Case Report
Middle East Journal of Cancer; October 2018; 9(4): 328-333

Unusual Site of Metastasis of Placental Site Trophoblastic Tumor: Case Report and Literature Review

Leila Mousavi Seresht*, Hamed Golmohamadzadeh, Zohreh Yousefi*♦, Amir Hosein Jafarian***, Ali Moghimi**, Mojgan Soltani***

**Department of Obstetrics and Gynecology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
***Department of Surgery, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
****Department of Pathology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

Abstract

Placental site trophoblastic tumor is a subtype of gestational trophoblastic neoplasm with unpredictable clinical behavior. Cytoreductive surgery is the cornerstone of treatment. The aim of this article is to present a case with an unusual site of metastases of placental site trophoblastic tumor. A 35-year-old woman was referred to the academic center of GTN as a persistent case gestational trophoblastic neoplasm for standard treatment. Based on pancreatic metastases in the patient's work-up, she underwent cytoreductive surgery that resulted in significant improvement in her condition. Proper surgical approach of placental site trophoblastic tumor has a major role in the remission of this disease.

Keywords: Placental site trophoblastic tumor, Gestational trophoblastic neoplasm, Pancreas metastasis

Introduction

Gestational trophoblastic disease (GTD) includes molar pregnancy and GTN subtypes which comprise choriocarcinoma, epithelioid trophoblastic tumors, and placental site trophoblastic tumor (PSTT). Placental site trophoblastic tumor is rare, 2%-3% of GTN with approximately 630 cases reported thus far.[1] The distinguishing feature of PSTT from other GTN subgroups is its capacity for slow growth and resistance to chemotherapy. This finding appears to be in 60% of cases.[2] Surgery and tumor elimination are the mainstay treatment, although adjuvant chemotherapy is not ineffective.[3] Careful history, βhCG level,

♦Corresponding Author:
Zohreh Yousefi, MD
Department of Obstetrics and Gynecology, Fellowship of Gynecology Oncology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
Tel: +985138412477
Email: Yousefiz@mums.ac.ir

Received: November 15, 2017; Accepted: February 12, 2018

histopathologic study, and the use of multiple and suitable imaging studies are helpful in diagnosis and management of this tumor.[4] Metastatic sites of PSTT include the liver, lungs, brain, lymph nodes, gastrointestinal and omentum, vertebra, bladder, and kidneys.[5-7] Only one case of pancreatic metastasis was reported in 2006 by Baergen et al. Fortunately, this patient was successfuly treated by combination surgery and chemotherapy after multi-disciplinary consultation.[8] Zeng et al. successfully managed other patient with pre- and post-operative chemotherapy.[9] Due to the rarity of this tumor and unpredictable clinical behavior compared to other GTN, here, we reported a rare, unusual site for PSTT metastasis. We reviewed studies in English indexed in PubMed from 1995 to 2017 that focused on epidemiology, pathology, diagnostic imaging, prognostic factors, and treatment of PSTT cases.

Case Report

A 35-year-old woman (gravida 3, para 2) was referred to the Oncology Department of an academic hospital affiliated with Mashhad University of Medical Sciences in 2017. She had a history of 2 months missed period, and dilation and curettage due to a suspicious missed abortion. The pathology report indicated only necrotic tissue. Based on continuous vaginal bleeding during 3 months and a plateau βhCG level of approximately 220 mIU/ml in consecutive weeks, chemotherapy with single agent (methotrexate) 50 mg/m^2 was administered. Due to the lack of response to this agent of chemotherapy of methotrexate (MTX) and poor response to a second drug (actinomycin), she underwent additional workup. Pelvic ultrasonography showed a 4×4 cm mass in the anterior wall of the uterus with a thin endometrial line. Pelvic MRI was suspicious for an invasive mole; thus, the patient underwent a hysterectomy. The histological report confirmed PSTT (Figure 1). In the subsequent follow-up, after a few weeks and despite single-agent chemotherapy (high dose MTX), βhCG levels had increased. Re-assessment of the patient showed pancreas and liver involvement. CT scan detected three large masses of 3.5 cm in the liver and one lesion in the pancreas (Figure 2). βhCG level was 95 mIU/ml; therefore, we prescribed the

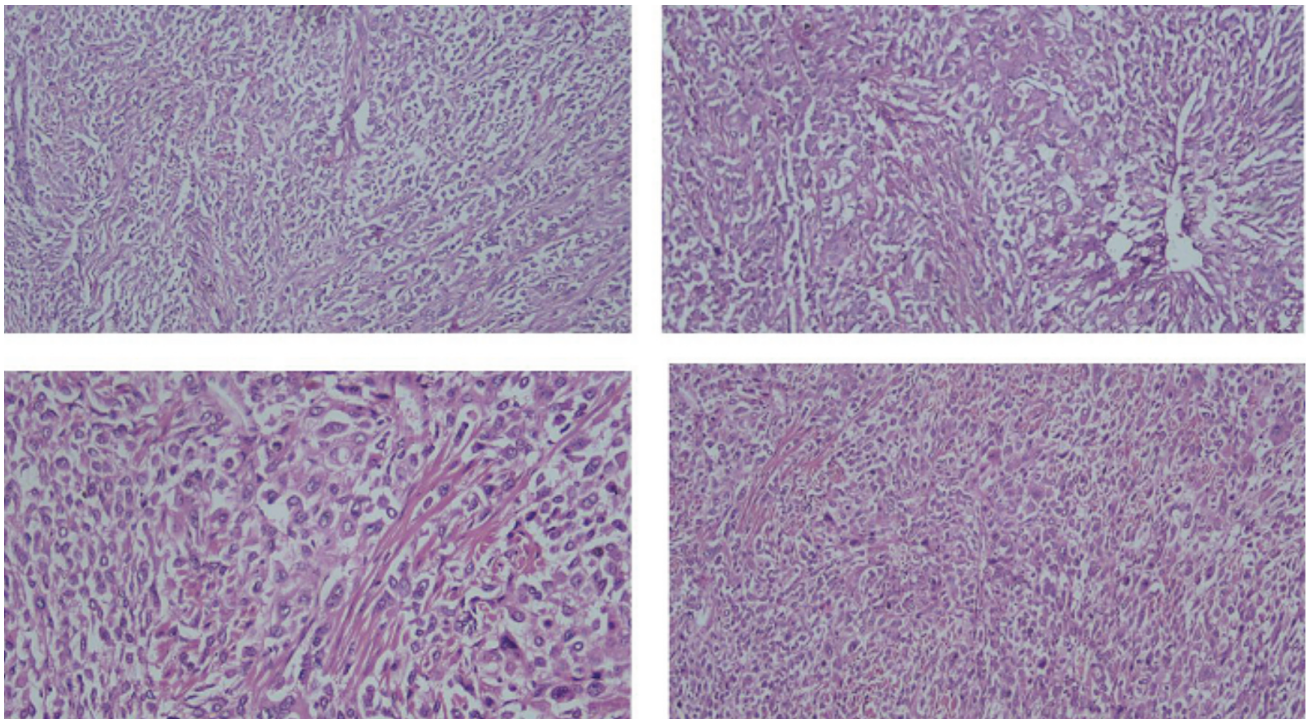

Figure 1. Histologic sections showing atypical trophoblastic cells with acidophilic cytoplasm and high mitotic rate and multiple nucleoli and entensive necrosis with myometrial invasion (H&E staining, 100×).

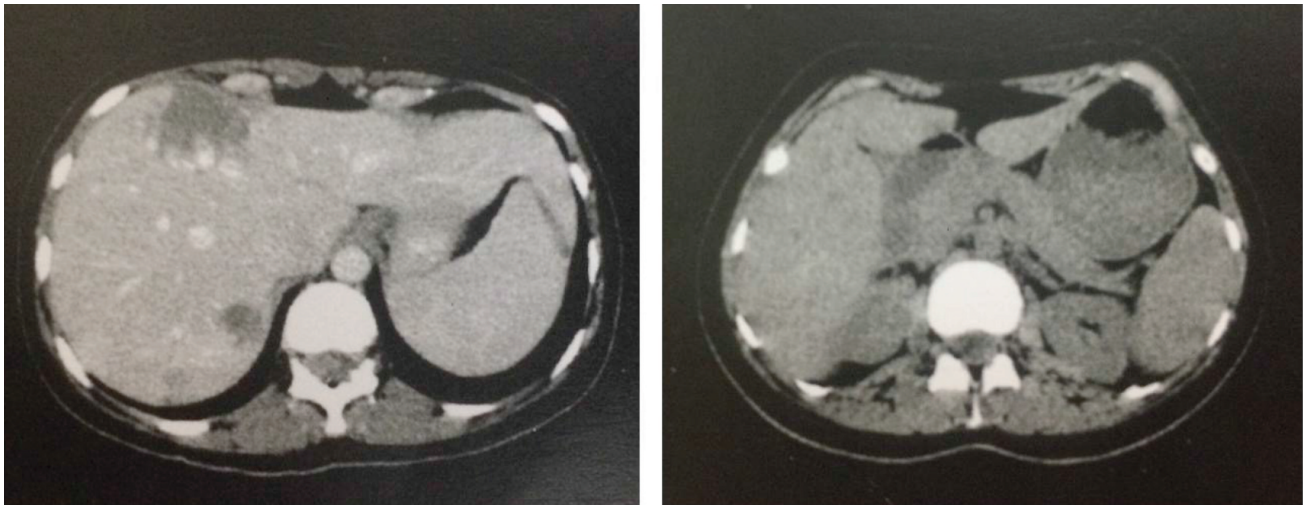

Figure 2. CT scan revealed multiple masses intra liver and pancreas.

standard combined chemotherapy regimen etoposide, MTX, dactinomycin, cyclophosphamide, and vincristine (EMA-CO). Despite two cycles of chemotherapy, the βhCG titer increased to 315 mIU/ml and she was given the chemotherapy regimen etoposide, MTX, actinomycin, cyclophosphamide, and cisplatin (EMA-EP). Because of poor response and increased βhCG level to 403 mIU/ml, she underwent a whole body PET scan which detected pancreatic metastasis (Figure 3). After multidisciplinary team recommendation, a laparotomy was performed. Extensive distal pancreatectomy along with splenectomy were performed (Figures 4, 5). After surgery, the βHCG titer in consecutive weeks was 13 mIU/ml. The patient has remained disease-free with no signs of recurrence at regular follow-up.

The patient provided written informed consent for publication of this case report and accompanying images.

Discussion

In this study, PSTT with metastasis to the pancreas has been successfully treated with appropriate surgery. Placental site trophoblastic tumor is a tumor that occurs in reproductive age women at a mean age of 32 years, which resembled the current patient. Histopathology analysis shows that intermediate trophoblastic

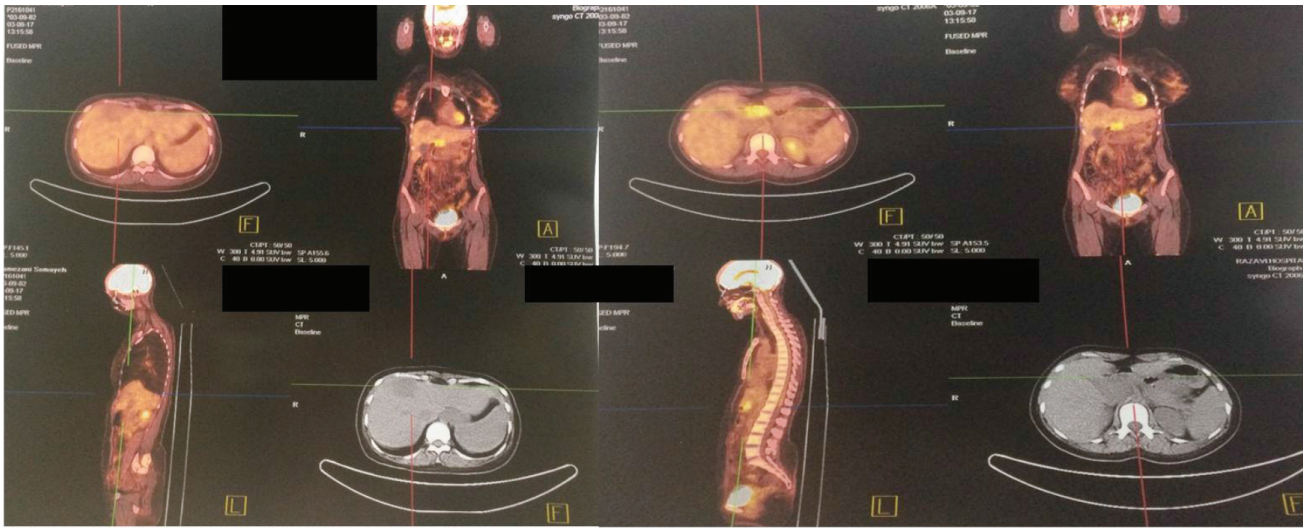

Figure 3. Whole body 18F-FDG PET/CT scan, show a 38×23 mm ill defied mass near the celiac, lesser curvature of the stomach near its antral part which is hyper metabolic and also a large mass in liver with no abnormal uptake and normal pancreas.

cells play a major role. Vascular invasion to muscle fibers, necrosis, and hemorrhage without chorionic villi are found in PSTT.[10] In addition, strongly positive staining HPL and cytokeratin are accepted methods for confirmation of PSTT.

Staining for pregnancy-associated major basic protein (pMBP), a specific marker of intermediate trophoblastic cells, is helpful to diagnose PSTT.[11] The symptoms of disease vary depending on the location of the tumor in the uterus, with amenorrhea or vaginal bleeding as with the current case, or metastatic symptoms in 30% of cases.[12] However, in some cases, the only symptom of the disease is increased βhCG titer (usually under 1000 mIU/ml).[13] There is no proposed specific imaging technique to diagnose PSTT. Ultrasound may show a solid or cystic mass in the fundus of the uterus similar to current case or another pelvic site. Moreover, CT scan and MRI may confirm the disease and identify distant metastasis.[14] Doppler ultrasonography is suggested because of the special feature of PSTT (low vascular resistance and high diastolic velocity of the tumor cells).[15] PET scan, as a new technique, is useful to identify the metastatic site and select a palliative or salvage treatment as with our complicated case.[16] Staging of PSTT is based on the GTN staging system, but GTN scoring is not suitable for management of PSTT.[17] The gold standard treatment for PSTT is surgery. Hysterectomy without bilateral salpingo-oophorectomy is performed. Since PSTT has a high potential for lymphatic spread, pelvic lymph node sampling and paraaortic lymphadenectomy in selected cases are recommended.[18] The role of chemotherapy in the adjuvant setting is unclear. Chemotherapy is recommended for: stages II and III cases, prolonged interval between the last pregnancy and disease (more than 2-4 years), high mitotic rate or deep myometrial invasion, age over 34 years, and βhCG over 1000 mIU/ml.[19]

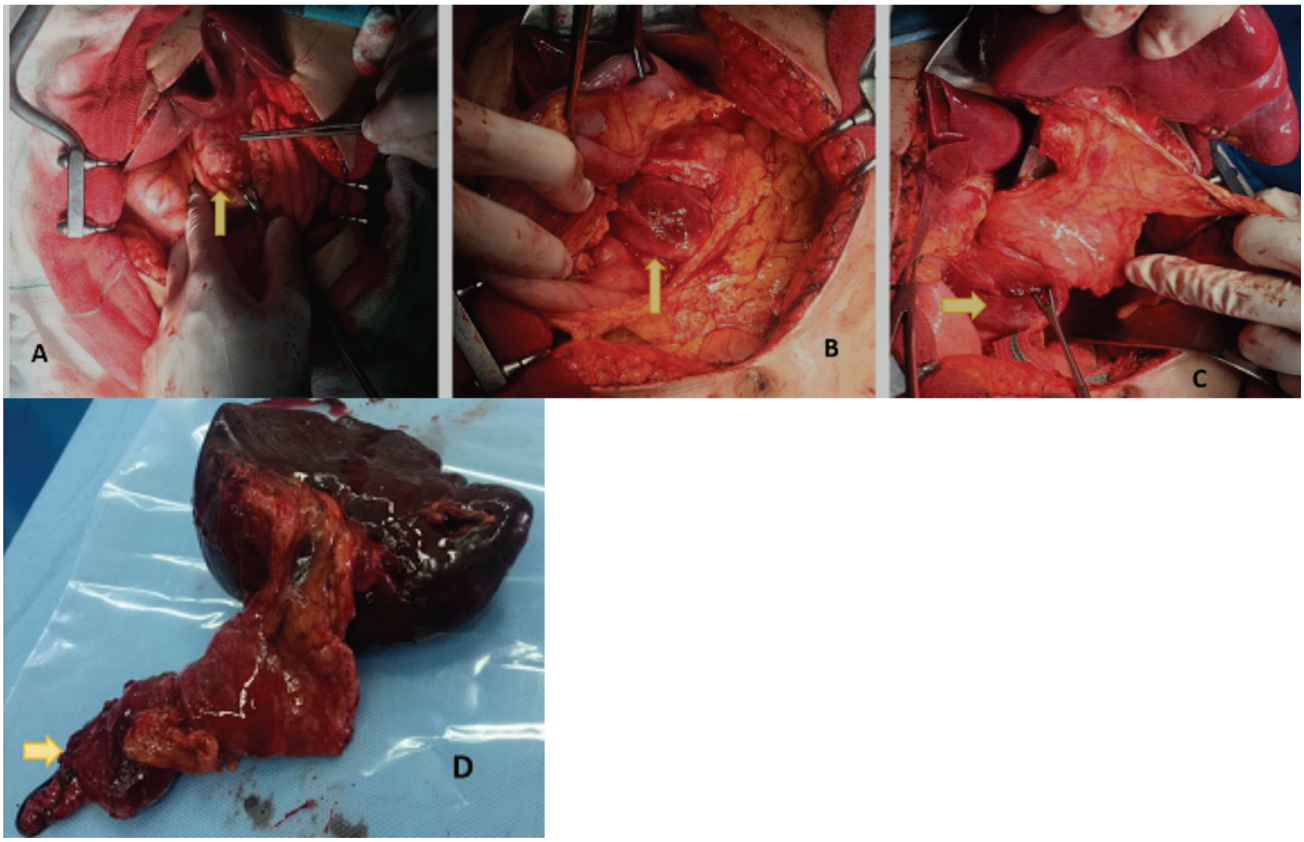

Figure 4. Laparotomy findings: A,B) Mass in the lesser sac-gastrocolic omentum. C) Mass in pancreas (arrow). D) Placental site trophoblastic tumor (PSTT) in pancreas after partial pancreatectomy plus splenectomy.

Physicians recommend the EMA-CO and EMA-EP regimens as first and second lines of treatment.[20] Huang et al. have reported the case of a 36-year-old Chinese woman with PSTT following a normal pregnancy; she was successfully treated with hysterectomy and pre- and post-operative EMA-CO regimen.[21] Overall survival for stage I disease is approximately 90% even without postoperative chemotherapy.[10,19] Close long-term follow-up of PSTT patients is needed due to potential risk for recurrence.[22]

Conclusion

Proper surgical approach of PSTT has a major role in the remission of this disease.

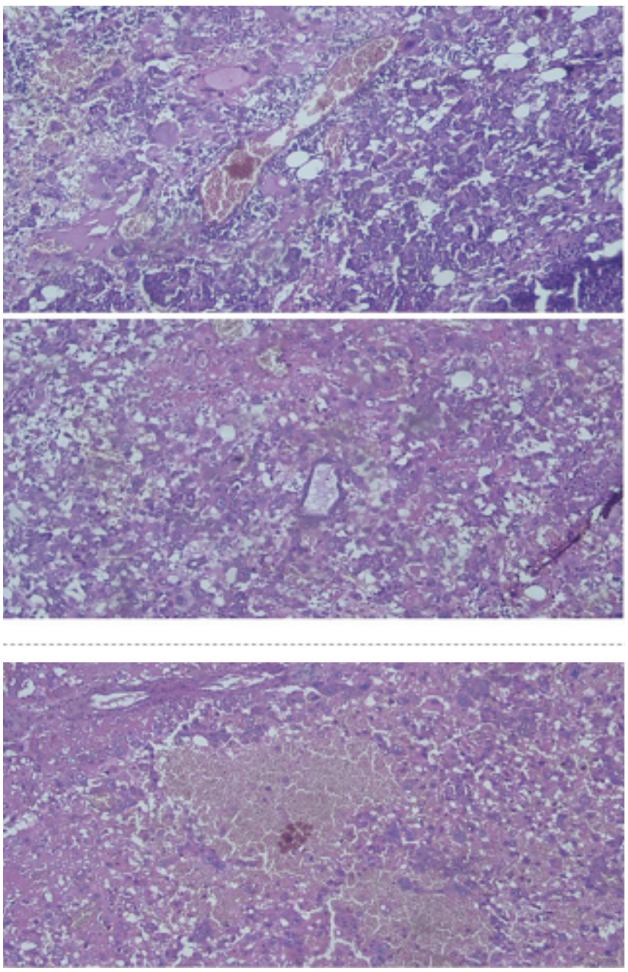

Figure 5. Histologic and immunohistochemistry of pancreatic mass. The results showed atypical trophoblastic cells with vascular nucleoli and acidophilic cytoplasm with focal necrosis and no chorionic villi (H & E staining, 100×).

Conflict of Interest

None declared.

References

1. Bouquet de la Jolinière J, Khomsi F, Fadhlaoui A, Ben Ali N, Dubuisson JB, Feki A. Placental site trophoblastic tumor: a case report and review of the literature. *Front Surg*. 2014;1:31.
2. Chiofalo B, Palmara V, Laganà AS, Triolo O, Vitale SG, Conway F, et al. Fertility sparing strategies in patients affected by placental site trophoblastic tumor. *Curr Treat Options Oncol.* 2017;18(10):58.
3. Santoro G, Laganà AS, Micali A, Barresi V, Giacobbe V, Palmara V. Historical, morphological and clinical overview of placental site trophoblastic tumors: from bench to bedside. *Arch Gynecol Obstet*. 2017;295(1):173-87.
4. Wang D, He Y, Hu Y, Xie C, Yin R. Placental site trophoblastic tumor with unusual presentation in the uterine cervix. *Eur J Obstet Gynecol Reprod Biol.* 2010;148(1):100-1.
5. Zwischenberger BA, Boren T. Placental site trophoblastic tumor presenting as a friable cervical mass. *Eur J Gynaecol Oncol.* 2010;31(5):570-2.
6. Pawar AA, Patil DB, Patel S, Mankad M, Dave P. Role of PET–CT Scan in Gynaeconcology. *J Obstet Gynaecol India.* 2016;66(5):339-44.
7. Niknejadi M, Ahmadi F, Akhbari F. Imaging and clinical data of placental site trophoblastic tumor: A case report. *Iran J Radiol.* 2016;13(2):e18480.
8. Baergen RN, Rutgers JL, Young RH, Osann K, Scully RE. Placental site trophoblastic tumor: a study of 55 cases and review of the literature emphasizing factors of prognostic significance. *Gynecol Oncol.* 2006;100(3): 511-20.
9. Zeng X, Liu X, Tian Q, Xue Y, An R. Placental site trophoblastic tumor: A case report and literature review. *Intractable Rare Dis Res*. 2015;4(3):147-51.
10. Monclair T, Abeler VM, Kærn J, Walaas L, Zeller B, Hilstrøm C. Placental site trophoblastic tumor (PSTT) in mother and child: first report of PSTT in infancy. *Med Pediatr Oncol.* 2002;38(3):187-91; discussion 192.
11. Zhang X. Coexisting epithelioid trophoblastic tumor and placental site trophoblastic tumor of the uterus following a term pregnancy: report of a case and review of literature. *Int J Clin Exp Pathol.* 2015;8(6):7254-9.
12. Denny LA, Dehaeck K, Nevin J, Soeters R, VAN AL WI, Megevand E, et al. Placental site trophoblastic tumor: three case reports and literature review. *Gynecol Oncol.* 1995;59(2):300-3.
13. Batra V, Kalra OP, Mathur P, Dev G. Membranous glomerulopathy associated with placental site trophoblastic tumour: a case report. *Nephrol Dial*

Transplant. 2007;22(6):1766-8.
14. Chang YL, Chang TC, Hsueh S, Huang KG, Wang PN, Liu HP, et al. Prognostic factors and treatment for placental site trophoblastic tumor-report of 3 cases and analysis of 88 cases. *Gynecol Oncol*. 1999;73(2):216-22.
15. Papadopoulos AJ, Foskett M, Seckl MJ, McNeish I, Paradinas FJ, Rees H, et al. Twenty-five years' clinical experience with placental site trophoblastic tumors. *J Reprod Med.* 2002;47(6):460-4.
16. Lucas R, Cunha TM, Santos FB. Placental site trophoblastic tumor: a case report and review of the literature. *J Radiol Case Rep.* 2015;9(4):14-22.
17. Lima LLA, Padron L, Câmara R, Sun SY, Rezende J Filho, Braga A. The role of surgery in the management of women with gestational trophoblastic disease. *Rev Col Bras Cir.* 2017;44(1):94-101.
18. Lan C, Li Y, He J, Liu J. Placental site trophoblastic tumor: lymphatic spread and possible target markers. *Gynecol Oncol.* 2010;116(3):430-7.
19. Papadopoulos AJ, Foskett M, Seckl MJ, McNeish I, Paradinas FJ, Rees H, et al. Twenty-five years' clinical experience with placental site trophoblastic tumors. *J Reprod Med.* 2002;47(6):460-4.
20. Schmid P, Nagai Y, Agarwal R, Hancock B, Savage PM, Sebire NJ, et al. Prognostic markers and long-term outcome of placental-site trophoblastic tumours: a retrospective observational study. *Lancet*. 2009;374(9683):48-55.
21. Huang F, Zheng W, Liang Q, Yin T. Diagnosis and treatment of placental site trophoblastic tumor. *Int J Clin Exp Pathol.* 2013;6(7):1448-51.
22. How J, Scurry J, Grant P, Sapountzis K, Ostor A, Fortune D, et al. Placental site trophoblastic tumor. Report of three cases and review of the literature. *Int J Gynecol Cancer.* 1995;5(4):241-9.