvement in bone pain and fever. The PSA level initially declined from 296.30 to 4.67 ng/mL in the first 4 months. However, subsequent evaluations revealed a progressive escalation in PSA levels, from 4.67 to 414.10 ng/mL by January 2022. The patient experienced a recurrence of skeletal discomfort. CT examination revealed a combination of osteolytic and osteoblastic metastases instead of the previously prevalent osteolytic lesions (Figure 4). Disease progression was also confirmed.

The patient underwent a therapeutic regimen involving docetaxel, goserelin, and bisphosphonates. However, the patient exhibited intolerance to the treatment, resulting in

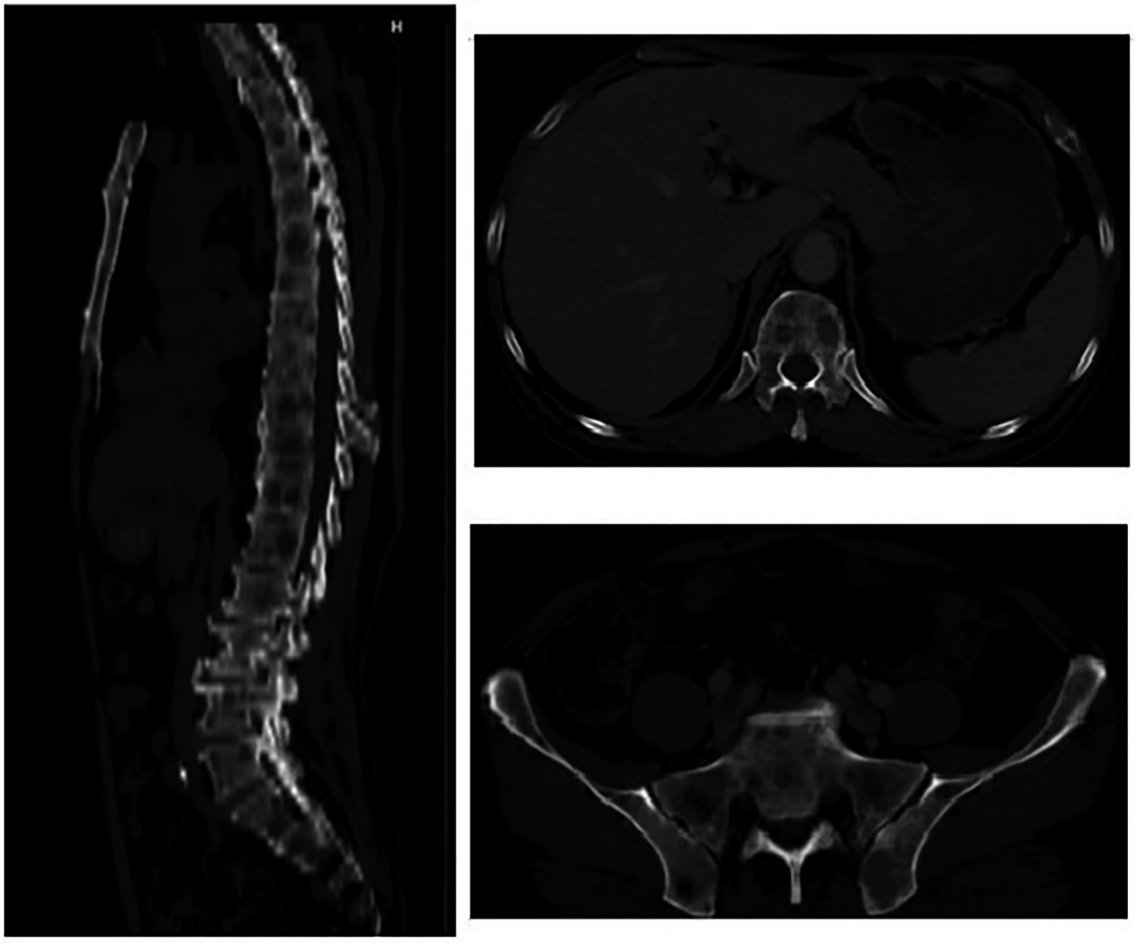

Figure 2: CT scans showed multiple lytic bone metastases in vertebral and pelvis bone in April 2021.

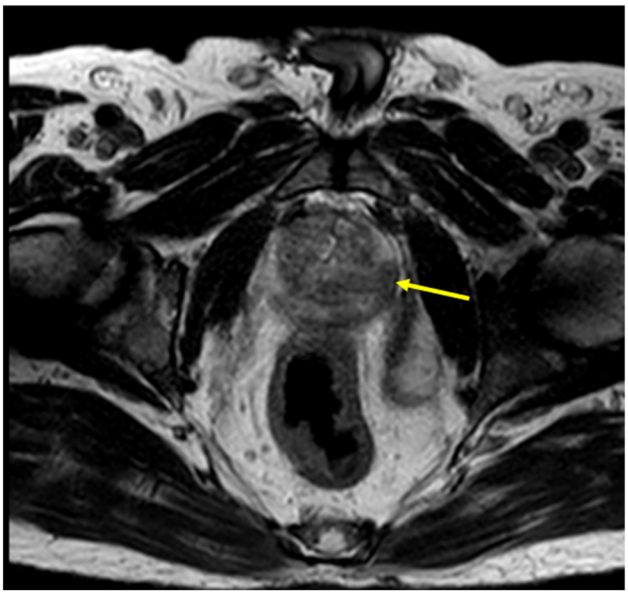

Figure 3: Prostate MRI demonstrated a convex contour of the prostate capsule lesion in T2-weighted (arrow).

grade 2 fatigue and anemia. Concurrently, the PSA level marginally decreased from 414.20 to 392.80 ng/mL within 2 months of treatment. However, it subsequently increased to 866.50 ng/mL by August 2022. This substantial elevation in PSA level strongly indicated an early progression of the disease. Subsequently, the patient received two cycles of ^{177}Lu-PSMA-617. *BRCA* testing for prostate was approved in our center in January 2023. NGS was performed on the patient's bone biopsy samples, revealing a mutation in the *BRCA2* gene at position 8364G>A. Nevertheless, the VAF index was less than 5 %. Further examination of blood samples confirmed the presence of a similar genetic mutation identified in the previous tissue sample. Unfortunately, several liver lesions were detected, and the patient's clinical status deteriorated within 1 month with liver failure, precluding the administration of PARPi. Consequently, the patient's overall survival duration was limited to 24 months.

Investigation exhibited a family history marked by a younger sister (III.4) diagnosed with breast cancer at the age

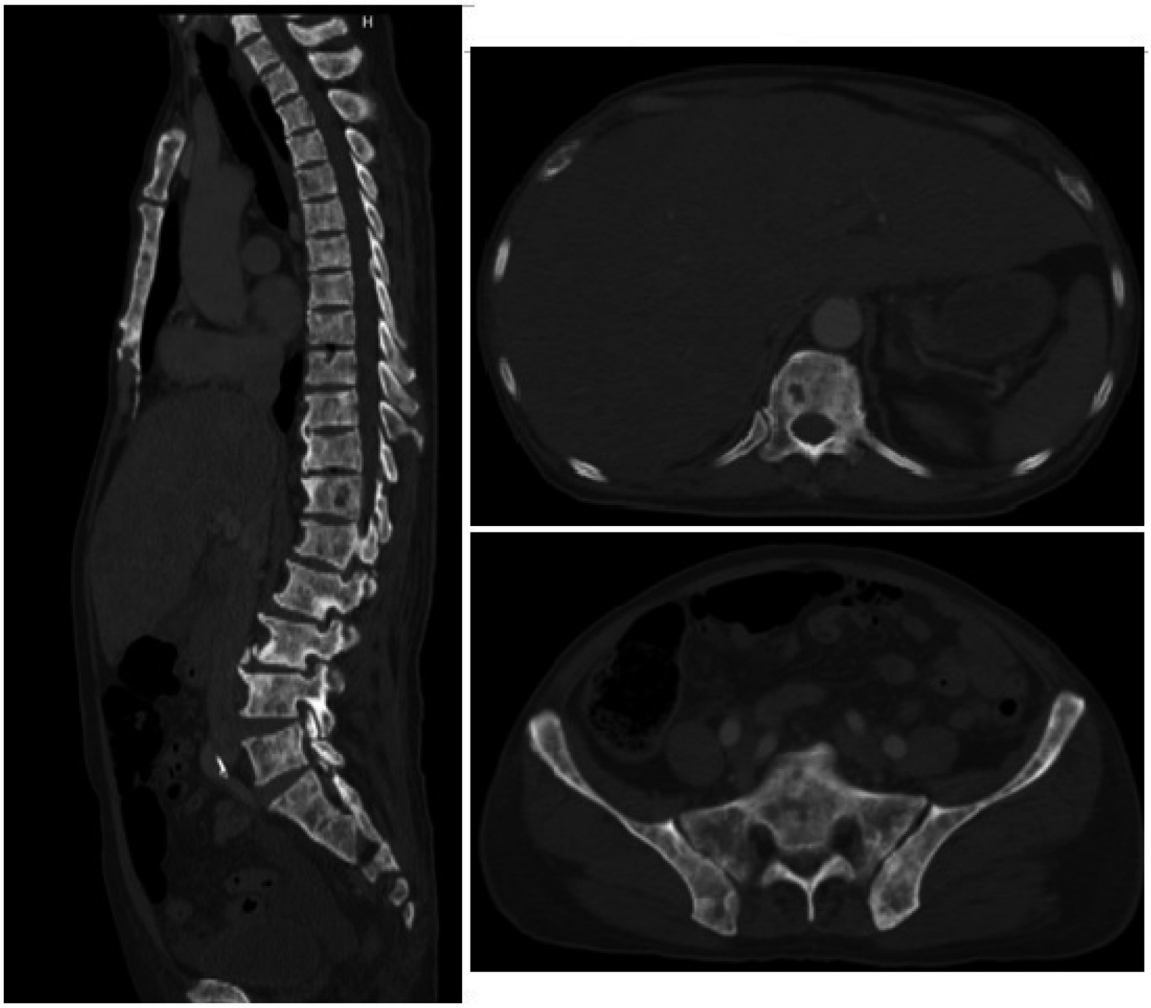

Figure 4: CT scans showed multiple combinations of osteolytic and osteoblastic metastasis in January 2022.

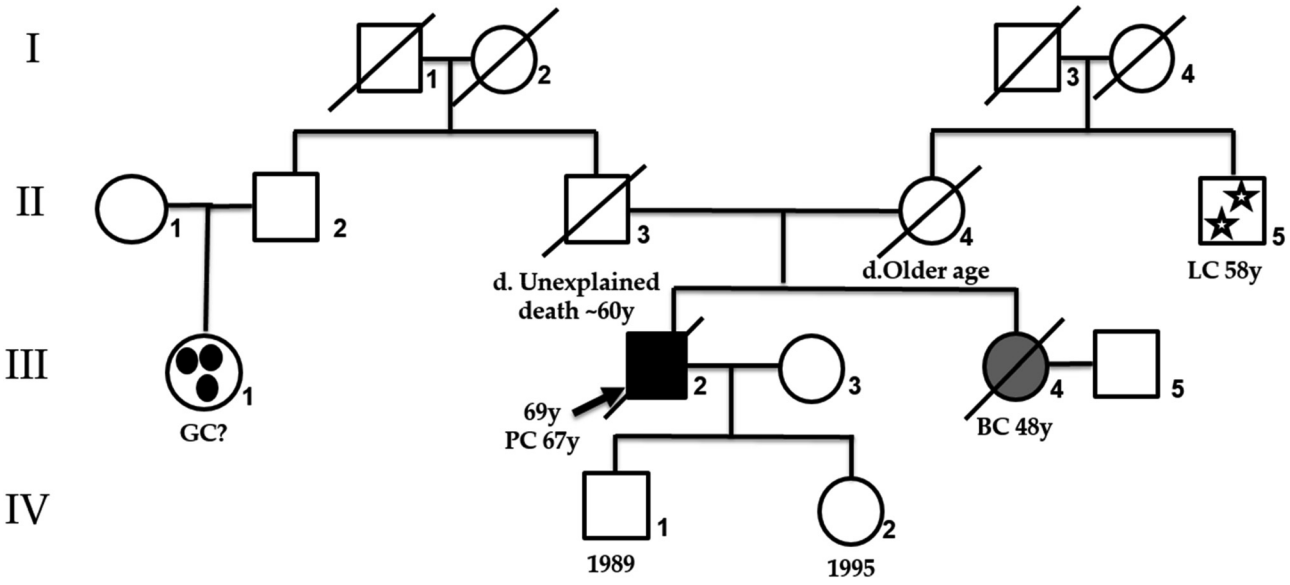

Figure 5: Pedigree chart of patient #1 (III.2) (PC, prostate cancer; BC, breast cancer; GC, gastric cancer; LC, lung cancer).

of 48. However, she died before the research timeframe rendering her sample unavailable. The patient's father (II.3) died from an unidentified disease at the age of 60. Additionally, the patient had a cousin (III.1) with gastric cancer and an uncle with lung cancer (age at diagnosis unknown) (Figure 5). Genetic counseling was conducted on the patient's relatives, while genetic testing was performed on the patient's children. Fortunately, the patient's children (IV.1 and IV.2) did not harbor the pathogenic variant.

Discussion

The patient had a germline mutation and a family history of breast cancer indicated hereditary breast and ovarian cancer syndrome. Having a younger sister (a first-degree relative) who was diagnosed with breast cancer before the age of 50 constituted a high-risk factor for being a germline mutation carrier in this patient. The occurrence of stomach cancer in a cousin and lung cancer in an uncle did not significantly contribute to the genetic predisposition. Simultaneously, the patient exhibited clinical features resistant early to non-PARP inhibitor treatment. Genetic counseling was conducted among the family members of the patient.

Additionally, in the presented case, the patient's tissue was obtained from a bone. Analysis of this sample may not provide sufficient information to diagnose the patient's genetic status. On the other hand, patients with a family history of cancer diagnosis at an early age, coupled with pathological features like treatment resistance, metastasis, and a high Gleason score, are more likely to harbor germline mutations. Therefore, a genetic mutation identification test in this patient was necessary.

Patient's perspective

Patient #1's wife, "If we had known about *BRCA* mutation sooner, maybe he could have lived longer. Fortunately, my children do not have these mutations, but we will screen them early for cancer."

Learning point

(1) *BRCA2* mutations can drive aggressive forms of prostate cancer.
(2) A detailed family history is crucial as it can provide clues to potential genetic predispositions.
(3) Genetic counseling and testing can offer valuable insights into disease management and prognosis.

Case 2

Case presentation

Patient #2, a 64-year-old man, presented with lower urinary tract symptoms. His medical and family histories were unremarkable. Further investigation with prostate MRI showed a direct extra-glandular tumor extension into the seminal vesicles and multiple common iliac lymph nodes (Figure 6).

A 12-core transrectal ultrasound-guided prostate needle biopsy revealed the presence of prostatic adenocarcinoma (Gleason score: 4+3=7). Genetic analysis was performed using the NGS technique and Sanger sequencing. *BRCA2*

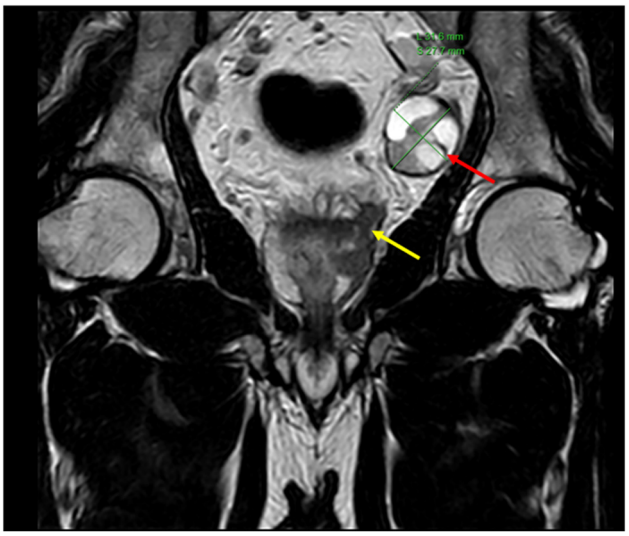

Figure 6: A prostate MRI showed a T2 hypointense lesions which invasion to seminal vesical (yellow arrow) and left common iliac lymph node (red arrow).

gene mutations were identified in tumor tissue samples (7879A>T) with a mutation frequency of 3.10 % (VAF). A blood test was performed, indicating the absence of germline mutations.

No evidence of distant metastasis was detected on both the 99mTc-MDP bone scan and whole-body CT scan; leading to the diagnosis of cT3bN1M0 (Gleason 4+3=7) prostate adenocarcinoma.

The patient subsequently underwent definitive radiotherapy and goserelin combined with bicalutamide. His PSA level reached a nadir of 0.03 ng/mL and maintained stability during the last assessment in October 2023.

Discussion

BRCA2 mutations were found in tumor tissue samples with a mutation frequency (VAF) of 3.1 %. It is noteworthy that in patients solely carrying mutations in the tumor tissues, the variant allele frequency may be relatively low.

Patients were screened, resulting in the detection of the disease at an early stage, and received early treatment. PARPi could be a potential therapy when resistance to alternative regimens emerges.

Patient's perspective

Patient, "I hope that when my cancer progresses, I can access targeted therapy".

Learning points

Testing for *BRCA* gene mutations should be conducted in prostate cancer patients (irrespective of the absence of a family history) to predict disease prognosis and to provide additional treatment methods (PARPi) in advanced-stage disease.

Discussion

In Vietnam, early detection, diagnosis, prognosis, and treatment of prostate cancer still pose many challenges when the early detection rate is low and the mortality rate from prostate cancer remains high. The application of specialized diagnostic and treatment techniques, such as biomarker analysis, contributes to individualized diagnosis and treatment and improves the cancer treatment capacity in Vietnam. Our study initially described the characteristics of prostate cancer patients with *BRCA* mutations, including the clinical characteristics such as age at diagnosis, pretreatment PSA concentration, Gleason score, metastasis status, and disease stage, and reported a case series of *BRCA* mutations.

Rate of detection of BRCA gene mutations in the study group

BRCA1 and *BRCA2* genes are the two most mentioned and researched genes related to breast and ovarian cancers. The role of *BRCA* gene mutations is not only being further studied in breast and ovarian cancers but is also expanding in other cancers, such as pancreatic and prostate cancers. A previous study reported a *BRCA1* gene mutation incidence of 3–9 % in prostate cancer patients, of which the rate of *BRCA2* mutations was 15–34 % [25]. In our study, 8.3 % of the patients had *BRCA2* mutations, while none had *BRCA1* mutations. Thus, *BRCA2* is closely associated with prostate cancer. Indeed, two recent studies by Silvestri et al., and colleagues showed that people carrying *BRCA2* mutations have a high risk of developing prostate cancer, especially in invasive and metastatic cases; the risk varies depending on family history and location of gene mutation [26]. Most studies have shown a stronger association between *BRCA2* mutations and prostate cancer than that with *BRCA1* mutations [27, 28].

Point and frameshift mutations frequently occur in the coding regions of the *BRCA1* and *BRCA2* genes [29]. A given population will circulate specific mutations within that population at a higher rate than in other populations [30]. In a study about heredity and Spain male breast cancer [31], mutations included 5530T>A in the *BRCA1* gene and 6860delA, 5374-5375del, and 03 cases have 9382C>T in the *BRCA2* gene. In our study, three patients demonstrated point mutations leading to nonsense and missense mutations: one patient had deletion, one had insertion, and none had frameshift mutation (Table 1). More research with

a bigger sample size is required to determine the features of the mutations in the Vietnamese population.

Some clinical characteristics and BRCA gene mutation status

The average age of the research group was 71.7 ± 8.2; ranging from 54 to 90. Most patients were aged between 60 and 79 years. The median PSA level at diagnosis was 202.10 ng/mL, and the highest level was 5,000.00 ng/mL. The lowest level was 1.80 ng/mL. Most of the patients had a PSA level of >100 ng/mL at diagnosis.

The average initial diagnosis age in the five patients with *BRCA* mutations was 66.2, tending to be lower than that of patients without *BRCA* mutations (72.2). The Gleason grade group in five patients with *BRCA* mutations also tended to be higher (80 %, Gleason scores: 4–5) compared with those in patients without mutations (78.5 %). The results of this study also demonstrated that the rates of lymph node metastasis and distant metastasis in patients with *BRCA* mutations were higher (60 and 80 % compared with 45.5 and 72.7 %, respectively) (Table 3).

These differences were not significant because of the low number of patients with *BRCA* mutations; however, this study also showed that *BRCA2* carriers tend to have a worse prognosis. In a large retrospective study on 2019 prostate cancer patients, there were 18 patients had *BRCA1* mutations, and 61 patients had *BRCA2* mutations. The *BRCA* carriers were more frequently associated with a higher Gleason score and more advanced stage at initial diagnosis than the frequency of non-carriers. Tryggvadottir et al. analyzed 89 prostate cancer patients in Iceland from 1955 to 2004. *BRCA* mutation carriers were diagnosed at a younger age (69 years) compared to non-carriers (74 years). Additionally, mutation carriers were admitted with a more advanced tumor stage and had poorer differentiated histology than non-carriers [32]. However, Thorne et al. showed no difference in the age of diagnosis or the initial serum PSA level between patients with and without mutation. However, *BRCA2* mutation patients presented with poorer differentiated and more advanced tumor stages compared to those observed in *BCRA* wild-type patients [18].

To our knowledge, this study is the first to report the gene carrier status of Vietnamese patients with prostate cancer as well as the accompanying clinical characteristics. However, due to the small sample size and low mutation detection rate, statistical analysis is not meaningful for assessing the relationship between gene carrier status and the pathological features of prostate cancer.

Conclusions

This study provides preliminary data on *BRCA* mutations in prostate cancer patients in Vietnam, suggesting that *BRCA2* mutations may be associated with more severe disease characteristics of prostate cancer. The reported cases provide further insight into the clinical significance of these mutations as well as suggestions for indications and testing procedures to determine the genetic carrier status for cases with these mutations.

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Research Ethics: This study was approved by the Ethics Committee of Bach Mai Hospital, Vietnam (approval number: 5362/BM-HĐĐĐ).

Informed consent: Informed consent was obtained from all subjects involved in the study.

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