Niraparib-Related Pulmonary Embolism During Ovarian Cancer Therapy

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Research Article

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Abstract

Niraparib, an oral, potent, highly selective poly (ADP-ribose) polymerase (PARP) inhibitor, has promising clinical benefit for maintenance treatment of patients with ovarian cancer in partial response to platinum-based chemotherapy, especially in patients with *BRCA* mutation. In publicly available niraparib-related treatment adverse events, gastrointestinal disorders and haematological toxicities were most commonly reported with manageable safety profile. Herein, we firstly describe a severe and never reported pulmonary embolism (PE) associated with the use of niraparib in a patient with *BRCA* mutation advanced high-grade serous ovarian cancer, and received anticoagulant therapy after PE. There have been no reports of PE caused by the use of niraparib in patients with advanced high-grade serous ovarian cancer, knowledge of the occurrence of PE after the use of niraparib may assist other clinicians in managing this rare but potentially serious toxic effect.

Main Text

Niraparib, an oral, potent, highly selective PARP inhibitor, has promising clinical benefit for maintenance treatment of patients with ovarian cancer in partial response to platinum-based chemotherapy, especially in patients with *BRCA* mutation or homologous recombination deficiency (HRD) positive disease.[1,2] In publicly available niraparib-related treatment adverse events, gastrointestinal disorders and haematological toxicities were most commonly reported with manageable safety profile.[1] Herein, we firstly describe a severe and never reported pulmonary embolism (PE) associated with the use of niraparib in a patient with advanced high-grade serous ovarian cancer.

A 55-year-old female patient was diagnosed with advanced high-grade serous ovarian cancer after comprehensive multidisciplinary consultation. Platinum-based chemotherapy was then administered as first-line treatment and the disease was evaluated as partial response. To seek for an effective maintenance therapy, tumor *BRCA* mutation and HRD status were analyzed using a next generation sequencing assay in patient providing tissue sample in a CAP authenticated lab. Subsequently, *BRCA2* c.6860G>T (1.85% abundance), *CDK12* c.956dupA (22.04% abundance) and *ATM* c.5692C>T (1.64% abundance) mutation (Fig. 1A-C) were detected and confirmed by polymerase chain reaction assay, suggesting PARP inhibitor may show promising clinical benefit for the maintenance treatment.

Two months after the last cycle of chemotherapy, niraparib (200mg once daily) was administered for the following maintenance treatment, clinical and radiological follow-up within the first 2 months showed no evidence of progression and severe adverse reaction. After taking niraparib for two and a half months, the patient was presented to the emergency room with the chief complaints of dyspnea and lower abdominal pain that had begun a few days earlier. Emergency contrast-enhanced computed tomography revealed dilated pulmonary veins with hypo-dense filling defect highlighting the presence of thrombosis (Fig. 1D, E). Meanwhile, a concurrent blood test revealed the serum D-dimer was 23.19 μg/ml (normal 0-0.55) and the serum fibrinogen was 4.38 μg/ml (normal 2-4). Based on the clinical presentation, CT images and remarkably increased serum D-dimer and fibrinogen levels, a diagnosis of PE was made, she was then

transported to the high care unit under anticoagulant therapy. Three days after the treatment, CT examination detected the remaining thrombi and her serum D-dimer decreased to 3.66 μg/ml.

There are several reports of PE occurring after operation or during chemotherapy in patients with ovarian cancer.[3,4] However, confirmed by publicly available niraparib-related treatment adverse events, there have been no reports of PE caused by the use of niraparib in patients with advanced high-grade serous ovarian cancer. Thus, knowledge of the occurrence of PE after the use of niraparib may assist other clinicians in managing this rare but potentially serious toxic effect.

Declarations

Ethics approval and consent to participate:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patient for participating this case.

Consent to publication:

Informed consent was obtained from the patient for publication of this case.

Availability of data and material:

Not applicable.

Competing interests:

The authors declare that they have no conflict of interest.

Funding:

Not applicable.

Authors' contributions:

We were all involved in the clinical care and management of the patient, collecting the data, and drafting the manuscript. Wei and Chen collected data and wrote the first draft of the manuscript. Liu supervised the work. All authors critically reviewed and approved the final version. Written consent for publication was obtained from the patient.

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Compliance with Ethical Standards section:

Disclosure of potential conflicts of interest:

The authors declare that they have no conflict of interest.

Research involving Human Participants and/or Animals:

YES, Research involving Human Participants. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent:

Informed consent was obtained from the patient for participating and publication of this case.

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Figures

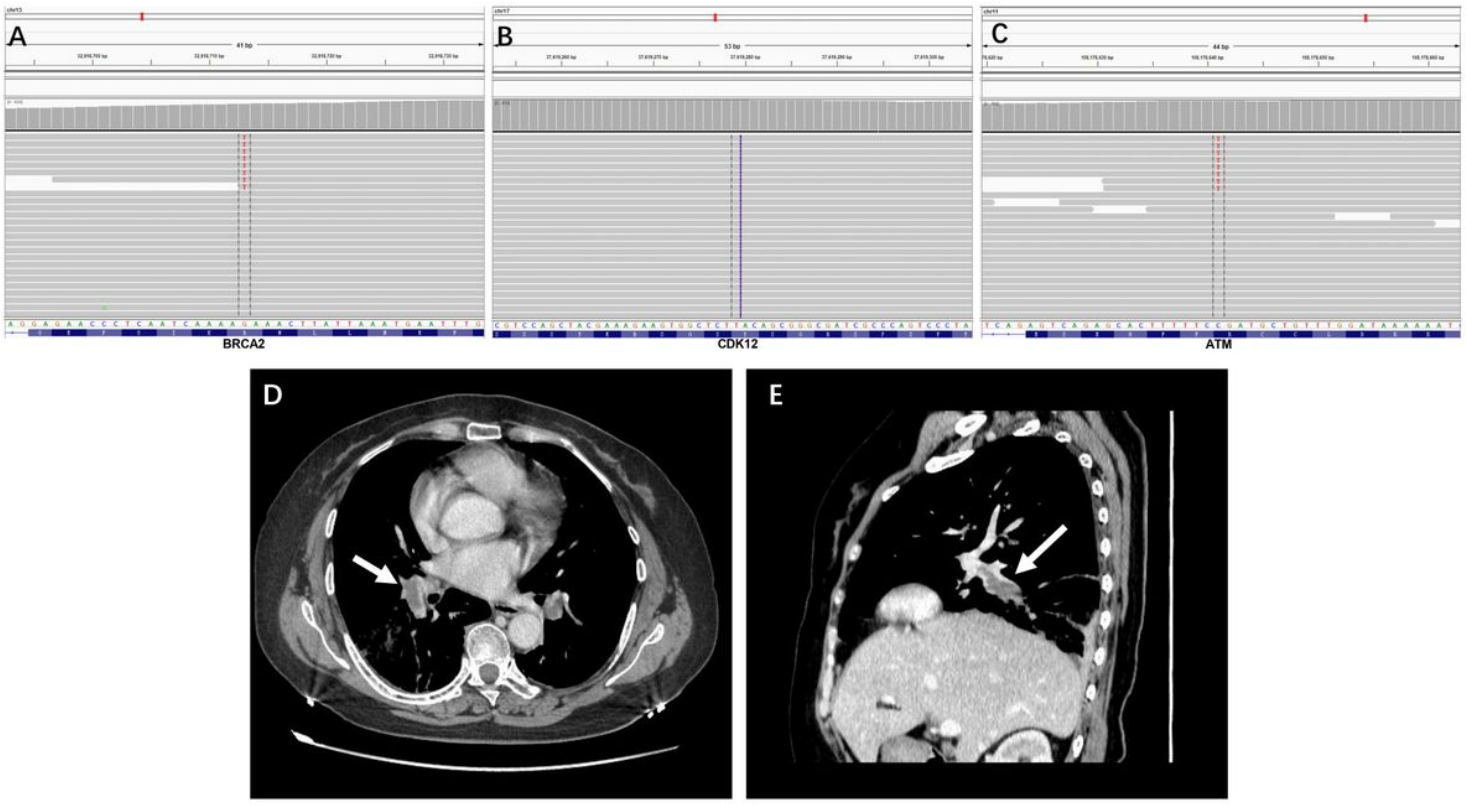

Figure 1

(A-C) the integrative genomics viewer snapshot of *BRCA2* c.6860G>T, *CDK12* c.956dupA and *ATM* c.5692C>T mutation. (D, E) contrast-enhanced computed tomography revealed dilated pulmonary veins with hypo-dense filling defect (E, 35.0×13.2 mm) highlighting the presence of thrombosis (arrow).