Case Report
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A Case of Primary Ovarian Primitive Neuroectodermal Tumor

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Abstract

Primitive neuroectodermal tumors (PNET) are a family of poorly differentiated malignant neoplasms of neuroectodermal origin. According to the location of origin, PNETs could be further categorized as central or peripheral. Peripheral PNET (pPNET) is an uncommon type that accounts for 1% of all soft tissue sarcomas and occurs outside the central and sympathetic nervous systems. Ovarian PNET is a very rare tumor with a high mortality rate. We report a case of pPNET originating from the pelvic cavity of a young woman. Ultrasound and Magnetic Resonance Imaging (MRI) findings demonstrated the presence of a high-grade malignant ovarian tumor. On microscopic evaluation, the tumor was composed of solid nests and sheets of small rounded cells, and on Immunohistochemical (IHC) evaluation, the tumor cells showed intense cell-membranous immunoactivity for MIC2 protein (CD99).
In the differential diagnosis of any invasive pelvic tumor in young women, pPNET should be considered.

Keywords: Primitive Neuroectodermal Tumor (PNET), Ovary, Magnetic Resonance Imaging (MRI) findings, Tumor, Diagnosis

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Introduction

The primitive neuroectodermal tumor (PNET) is a group of malignant neoplasms that originates from neuroectodermal cells belonging to the family of small round cell tumors (1). It is the second most common type of sarcoma that occurs in young adults and children (2). PNETs exhibit characteristic immunophenotypical and genetic features, which can be distinguished from other small-round-cell tumors (3).

Tumors are classified into two groups based on the cell of origin and location: peripheral and central types (4). Immunohistochemically, Peripheral PNETs differ from central ones in that these tumors typically show high amounts of the MIC2 antigen (CD99) and express characteristic chromosomal translocation (5).

Peripheral PNETs most commonly occur in the thoracopulmonary region, known as Askin tumor, the retroperitoneal paravertebral soft tissues, head and neck soft tissues, and soft tissues of intra-abdominal, intra-pelvic, and extremities (6).

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↑What is "already known" in this topic:
Primitive Neuroectodermal Tumor (PNET) is an uncommon tumor that accounts for 1% of all soft tissue sarcomas. PNET could be further categorized as central or peripheral. Ovarian PNET is a very rare tumor with high mortality rate. Few of the reported cases discussed imaging.

→What this article adds:
We report a case of peripheral PNET originating from the pelvic cavity of a young woman. Ultrasound and Magnetic Resonance Imaging (MRI) findings demonstrated the presence of a high-grade malignant ovarian tumor. As shown in this case report, imaging findings in association with clinical and laboratory findings can help to predict the differential diagnosis.

PNETs of the female genital tract are a rare entity and may originate from the uterine corpus, ovaries, cervix, and vulva (7).

We report a case of PNET originating from the pelvic cavity of a young woman, with a focus on the imaging findings.

Case Presentation

The patient was a 21-year-old white virgin woman who presented to the gynecology clinic with an irregular menstrual period and abdominal distension for the past few months. She had no significant familial or personal history of genital tract or other abdominopelvic cancers. Physical examinations revealed abdominal distension, which was firm and nodular in deep palpation. The vital signs were stable.

Laboratory evaluation revealed an elevated CA-125 concentration of 1072 U/ml, while the other tumor markers were within normal limits (CA19-9=9.2 U/ml, AFP=2.3 ng/ml, βHCG < 1 mU/ml).

Transabdominal ultrasound examination showed multiple complex nodules of tumor involving the pelvic cavity diffusely. The largest component, measuring approximately 77×56 mm2, was located on the right side of the pelvis and showed central necrotic areas with a thickened peripheral solid component (Figure 1). The ovaries were not separately detectable from the tumor. Peritoneal thickening and moderate amounts of ascites in the pelvic cavity were evident. Doppler evaluation showed vascularity in the solid components with the following Doppler parameters (Figure 2):

Peak systolic velocity (PSV)=42.07 cm/s
End diastolic velocity (EDV)=19.59 cm/s
Resistive index (RI)=0.53
Pulsatility index (PI)=0.71

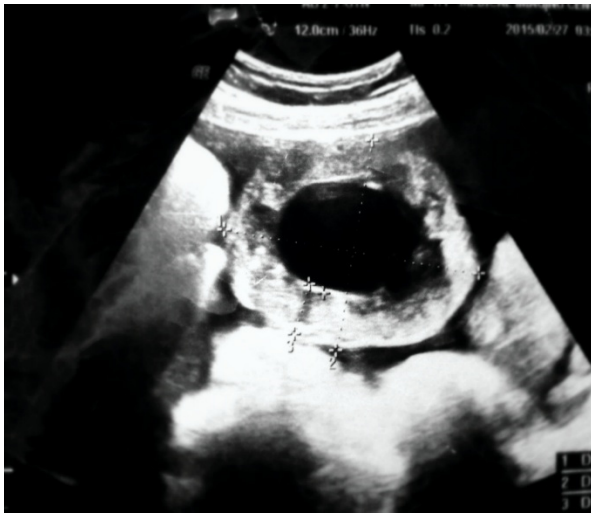


Figure 1. Multiple tumor nodules in the pelvic cavity with the largest component measuring about 77×56 mm^2 on the right side which shows a central necrotic area with thick peripheral solid component

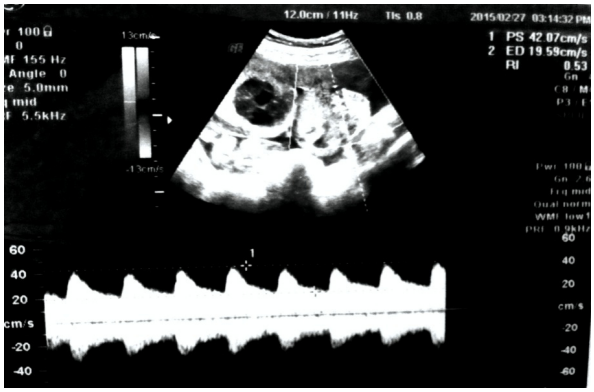


Figure 2. Doppler parameters of the solid components shows, PS=42.07 cm/s, ED=19.59 cm/s, RI=0.53, PI=0.71

To evaluate the extension of the tumor and to possibly collect more diagnostic information, the patient was prescribed anatomical and advanced MR imaging (dynamic contrast-enhanced (DCE) and diffusion-weighted imaging (DWI)).

The MRI scans were performed on a 3-Tesla MRI system (Tim Trio, Siemens, Erlangen, Germany) using a body phased-array coil. Prior to contrast administration, the following sequences were acquired: axial T2-weighted turbo spin-echo, sagittal T2-weighted turbo spin-echo, axial T1-weighted gradient-echo with and without fat suppression, and diffusion-weighted imaging.

Then, Gadolinium chelate (Dotarem 15mg) at a dose of 0.2 mL.kg^{-1} with a rate of 2 mL. s^{-1} was given, followed by flushing the tubing with 20 mL of normal saline. Images were obtained before the bolus injection at 7.6-s intervals beginning 10 s, for a total of 380 s and a total of 50-time frames. At the end, 6 minutes after gadolinium injection, delayed-enhanced axial and sagittal T1-weighted gradient-echo images with breath-hold were acquired.

MRI findings showed multiple heterogeneous nodules of complex masses filling the pelvic cavity on both sides and in the presacral region, which showed intermediate signal intensity on T1-weighted and high signal intensity on T2-weighted imaging. The tumor also showed small areas of T1 high signal intensity compatible with intra-tumoral hemorrhagic foci (Figure 3). Suspicious adhesions to the rectum and to some of the small bowel loops were evident.

There were also significant amounts of ascites with high signal intensity components in favor of bloody materials, along with omental thickening and nodularity. The solid components of the tumor showed marked enhancement after contrast administration (Figure 4).

Dynamic contrast-enhanced (DCE) MRI analysis revealed a type-3 curve of enhancement (Figure 5).

Semiquantitative analysis showed the following parameters:

SI max=352.8, SI peak=317.52, SI rel=317.02, WIR=0.98, WOR=0.036 and AUC=5533.56

Finally, on quantitative analysis, pharmacokinetic parameters were compatible with a malignant tumor (K_{trans} = 0.264 (s^{-1}), K_{ep} = 0.008 (s^{-1}), V_p = 36.1%) (Figure 6).

On DW images, the solid tumor showed areas of diffusion restriction (Figure 7).

According to the Ovarian-Adnexal Reporting and Data

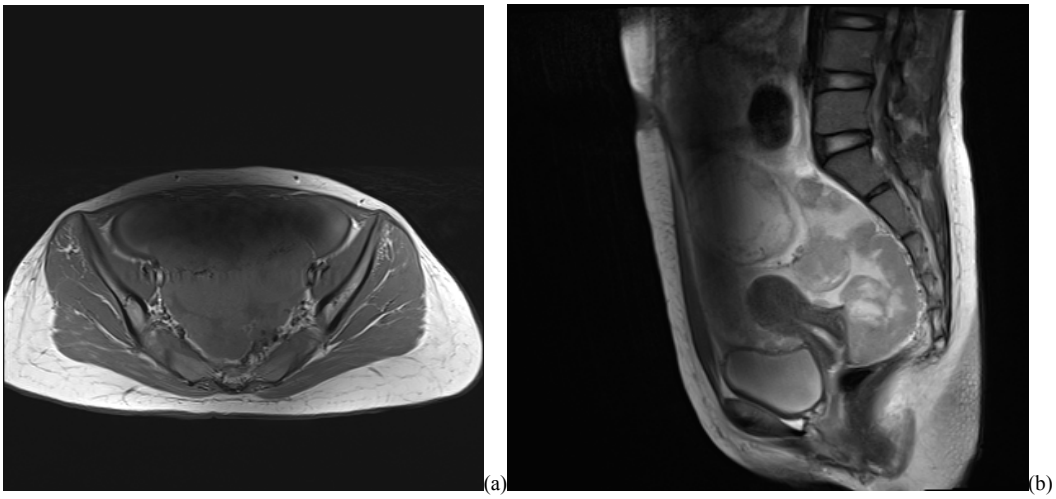


Figure 3. MRI findings of the pelvic tumor, as shown on the axial T1 weighted (a) sagittal T2 weighted (b) images, revealed a complex heterogeneous mass that filled the pelvic cavity on both sides and also in the presacral region. The mass also showed intermediate signal intensity and high signal intensity on T1WI and T2WI respectively. The mass also showed small regions of T1 high signal intensity compatible with intratumoral hemorrhagic foci.

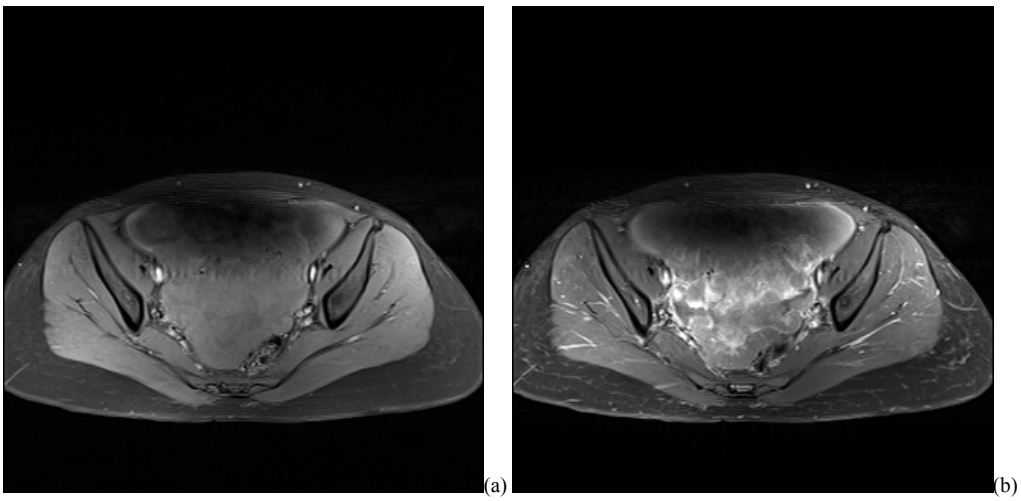


Figure 4. The tumor solid components showed marked enhancement after contrast administration (b) in comparison with pre-contrast images(a)

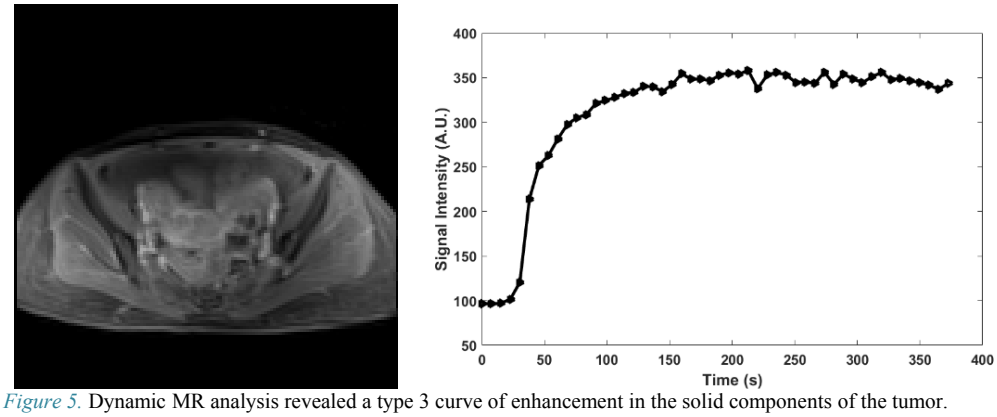


Figure 5. Dynamic MR analysis revealed a type 3 curve of enhancement in the solid components of the tumor.

System (ORADS) criteria published by the American College of Radiology, this ovarian lesion was classified as ORADS 5 on both ultrasound and MRI, indicating a high probability of malignancy.

During the exploratory laparotomy, a large, vegetative tumor was observed filling the pelvic cavity and cul-de-sac. The tumor was friable and hemorrhagic, with areas of cystic and necrotic components. The omentum was infiltrated by the tumor, and an omentectomy was performed. Adhesions were also evident to the rectum, bowel loops, serosal surface of both kidneys and the inferior surface of the liver.

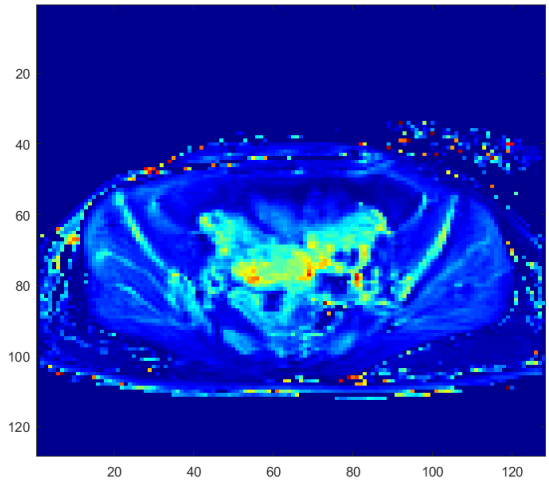
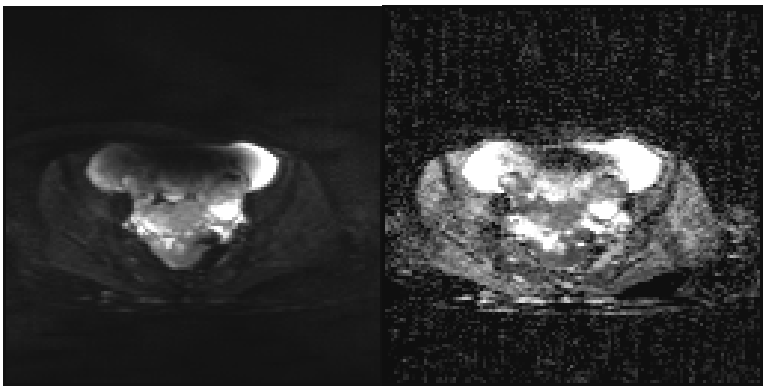


Figure 6. The Ktrans-encoded color map obtained from the pharmacokinetic quantitative analysis of the DCE-MRI shows warm and hot areas, representing areas of high-grade malignancy.



(a) (b)

Figure 7. In DWI (a) and ADC (b) sequences, the solid tumor showed areas of restriction.

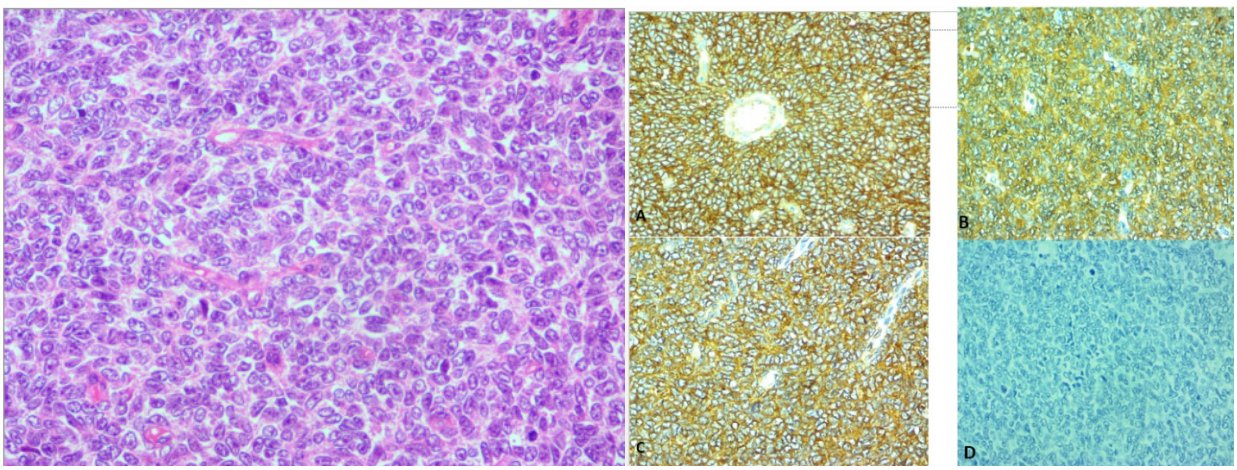


Figure 8. H&E stained sections show small round cells with scant cytoplasm arranged in a diffuse pattern with little structure. Mitotic activity is high. IHC study shows the positive reaction of tumor cells with CD99, NSE, Synaptophysin and negative results with LCA and CK.

Both ovaries were infiltrated and replaced completely by tumorous tissue and could not be detected during surgery. The frozen section reported poorly differentiated carcinoma.

Because of a severely hemorrhagic fragile tumor and diffuse involvement of the pelvic organs, the patient was considered non-operable and was scheduled for neo-adjuvant chemotherapy.

Permanent section profiles showed very crowded small

cells and a high nuclear-cytoplasmic ratio in neoplastic tissue arranged in sheets with occasional organoid patterns.

An immunohistochemical study revealed positive immunoreactivity for MIC 2 (CD99), NSE, Synaptophysin,Vimentine as well as negative immunostaining for CK7, CK20, EMA, Inhibin, Calretinine, LCA, WTI, GFAP and P53. These findings allowed the pathologist to make the diagnosis of a primitive neuroectodermal tumor (PNET).

Discussion

PNETs account for 1% of all soft tissue sarcomas. Approximately 80% of the patients are less than 20 years old (8). Regarding the location, the PNET family could be classified into the following two groups (9):

- Central PNETs could be subdivided into two groups: CNS primitive neuroectodermal tumors (PNETs) and autonomic nervous system Neuroblastoma
- Peripheral primitive neuroectodermal tumors (pPNETs) - Tumors originate from tissues outside the autonomic and central nervous system

As described previously, the thoraco-pulmonary region is the most common location of pPNETs, called Askin tumor, the retroperitoneal paravertebral soft tissues, head and neck soft tissues, and soft tissues of intra-abdominal, intra-pelvic, and extremities (6).

Only rare cases of female pelvis PNET have been reported, which can arise from the uterus body, ovaries, or less commonly broad ligaments (3, 10, 11).

In PNETs, clinical symptoms, such as swelling of the surrounding organs and pain, are related to the tumor location and are nonspecific.

Serum CA125 levels may increase and this marker is important for diagnosis, follow-up, and prognosis of PNET of the female internal genital tract (12). As the patient reported here, other tumor markers may not show any significant elevation.

In some articles, imaging features of pelvis PNET have been described. In a case, a pelvic mass measuring 110 x 90 x 90 mm was observed on MRI. The described mass had inhomogeneous T1 and T2 signal, with areas of T2 isosignal and T1 hypersignal within and minimal, non-gadolinophilic, diffusion restriction (13). In another article, Abdominal and pelvic MRI revealed a large mass in the abdominal and pelvic cavity, which showed a low and intermediate T1 signal intensity and a high, heterogeneous T2 signal intensity, with good enhancement (14).

However, the role of imaging in diagnosing PNET prior to histopathological evaluation has not been studied before. As shown in this case report, imaging findings in association with clinical and laboratory findings can help to predict the differential diagnosis. When a tumor has filled the pelvic cavity, evaluation of pelvic organs by imaging could be helpful in distinguishing the organ of origin. Since the PNETs usually arise in young patients, and ovaries are always easily detectable in this age group (due to their significant size and the presence of follicles), the absence of any ovarian tissue in the imaging examinations could be suggestive of the ovarian origin of the PNET tumor, as in our patient.

The imaging findings play a crucial role in estimating the local extension of the tumor, which is essential for treatment planning. When the tumor invades the adjacent organs, neoadjuvant chemotherapy is often considered for the patient rather than a surgical approach, which carries a higher risk due to the severely hemorrhagic nature of the tumor.

While no single imaging modality can predict the diagnosis of PNETs with high certainty, newer techniques, such as quantitative dynamic contrast-enhanced MRI (DCE-MRI), may aid in the differential diagnosis. In this case, we have also evaluated the semiquantitative and pharmacokinetic parameters of the tumor on DCE-MRI, all of which were compatible with a highly aggressive malignant neoplasm. This finding, combined with the elevated serum CA-125 level in a young patient, raises suspicion for PNET to be included in the differential diagnosis.

Conclusion

Although PNET is a rare disease, it can be included in the differential diagnosis of other pelvic masses by using imaging and clinical findings.

Authors' Contributions

All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors. Sara Parviz, Masoumeh Gity and Fahimeh Zeinalkhani contributed to the study design. Anahita Fathi Kazerooni and Hamidreza Saligheh Rad contributed to the data acquisition and analysis. Fahimeh Zeinalkhani and Fatemeh Nili contributed to the data interpretation. Hadise Zeinalkhani and Peyman Kamali Hakim drafted or substantially contributed to revising the work. All authors read and approved the manuscript.

Ethical Considerations

Informed consent was obtained from the patient to publish the information, and the patient's name was not mentioned anywhere according to her request.

Acknowledgment

The authors thank all those who contributed to this study.

Conflict of Interests

The authors declare that they have no competing interests.

References

1. Yousefi Z, Sharifhi N, Hasanzadeh M, Mottaghi M Bolandy S. Peripheral Primitive Neuroectodermal Tumor of the Pelvis. Iran J Med Sci. 2014 Jan;39(1):71-74.
2. Kim KJ, Jang BW, Lee SK, Kim BK, Nam SL.A case of peripheral primitive neuroectodermal tumor of the ovary. Int J Gynecol Cancer. 2004 Mar-Apr;14(2):370-2.
3. Schmidt D. Malignant peripheral neuroectodermal tumor. Curr Top Pathol. 1995;89:297–312
4. Armbruster C, Huber M, Prosch H, Dworan N, Attems J. Ewing's sarcoma and peripheral primitive neuroectodermal tumor in adults: different features of a rare neoplasm. Onkologie. 2008;31:179–84.
5. Dedeurwaerdere F, Giannini C, Sciot R, Rubin BP, Perilongo G, Borghi L, et al. Primary peripheral PNET/Ewings's sarcoma of the dura: a clinicopathologic entity distinct from central PNET. Mod Pathol.

2002;15:673–678
6. Jurgens H, Bier V, Harms D, Beck J, Brandeis W, Etspuler G, et al. Malignant peripheral neuroectodermal tumors: a retrospective analysis of 42 patients. Cancer. 1988;61:349–357
7. Park JY, Lee S, Kang HJ, Kim HS, Park SY. Primary Ewing's sarcoma-primitive neuroectodermal tumor of the uterus: a case report and literature review. Gynecol Oncol. 2007;106:427-32.
8. Bernstein M, Kovar H, Paulussen M, Randall RL, Schuck A, Teot LA, et al. Ewing's sarcoma family of tumors: current management. Oncologist. 2006;11:503–19.
9. Batsakis JG, Mackay B, el-Naggar AK. Ewing's sarcoma and peripheral primitive neuroectodermal tumor: an interim report. Ann Otol Rhinol Laryngol. 1996 Oct;105(10):838-43.
10. Wang F, Zhang X, Shen Y, Li S, Lv M, Li C, et al. Primary primitive neuroectodermal tumor in pelvic cavity: an unusual case and literature review. Int J Clin Exp Med. 2016;9(2):4767-4774.
11. Tiong FL. A Rare Case of Pelvic Primitive Neuroectodermal Tumor in a 37-Year-Old Patient. J Med Cases. 2016;7(2):58-59.
12. Xiao C, Zhao J, Guo P, Wang D, Zhao D, Ren T, et al. Clinical analysis of primary primitive neuroectodermal tumors in the female genital tract. int J Gynecol Cancer. 2014 Mar;24(3):404-9.
13. Grigoriu C, Terzea DC, Lisievici AC, Georgescu TA, Constantin AE, Bacalbașa N, et al. Peripheral-type primitive neuroectodermal tumor of the ovary with EWSR1-FLI1 fusion transcript: a case report and brief review of literature. Rom J Morphol Embryol. 2021 Apr-Jun;62(2):581-586.
14. Chao X, Bi Y, Li L. Ovarian primary primitive neuroectodermal tumor: a review of cases at PUMCH and in the published literature. Orphanet J Rare Dis. 2019;14(1):147.